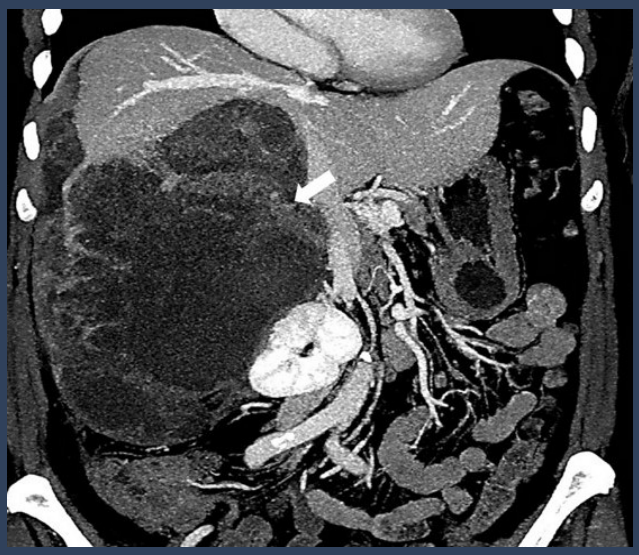
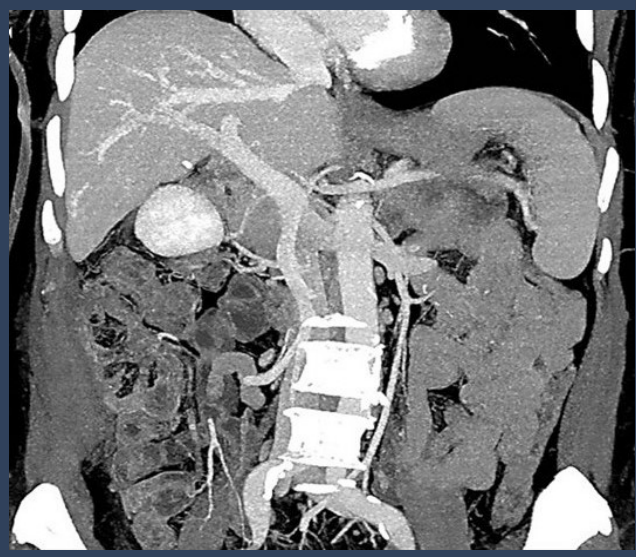
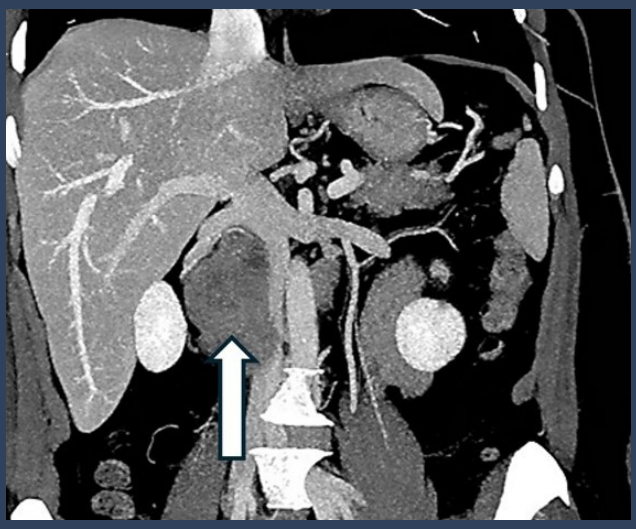
The Official Journal of the Inonu Liver Transplantation Institute

Journal of Inonu Liver Transplantation Institute







Treatment of Recurrent Granulosa Cell Tumors of the Ovaries: Single-center Experience

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Journal of Inonu Liver Transplantation Institute

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Language of Publication: English
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Journal of Inonu Liver Transplantation Institute

Aim and Scope

Aim

The Journal of Inonu Liver Transplantation Institute is a peer-reviewed open-access e-only publication in the field of liver transplantation publishing research articles on clinical, experimental liver transplantation, combined liver and other organ transplantation, and liver diseases. The journal welcomes original research articles, reviews, meta-analyses, case reports, and letters.

Overview

Journal of Inonu Liver Transplant Institute has been founded and established by Inonu Liver Transplant Institute in order to form a source of high-quality research in diseases and therapy of the liver and biliary tract. Both clinicians and basic science researchers are the target population of our journal.

Scope

Hepatobiliary disorders are a complex spectrum of diseases, usually requiring a multi-disciplinary approach that involves interventional radiologists, hepatologists, oncologists, hepatobiliary-transplant surgeons and translational researchers. The Journal of Inonu Liver Transplant Institute (JILTI) is internationally peer reviewed and provides a source for articles on prevention, diagnosis and cutting-edge therapy of hepatobiliary diseases and cancers which also includes liver transplantation, complex hepatobiliary surgical procedures, medical and immune therapies. In accordance with our aims, basic and translational research as applied to these diseases have utmost importance for our journal.

Keywords: Hepatobiliary diseases and cancers, liver surgery, liver transplantation, advanced therapy of hepatobiliary diseases, basic and translational research on hepatobiliary diseases.

Ethics and Policies

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Drafting the work or revising it critically for important intellectual content; AND
Final approval of the version to be published; AND
Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
In addition to being accountable for their own work, authors should have confidence in the integrity of the contributions of their co-authors and each author should be able to identify which co-authors are responsible for other parts of the work.
All of those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who provided a contribution but do not meet all four criteria should be recognized separately on the title page and in the Acknowledgements section at the conclusion of the manuscript.
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Ethics Policy

The Editorial Board of the Journal of Inonu Liver Transplantation Institute and the Publisher adheres to the principles of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the US National Library of Medicine (NLM), the World Medical Association (WMA) and the European Association of Science Editors (EASE).
In accordance with the journal's policy, an approval of research protocols by an ethics committee in accordance with international agreements "WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (last updated: October 2013, Fortaleza, Brazil)" , "Guide for the care and use of laboratory animals (8th edition, 2011)" and/or "International Guiding Principles for Biomedical Research Involving Animals (2012)" is required for all research studies. If the submitted manuscript does not include ethics committee approval, it will be reviewed according to COPE's guideline (Guidance for Editors: Research, Audit and Service Evaluations). If the study should have ethical approval, authors will be asked to provide ethical approval in order to proceed the review process. If they cannot provide ethical approval, their manuscript will be rejected and also their institutions and when needed, the related bodies in their country will be informed that such studies must have ethics committee approval. If they provide approval, review of the manuscript will continue.
For articles concerning experimental research on humans, a statement should be included that shows informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. The journal may request a copy of the Ethics Committee Approval received from the relevant authority. Informed consent must also be obtained for case reports and clinical images.
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1. Use of AI Tools in Manuscript Preparation

According to the ICMJE recommendations, authors must disclose any use of generative AI or AI-assisted technologies (e.g., ChatGPT, Claude, Gemini) in the preparation of their manuscript. This includes specifying the tool's name, version, and purpose in the appropriate section of the manuscript (e.g., Acknowledgments for writing assistance, or Methods for data analysis)
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- Are adequate references made to other Works in the field?
- Is the language acceptable?

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All authors are required to declare what support they received to carry out their research. Declaring funding sources acknowledges funders' contributions, fulfills funding requirements, and promotes greater transparency in the research process.
Each author must individually declare all sources of funding received for the research submitted to the journal. This information includes the name of granting agencies, grant numbers, and a description of each funder's role. If the funder has played no role in the research, this must be stated as well.
Authors are not required to provide the complete list of every single grant that supports them if the grant is not related to the research published.

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Journal of Inonu Liver Transplantation Institute

Information for the Authors

THE JOURNAL

The Journal of Inonu Liver Transplantation Institute (The Journal) is an international, scientific, open access periodical published in accordance with independent, unbiased, and double-blinded peer-review principles. The journal is the official publication of the Inonu Liver Transplantation Institute, and it is published in April, August and December, three times a year. The publication language of the journal is English.

The Journal aims to contribute to international literature by publishing high-quality manuscripts in the field of diseases and therapy of the liver and biliary tract. The journal's target audience includes academics and expert physicians working in transplantation surgery specialists.

REVIEW PROCESS

Manuscripts submitted to the Journal will undergo a double-blind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in their field in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation process of manuscripts submitted by editors or by the editorial board members of the journal. The editor-in-chief is the final authority in the decision-making process for all submissions.

Reviews are typically completed within one month of submission to the journal. Authors will be sent constructive reviewer comments intended to be useful. In general, the instructions, objections, and requests made by the reviewers should be followed. The revised manuscript should clearly and precisely indicate every step taken in accordance with the reviewers' notes. A list of responses and the corrections made to each comment should be provided.

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Each individual listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship be based on the following 4 criteria:

Substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work; AND

Drafting the work or revising it critically for important intellectual content; AND

Final approval of the version to be published; AND

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for their own work, authors should have confidence in the integrity of the contributions of their co-authors and each author should be able to identify which co-authors are responsible for other parts of the work.

All of those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged on the title page of the manuscript.

The Journal requires that corresponding authors submit a signed and scanned version of the authorship contribution form (available for download through www.jilti.org) during the initial submission process in order to appropriately indicate and observe authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without further review. As part of the submission of the manuscript, the corresponding author should also send a short statement declaring that they accept all responsibility for authorship during the submission and review stages of the manuscript.

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Key Features:

- The "Letter to the Editor" should be unstructured and should not include an abstract, keywords, tables, figures, images, or other media.
- The manuscript being commented on must be properly cited within the "Letter to the Editor."
- Our journal considers all feedback on published articles. However, we emphasize that comments should be scientifically relevant and meaningful to the discussion. Irrelevant or unfounded comments may be rejected.

ICMJE Guidelines:

Our journal adheres to the guidelines set forth by the ICMJE (International Committee of Medical Journal Editors). According to ICMJE, "Letters to the Editor" should be a platform for responsible debate, critique, and discussion. These letters may raise substantial criticisms or questions about previously published articles, and authors of the discussed articles are expected to respond to these criticisms.

ICMJE also notes that editors have the right to edit these letters for length, grammar, and style. However, all letters should contribute constructively to the academic discussion and critique, and those deemed irrelevant or unfounded may be rejected.

You can view the ICMJE guidelines on "Correspondence" here.

Table 1. Limitations for each manuscript type.

Type of manuscript	Wordlimit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	4000-5000	350-400	40-50	6	6
Review Article	5000-6000	350-400	50-60	6	10
Meta analysis	5000	350	50	6	10
Case Report	1500	200	20	No tables	5
Letter to the Editor	1000	No abstract	10	No tables	1

Title page: A separate title page should be submitted with all submissions and this page should include:

The full title of the manuscript as well as a short title (running head) of no more than 50 characters

Name, affiliation, ORCID ID number, and highest academic degree of the author(s)

Funding and other material support

Name, address, phone number(s), fax number, and email address of the corresponding author

Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria

Manuscripts that have been presented orally or as a poster should include the name, date and place of the event

Abstract: An English-language abstract is required with all submissions except editorial comments, images, and letters to the editor. Systematic reviews and original articles should contain a structured abstract of maximum 350*400 words with the subheadings of objective, methods, results, and conclusion.
Keywords: Each submission must be accompanied by a minimum of three and a maximum of six keywords for subject indexing included at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (https://www.nlm.nih.gov/mesh/MBrowser.html).
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All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition. Units should be prepared in accordance with the International System of Units (SI). When a drug, device, hardware, or software program, or other product is mentioned within the main text, the name of the product, the manufacturer/copyright holder of the product (not simply the vendor), and city and the country of the company (including the state, if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric Co., Boston, MA, USA)"
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Limitations, drawbacks, and shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.
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Journal article: van Erk MD, Dam-Vervloet AJ, de Boer FA, Boomsma MF, van Straaten H, Bosschaart N. How skin anatomy influences transcutaneous bilirubin determinations: an in vitro evaluation. Pediatr Res 2019;86:471-7.
Epub ahead-of-print article: Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead-of-print].
Manuscript published in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlEID/cid.htm.
Book section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.2290-308.
Books with a single author: Sweetman SC. Martindale the Complete Drug Reference. 34th ed. London: Pharmaceutical Press; 2005.
Editor(s) as author: Huizing EH, de Groot JAM, editors. Functional reconstructive nasal surgery. Stuttgart-New York: Thieme; 2003.
Conference proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.
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Original Research

Treatment of Recurrent Granulosa Cell Tumors of the Ovaries: Single-center Experience

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Abstract

Objectives: Granulosa cell tumors (GCTs) are rare ovarian tumors with a high rate of late recurrence, which can present a significant challenge for surgical management. This study aims to evaluate the outcomes of debulking surgery for recurrent GCTs that involve major abdominal vessels and the liver.

Methods: We present a retrospective case series of three patients with recurrent GCTs who were treated at our reference center between 2024 and 2025. We collected data on patient demographics, medical history, recurrence location, treatment details, and follow-up. All data are presented descriptively.

Results: The patients' ages ranged from 53 to 70 years. The time from initial surgery to the first recurrence ranged from 6 to 26 years. Two patients experienced extra-pelvic recurrences in the retroperitoneal space, while one had a pelvic recurrence. All three patients underwent debulking surgery, with two patients experiencing second recurrences and one patient experiencing a third. One patient required anterior wall resection and reconstruction of the Inferior Vena Cava (VCI). Notably, two patients had elevated levels of CEA and CA-125 that peaked before recurrence.

Conclusion: Our findings suggest that the number of GCT recurrences is not as critical as the ability to perform a complete, safe resection. Surgery alone, with a focus on radical resection of recurrent foci, appears to be the primary determinant of favorable patient survival, even when it involves complex procedures like oncovascular resection. Repeated resections, even for multiple recurrences, can lead to favorable long-term outcomes.

Keywords: Granulosa Cell Tumors, Recurrent Ovarian Cancer, Radical Surgery, Repeated Resections

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Granulosa cell tumors (GCTs) originate from the granulosa cells of the sex cords, which are responsible for producing sex steroids and peptides essential for folliculogenesis.[1] GCTs are a rare type of ovarian tumor, constituting less than 5% of all cases. They are classified into two main types: adult GCT and juvenile GCT.[1]

Adult GCT is the more common form, making up 95% of cases, and typically affects perimenopausal women in their fifth decade. Juvenile GCT is rare and is more commonly diagnosed in premenarchal females.[1] A key characteristic of these tumors is their early-stage presentation, often accompanied by symptoms of hyperestrogenism. The prog-

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nosis for GCTs is generally better than for other epithelial ovarian tumors, especially when treated with radical surgery, which can be curative.[2]

The development of GCTs involves an accumulation of genetic and epigenetic changes. Genetic aberrations have been noted on chromosomes 1, 3, 6, 11, 12, 15, 17, and X, along with chromosomal microsatellite instability and loss of heterozygosity.[3] Epigenetic changes, such as hypermethylation, have also been reported in various gene loci, including p16, estrogen receptor-α (ER-α), BRCA1, and others.[3] The inherited component of GCT is suggested by its association with conditions like Peutz-Jeghers and Potters syndromes, and in the case of juvenile GCT, with Ollier and Maffucci diseases.[3]

GCTs are typically slow-growing tumors that often present cystic and hemorrhagic components.[1] Common symptoms include palpable mass and hyperestrogenism-related symptoms.[4, 5] Several factors influence prognosis, including patient age, tumor size, rupture, mitotic index (Ki-67), nuclear atypia, aneuploidy, and p53 overexpression.[1, 6] The primary surgical treatment for GCTs with a high probability of survival is surgical debulking combined with the excision of metastatic lymph nodes.[7]

Unfortunately, GCT recurrence is often insidious and can occur decades after initial treatment. More than 20% of stage I GCTs will recur within 5-10 years post-surgery.[8-11] A study by Lee et al. reported an 8 out of 38 recurrence rate in adult GCT patients, with the most common sites being the pelvis and the liver.[8] For recurrent disease, effective debulking surgery combined with radiation and chemotherapy offers a high probability of survival.[9, 10] The prognosis for recurrent disease is determined by the age at recurrence and the treatment modality used. Patients under 50 at recurrence or those who receive single-modality treatment (surgery or chemotherapy alone) have a more than tenfold increased risk of cancer-related death compared to those who receive combination therapy.[10]

Extensive vascular reconstruction combined with debulking surgery for ovarian tumors is extremely rare. Finch et al. reported a case involving combined vena cava and aortic reconstructions in a 76-year-old patient with recurrent GCT.[11] Similarly combined resection of the liver and other viscera during debulking surgery for recurrent GCT is very rare, but successful resection provides an overall favorable outcome.[12] Given this rarity, our study aims to evaluate the outcomes of debulking surgery in patients with recurrent GCT that involves major abdominal vessels and the liver.

Methods

We serve as a reference center for primary and metastatic liver tumors. Between 2024 and 2025 we treated 3 cases of recurrent GCT. The details of the procedures are provided here in our case series. Since we are retrospectively presenting these cases, we did not require institutional review board approval for the ethical and scientific aspects of our study.

Study Parameters

We provide data about the patient's medical history, including when the index event occurred. The location of the recurrence and how it was diagnosed. Furthermore, we give the details of how we treated the patient. In addition, we provide the demographic details of the patients, including their age, information regarding pregnancies.

Laboratory data included the findings on the imaging procedures, and information regarding extreme laboratory findings is given. Furthermore, the macroscopic and macroscopic characteristics of the tumors are also summarized for each patient.

Statistical Analysis

All data are presented as descriptive data for patients. Age of the patients and duration between the index operation and the recurrences are expressed as a range. All statistical analyses were performed using Statistical software Package for Social Sciences version 24 (SPSS v24, Armonk, USA).

Results

Patient Demographics and Initial Surgeries

Table 1 summarizes the demographic, clinical, tumor, and laboratory characteristics of the three patients. Their ages ranged from 53 to 70 years. Two patients had a total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), along with appendectomy and pelvic paraaortic lymph node dissection (PPaLND). The third patient underwent TAH, unilateral salpingo-oophorectomy (USO), PPaLND, and appendectomy. Notably, one patient had her initial operation at a different medical center. All the patients had adult-type GCT (Fig. 1A-C).

Recurrence and Subsequent Operations

The time from the initial operation to the first recurrence ranged from 6 to 26 years. The first recurrences were typically in the retroperitoneal space (two patients), with one patient's recurrence located in the left upper and lower quadrants. These were nearly always resected without needing to remove other organs. However, in Patient 3, a single recurrence occurred 26 years after the initial surgery

Table 1. Summary of the demographic and clinical characteristics of the Patients with GCT

Patient ID	Age	Duration and type of index operation	Chemotherapy	1st recurrence and timing	2nd recurrence and timing	3rd recurrence and timing	Elevation in tumor markers
Patient 1	70y	6 years TAH+BSO	None	Left UQ and Left LQ spaces 5 years after index operation	Right UQ and retroperitoneum 6 years after index operation (4 months after the first recurrence)	Pelvic 6 years after the index operation (5 months after the second recurrence)	None
Patient 2	53y	5 years TAH+ left USO	None	Retroperitoneal mass starting from SMA 5 years after the index operation	Right UQ and R LQ mass invading VCI. 5 years after the index operation (4 months after the first recurrence)	None	CEA was elevated since 1st year after the index operation and reduced after the operations for the two recurrences (currently 8 ng/ml)
Patient 3	68y	TAH+BSO PPaLND 26 yeas ago	Bleomycin, etoposide, and cisplatin	Retroperitoneal mass on the right extending to the right subdiaphragmatic region 26 years after the index operation	None	None	CA-125 was elevated since the recurrence, but is decreasing) (currently 38U/ml

*TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo-oopherectomy; USO: Unilateral salpingo-oopherectomy; PPaLND: Pelvic and para-aortic lymph node dissection; UQ: Upper quadrant; LQ: Lower quadrant; VCI: Vena cava inferior; CEA: Carcinoembryonic antigen; CA-125: Carbohydrate Antigen-125.

(Table 1). This mass extended from the right lower quadrant to the subdiaphragmatic space, necessitating a diaphragmatic resection (Fig. 2A-C).

Patients 1 and 2 experienced second recurrences in the retroperitoneal space and the right upper and lower quadrants, respectively, both diagnosed four months after the first recurrence. While the recurrent tumor in Patient 1 was resected without complications, Patient 2 required an excision of the anterior wall of the VCI, which was then reconstructed with a cryopreserved venous patch (Fig. 3A-C). Patient 3 had a third recurrence in the pelvis, diagnosed five months after the second, which was also successfully resected.

Tumor markers were elevated in two patients (Patients 2 and 3), and they reached peak levels before the recurrences. Carcinoembryonic antigen (CEA) and carbohydrate antigen-125 (CA-125) were the two markers that were elevated. Only one patient received adjuvant chemotherapy after the index operation. It included bleomycin, etoposide, and cisplatin.

Discussion

GCTs constitute 2-5% of all ovarian tumors, with the adult-type being classified as sex cord tumors of the ovaries. After initial surgery, the recurrence rate is 25%,[13] with one-third of recurrences happening within five years and nearly 20% within ten years.[13] Once recurrence occurs, the survival rate drops to less than 50%.[13]

Several factors predict a poor prognosis and a higher likelihood of recurrence, including the patient's age at initial diagnosis, the primary tumor's size, and specific histopathological characteristics like the mitotic index.[14] Leaving a residual tumor after the primary tumor's resection has been identified as the main determinant of a poor prognosis. The most common sites for recurrence are the pelvic cavity, liver, and lungs.[14]

The treatment of recurrence is a controversial topic; however, multimodal therapy, which includes effective debulking surgery, is typically recommended. Even with multimodality treatment, 60% of patients who experience an initial recurrence are reported to have a second or third recurrence.[15]

In our case series, two patients developed extra-pelvic recurrence, including one with a mass in the right retroperitoneal space. The third patient had a pelvic recurrence. All patients initially TAH + BSO. Our findings are consistent with previous case series.[14, 15] While we did not observe any extra-abdominal recurrences in our study, the pelvic recurrences were massive, requiring the concomitant resection of abdominal structures like the VCI in one patient.

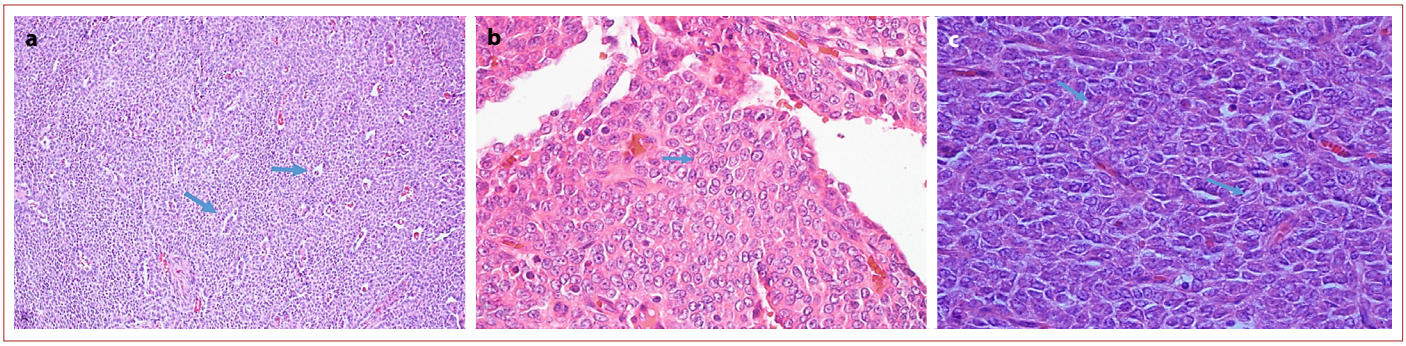

Figure 1. Summary of the different pathognomonic histological findings. **(a)** The most characteristic pattern of ovarian adult-type granulosa cell tumors is a microfollicular architecture, defined by the presence of Call-Exner bodies. These rosette-like structures resemble the Call-Exner bodies found in a Graafian follicle. Their centers are small, rounded spaces filled with eosinophilic cellular debris or hyaline basement membrane material, which are surrounded by numerous layers of granulosa cells. The image you're referring to is a hematoxylin and eosin (H&E) stain at 100x magnification, with arrows pointing to the characteristic pattern. **(b)** Coffee bean-like cells showing nuclear grooves (arrow), HE, 400X, **(c)** Grooved nuclei that look like coffee beans (arrows), HE, 200x.

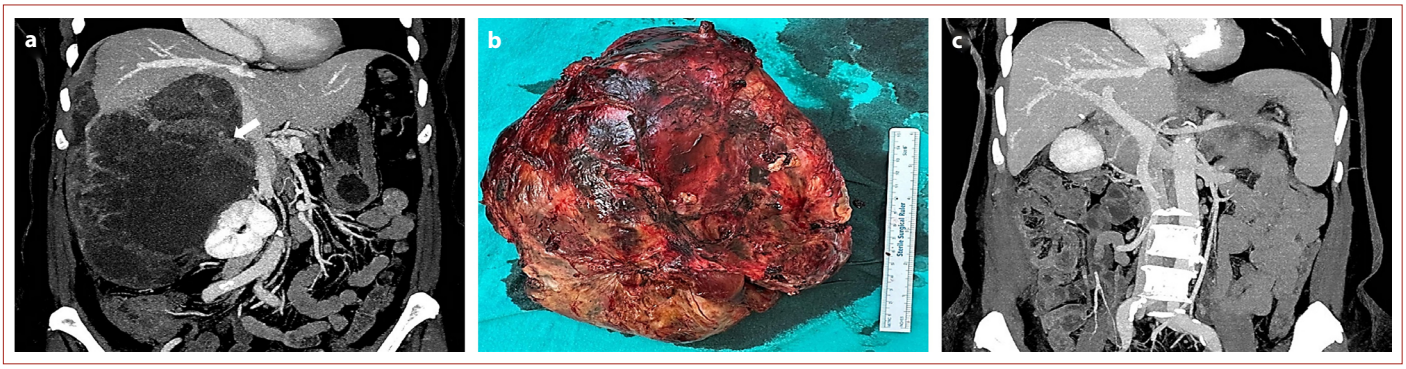

Figure 2. Summary of the large recurrent tumor. **(a)** The preoperative computerized tomography (CT) scan showing the large recurrent mass (arrow). **(b)** Shows the resection material intraoperatively. **(c)** Postoperative follow-up CT showing no recurrences.

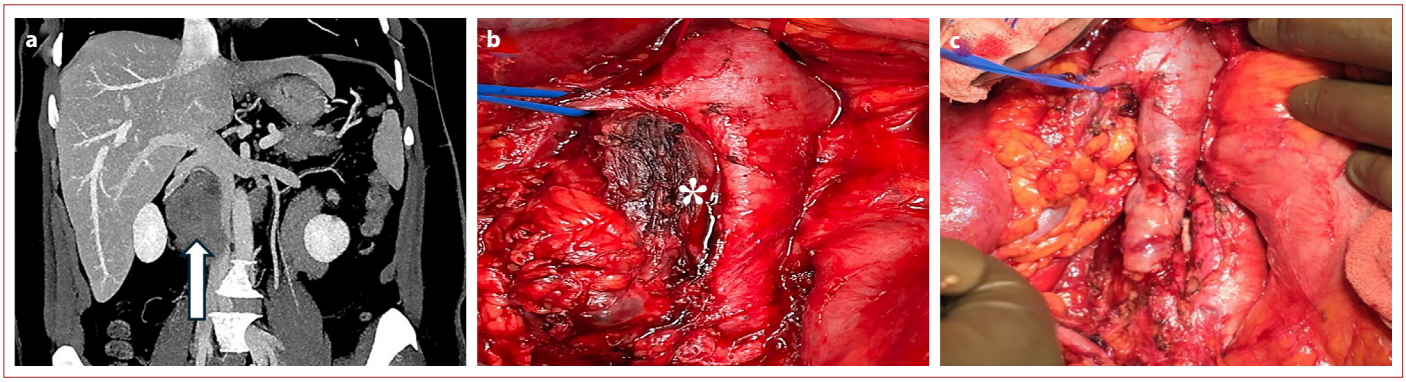

Figure 3. Summary of the patient with a recurrent tumor invading the infrarenal Vena Cava Inferior (IVC). **(a)** CT images of the recurrent mass (arrow). As shown, the mass is located inferior to the renal vein. **(b)** Intraoperative view showing the invasion of the anterior wall of the Vena Cava Inferior (asterisk). **(c)** The post-resection view showing the reconstructed IVC.

Complex oncovascular resections have been reported for epithelial ovarian tumors, and patient outcomes are usually favorable.[18] We performed a VCI anterior wall resection on one patient, and her follow-up has been uneventful, with no evidence of recurrence since the resection. Based on our data, oncovascular resections appear to have favorable outcomes.

The duration of progression-free survival is reported to determine the patient's prognosis.[11] However, our data shows that two-thirds of our patients had multiple recurrences that were successfully resected. Follow-up of these patients shows no evidence of recurrence. Similarly, Finch et al.[12] have reported a patient with multiple recurrences who was treated with repeated resections, including on-

covascular resections of the VCI. Therefore, repeated recurrences in GCT patients should not be considered an indication of an insufficient initial resection. We propose that the number of recurrences is not the primary concern, as long as each subsequent resection can be performed safely. This is further supported by Yumru Celiksoy et al.,[17] who demonstrated that different adjuvant therapies had no beneficial effect on disease-free survival in patients with recurrent adult GCTs.

Gurumuthy et al.[14] conducted a meta-analysis that evaluated five retrospective cohort studies, which included 535 women with GCT. Only one of these studies reported a beneficial effect of adjuvant chemotherapy, noting that it provided prolonged patient survival.[14] Also, other studies fail to show a survival benefit of adjuvant systemic chemotherapy following surgery for adult GCTs.[18-20] In our study, one patient who received adjuvant therapy following the index operation experienced a recurrence twenty-six years later. Therefore, adjuvant therapy can prolong the disease-free survival in selected patients.

Several markers, including inhibin, estradiol, and Müllerian-inhibiting substance, as well as histopathological parameters like Ki67, p53, and cluster of differentiation (CD) 56 expression, have been identified for the follow-up of GCTs.[21, 22] However, no single marker has definitive diagnostic or prognostic significance. In our study, we observed that CEA and CA-125 levels were elevated in our patients, with levels peaking before recurrence episodes.

The major limitation of our study is the small number of patients included. Nevertheless, we can still draw some conclusions from their clinical and tumor-related characteristics.

In conclusion, recurrent GCTs present a significant challenge from an oncologic surgery perspective. The number of recurrences is less important than the ability to achieve a complete resection of the recurrent tumor. The ability to perform a radical resection of recurrences, through surgery alone, appears to be the primary determinant of favorable patient survival. Furthermore, no tumor markers are currently reliable for the prognostication or diagnosis of these tumors.

Disclosures

Ethics Committee Approval: Ethics approval was not required for this retrospective study.

Informed Consent: Written and verbal informed consent was obtained from all patients.

Conflict of Interest: The authors declare that they have no conflicts of interest.

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References

1. Biju Azariah M, Manisha V, Anuja K, Jayaprakash PG. Granulosa Cell Tumors of Ovary – A Systematic Review. Sch J Med Case Rep, 2021, 9(7): 690-695.
2. Inada Y, Nakai G, Yamamoto K, Yamada T, Hirose Y, Terai Y, Ohmichi M, Narumi Y. Rapidly growing juvenile granulosa cell tumor of the ovary arising in adult: a case report and review of the literature. J Ovarian Res. 2018 Dec 14;11(1):100. doi: 10.1186/s13048-018-0474-0. PMID: 30547828; PMCID: PMC6293549.
3. Dhillon VS, Aslam M, Husain SA. The contribution of genetic and epigenetic changes in granulosa cell tumors of ovarian origin. Clin Cancer Res. 2004 Aug 15;10(16):5537-45. DOI: 10.1158/1078-0432.CCR-04-0228. PMID: 15328194.
4. Kottarathil VD, Antony MA, Nair IR, Pavithran K. Recent advances in granulosa cell tumor ovary: a review. Indian J Surg Oncol. 2013 Mar;4(1):37-47. doi: 10.1007/s13193-012-0201-z. Epub 2012 Dec 7. PMID: 24426698; PMCID: PMC3578540.
5. Koukourakis GV, Kouloulias VE, Koukourakis MJ, Zacharias GA, Papadimitriou C, Mystakidou K, Pistevou-Gompaki K, Kouvaris J, Gouliamos A. Granulosa cell tumor of the ovary: tumor review. Integr Cancer Ther. 2008 Sep;7(3):204-15. doi: 10.1177/1534735408322845. PMID: 18815151.
6. Adefris M, Fekadu E. Postmenopausal mild hirsutism and hyperandrogenemia due to granulosa cell tumor of the ovary: a case report. J Med Case Rep. 2017 Aug 30;11(1):242. doi: 10.1186/s13256-017-1411-3. PMID: 28851436; PMCID: PMC5576087.Integr Cancer Ther. 2008 Sep;7(3):204-15. doi: 10.1177/1534735408322845. PMID: 18815151.
7. Dolkar T, Rayapureddy AK, Kadakia N, Bellamkonda A, Kalavar M. Recurrent Granulosa Cell Tumor in a Postmenopausal Woman: A Case Report and Literature Review. Cureus. 2023 Aug 12;15(8):e43368. doi: 10.7759/cureus.43368. PMID: 37700975; PMCID: PMC10494553.
8. Lee YK, Park NH, Kim JW, Song YS, Kang SB, Lee HP. Characteristics of recurrence in adult-type granulosa cell tumor. Int J Gynecol Cancer. 2008 Jul-Aug;18(4):642-7. doi: 10.1111/j.1525-1438.2007.01065.x. Epub 2007 Sep 14. PMID: 17868338.
9. Yasukawa M, Matsuo K, Matsuzaki S, Dainty LA, Sugarbaker PH. Management of recurrent granulosa cell tumor of the ovary: Contemporary literature review and a proposal of hyperthermic intraperitoneal chemotherapy as novel therapeutic option. J Obstet Gynaecol Res. 2021 Jan;47(1):44-51. doi: 10.1111/jog.14494. Epub 2020 Oct 25. PMID: 33103312.
10. Salkeni MA, Shin S, Takebe N, Stevens S, Chen A. Advanced Gran-

ulosa Cell Tumors of the Ovary: A Review with a Focus on Current and Novel Therapeutic Approaches. J Immunother Precis Oncol. 2024 Aug 1;7(4):263-271. doi: 10.36401/JIPO-23-40. PMID: 39524463; PMCID: PMC11541922.

11. Zhao D, Zhang Y, Ou Z, Zhang R, Zheng S, Li B. Characteristics and treatment results of recurrence in adult-type granulosa cell tumor of ovary. J Ovarian Res. 2020 Feb 14;13(1):19. doi: 10.1186/s13048-020-00619-6. PMID: 32059683; PMCID: PMC7020364.
12. Finch L, Ellozy S, Sandhu J, Patel T, Tew WP, Chi DS. Vascular resection and reconstruction in recurrent granulosa cell tumor. Gynecol Oncol Rep. 2024 Aug 31;55:101496. doi: 10.1016/j.gore.2024.101496. PMID: 39297077; PMCID: PMC11408049.
13. Aleter A, Mahajan PS, Petkar MA, Abdulmajeed HA, Khalaf H, Elmoghazy W, Elaffandi A. Late Cystic Metastasis of an Ovarian Granulosa Cell Tumor to the Liver. Cureus. 2021 Sep 17;13(9):e18051. doi: 10.7759/cureus.18051. PMID: 34671531; PMCID: PMC8520693.
14. Gurumurthy M, Bryant A, Shanbhag S. Effectiveness of different treatment modalities for the management of adult-onset granulosa cell tumours of the ovary (primary and recurrent). Cochrane Database Syst Rev. 2014 Apr 21;2014(4):CD006912. doi: 10.1002/14651858.CD006912.pub2. PMID: 24753008; PMCID: PMC6513416.
15. Seagle BL, Ann P, Butler S, Shahabi S. Ovarian granulosa cell tumor: A National Cancer Database study. Gynecol Oncol. 2017 Aug;146(2):285-291. doi: 10.1016/j.ygyno.2017.05.020. Epub 2017 May 19. PMID: 28532858.
16. Uccella S, Bosco M, Mezzetto L, Garzon S, Maggi V, Giacopuzzi S, Antonelli A, Pinali L, Zorzato PC, Festi A, Polati E, Montemezzi S, De Manzoni G, Franchi MP, Veraldi GF. Major vessel resection for complete cytoreduction in primary advanced and recurrent ovarian malignancies: A case series and systematic review of the literature - pushing the boundaries in oncovascular surgery. Gynecol Oncol. 2023 Dec;179:42-51. doi: 10.1016/j.ygyno.2023.10.021. Epub 2023 Nov 1. PMID: 37922861.
17. Yumru Celiksoy H, Dickie C, Seckl MJ, Aydın E, Sozen H, Topuz S, Fotopoulou C. Effectiveness of adjuvant systemic therapy following complete cytoreductive surgery in patients with recurrent granulosa cell tumours of the ovary. Sci Rep. 2024 Jan 10;14(1):993. doi: 10.1038/s41598-024-51752-x. PMID: 38200105; PMCID: PMC10781791.
18. Wang D, Xiang Y, Wu M, Shen K, Yang J, Huang H, Ren T. Is adjuvant chemotherapy beneficial for patients with FIGO stage IC adult granulosa cell tumor of the ovary? J Ovarian Res. 2018 Mar 27;11(1):25. doi: 10.1186/s13048-018-0396-x. PMID: 29587835; PMCID: PMC5870389.
19. Mangili G, Ottolina J, Cormio G, Loizzi V, De Iaco P, Pellegrini DA, Candiani M, Giorda G, Scarfone G, Cecere SC, Frigerio L, Gadducci A, Marchetti C, Ferrandina G. Adjuvant chemotherapy does not improve disease-free survival in FIGO stage IC ovarian granulosa cell tumors: The MITO-9 study. Gynecol Oncol. 2016 Nov;143(2):276-280. doi: 10.1016/j.ygyno.2016.08.316. Epub 2016 Sep 3. PMID: 27597380.
20. Plett H, Ricciardi E, Vacaru V, Ramspott JP, Colombo N, Sehouli J, du Bois A, Garbi A, Richter R, Ataseven B, Aletti G, Braicu E, Heitz F, Portuesi R, Muallem MZ, Dagres T, Parma G, Roser E, Traut A, Multinu F, Harter P. Adult ovarian granulosa cell tumors: analysis of outcomes and risk factors for recurrence. Int J Gynecol Cancer. 2023 May 1;33(5):734-740. doi: 10.1136/ijgc-2022-003854. PMID: 36759002.
21. Jung D, Almstedt K, Battista MJ, Seeger A, Jäkel J, Brenner W, Hasenburg A. Immunohistochemical markers of prognosis in adult granulosa cell tumors of the ovary - a review. J Ovarian Res. 2023 Mar 3;16(1):50. doi: 10.1186/s13048-023-01125-1. PMID: 36869369; PMCID: PMC9983179.
22. Nofech-Mozes S, Ismiil N, Dubé V, Saad RS, Khalifa MA, Moshkin O, Ghorab Z. Immunohistochemical characterization of primary and recurrent adult granulosa cell tumors. Int J Gynecol Pathol. 2012 Jan;31(1):80-90. doi: 10.1097/PGP.0b013e318224e089. PMID: 22123727.

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Case Report

Management of Late Hemorrhage from Hepatic Artery Pseudoaneurysm after Gallbladder Cancer Surgery: A Case Report

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Abstract

Gallbladder cancer carries a poor prognosis, with surgical resection being the only curative option. However, complex anatomy can lead to serious postoperative complications.

We present a case of a 58-year-old male who developed a hepatic artery pseudoaneurysm following radical laparoscopic cholecystectomy for gallbladder cancer. The procedure was complicated by an aberrant bile duct injury, requiring hepaticoduodenostomy. He had a high-flow biliary fistula postoperatively. On postoperative day 7, he presented with hemorrhage and hemodynamic instability. CT angiography revealed a pseudoaneurysm of hepatic artery, and emergency surgical exploration was performed after failed coil embolization. The pseudoaneurysm was repaired, and segment 6 resection was performed for anastomotic dehiscence and necrosis. The patient recovered, received adjuvant chemotherapy, and experienced no further complications.

This case emphasizes the need for multidisciplinary management in complex biliary surgery and highlights the potential for rare but serious complications like pseudoaneurysms.

Keywords: Biliary Fistula, Hepaticojejunostomy, Hepatectomy, Bleeding, Cholecystectomy

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Gallbladder cancer is a rare malignancy with poor prognosis, and surgical resection remains the only curative treatment. However, the best surgical approach is still debated, particularly regarding the need for extended lymphadenectomy, hepatectomy, and complete extrahepatic bile duct resection.[1] Regardless of these debates, the complex anatomy of the biliary tree and its proximity to vital structures pose challenges, including the risk of pseudoaneurysm formation from surgical trauma, which can cause delayed and severe pulsatile bleeding. This case report depicts a rare presentation of early postoperative hemorrhage due to a hepatic artery pseudoaneurysm in a gallbladder cancer patient and highlights the role of combined management with interventional radiology and surgery. Institutional Re-

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view Board (IRB) approval was not required by IRB for the preparation of this report, but written informed consent was obtained from the patient for publication.

Case Report

A 58-year-old male with a history of subtotal gastrectomy with Billroth II anastomosis for peptic ulcer perforation presented with abdominal pain and 9 kg weight loss over 5 months. Imaging revealed a 25x23x24 mm gallbladder mass, connected to segment 6 of the liver, suggesting malignancy. MRI confirmed a gallbladder mass with fistulation to the duodenum and MRCP showed low insertion of the segment 6 bile duct into main bile duct (Fig. 1).

The patient underwent laparoscopic radical cholecystectomy with gallbladder bed resection and lymphadenectomy, complicated by segment 6 bile duct injury but no vascular damage. The injury was identified intraoperatively and reconstructed with a laparoscopic hepaticoduodenostomy. The right hepatic artery was located near the gallbladder bed and common bile duct with a short trunk of cystic artery which was ligated from the root by energy a device during cholecystectomy.

Bile fistula, 300 ml daily, was developed at the 3rd day of the surgery possible due to the tight hepaticoduodenostomy, it was planned to treat conservatively. On postoperative day 7, the patient presented with hemorrhagic drainage of 500 ml from the liver bed drain and he had lethargy. A CT angiography revealed a 4-centimeter pseudoaneurysm close to the right hepatic artery (Fig. 2). Coil embolization via mesenteric angiography was attempted but failed due to the artery's anatomical configuration.

Surgical exploration was performed emergently after failed embolization due to hypotension. Pseudoaneurysm of the hepatic artery was detected; and repaired with 5-0 polypropylene sutures after the excision of the pseudoaneurysm. Hepaticoduodenostomy leakage and additionally cystic duct leakage due to the necrosis of the remnant were seen; segment 6 resection with T tube placement to the cystic duct root was performed and duodenum orifice was controlled by 16 French Petzer drain placement.

In the early postoperative period, T-tube was non-functioning and high flow biliary fistula was treated by placing an external PTC catheter. Postoperative follow-up showed no bleeding or cholangitis recurrence. Histopathology confirmed poorly differentiated adenosquamous carcinoma with perifibromuscular connective tissue invasion but no lymph node metastasis (pT2bN0, AJCC 2017). Patient was discharged at the 4th week of the surgery and started the adjuvant chemotherapy at the 8th week of the surgery. The patient had received adjuvant chemotherapy without any complications and remains free of late surgical complications and recurrence.

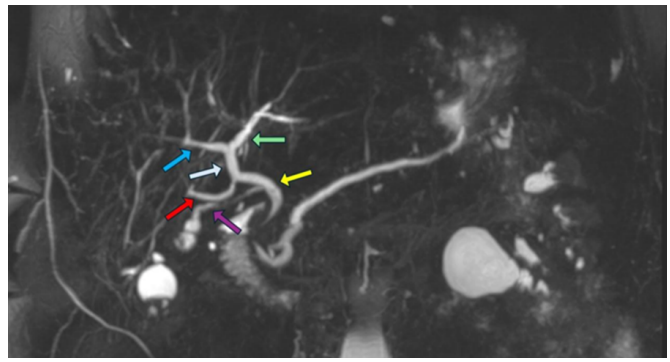

Figure 1. Digital reconstruction of Preoperative Magnetic Resonance Cholangiopancreatography Image.

Red Line: Bile duct of Segment 6 of liver. (Note the low insertion at common hepatic duct level). Blue Line: Right lobe bile duct. Green line: Left lobe bile duct. White Line: Common hepatic duct. Purple line: Cystic duct. Yellow line: Common bile duct.

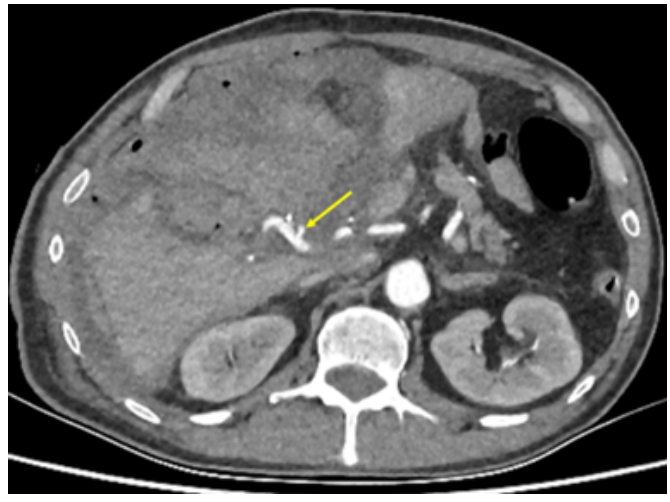

Figure 2. Hepatic artery pseudoaneurysm which caused post operative bleeding. (Shown in yellow arrow).

Discussion

Pseudoaneurysm is a false arterial dilatation caused by trauma, where the false lumen does not connect to the true lumen. Postoperative pseudoaneurysm bleeding is typically pulsatile, intermittent, and delayed. Most common reason for the visceral pseudoaneurysm is iatrogenic trauma of the artery; particularly after laparoscopic dissection by energy devices, as seen in this case involving a hepatic artery pseudoaneurysm.

Hepatic artery pseudoaneurysms are rare and can pose significant challenges in diagnosis and management. Data on bleeding and reintervention rates in gallbladder cancer

surgery are limited; but Arteaga et al. and Frankhauser et al. reported acute bleeding mortality rates of 3–4% and re-intervention rates of 3–5% in hepatopancreatobiliary surgery.[2,3] Dou et al. found lower blood loss in laparoscopic gallbladder cancer surgery compared to conventional approaches, consistent with our institutional experience.[4]

The laparoscopic approach was chosen for its minimally invasive benefits, including reduced recovery time and postoperative pain. However, the complex biliary anatomy, especially with advanced disease or anatomical variations, increases the risk of bile duct injury.[5,6] Limited visualization and instrument maneuverability in laparoscopy can delay injury recognition and management.[7] In this case, the Segment 6 bile duct drained directly into the common hepatic duct, running parallel to the cystic duct (Fig. 1). Despite these challenges, the procedure was successfully completed laparoscopically. At our institution, most hepatopancreatobiliary surgeries are performed laparoscopically, with success rates comparable to open procedures, allowing for precise anatomical assessment and management.

The pseudoaneurysm underscores the complexity of biliary surgery, especially with prior anatomical distortion.[8] The right hepatic artery's proximity to the gallbladder bed and common bile duct contributed to its formation. Management required a multidisciplinary approach. Coil embolization failed due to challenges in catheterizing the artery, reflecting the difficulties of endovascular procedures in complex vascular anatomy.[9] Persistent bleeding necessitated surgical exploration and repair.

The surgery was complicated by adhesions, bilioenteric anastomosis avulsion, and Segment 6 necrosis. Hemostasis and biliary drainage required meticulous dissection and reconstruction. Temporary T-tube and a PTC catheter drainage managed the biliary fistula, allowing the patient to start adjuvant chemotherapy within the optimal 6 to 8 weeks. Despite no lymph node metastasis, the diagnosis of adenosquamous carcinoma necessitates adjuvant therapy and long-term monitoring due to its aggressive nature.[10]

Conclusion

This case highlights the importance of meticulous surgical technique and careful patient selection in managing gallbladder cancer. The development of a pseudoaneurysm and the need for additional surgery emphasize the risk of serious complications in advanced gallbladder disease. A successful outcome was achieved through a multidisciplinary approach, combining surgery, radiology, and psychological care. Despite initial complications and a second, more extensive surgery, the patient recovered well, underscoring the value of comprehensive patient care.

Disclosures

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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References

1. Benson AB, D'Angelica MI, Abbott DE, Anaya DA, Anders R, Are C, et al. Hepatobiliary Cancers, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2021;19(5):541-65.
2. Fankhauser GT, Stone WM, Naidu SG, Oderich GS, Ricotta JJ, Bjarnason H, et al. The minimally invasive management of visceral artery aneurysms and pseudoaneurysms. J Vasc Surg. 2011;53(4):966-70.
3. Sanchez Arteaga A, Orue-Echebarria MI, Zarain L, Lusilla A, Martinez CM, Moreno A, et al. Acute bleeding from pseudoaneurysms following liver and pancreatobiliary surgery. Eur J Trauma Emerg Surg. 2017;43(3):307-11.
4. Dou C, Zhang Y, Liu J, Wei F, Chu H, Han J, et al. Laparoscopy versus laparotomy approach of a radical resection for gallbladder cancer: a retrospective comparative study. Surg Endosc. 2020;34(7):2926-38.
5. Richardson MC, Bell G, Fullarton GM. Incidence and nature of bile duct injuries following laparoscopic cholecystectomy: an audit of 5913 cases. West of Scotland Laparoscopic Cholecystectomy Audit Group. Br J Surg. 1996;83(10):1356-60.
6. Davidoff AM, Pappas TN, Murray EA, Hilleren DJ, Johnson RD, Baker ME, et al. Mechanisms of major biliary injury during laparoscopic cholecystectomy. Ann Surg. 1992;215(3):196-202.
7. Stewart L, Way LW. Bile duct injuries during laparoscopic cholecystectomy. Factors that influence the results of treatment. Arch Surg. 1995;130(10):1123-8; discussion 9.
8. Harvey J, Dardik H, Impeduglia T, Woo D, DeBernardis F. Endovascular management of hepatic artery pseudoaneurysm hemorrhage complicating pancreaticoduodenectomy. J Vasc Surg. 2006;43(3):613-7.
9. Cheung PL, Lee YS, Tan CB, Lau HY, Siu CW, Chan CX, et al. Endovascular Management of Hepatic Artery Pseudoaneurysms: A Case Series. Vasc Specialist Int. 2023;39:1.
10. Benson AB, D'Angelica MI, Abrams T, Abbott DE, Ahmed A, Anaya DA, et al. NCCN Guidelines® Insights: Biliary Tract Cancers, Version 2.2023. J Natl Compr Canc Netw. 2023;21(7):694-704.

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Case Report

A Rare Tumor of the Liver: Mucinous Cystic Neoplasm

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Abstract

Mucinous cystic neoplasms (MCNs) are rare hepatic lesions with malignant potential, most commonly occurring in middle-aged women. Due to the lack of specific diagnostic tests and pathognomonic radiologic findings, establishing a preoperative diagnosis is challenging. The recommended primary treatment is complete surgical resection, while definitive diagnosis is typically made through histopathological evaluation.

A 24-year-old female patient, initially operated on with a preoperative diagnosis of hydatid cyst, was found on imaging to have a 9 × 4.5 cm cystic mass predominantly located in segment 4B of the liver, with partial extension toward segment 5. The patient underwent a left hepatectomy. Her postoperative course was uneventful, and histopathological analysis revealed a low-grade MCN.

There is limited information in the literature regarding MCNs of the liver. Accurate management of these patients is crucial due to their potential association with invasive carcinoma. Therefore, this entity should be considered in the differential diagnosis of hepatic cystic lesions, and curative surgical resection should be pursued whenever feasible.

Keywords: Mucinous Cystic Neoplasm, Liver, Ovarian-Like Stroma

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Mucinous cystic neoplasms (MCNs) of the liver are rare tumors that typically occur in middle-aged women, accounting for less than 5% of all hepatic cysts.[1,2] Although these tumors are generally benign, they carry a 3–5% risk of malignancy, which creates challenges in both diagnosis and management.[3] The exact origin of MCNs remains uncertain; however, histopathological studies suggest a possible association with ectopic ovarian-like stroma within the liver.[4]

Current knowledge about MCNs is primarily derived from case reports and small-scale studies, leaving no clear consensus on their optimal diagnosis and treatment strategies. Given their rarity and malignant potential, accurate clinical management is essential. In this report, we present the diagnostic and therapeutic management of a 24-year-old female with a hepatic MCN.

Case Report

A 24-year-old female patient who presented to another centre two months ago with complaints of abdominal pain and bloating was found to have a mass consistent with a hydatid cyst in the left lobe of the liver during the examinations performed. The patient underwent a partial cystectomy, and her postoperative course was uneventful.

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Histopathological examination of the surgical specimen removed from the cyst wall revealed it to be a MCN without dysplasia or invasive malignancy. The patient was then referred to us.

The patient had no significant comorbidities, and abdominal examination was unremarkable. Laboratory tests, including liver function tests and tumor markers, were within normal limits. Contrast-enhanced computed tomography and magnetic resonance imaging revealed a lobulated, multilocular cystic mass with thin septations, predominantly located in segment 4B of the liver, with partial extension into segment 5, measuring 9 × 4.5 cm at its widest dimension (Fig. 1).

A left hepatectomy was performed, ensuring tumor-free surgical margins. The postoperative period was uneventful. Histopathological examination of the hepatectomy specimen revealed MCN containing low-grade dysplasia measuring 9x7x4 cm (Fig. 2). The patient was subsequently placed under follow-up by the medical oncology department without adjuvant therapy (Fig. 3).

Discussion

MCNs were previously classified as biliary cystadenomas or cystadenocarcinomas. In 2010, the World Health Organization (WHO) reclassified these mucin-producing biliary tumors into two distinct entities: MCNs and intraductal papillary mucinous neoplasms (IPMNs) of the bile duct.[5] Hepatic IPMNs are considered the biliary counterpart of pancreatic IPMNs. Unlike MCNs, IPMNs tend to communicate with the bile ducts, are slightly more common in males, and typically lack ovarian-like stroma.

Histopathologically, MCNs are cyst-forming epithelial tumors lined by mucin-producing cuboidal or columnar epithelium, usually without communication with the bile ducts, and characterized by the presence of ovarian-like stroma. According to the WHO classification, the presence of ovarian-like stroma is a defining diagnostic criterion for MCNs. These tumors can exhibit low-, intermediate-, or high-grade dysplasia and, in some cases, progress to invasive carcinoma.

Nearly all MCNs occur in female patients and are most commonly located in the left lobe of the liver.[6] Our patient is similarly a female patient with a left lobe lesion. Interestingly, a significant proportion of cases originate from segment 4, as observed in our case, although the exact reason for this remains unclear. The average age at presentation is typically between 40 and 70 years, but, as in our case, MCNs

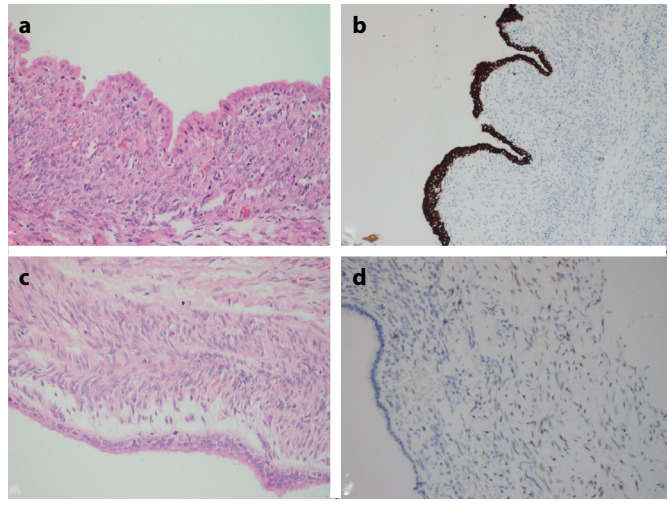

Figure 2. (a) Cyst surface surrounded by single-layered cuboidal cells (HE; 200X). **(b)** CK7 positivity in single-layered cuboidal cells (CK7; 200X). **(c)** Ovarian stroma with a spindle cell appearance beneath the epithelium (HE; 200X). **(d)** Estrogen receptor positivity in the ovarian stroma area (Estrogen receptor; 200X).

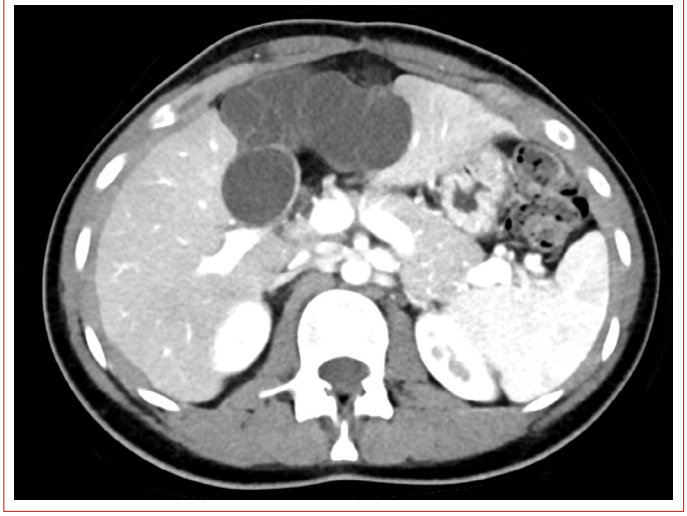

Figure 1. Preoperative septated cystic lesion in liver segment 4B-5.

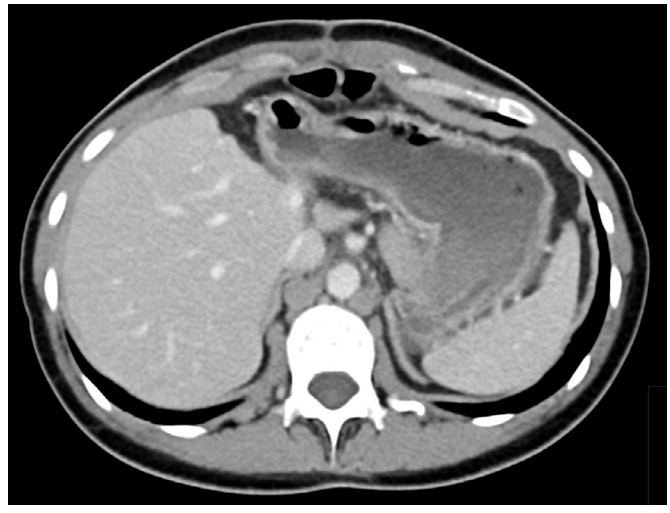

Figure 3. The post-operative CT scan at the 3-month follow-up.

may also present in younger patients, with only a few cases reported in individuals under 25.

In their early stages, MCNs are usually asymptomatic, and diagnosis often occurs when the lesions enlarge to approximately 10 cm.[7] When symptomatic, patients most commonly present with epigastric pain, abdominal fullness, and anorexia. Depending on the tumor's location, obstructive jaundice may also occur. Laboratory findings are often unremarkable unless there is biliary obstruction or communication with the bile ducts, and serum CA19-9 levels may be elevated. Our patient had abdominal pain and bloating, but no biliary problems, and her CA 19-9 was within normal limits.

On imaging, MCNs typically appear as multiloculated cystic tumors with septated walls that do not communicate with the bile ducts.[8] Due to these nonspecific imaging characteristics, they are frequently misdiagnosed as simple hepatic cysts, hydatid cysts, liver abscesses, or cholangiocarcinomas. In our patient, the lesion was initially misdiagnosed at another center, leading to an incomplete resection and potential risk of recurrence.

Definitive diagnosis relies on histopathological evaluation. The hallmark feature of MCNs is the presence of mucin-secreting biliary-type epithelium accompanied by dense subepithelial ovarian-type stroma that expresses female sex hormone receptors.

Although rare, MCNs carry a risk of malignant transformation. Due to the limited number of cases reported, the incidence of invasive carcinoma has been reported to range between 2% and 15.4%.[7,9] However, the absence of specific radiological features makes distinguishing benign from malignant lesions challenging.[10]

The recommended primary treatment for these tumors is curative surgical resection, aimed at preventing recurrence and malignant transformation.[11] Recurrence rates are high after partial resection (up to 80%). Prognosis largely depends on the presence or absence of invasion. In benign lesions, five-year survival after complete resection approaches 100%, with 18-year survival rates around 90%, whereas in cases associated with invasive carcinoma, five-year survival declines to 65–70%.[12,13]

Conclusion

In conclusion, MCNs of the liver are rare lesions with an uncertain etiopathogenesis and no specific diagnostic tests. Due to the limited number of reported cases, data regarding optimal management are scarce. Given their malignant potential, increasing awareness of these lesions and reporting more cases are essential to improve diagnostic accuracy and therapeutic strategies.

Disclosures

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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References

1. Marrero JA, Ahn J, Rajender Reddy K, Americal College of Gastroenterology. ACG clinical guideline: the diagnosis and management of focal liver lesions. Am J Gastroenterol. 2014 Sep;109(9):1328–47; quiz 1348.
2. Zen Y, Pedica F, Patcha VR, Capelli P, Zamboni G, Casaril A, et al. Mucinous cystic neoplasms of the liver: a clinicopathological study and comparison with intraductal papillary neoplasms of the bile duct. Mod Pathol. 2011 Aug;24(8):1079–89.
3. Van Treeck BJ, Lotfalla M, Czeczok TW, Mounajjed T, Moreira RK, Allende DS, et al. Molecular and Immunohistochemical Analysis of Mucinous Cystic Neoplasm of the Liver. Am J Clin Pathol. 2020 Nov 4;154(6):837–47.
4. Quigley B, Reid MD, Pehlivanoglu B, Squires MH, Maithel S, Xue Y, et al. Hepatobiliary Mucinous Cystic Neoplasms With Ovarian Type Stroma (So-Called "Hepatobiliary Cystadenoma/Cystadenocarcinoma"): Clinicopathologic Analysis of 36 Cases Illustrates Rarity of Carcinomatous Change. Am J Surg Pathol. 2018 Jan;42(1):95–102.
5. Kubota K, Nakanuma Y, Kondo F, Hachiya H, Miyazaki M, Nagino M, et al. Clinicopathological features and prognosis of mucin-producing bile duct tumor and mucinous cystic tumor of the liver: a multi-institutional study by the Japan Biliary Association. J Hepatobiliary Pancreat Sci. 2014 Mar;21(3):176–85.
6. Kośnik A, Stadnik A, Szczepankiewicz B, Patkowski W, Wójcicki M. Spontaneous rupture of a mucinous cystic neoplasm of the liver resulting in a huge biloma in a pregnant woman: A case report. World J Clin Cases. 2021 Oct 26;9(30):9114–21.
7. Zen Y, Jang KT, Ahn S, Kim DH, Choi DW, Choi SH, et al. Intraductal papillary neoplasms and mucinous cystic neoplasms of the hepatobiliary system: demographic differences between Asian and Western populations, and comparison with pancreatic counterparts. Histopathology. 2014 Aug;65(2):164–73.
8. Moriuchi T, Hashimoto M, Kuroda S, Kobayashi T, Ohdan H, Moriuchi T, et al. Mucinous Cystic Neoplasm of the Liver in a Teenager: A Case Report. Cureus. 2024 Jul 30;16.

9. Shibata H, Ohike N, Norose T, Isobe T, Suzuki R, Imai H, et al. Mucinous Cystic Neoplasms Lined by Abundant Mucinous Epithelium Frequently Involve KRAS Mutations and Malignant Progression. Anticancer Res. 2017 Dec;37(12):7063–8.
10. Takano Y, Nagahama M, Yamamura E, Maruoka N, Mizukami H, Tanaka J ichi, et al. Prolapse into the bile duct and expansive growth is characteristic behavior of mucinous cystic neoplasm of the liver: report of two cases and review of the literature. Clin J Gastroenterol. 2015;8(3):148–55.
11. Tekin E, Taşkın T, Ayhan S. Musinous cystic neoplasia mimicking hydatid cyst in the liver: Two rare cases. Turk J Surg. 2024 Mar 23;40(1):82–6.
12. Soares KC, Arnaoutakis DJ, Kamel I, Anders R, Adams RB, Bauer TW, et al. Cystic neoplasms of the liver: biliary cystadenoma and cystadenocarcinoma. J Am Coll Surg. 2014 Jan;218(1):119–28.
13. Lee CW, Tsai HI, Lin YS, Wu TH, Yu MC, Chen MF. Intrahepatic biliary mucinous cystic neoplasms: clinicoradiological characteristics and surgical results. BMC Gastroenterol. 2015 Jun 10;15:67.

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Case Report

Evaluation of a Case with Biliary Atresia and Heterotaxy Syndrome (Left Isomerism) in Terms of Liver Transplantation: A Case Report

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Abstract

Left isomerism, a subtype of heterotaxy marked by multiple spleens and abnormal organ positioning, poses additional complexity when coexisting with biliary atresia, the leading cause of neonatal cholestasis and pediatric liver transplantation. We report a 5-month-old male infant with biliary atresia and left isomerism, presenting with persistent jaundice, acholic stools, and dark urine. Despite undergoing Kasai portoenterostomy at one month, clinical and laboratory parameters did not improve. Cardiac assessment revealed left atrial isomerism, atrioventricular septal defect, pulmonary atresia, and patent ductus arteriosus. Abdominal CT showed a midline liver, polysplenia, absent inferior vena cava with azygos-hemiazygos continuation, preduodenal portal vein, intestinal malrotation, and visceral heterotaxy. Laboratory tests indicated severe cholestasis, hepatocellular injury, and impaired liver function. The patient was evaluated and listed as a liver transplant candidate. The coexistence of biliary atresia and left isomerism complicates both diagnosis and treatment. Early imaging, multidisciplinary management, and timely transplantation are essential to improve outcomes. This case underscores the importance of a comprehensive, individualized approach in managing biliary atresia with complex congenital anomalies.

Keywords: Biliary Atresia, Heterotaxy Syndrome, Liver Transplantation

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Left isomerism, also known as polysplenia syndrome, is a form of heterotaxy characterized by the presence of multiple spleens and other deviations from normal organ positioning. This condition is classified as situs ambiguus or heterotaxy, where the organs do not follow the typical left-right arrangement seen in standard anatomical structures. In left isomerism, the body may exhibit bilateral left-sidedness; that is, structures usually found on the left side of the body may be mirrored on both sides.[1] This is often associated with variations in the arrangement of major blood vessels and internal organs.[2]

Biliary atresia is a rare neonatal disease caused by obstruction of the bile ducts, leading to severe cholestasis, fibrosis, and cirrhosis. Although it is the primary cause of neonatal cholestasis, it is also the most common reason for liver transplantation in children. Although the exact etiology remains unknown, early surgical intervention and disease management through the Kasai procedure are of great im-

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portance to control the disease and delay the need for liver transplantation.[3, 4]

The coexistence of left isomerism and biliary atresia is clinically significant because of the complexity created by having to manage both conditions simultaneously. Additional congenital defects are observed in approximately 10% of infants with biliary atresia, often involving left-right axis abnormalities, such as situs inversus and polysplenia. This association suggests a possible underlying genetic factor in the disease.[1] The presence of left isomerism can complicate the diagnosis and treatment of biliary atresia, as it may mask typical signs of anatomical abnormalities or affect surgical outcomes.

The incidence of biliary atresia is estimated to be between 1 in 5,000 and 1 in 20,000 live births, with higher incidence rates observed in Asia.[5] When seen in conjunction with conditions such as left isomerism, early and accurate diagnosis is crucial; timely intervention and prevention of serious complications help achieve the best possible surgical outcomes.[3]

In children with biliary atresia, especially when accompanied by complex conditions such as left isomerism, liver transplantation is a vital treatment option. In cases where biliary atresia coexists with left isomerism, additional anatomical variations, such as the absence or abnormal structure of the portal veins, may render traditional liver transplantation techniques unfeasible.[6] These vascular anomalies require special surgical approaches and preoperative imaging to ensure successful liver transplantation.[7] Surgical management of these patients requires a multidisciplinary approach to optimize outcomes and address preoperative challenges, such as malnutrition and portal hypertension.[8]

In conclusion, liver transplantation is a vital option for the treatment of biliary atresia, especially in complex clinical situations in which concurrent left isomerism is present.

Case Report

A five-month and fourteen-day-old male patient was evaluated at an outside center for persistent jaundice during the first weeks after birth, acholic stools, and dark-colored urine. Imaging and biochemical tests led to a diagnosis of biliary atresia. Kasai portoenterostomy was performed in the first month of life. However, since there was no improvement in clinical and laboratory findings postoperatively and jaundice persisted, the patient was referred to our center for further evaluation.

On evaluation of the cardiac system, transthoracic echocardiography revealed left atrial isomerism, complex atrioventricular septal defect (AVSD), pulmonary valve atresia, and patent ductus arteriosus (PDA). The pulmonary arteries were perfused by means of a stent placed in the PDA, and there was mild regurgitation in the atrioventricular valves. On contrast-enhanced thoracic CT, a right aortic arch and an AVSD are observed (Fig. 1). The patient's overall hemodynamic status was stable, and cardiac surgery was postponed to a later date. Given the presence of cardiac and major vascular structural anomalies, recognition of cardiac anomalies before liver transplantation may be important.

Abdominal CT tomography showed that the liver was displaced toward the midline and shifted to the left. In addition, polysplenia consistent with multiple small nodular splenic structures, absence of the inferior vena cava (IVC), and, secondary to this, azygos-hemiazygos vein dilatation, preduodenal portal vein, short pancreas, intestinal malrotation, loss of visceral symmetry (Fig. 2) were detected. These findings support the presence of heterotaxy syndrome (left isomerism) in this patient.

Laboratory evaluations revealed that the total bilirubin level was 17.84 mg/dL and the direct bilirubin level was 8.78 mg/dL, indicating significant cholestatic jaundice.

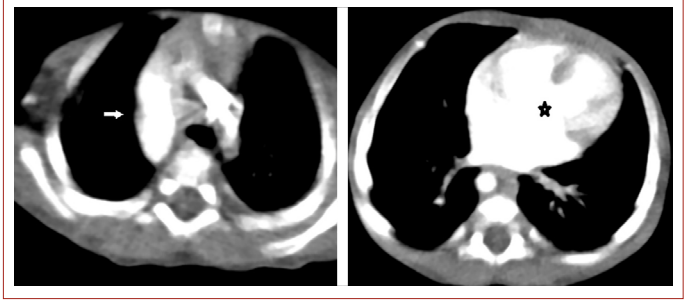

Figure 1. Contrast-enhanced thoracic CT images show a right-sided aortic arch (white arrow) and an atrioventricular septal defect (AVSD) (asterisk).

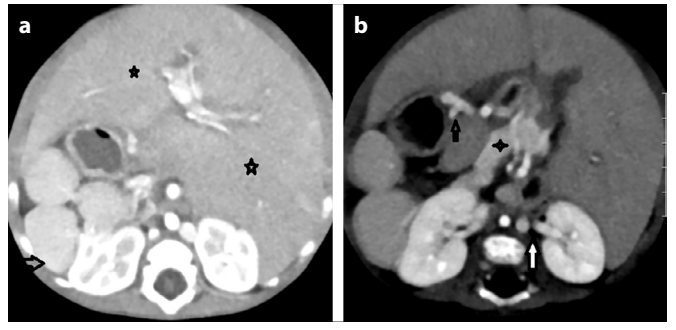

Figure 2. Contrast-enhanced abdominal CT images. **(a)** The liver is located in the midline, and both lobes exhibit a left-lobe configuration (asterisks). Multiple splenules consistent with polysplenia are seen (arrow). **(b)** A right-sided stomach, a preduodenal portal vein (black arrow), a shortened pancreas (asterisk), and a dilated azygos vein (white arrow) are observed.

There was a notable elevation in transaminase levels (AST, 647 U/L; ALT, 300 U/L), which was consistent with active hepatocellular injury. The LDH level was 281 U/L, indicating nonspecific cellular damage. The serum albumin level was below the reference values of 3.0 g/dL, showing decreased protein synthesis capacity of the liver. There was also a disturbance in coagulation parameters: INR was 1.61, and prothrombin activity was 38.4%. These findings indicate that the patient experienced advanced hepatic dysfunction and impaired liver reserve.

In light of these clinical, laboratory, and radiological findings, the patient was evaluated by a multidisciplinary council for liver transplantation and has been placed under follow-up as a transplant candidate.

Discussion

Left isomerism is mostly associated with polysplenia syndrome and presents unique challenges when accompanied by biliary atresia. Left isomerism encompasses a spectrum of cardiac and extracardiac anomalies, including[2] interruption of the inferior vena cava, complete atrioventricular septal defect, and complete heart block. These anomalies complicate the diagnosis and treatment of biliary atresia, which, due to progressive fibrosis of the biliary tree, leads to cholestasis and liver damage, and is the most common cause of neonatal cholestasis and pediatric liver transplantation.[4]

The presence of laterality defects, such as left isomerism, increases the complexity of genetic and environmental factors in the management of these cases. Studies suggest that genetic mutations affecting the determination of the left-right axis, such as the CFC1 gene, may predispose patients to both left isomerism and biliary atresia; however, other genetic or environmental factors may also contribute to this phenotype.[1]

Early diagnosis of biliary atresia is crucial for effective treatment, with interventions such as hepatoportoenterostomy ideally performed within the first 45 days of life yielding the best outcomes. This surgical procedure aims to restore bile flow from the liver to the intestine, potentially slowing the progression of liver damage. However, despite early intervention, the majority of patients with biliary atresia eventually require liver transplantation because of ongoing liver deterioration.The progressive nature of biliary atresia means that even with successful initial treatment, long-term liver health remains a significant concern. As patients age, the cumulative effects of cholestasis and fibrosis often lead to cirrhosis and liver failure. This necessitates close monitoring of liver function and regular follow-up throughout childhood and adolescence. Liver transplantation, when required, offers these patients the best chance for long-term survival and improved quality of life, addressing both biliary obstruction and the resultant liver damage.[3, 4]

In such complex cases, radiology, a multisystemic approach involving pediatric surgeons, hepatologists, cardiologists, and geneticists, is required. This comprehensive approach enables the early detection of various complications arising from the coexistence of left isomerism and biliary atresia and facilitates the development of personalized treatment strategies.[9]

Improvements in management may include the development of screening protocols for the early detection of biliary atresia and associated anomalies, as well as ongoing research on genetic factors and potential environmental triggers involved in the etiology of these combined conditions.[10]

Conclusion

Heterotaxy syndrome accompanied by biliary atresia (especially left isomerism) can lead to significant anatomical and physiological challenges in liver transplant planning. In such cases, early diagnosis, detailed imaging, multidisciplinary evaluation, and timely transplantation decisions play decisive roles in reducing mortality and morbidity. This presentation provides a remarkable example of the approach to liver transplantation in cases of biliary atresia associated with complex congenital anomalies.

Disclosures

Informed Consent: Written, informed consent was obtained from the patient's family for the publication of thís case report and the accompanying images.

Conflict of Interest: None declared.

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References

1. Jacquemin E, Cresteil D, Hadchouel M, Raynaud N (2002) CFCI gene mutation and biliary atresia with polysplenia syndrome. Journal of Pediatric Gastroenterology and Nutrition 34:326.
2. Tawfik AM, Zaky MM, Eladalany MA, Elmokadem AH, Batouty NM (2013) Polysplenia syndrome: a review of the relationship with viscero-atrial situs and the spectrum of extra-cardiac anomalies. Surgical and Radiologic Anatomy 35:647–653.

3. Schreiber RA, Harpavat S, Hulscher JBF, Wildhaber BE (2022) Biliary Atresia in 2021: Epidemiology, Screening and Public Policy. Journal of Clinical Medicine 11:999.
4. Feldman AG, Mack CL (2015) Biliary Atresia: Clinical Lessons Learned. Journal of Pediatric Gastroenterology and Nutrition 61:167–175.
5. Tam PKH, Wells RG, Tang CSM, Lui VCH, Hukkinen M, Luque CD, De Coppi P, Mack CL, Pakarinen M, Davenport M (2024) Biliary atresia. Nature reviews Disease primers.
6. Ledesma-Medina J, Bron KM, Dominguez R, Bowen A, Young LW (1985) Pediatric liver transplantation. Part I. Standardization of preoperative diagnostic imaging. Radiology 157:335–338.
7. Barshes NR, Lee TC, Goss JA, Carter BA, Balkrishnan R, Karpen SJ (2005) Orthotopic Liver Transplantation for Biliary Atresia. Liver Transplantation 11:1193–1200.
8. Sundaram SS, Mack CL, Sokol RJ, Feldman AG (2016) Biliary atresia: Indications and timing of liver transplantation and optimization of pretransplant care. Liver Transplantation 23:96–109.
9. Bezerra JA, Karpen SJ, Hoofnagle JH, Mack CL, Sokol RJ, Wells RG, Doo E (2018) Biliary Atresia: Clinical and Research Challenges for the Twenty-First Century. Hepatology 68:1163–1173.
10. Wang KS, Karpen SJ, Holcomb G, et al (2015) Newborn Screening for Biliary Atresia. Pediatrics 136:e1663–e1669.

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Case Report

Wolman's Disease, Haemopagocytic Lymphohistiocytosis and Cytomegalovirus Infection: Association or Coincidence?

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Abstract

Wolman's disease, an infantile form of lysosomal acid lipase deficiency, is very rare and usually fatal in infancy. In this article we present two infants with Wolman's disease associated with cytomegalovirus infection, one with surrenal calcifications and the other with histopathological liver calcifications and haemophagocytic lymphohistiocytosis.

Both cases had complaints of vomiting and fever for two months. A family history of consanguinity and infant deaths of unknown cause was reported. Physical examination revealed jaundice and hepatosplenomegaly. Cytomegalovirus infection, unresponsive to ganciclovir treatment, was diagnosed in both cases. While haemophagocytic lymphohistiocytosis and histopathological calcifications in the liver were observed in the first case, classical surrenal calcifications were seen in the second case.

It is not clear whether the presence of cytomegalovirus infection in both cases and haemophagocytic lymphohistiocytosis in one case are coincidental. Furthermore, histopathological calcification in the liver appears to be a diagnostic criterion, as is adrenal calcification, although it has never been reported before.

Keywords: Hemophagocytic Lymphohistiocytosis, Cytomegalovirus Infection, Wolman's Disease

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Lysosomal acid lipase deficiency (LAL-D) is a rare autosomal recessive lysosomal storage disorder caused by LIPA gene variants (chromosome 10q23.2-q23.3), resulting in defective hydrolysis of cholesteryl esters and triglycerides and subsequent accumulation in multiple organs. Two clinical forms are recognized: Wolman disease (WD), the severe infantile form, and cholesteryl ester storage disease (CESD), the milder phenotype due to partial enzyme activity. Affected individuals are homozygous or compound heterozygous for LIPA variants, and more than 100 variants have been described.[1,2] Severe variants, such as nonsense or frameshift changes, typically present in infancy. The most common (>50%) variant is E8SJM (c.894G>A).[1]

In WD, fetal ascites and polyhydramnios may be observed in utero. The incidence is estimated at 1:100,000–1:300,000 live births. The disease manifests in early infancy with absent LAL activity. The hallmark feature is adrenal enlargement with calcifications, frequently detected on imaging, although not mandatory for diagnosis. Adrenal insufficiency has also been reported.[1]

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Secondary hemophagocytic lymphohistiocytosis (HLH) may complicate WD, and cytomegalovirus (CMV) infection is among the recognized infectious triggers of HLH. Here, we present two cases of WD: the first with HLH secondary to CMV infection and hepatic calcifications identified on histopathology, and the second with adrenal calcifications and a strong family history of infantile deaths.

Case Report

Case 1 – A two-month-old girl presented with persistent vomiting since birth, worsening over the last 20 days, fever, and weight loss for one week. The parents were second-degree relatives. In the extended family, the mother's aunt and uncle had died in infancy with a suspected storage disorder.

Examination: Body temperature: 38.5 °C; weight: 4 kg (3rd–10th percentile); height: 60 cm (75th percentile). Hepatomegaly (liver palpable 4 cm below the right costal margin) and splenomegaly (2 cm below the left costal margin) were noted.

Laboratory tests: WBC 30,000/µL; Hb 7.9 g/dL; PLT 109,000/µL; INR 2.2; AST 1456 U/L; ALT 287 U/L; total protein 5.2 g/dL; albumin 2 g/dL; total bilirubin 1.09 mg/dL; direct bilirubin 0.58 mg/dL; ALP 148 U/L; GGT 150 U/L; LDH 2726 U/L; TG 923 mg/dL; cholesterol 136 mg/dL; HDL 9 mg/dL; LDL 55 mg/dL.

Microbiology: CMV IgM and CMV PCR were positive. Empirical cefotaxime and amikacin were started, and ganciclovir was initiated for CMV.

Follow-up: One week later, fever persisted, WBC decreased to 2100/µL, Hb 7.4 g/dL, and PLT 27,000/µL. Peripheral smear showed vacuolization of lymphocytes; bone marrow aspiration demonstrated foam cells with hemophagocytosis. HLH criteria were fulfilled (ferritin 2500 µg/mL, fibrinogen 64 mg/dL). HLH-2004 protocol was initiated.

Enzyme studies: Lysosomal acid lipase activity <0.02 nmol/h/mg (normal 0.37–2.30). Diagnosis: WD with secondary HLH triggered by CMV. The patient died one day later before enzyme replacement therapy could be started.

Histopathology: Post-mortem liver biopsy showed diffuse macrovesicular steatosis, pericentral hepatocyte loss, calcification and fibrosis, ductular proliferation with bile plugs, and severe pericellular/central fibrosis. Findings were consistent with a metabolic storage disorder with lipid accumulation.

Case 2 – A two-month-old boy presented with vomiting, one month of abdominal distension (worsening in the last few days), and fever for three days. The parents were first-degree relatives. Eight of the father's siblings had died in infancy of unknown causes.

Examination: Body temperature: 38.6 °C; weight: 5 kg (50th percentile); height: 60 cm (75th percentile); icterus, abdominal distension, and hepatosplenomegaly (liver and spleen palpable 4 cm below the costal margins).

Laboratory tests: WBC 17,000/µL; Hb 6.3 g/dL; PLT 65,000/µL; INR 3.5; AST 1522 U/L; ALT 541 U/L; total protein 4.7 g/dL; albumin 2 g/dL; total bilirubin 4 mg/dL; direct bilirubin 3.1 mg/dL; GGT 118 U/L; LDH 4046 U/L; TG 613 mg/dL; cholesterol 130 mg/dL; HDL 29 mg/dL; LDL 21 mg/dL.

Microbiology: CMV IgM and CMV PCR positive; ganciclovir was initiated.

Imaging: Abdominal tomography demonstrated bilateral adrenal calcifications.

Enzyme studies: Lysosomal acid lipase activity <0.02 nmol/h/mg. Diagnosis: WD. The patient died three days later before therapy could be initiated.

Histopathology: Post-mortem liver biopsy showed diffuse macro- and microvesicular steatosis, scattered necrosis, and extramedullary hematopoiesis.

Discussion

WD typically presents within the first weeks of life with vomiting, diarrhea, hepatosplenomegaly, and cachexia, progressing rapidly to death within 2–6 months. CESD is milder, often presenting later in childhood with deficient, but not absent, LAL activity.[3,4]

Our first case presented with fever, hepatosplenomegaly, hypertriglyceridemia, and liver failure at two months, and developed HLH secondary to CMV infection. The second case exhibited adrenal calcifications, a classic feature, but bone marrow examination could not be performed due to coagulopathy. Both cases showed marked hypertriglyceridemia with low HDL and LDL cholesterol, consistent with the characteristic dyslipidemia of LAL-D.[5] Elevated LDH and prolonged INR indicated severe hepatocellular injury and impaired synthetic function.

Histopathology in WD usually demonstrates micro- and macrovesicular steatosis, periportal fibrosis, and lipid-laden histiocytes.[6-8] In our first case, hepatic calcification was also noted—an unusual finding. While adrenal calcification is well described in WD, hepatic calcification is rarely reported. Given the concomitant CMV infection, it remains uncertain whether hepatic calcification represents an atypical manifestation of WD or a secondary effect of CMV infection.

Reports have described WD complicated by HLH, but infection-associated HLH in this context is rarely documented. The proposed mechanism involves cholesteryl ester crystal accumulation in macrophages, triggering cytokine release

and HLH activation.[9,10] Despite initiation of HLH therapy and antiviral treatment, the outcome remained fatal, underscoring the severity of this association.

Conclusion

LAL-D should be considered in infants with consanguinity, family history of infant deaths, persistent vomiting, hepatosplenomegaly, hypertriglyceridemia, low HDL, cholestasis, and adrenal calcifications. Infants presenting with HLH should also be screened for WD. Although hepatic calcifications are not a specific finding, their presence, as in our case, highlights the need for further studies on their diagnostic significance.

Disclosures

Informed Consent: Written informed consent was obtained from the patients' legal guardians for publication of this case report and accompanying images.

Conflict of Interest: None declared.

Financial Disclosure: None.

Authorship Contributions: Concept – Ş.G.; Design – Ş.G., F.İ.V., M.A.S.; Supervision – M.A.S.; Materials – Ş.G., F.İ.V., E.G.; Data collection &/or processing – N.K.S., E.S. ; Analysis and/or interpretation – N.K.S., E.S., A.A, Y.D.O, B.M.; Literature search – Ş.G.; Writing – Ş.G.; Critical review – M.A.S.

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References

1. Wilson DP, Patni N. Lysosomal Acid Lipase Deficiency. 2023 Mar 15. In: Feingold KR, et al. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–. PMID: 27809430.
2. Korbelius M, Kuentzel KB, Bradić I, Vujić N, Kratky D. Recent insights into lysosomal acid lipase deficiency. Trends Mol Med. 2023 Jun;29(6):425-438. doi:10.1016/j.molmed.2023.03.001.
3. Burton BK, Balwani M, Feillet F, et al. A phase 3 trial of sebelipase alfa in lysosomal acid lipase deficiency. N Engl J Med. 2015;373:1010-1020.
4. Ikari N, Shimizu A, Asano T. Lysosomal Acid Lipase Deficiency in Japan: A Case Report of Siblings and a Literature Review. J Nippon Med Sch. 2018;85(2):131-137. doi:10.1272/jnms.2018_85-20.
5. Curiati MA, Kyosen SO, Pereira VG, Patrício FRDS, Martins AM. Lysosomal Acid Lipase Deficiency: Report of Five Cases across the Age Spectrum. Case Rep Pediatr. 2018;2018:4375434.
6. Ikari N, Shimizu A, Asano T. Lysosomal Acid Lipase Deficiency in Japan: A Case Report of Siblings and a Literature Review of Cases in Japan. J Nippon Med Sch.2018;85(2):131-137. doi: 10.1272/jnms.2018_85-20. PubMed PMID: 29731497.
7. Curiati MA, Kyosen SO, Pereira VG, Patrício FRDS, Martins AM. Lysosomal Acid Lipase Deficiency: Report of Five Cases across the Age Spectrum. Case Rep Pediatr. 2018 Jan 21;2018:4375434. doi: 10.1155/2018/4375434.
8. Boldrini R, Devito R, Biselli R, Filocamo M, Bosman C. WD and CESD diagnosed by histological and ultrastructural examination of intestinal and liver biopsy. Pathol Res Pract. 2004;200(3):231-240.
9. Tinsa F, Ben Romdhane M, Boudabous H, et al. A Novel Mutation ... Unusual Presentation: HLH. J Pediatr Hematol Oncol. 2018. doi:10.1097/MPH.0000000000001192.
10. Santos Silva E, Klaudel-Dreszler M, Bakuła A, et al. Early onset LAL deficiency presenting as secondary HLH: Two infants treated with sebelipase alfa. Clin Res Hepatol Gastroenterol. 2018. doi:10.1016/j.clinre.2018.03.012.

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Case Report

Surgical Treatment of Tumor Thrombus Extending into the Right Atrium in Hepatocellular Carcinoma: Case Report

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Abstract

Hepatocellular carcinoma (HCC) stands as a primary contributor to cancer-related mortality across the globe. While intrahepatic vascular invasion is a frequent finding in individuals with HCC, the progression of a tumor thrombus through the inferior vena cava (IVC) and into the right atrium is an infrequent event. This report details the surgical handling of a 72-year-old male patient diagnosed with HCC in the right hepatic lobe, which was complicated by a tumor thrombus extending into the inferior vena cava and approaching the right atrium. The patient successfully underwent a right hepatectomy combined with thromboendovenectomy and had an unremarkable postoperative course. At a 10-month follow-up, no signs of recurrence were detected. This case underscores the beneficial effect of meticulously planned surgical procedures on the survival of patients with advanced HCC and brings attention to the value of employing aggressive surgical strategies.

Keywords: Inferior Vena Cava, Hepatocellular Carcinoma, Right Atrial Invasion, Tumor Thrombus

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Constituting around 90% of all primary liver cancers, hepatocellular carcinoma (HCC) represents a major factor in cancer-related deaths worldwide.[1] Key risk factors predisposing individuals to HCC development include cirrhosis, chronic infections from hepatitis B and C, and non-alcoholic fatty liver disease. From a clinical standpoint, HCC may not show any symptoms, or in some cases, it can manifest with signs like abdominal pain, fatigue, encephalopathy, or ascites.[2]

Although intrahepatic vascular invasion is observed in 10–40% of HCC cases, a tumor thrombus that extends into the IVC and right atrium is present in merely 1–4% of these patients.[3, 4] The presence of such a widespread thrombus carries the risk of life-threatening events, including right heart failure and pulmonary embolism. In these situations, palliative treatments are generally the standard recommendation; however, surgical intervention has the potential to markedly enhance the prognosis for carefully chosen patients.[5-9] This case report outlines the successful surgical management, involving right hepatectomy and thromboendovenectomy, of an individual with primary HCC whose tumor thrombus extended into the right atrium.

Case Report

A 72-year-old male sought medical attention with complaints of fatigue and pain in the right upper quadrant. A

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mass measuring 140 × 130 × 115 mm, consistent with HCC, was identified in the right hepatic lobe via triphasic dynamic tomography. The imaging further revealed a tumor thrombus that progressed from the right hepatic vein and IVC up to the level of the right atrium (Fig. 1).

Laboratory analyses indicated a serum Alpha-fetoprotein level of 19.6 ng/mL, with the normal range being 0.9–9.0 ng/mL. Preoperative levels of other tumor markers were also within normal limits, including CEA at 1.1 ng/mL (normal range: 0–3) and CA 19-9 at 21.4 U/mL (normal range: 0–35). Tests for viral hepatitis came back negative, while esophagogastroduodenoscopy and colonoscopy yielded normal findings. The patient's medical history included benign prostatic hyperplasia, with no familial background of cirrhosis or cancer. A sufficient remnant liver volume (%35.4) in the left lobe was confirmed by radiological evaluation. Classified as Child-Pugh A and American Society of Anesthesiologists physical status of 2, the patient was considered a suitable candidate for surgery.

Surgical Technique

The procedure was conducted under general anesthesia using a median and right lateral incision. Mobilization of the right lobe was achieved by carefully dividing the right hepatic triangular and coronary ligaments. To clearly define the anatomical relationship between the liver and the IVC, the hanging maneuver was utilized. A foremost objective during the operation was to mitigate the embolic risk posed by the tumor thrombus.

The suprahepatic and infrahepatic portions of the IVC were prepared with great care for clamping. Following this, the right hepatic artery and right portal vein were dissected, ligated, and then transected. The CUSA system was used to transect the liver parenchyma, effectively separating the right and left lobes, and the specimen was then removed as a single block. Subsequent to the transection of the right hepatic vein, the tumor thrombus was meticulously extracted from the IVC and right atrium by means of thromboendovenectomy (Fig. 2). After ensuring hemostasis was complete, the procedure was concluded with the placement of a single drain.

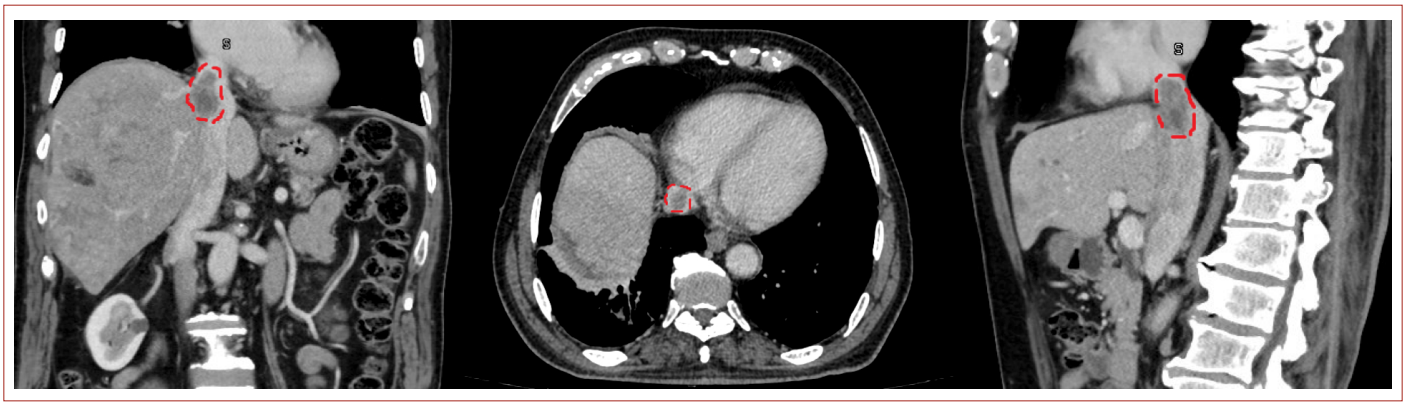

Figure 1. CT image showing tumor in the right lobe of the liver and extension of tumor thrombus from the IVC to the right atrium, delineated by red lines.

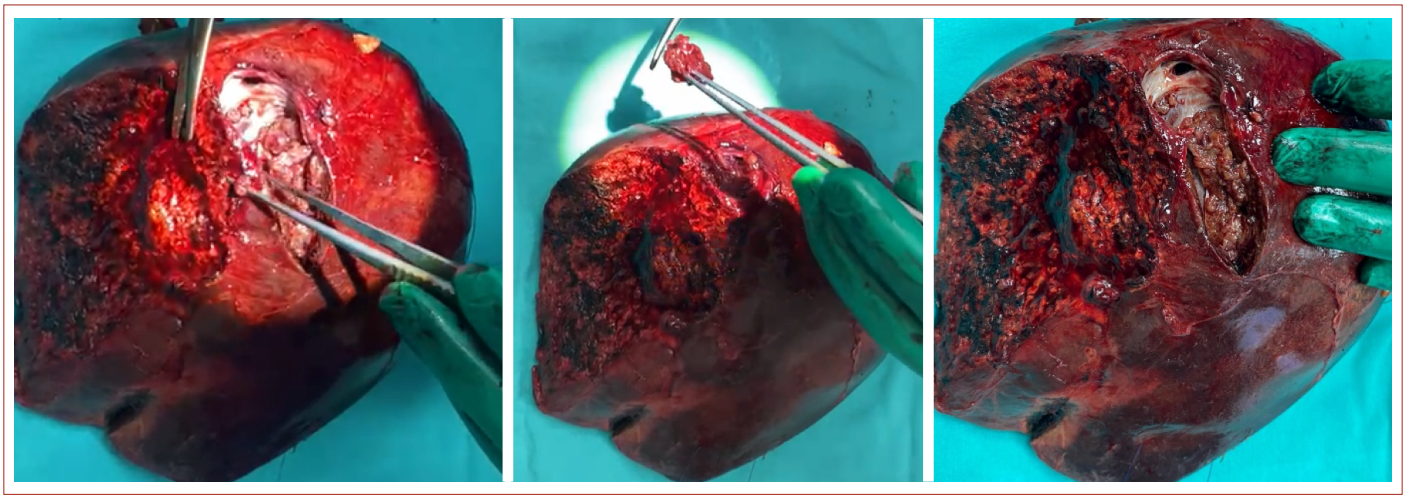

Figure 2. Tumor thrombus invasion in the right hepatic vein in the specimen.

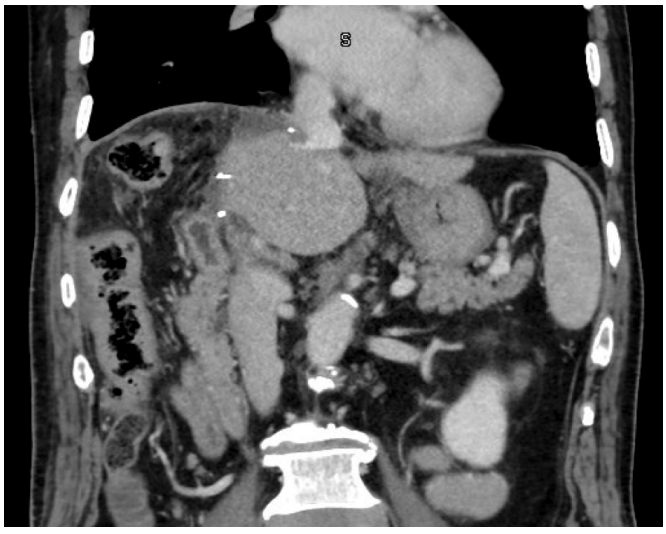

Figure 3. Control CT image at 5th months postoperatively.

Pathology Findings and Follow-Up

The patient was moved from the intensive care unit to the ward on the first day after surgery. The abdominal drain was taken out on the third day, and on the fifth day, the patient was discharged without any complications. The pathological analysis identified a poorly differentiated HCC (nuclear grade 3) of 16.5 × 14 × 9.5 cm in size, accompanied by two satellite tumors measuring 2.8 and 0.7 cm. The tumor was situated adjacent to the liver capsule but did not invade it. An examination of the surgical margins showed no evidence of tumor infiltration.

During the follow-up at the 5th month, the patient's serum Alpha-fetoprotein level had fallen to 3.8 ng/mL, and imaging scans revealed no indication of recurrence (Fig. 3). The patient is currently in his 10th month of follow-up, which is proceeding without any issues.

Discussion

The extension of a tumor thrombus into the right atrium is an uncommon yet severe complication associated with HCC. A Japanese study documented the incidence of HCC-related tumor thrombus affecting the IVC and right atrium to be 2.9% on imaging studies, 0.7% in surgical cohorts, and 18.2% in autopsy findings.[9]

Typically, cases of advanced HCC are addressed with non-surgical methods like conservative therapy, transarterial chemoembolization, or radiotherapy. Nevertheless, for patients with a tumor thrombus that involves the right atrium, these treatments often result in poor outcomes, and the prognosis continues to be bleak.[10, 11] When metastatic disease extends to the IVC and right atrium, survival is typically between 2 days and 3 months with palliative care or no treatment; however, surgical resection has been linked to a notably longer median survival of 9 to 33 months.[2, 12, 13] Published reports show survival durations of 5–56 months following surgical resection and thrombectomy.[6, 14]

Patients with HCC frequently manifest with a range of symptoms, including pain in the right upper quadrant, fatigue, anorexia, weight loss, abdominal swelling, jaundice, pruritus, or encephalopathy.[15] Although 70–90% of HCC instances arise in cirrhotic livers, a notable 10–30% develop in livers without cirrhosis.[16] The patient in this report did not have a cirrhotic history and presented with symptoms of fatigue and right upper quadrant pain.

In HCC cases involving a tumor thrombus, surgical intervention can markedly enhance progression-free survival rates. One particular study highlighted a 40% 1-year survival rate achieved with surgical treatment, underscoring the necessity of prompt surgical action. Such operations can avert life-threatening events like right ventricular outflow obstruction, cardiac valve failure, and pulmonary embolism, thus offering a distinct survival benefit.[9, 13, 17]

HCC accompanied by a tumor thrombus is categorized into three types based on its anatomical relationship to the heart: type I refers to a thrombus located within the inferior vena cava (IVC) below the diaphragm ; type II describes a thrombus situated in the IVC above the diaphragm but still external to the right atrium ; and type III, known as the intracardiac type, involves the tumor thrombus being located above the diaphragm and having penetrated the right atrium.[18] In the case of our patient, the tumour thrombus was classified as type II and was positioned in the IVC above the diaphragm, but had not reached the right atrium.

For non-cirrhotic HCC patients who have adequate remnant liver, surgical resection continues to be a practical treatment choice. In the present case, the decision to proceed with resection was bolstered by preoperative imaging, which verified that the upper portion of the IVC thrombus was accessible for clamping. Although brachytherapy can be considered as an alternative treatment option in selected HCC cases with vascular invasion, previous studies have reported an increased risk of embolic events associated with intravascular tumor thrombus and lower treatment efficacy compared to surgery.[19] Similarly, while external beam radiotherapy (EBRT) has shown promising results, with reported 1-year and 2-year overall survival rates of 53.6% and 36.9%, respectively, in comparable patient populations, its effectiveness is often limited in the presence of large tumor burdens or extensive vascular invasion.[20] Moreover, EBRT may not prevent catastrophic events such as pulmonary embolism or cardiac obstruction caused by tumor thrombi. In the present case, given the patient's favorable anatomy, adequate future

liver remnant, and absence of extrahepatic disease, surgical resection was considered the most appropriate and potentially curative treatment approach.

The role of adjuvant chemotherapy in HCC has been extensively investigated. Recent evidence indicates that adjuvant immunotherapy, particularly the combination of atezolizumab and bevacizumab, may improve recurrence-free survival in patients undergoing curative-intent resection for HCC (20). In our patient, no adjuvant chemotherapy was administered during follow-up at our institution, as no evidence of recurrence or metastasis was detected in radiological imaging or alpha-fetoprotein (AFP) levels. However, since the patient continued follow-up at another center after the tenth postoperative month, it remains unknown whether adjuvant systemic therapy was subsequently administered.

In summary, while advanced HCC with a right atrial thrombus presents an aggressive condition, it can be managed effectively with surgical treatments in appropriately selected patients. It is advisable that these high-risk surgical procedures be carried out in transplant centers where donor availability is assured.

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References

1. Forner A, Reig M, Bruix J. Hepatocellular carcinoma. Lancet. 2018;391(10127):1301-14.
2. Wu K, Travaline CE, Elliot L. Right atrial tumor invasion: a rare presentation of hepatocellular carcinoma. Cureus. 2022; Mar 6.
3. Li W, Wang Y, Gao W, Zheng J. HCC with tumor thrombus entering the right atrium and inferior vena cava treated by percutaneous ablation. BMC Surg. 2017;17(1).
4. Quirk M. Management of hepatocellular carcinoma with portal vein thrombosis. World J Gastroenterol. 2015;21(12):3462.
5. Galle PR, Forner A, Llovet JM, Mazzaferro V, Piscaglia F, Raoul JL, et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol. 2018;69(1):182-236.
6. Tomita K, Shimazu M, Takano K, Gunji T, Ozawa Y, Sano T, et al. Resection of recurrent hepatocellular carcinoma with thrombi in the inferior vena cava, right atrium, and phrenic vein: a report of three cases. World J Surg Oncol. 2020;18(1).
7. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2018;68(2):723-50.
8. Wang Y, Yuan L, Ge RL, Sun Y, Wei G. Survival benefit of surgical treatment for hepatocellular carcinoma with inferior vena cava/right atrium tumor thrombus: results of a retrospective cohort study. Ann Surg Oncol. 2013;20(3):914-22.
9. Tashiro S, Miyake H. Extended left and caudal lobectomy with removal of tumor thrombus extending into the right atrium for hepatocellular carcinoma by total hepatic vascular exclusion using cardiopulmonary bypass. In Operation Atlas of Hepato-Pancreato-Biliary Surgery: Collected Case Studies (pp. 67-75).
10. Uemura M, Sasaki Y, Yamada T, Eguchi H, Ohigashi H, Doki Y, et al. Surgery for hepatocellular carcinoma with tumor thrombus extending into the right atrium:. report of a successful resection without the use of cardiopulmonary bypass. Hepatogastroenterology. 2004;51(59):1259-62.
11. Sengodan P, Grewal H, Gandhi S. Invasive hepatocellular carcinoma with recurrent pulmonary embolism: use of AngioVac cannula thrombectomy device for mechanical aspiration. J Invasive Cardiol. 2014;26(7):E100-3.
12. Wang W, Wei C. Advances in the early diagnosis of hepatocellular carcinoma. Genes Dis. 2020;7(3):308-19.
13. Amin S, Shahab A, Qazi AR, Yunus H, Saeed L, Khan AA, et al. A rare incidence of hepatocellular carcinoma with tumor thrombus extending to the right heart. Cureus. 2023; Aug 23.
14. Pesi B, Giudici F, Moraldi L, Montesi G, Romagnoli S, Pinelli F, et al. Hepatocellular carcinoma on cirrhosis complicated with tumoral thrombi extended to the right atrium:. results in three cases treated with major hepatectomy and thrombectomy under hypothermic cardiocirculatory arrest and literature review. World J Surg Oncol. 2016;14(1).
15. McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of hepatocellular carcinoma. Hepatology. 2021;73(Suppl 1):4-13.
16. Singal AG, Lampertico P, Nahon P. Epidemiology and surveillance for hepatocellular carcinoma: new trends. J Hepatol. 2020;72(2):250-61.
17. Lin HH, Hsieh CB, Chu HC, Chang WK, Chao YC, Hsieh TY. Acute pulmonary embolism as the first manifestation of hepatocellular carcinoma complicated with tumor thrombi in the inferior vena cava: surgery or not? Dig Dis Sci. 2007;52(6):1554-7.
18. Li AJ, Zhou WP, Lin C, Lang XL, Wang ZG, Yang XY, et al. Surgical treatment of hepatocellular carcinoma with inferior vena cava tumor thrombus: a new classification for surgical guidance. Hepatobiliary Pancreat Dis Int. 2013;12(3):263-9.
19. Li Y, Li H, Hu H, Yuan H, Zhao Y. Efficacy and safety of transcatheter arterial chemoembolization combined with either 125I seed implantation or apatinib in hepatocellular carcinoma with portal vein tumor thrombosis:. A retrospective comparative study. J Cancer Res Ther. 2020;16(7):1691-1697.
20. Singal AG, Yarchoan M, Yopp A, Sapisochin G, Pinato DJ, Pillai A. Neoadjuvant and adjuvant systemic therapy in HCC: Current status and the future. Hepatol Commun. 2024;8(6):e0430.

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Case Report

Multidisciplinary Management of Alveolar Echinococcosis With Bilateral Pulmonary Involvement: A Case Report

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Abstract

Alveolar echinococcosis (AE) is a rare, chronic, and invasive parasitic zoonosis caused by the larval stage of the helminth Echinococcus multilocularis, which can often mimic malignancy. While this disease particularly affects the liver, pulmonary involvement is less commonly seen. Bilateral pulmonary involvement has been reported in a very limited number of cases in the literature.

In this study, we present a 45-year-old male patient with liver and bilateral pulmonary involvement. Imaging studies of the patient who presented with abdominal pain revealed an irregularly bordered mass in the right hepatic lobe, a lobulated contoured lesion approximately 2x3 cm in size with calcified areas in the center located subpleurally in the right upper lung lobe, and a lesion approximately 1x2 cm in size in the left lower lung lobe were detected. Under multidisciplinary council management, uniportal VATS wedge resection was applied to the left lower lobe, and the pathology was confirmed as echinococcus alveolaris. Subsequently, wedge resection was performed to the right upper lobe and right hepatectomy was performed for liver involvement.

Following surgical treatment with multidisciplinary approach, the patient was discharged with recovery.

Keywords: Echinococcus Alveolaris, Alveolar Cyst, Pulmonary Cyst, Minimally Invasive Surgery, Zoonotic Disease, Major Hepatectomy

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Alveolar echinococcosis (AE) is a parasitic zoonosis caused by the metacestode (larval) stage of Echinococcus multilocularis, a helminth from the cestode class.[1]

It is more commonly encountered in the Eastern Anatolia region of Türkiye. The global incidence is estimated at 0.03-1.2/100,000 per year, but this rate is higher in endemic areas.

Following infection, parasite larvae primarily settle in the liver through portal circulation and form the main disease focus there. From the liver, it can spread to other organs through hematogenous, lymphatic, or direct invasion routes. Primary pulmonary involvement is quite rare; in most cases, hematogenous spread of infection that initially begins in the liver is involved.[2,3] Pulmonary involvement is seen in approximately 20% of cases, while bilateral pulmonary involvement is quite rare and has been reported in a limited number of cases in the literature.

AE develops as a lesion that progresses chronically, is characterized by a long asymptomatic period (5-15 years), and develops in the form of an invasive malignancy-like, multiple, and exogenously budding lesion, so its detection is

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usually incidental or diagnosis is made when symptoms appear in advanced stages.[4] Due to this characteristic, it is also called "parasitic cancer."

Imaging methods play an important role in diagnosis. Ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) are frequently used modalities. Radiologically, pulmonary AE, which is observed as nodular lesions containing calcifications, irregularly bordered, harboring necrotic areas, and having an infiltrative character, can be confused with primary lung malignancies or metastatic lesions.[5,6] Therefore, pulmonary tuberculosis, lung carcinoma, metastatic lesions, and other infectious pathologies should be considered in differential diagnosis. Serological tests, especially in endemic areas, can be helpful in diagnosis. Enzyme-linked immunosorbent assay (ELISA) and Western blot techniques are the most commonly used serological methods.[2,5]

In this case, we present an alveolar echinococcosis case with both hepatic and bilateral pulmonary involvement that mimics malignancy.

Case Report

A 45-year-old male patient with no known medical history, engaged in farming and living in a rural area, presented to an external center with complaints of right upper quadrant pain that had been continuing for 3 months and had intensified in the last 2 weeks. The patient was diagnosed with E. alveolaris with accompanying hepatic and bilateral pulmonary involvement, and due to biliary obstruction, a stent was placed in the right bile duct via ERCP and he was referred to our center for further treatment.

Upon evaluation at our hospital, physical examination revealed tenderness in the right upper quadrant and hepatomegaly, with no other pathological findings. Respiratory system examination showed no pathological findings. The patient's temperature was 36.8°C, pulse 78/min, blood pressure 130/80 mmHg, respiratory rate 16/min, oxygen saturation 97%, blood type A Rh (+), height 170 cm, and weight 66 kg.

Laboratory tests revealed leukocyte count 9,470/mm^3, eosinophil ratio 1.5%, hemoglobin 12.9 g/dL, platelet count 550,000/mm^3, ALT 48 U/L, AST 54 U/L, GGT 99 U/L, ALP 264 U/L, total bilirubin 0.77 mg/dL, direct bilirubin 0.25 mg/dL, sedimentation rate 42 mm/hour, and C-reactive protein 16.9 mg/dL.

Abdominal ultrasonography revealed a heterogeneous, irregularly bordered, hypoechoic solid lesion in the right hepatic lobe. Abdominal computed tomography showed a mass lesion with heterogeneous structure, irregular borders, and areas of calcification and necrosis filling the right hepatic lobe, and a stent was observed in the right bile duct (Fig. 1a).

The patient's posteroanterior chest radiograph showed irregularly bordered nodules in the right middle lung zone and left lower lung zone (Fig. 1b), and thoracic tomography revealed a lobulated contoured lesion approximately 2x3 cm in size with calcified areas in the center located subpleurally in the right upper lung lobe and an irregularly bordered lesion approximately 1x2 cm in size in the left lower lung lobe (Fig. 1c, d). These findings suggested primary lung malignancy or metastatic lesions.

Serological tests showed positive Anti Echinococcus multilocularis antibodies by ELISA.

In the multidisciplinary tumor council, the patient was evaluated as having E. alveolaris filling the right hepatic lobe with suspected inferior vena cava invasion and also bilateral pulmonary involvement. It was decided that lung lesions would first be resected by thoracic surgery, followed by treatment of the liver lesion by general surgery. For the patient with extensive hepatic involvement, it was decided to perform ICG R15 testing and calculate remaining liver volume to evaluate resectability.

First, wedge resection was applied to the lesion in the left lung via uniportal VATS (Video Assisted Thoracoscopic Surgery), then to the right lung. Intraoperatively, a subpleurally located, hard, white-yellow colored, irregularly bordered

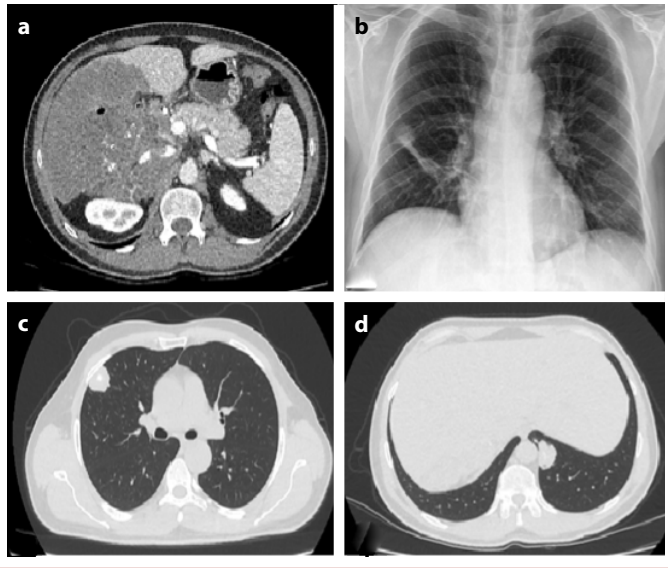

Figure 1. (a) Preoperative tomographic image of Echinococcus alveolaris in the right hepatic lobe. **(b)** Preoperative posteroanterior chest radiograph image of Echinococcus alveolaris. **(c)** Preoperative axial section tomographic image of Echinococcus alveolaris in the right lung. **(d)** Preoperative axial section tomographic image of Echinococcus alveolaris in the left lung.

lesion was observed. Histopathological examination revealed the diagnosis of echinococcus alveolaris with laminar membrane structures and alveolar pattern showing the development of characteristic daughter vesicles. Immunohistochemical staining yielded positive reactions against parasite antigens. Two weeks later, wedge resection was also applied to the lesion in the right upper lung lobe, and the histopathology of this lesion was also compatible with echinococcus alveolaris.

Two months after lung surgery, the patient was re-evaluated by general surgery for liver treatment. Volumetric examination calculated FRL (left lobe) as 630cc, GRWR >0.8%. ICG testing could not be performed due to technical reasons. The patient, who was suitable for major hepatectomy, underwent surgery. Right hepatectomy was completed with placement of a T-tube in the choledochus. Histopathological examination of the liver specimen was also reported as compatible with echinococcus alveolaris.

In the postoperative period, the patient developed bile leak and biloma. The biloma was percutaneously drained and the bile leak was controlled with percutaneous and endoscopic methods. Albendazole treatment was started (at a dose of 10-15 mg/kg/day for 2 years) and the patient was called for regular follow-ups (Fig. 2). Recurrence was not detected in control imaging at 18 months postoperatively.

Discussion

Alveolar echinococcosis is a rare parasitic disease that primarily affects the liver and has a mortality rate of up to 90% if left untreated.[1,3] Delays in diagnosis may occur due to its long asymptomatic course and incidental onset. Primary pulmonary involvement is quite rare. Studies have reported primary pulmonary involvement in less than 2% of AE cases.[2] Bilateral pulmonary involvement, as in our case, is reported even more rarely in the literature.

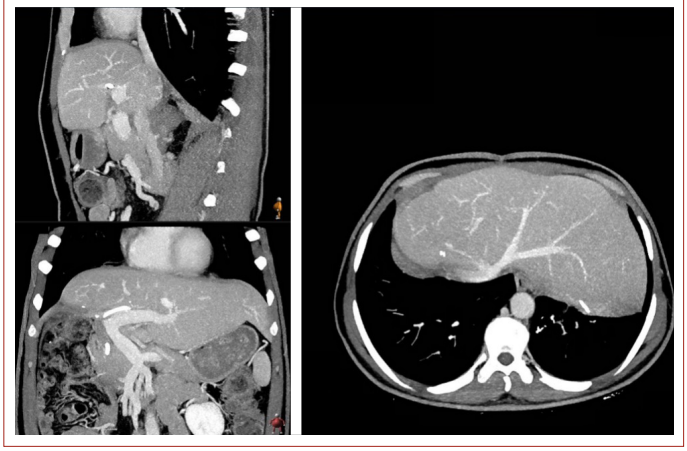

Figure 2. Post-hepatectomy 6 month images.

The main approach in AE treatment is surgical excision and long-term antiparasitic chemotherapy. Radical resection is recommended when surgical excision of lesions is possible, as in our case.[3,5] In the WHO guidelines published in 2010, surgical treatment is recommended as the first choice in cases where R0 resection can be performed in AE treatment. With the development of minimally invasive surgical techniques in recent years, resection can be performed with approaches such as VATS in appropriate cases. This method was preferred and successfully applied in our case.

Antiparasitic chemotherapy can be applied as a complement to surgical treatment or alone in inoperable cases. Benzimidazole derivatives (albendazole and mebendazole) are the most commonly used agents. Albendazole is preferred because it shows better bioavailability than mebendazole.[1,7] Albendazole treatment is generally recommended at a dose of 10-15 mg/kg/day for two years or longer.

Brunetti et al.[1] emphasized the importance of a multidisciplinary approach in AE treatment in the WHO guidelines they published. In our case, successful treatment results were obtained through coordinated work of thoracic surgery, general surgery, radiology, and hepatology departments.

Early diagnosis and appropriate treatment approach are determining factors in the prognosis of alveolar echinococcosis. In a study by Tichý et al.,[7] they reported that the 10-year survival rate in cases undergoing R0 resection was over 90%. Curative surgery can be performed in 35% of cases, and in unresectable cases, the only curative surgery is liver transplantation.[8] In inoperable cases, 5-year survival is around 80% with long-term albendazole treatment. Radical surgical approach was applied in this patient and albendazole treatment was started. No recurrence was detected at the 18-month postoperative control, but long-term follow-up is recommended due to the risk of late recurrence of AE.

Our study has several important clinical and scientific features. First, it is an AE case with bilateral pulmonary involvement, which is rarely seen. Second, having a radiological appearance that mimics malignancy shows that AE should also be considered in differential diagnosis. Third, successful treatment results were obtained with minimally invasive surgical techniques. Finally, it emphasizes the importance of a multidisciplinary approach in both treatment planning and post-treatment management in cases with liver and lung involvement.

Conclusion

In this case of primary hepatic E.A. accompanied by bilateral pulmonary involvement, lung lesions were first treated minimally invasively, and subsequently, the highly complicated case was curatively treated with major hepatectomy. Management of E.A. cases should be multidisciplinary.

Disclosures

Informed Consent: Written informed consent was obtained from the patient while maintaining confidentiality of patient identity.

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References

1. Brunetti E, Kern P, Vuitton DA. Writing Panel for the WHO-IWGE. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. Acta Trop. 2010;114(1):1-16.
2. Bulakçı M, Kartal MG, Yılmaz S, et al. Multimodality imaging in diagnosis and management of alveolar echinococcosis: An update. Diagn Interv Radiol. 2016;22(3):247-256.
3. Özdemir A, Bozdemir ŞE, Akbiyik D, et al. Pulmonary alveolar echinococcosis: a case report. Turkiye Parazitol Derg. 2021;45(2):147-150.
4. Bresson-Hadni S, Delabrousse E, Blagosklonov O, et al. Imaging aspects and non-surgical interventional treatment in human alveolar echinococcosis. Parasitol Int. 2006;55 Suppl: S267-S272.
5. Kayaalp C, Dirican A, Aydin C. Primary hepatic alveolar echinococcosis: a critical review of the literature. World J Gastroenterol. 2022;28(2):226-239.
6. Kern P, Bardonnet K, Renner E, et al. European echinococcosis registry: human alveolar echinococcosis, Europe, 1982-2000. Emerg Infect Dis. 2003;9(3):343-349.
7. Tichý E, Torbašinović I, Kolářová L, et al. Surgical treatment outcomes of alveolar echinococcosis: A 25-year single-centre experience. PLoS Negl Trop Dis. 2022;16(5):e0010408.
8. Ozdemir F, Ince V, Barut B, Onur A, Kayaalp C, Yilmaz S. Living donor liver transplantation for Echinococcus Alveolaris: single-center experience. Liver Transpl. 2015;21(8):1091-5.