Case Report

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A Case Study on the Diagnostic Complexity of Krukenberg Tumor in Pregnancy: Clinical Insights and Management

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ABSTRACT

Krukenberg tumors, metastatic ovarian carcinomas primarily originating from gastrointestinal malignancies, present significant diagnostic and therapeutic challenges during pregnancy. We report a case of a 39-year-old pregnant woman initially diagnosed with autoimmune pancreatitis (AIP) and cholestasis of pregnancy, later found to have metastatic signet ring cell carcinoma of the stomach with ovarian involvement. This case highlights the complexities in differentiating malignancy from benign hepatobiliary disorders during pregnancy, emphasizing the need for a multidisciplinary approach. Early integration of tumor markers, advanced imaging, and HISORt criteria can facilitate timely diagnosis and improve clinical outcomes.

Introduction

Adnexal masses detected during pregnancy are predominantly benign, with most resolving spontaneously [1]. However, ovarian malignancies, though rare (4–8 per 100,000 pregnancies), pose significant diagnostic challenges, especially when metastatic [2]. Among these, Krukenberg tumors metastatic ovarian carcinomas primarily originating from gastric cancer are clinically significant due to their aggressive nature and poor prognosis [3].

Gastric cancer during pregnancy is rare but often diagnosed at an advanced stage due to symptom overlap with common pregnancy-related conditions [4]. This delay frequently leads to widespread metastasis, including ovarian dissemination [5]. The management of Krukenberg tumors during pregnancy requires a multidisciplinary approach to balance maternal and fetal health while addressing the malignancy's aggressive progression. Jaundice, a symptom of intrahepatic cholestasis of pregnancy, may also indicate liver metastasis or biliary tract obstruction due to malignancy [6]. This overlap complicates early diagnosis, emphasizing the importance of a structured diagnostic framework.

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Case Presentation

A 39-year-old woman, gravida 6, para 1, at 19 weeks and 5 days gestation, presented with jaundice and pruritus. Laboratory evaluation revealed elevated liver enzymes (AST: 43 U/L, ALT: 82 U/L) and hyperbilirubinemia (total bilirubin: 5.2 mg/dL, direct bilirubin: 2.8 mg/dL). Initial blood work demonstrated significantly elevated pancreatic enzymes—amylase at 420 U/L and lipase at 610 U/L. Complete blood count revealed hemoglobin of 11.0 g/dL, WBC count of 13.4×10^9/L, and platelets at 213×10^9/L. Inflammatory markers were also raised, including CRP at 26.2 mg/L, ESR at 56 mm/hr, and LDH at 423 U/L.

Abdominal ultrasound showed a dilated common bile duct (CBD) without stones and gallbladder sludge.

The patient's liver enzymes fluctuated over time, and further investigations included:

- **Bile Acids:** 113 µmol/L

- **CA19-9:** 63.6 U/mL

- **Autoimmune Panel:** ANA, anticardiolipin antibody, lupus anticoagulant, and anti-β2-glycoprotein (all negative)

- **IgG4:** Normal

Advanced Imaging Findings:

- **MRCP:** Thickened intra- and extrahepatic bile ducts, no stones, normal pancreatic duct.

- **CT Abdomen and Pelvis:** Dilated CBD (16 mm), splenomegaly (135 mm), thickened posterior gastric wall, omental edema, lymphadenopathy.

- **EUS:** Thickened CBD with sludge, gallbladder thickening, edematous pancreas, peri-portal lymph nodes.

CT of the abdomen was performed with the patient's informed consent due to clinical deterioration and inconclusive MRCP findings. CT pelvis was not performed due to maternal refusal. The choice of CT, despite pregnancy, followed multidisciplinary discussion prioritizing maternal health and immediate diagnostic needs.

Initially diagnosed with AIP and cholestasis, The diagnosis of autoimmune pancreatitis (AIP) was initially considered based on elevated amylase and lipase levels and imaging findings on MRCP and EUS, which showed an edematous pancreas and ductal abnormalities. Although IgG4 levels were normal, the clinical picture and the patient's response to steroids supported this diagnosis. Due to concerns for biopsy-related complications during pregnancy and the patient's reluctance to undergo EUS-guided biopsy, a non-invasive treatment strategy with corticosteroids was initiated based on multidisciplinary consensus.

She was treated with ursodeoxycholic acid, cholestyramine, and prednisone. However, she was readmitted one month later with worsening nausea, vomiting, and hypertension, necessitating an emergency cesarean section at 26 weeks and 3 days.

The indication for pregnancy termination at 26 weeks was severe preeclampsia, unresponsive to antihypertensive therapy, accompanied by elevated liver enzymes and rising LDH levels. The maternal condition was deemed life-threatening, and cesarean delivery was recommended as a lifesaving measure.

Cesarean section was performed via a Pfannenstiel incision. During surgery, bilateral adnexal masses (Figure1) were palpated, raising suspicion for Krukenberg tumors. An intraoperative exploratory maneuver through the same incision led to identification of a firm gastric mass posterior to the stomach, prompting oncologic referral. Histopathology confirmed **signet ring cell carcinoma of the stomach with ovarian metastases (Krukenberg tumor) (Figure2).

Postoperative findings included:

- **CA125:** 471 U/mL

- **CA19-9:** >1200 U/mL

- **AST:** Increased from 64 to 211 U/L

- **ALT:** Increased from 84 to 171 U/L

- **Total Bilirubin:** Increased from 6.2 to 6.6 mg/dL

- **CT Scan:** Bilateral pleural effusion, basal lung consolidation (aspiration pneumonia), gastric mass invading the CBD, mesenteric lymphadenopathy, blastic vertebral lesions (metastases). Post-cesarean follow-up evaluations were conducted within the first two weeks. These included imaging and endoscopic assessments that confirmed the gastric origin of the malignancy. The prompt scheduling of these follow-ups facilitated early oncology referral and planning of palliative care.

An attempted ERCP for biliary drainage was unsuccessful, leading to percutaneous CBD drainage. Given widespread metastasis, the patient was transitioned to palliative care.

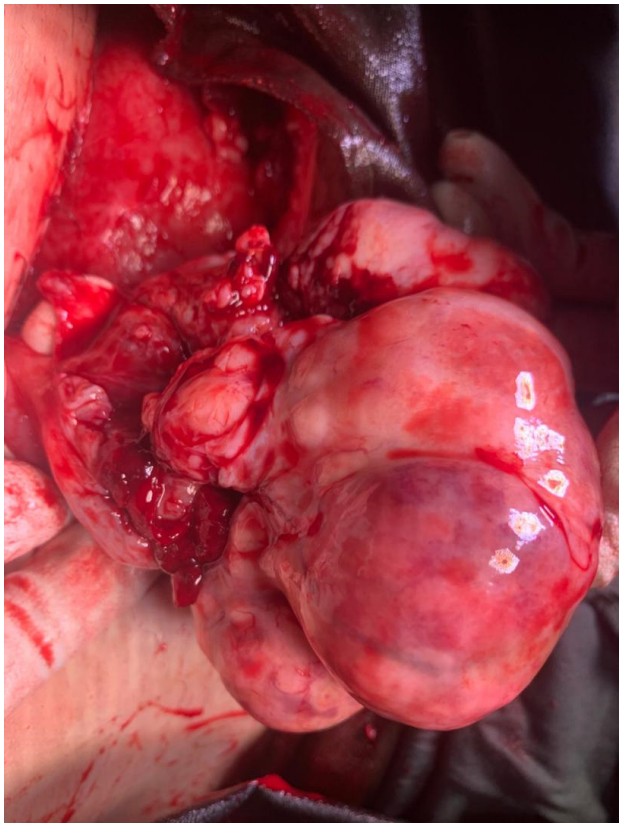

Fig. 1. This image shows a large mass removed following surgery.

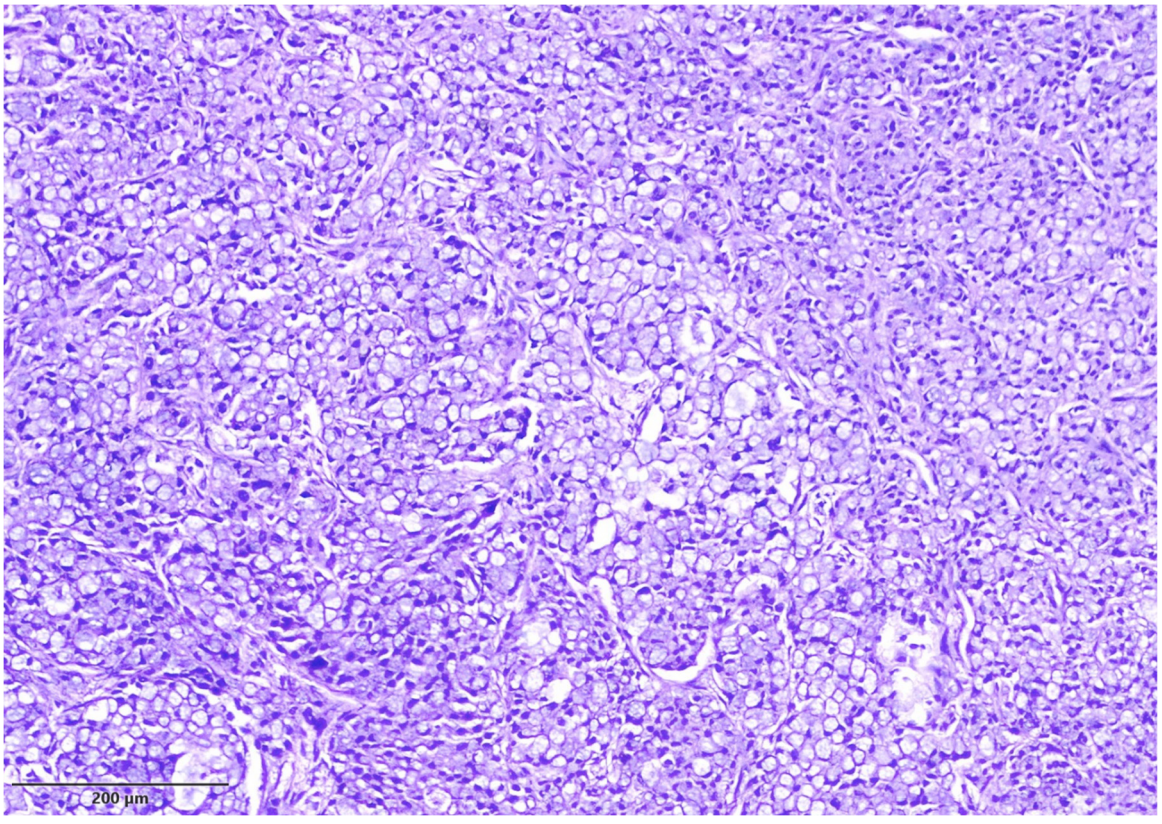

Fig. 2. Histopathological view of the adnexal lesion

Discussion

Krukenberg tumors, as metastatic ovarian carcinomas originating primarily from gastrointestinal malignancies, pose significant diagnostic and therapeutic challenges, particularly during pregnancy [7]. This case exemplifies the complexity of differentiating between pregnancy-related hepatobiliary conditions and malignancy, especially in the presence of overlapping symptoms. Initially diagnosed with autoimmune pancreatitis (AIP) and cholestasis of pregnancy, the patient later presented with a diagnosis of signet ring cell carcinoma of the stomach with metastasis to the ovaries. It is noteworthy that although the patient underwent an initial abdominal ultrasound, no adnexal masses were identified. The absence of pelvic CT due to maternal refusal and the physiological limitations of ultrasound in late second trimester may have contributed to the missed diagnosis. Krukenberg tumors, being rapidly growing metastatic lesions, may develop swiftly and remain undetectable in early imaging. This highlights the inherent challenge of diagnosing adnexal metastases without comprehensive imaging in pregnancy. This case highlights the critical importance of a comprehensive, multidisciplinary approach to ensure timely diagnosis and optimal management of such complex conditions.

Diagnostic Challenges and Lessons Learned:1. Initial Misdiagnosis of Autoimmune Pancreatitis (AIP): The initial diagnosis of AIP was made based on endoscopic findings suggesting pancreatic edema. The HISORt criteria [8], however, were not fully met in this case, and the normal IgG4 levels should have prompted a more thorough investigation for malignancy. Despite the rarity of AIP during pregnancy, the patient's positive response to corticosteroids initially supported this diagnosis. However, the lack of confirmation with tumor markers and the absence of typical red flags for AIP ultimately complicated the diagnostic process.

2. Overlap of Symptoms:Symptoms of cholestasis of pregnancy, such as jaundice and pruritus, often overlap with signs of malignancy, leading to potential diagnostic delays. The imaging findings, including biliary dilation, pancreatic changes, and gallbladder sludge, were not definitive, and the malignancy was not initially suspected. The absence of classic symptoms of malignancy, such as significant weight loss or anemia, further contributed to the delay in diagnosis, making it more difficult to differentiate between pregnancy-related complications and underlying. cancer.

3. Limitations of Diagnostic Tools during Pregnancy: Pregnancy imposes significant limitations on diagnostic modalities [9]. The patient was not a candidate for contrast-enhanced CT scans due to concerns about fetal safety, which hindered a comprehensive evaluation of potential malignancy. Furthermore, ultrasound-guided biopsy, a method that could have provided a more timely diagnosis, was not initially pursued. The need to balance the safety of the fetus while achieving a definitive diagnosis underscores the challenges faced in managing pregnant patients with potential malignancies. Role of Severe Preeclampsia in Uncovering Malignancy.

The development of severe preeclampsia, which necessitated an emergency cesarean section at 26 weeks and 3 days of gestation, was a pivotal moment in the diagnosis of signet ring cell carcinoma. Without this complication, the malignancy may have remained undiagnosed for a longer period, which could have worsened the patient's prognosis. This case underscores the critical importance of considering malignancy in the differential diagnosis when atypical presentations of pregnancy-related conditions arise, particularly when symptoms do not improve with standard treatment.

Given the complexity of diagnosing and managing this case, a multidisciplinary approach involving obstetricians, gastroenterologists, oncologists, and radiologists was essential. Each specialist contributed to the timely identification and management of both the pregnancy-related and oncological concerns. Early integration of tumor markers and advanced imaging techniques could have facilitated a faster diagnosis, as demonstrated by the patient's later progress with markedly elevated CA125 and CA19-9 levels.

Diagnostic Pitfall, Recommended Evidence-Based Strategy

- AIP vs. Malignancy: Rigorously apply HISORt criteria; consider biopsy early.
- Delayed tumor marker assessment: Include CA125, CEA, and MRI earlier in the workup.
- Limited imaging options in pregnancy: Optimize ultrasound-guided biopsy and use MRI with fetal-safe contrast.
- Late oncologic referral: Involve oncology at first suspicion of malignancy.

The revised strategies are based on HISORt criteria, international imaging safety guidelines during pregnancy, and recent literature on tumor marker interpretation in gravid patients. Each item reflects a synthesis of evidence-based best practices for

managing diagnostic uncertainty in complex obstetric-oncologic cases.

Implications for Clinical Practice

- **Early integration of tumor markers (CA19-9, CA125, CEA) in patients with persistent hepatobiliary symptoms can expedite malignancy detection.**

- **MRI with safe contrast alternatives should be prioritized in suspected malignancies during pregnancy.**

- **A multidisciplinary team approach is crucial for balancing maternal-fetal outcomes while managing aggressive malignancies.**

This case further reinforces the idea that pregnancy inherently complicates the diagnostic process due to physiological changes such as elevated liver enzymes and hyperbilirubinemia, which can mask underlying malignancies. These factors, in combination with the limited availability of imaging tools, complicate timely and accurate diagnosis, particularly in cases where malignancy is not initially suspected. The rapid progression of the cancer in this patient, with metastasis to the ovaries and other distant sites, emphasizes the need for early detection and prompt intervention. Although serum levels of CA125 and CA19-9 may physiologically increase during pregnancy, markedly elevated values such as CA19-9 above 1000 U/mL should not be disregarded. Ercan et al. 2011, [10] and Han et al. 2012, [11] have shown that while some tumor markers (especially CA125) may rise during early gestation, CA19-9 generally remains within or close to normal ranges. Therefore, significant elevations beyond expected values should raise concern. According to Zhang et al. 2023, [12] elevated tumor markers in pregnant patients, especially when accompanied by nonspecific gastrointestinal or hepatobiliary symptoms, warrant thorough investigation. Dłuski et al. 2023, [13] also emphasized that such levels in the setting of metastatic gastric cancer retain diagnostic significance during pregnancy. In our case, the patient's CA19-9 level exceeded 1200 U/mL postpartum, but had already reached 63.6 U/mL earlier in gestation. In retrospect, giving more clinical weight to these abnormal tumor markers, in conjunction with imaging, might have facilitated an earlier diagnosis.

Aggressive Nature of Signet Ring Cell Carcinoma

Signet ring cell carcinoma, an aggressive form of gastric cancer, often presents at an advanced stage with rapid metastasis to distant organs, as was the case in this patient. The malignancy spread to the ovaries, lymph nodes, and vertebrae, further complicating management and prognosis. This underscores the importance of early recognition of potential malignancy and the necessity of timely treatment to improve clinical outcomes. Given the aggressive nature of the disease, a prompt diagnosis and early initiation of therapy are crucial in improving the chances of survival for patients with this condition.

Conclusion

Krukenberg tumors in pregnancy present significant diagnostic and management challenges. The overlap of symptoms from pregnancy-related conditions and malignancy, as well as the limitations of diagnostic tools during pregnancy, complicates timely diagnosis. This case highlights the importance of a rigorous differential diagnosis, early involvement of oncology, and the need for a multidisciplinary team to navigate complex cases involving both pregnancy and malignancy. Optimizing diagnostic strategies, including early tumor marker assessment and the use of safe imaging techniques, can significantly improve the chances of timely diagnosis and intervention, ultimately enhancing maternal and fetal outcomes.

Ethical Considerations

Informed Consent

Informed consent was obtained from the patient involved in this case report. The patient and their family consented to the publication of all images, clinical data, and other information included in this manuscript.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the appropriate institutional review board (IRB).

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Conflict of Interests

The authors declare no conflicts of interest related to this study.

Availability of data and materials

The data that support the findings of this study are available but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [Shirin Souri].

References

[1] Hakoun AM, AbouAl-Shaar I, Zaza KJ, Abou-Al-Shaar H, A Salloum MN. Adnexal masses in pregnancy: An updated review. Avicenna J Med. 2017 Oct-Dec;7(4):153-7. https://doi.org/10.4103/ajm.AJM_22_17

[2] Franciszek Dłuski D, Mierzyński R, Poniedziałek-Czajkowska E, Leszczyńska-Gorzelak B. Ovarian Cancer and Pregnancy-A Current Problem in Perinatal Medicine: A Comprehensive Review. Cancers (Basel). 2020 Dec 16;12(12):3795. https://doi.org/10.3390/cancers12123795

[3] Kubeček O, Laco J, Špaček J, Petera J, Kopecký J, Kubečková A, Filip S. The pathogenesis, diagnosis, and management of metastatic tumors to the ovary: a comprehensive review. Clin Exp Metastasis. 2017 Jun;34(5):295-307. https://doi.org/10.1007/s10585-017-9856-8

[4] Cift T, Aydogan B, Akbaş M, Aydın B, Demirkiran F, Bakkaloglu DV, Ilvan S. Case report: gastric carcinoma diagnosed at the second trimester of pregnancy. Case Rep Obstet Gynecol. 2011;2011:532854. https://doi.org/10.1155/2011/532854

[5] Lengyel E. Ovarian cancer development and metastasis. Am J Pathol. 2010 Sep;177(3):1053-64. https://doi.org/10.2353/ajpath.2010.100105

[6] Zhang J, Peng P, Cao D, Yang J, Shen K. Clinicopathological features and maternal and foetal management of pregnancy-complicating Krukenberg tumours. Mol Clin Oncol. 2020 Jun;12(6):581-7. https://doi.org/10.3892/mco.2020.2025

[7] Uyeturk U, Arslan SH, Bal O, Arslan UY, Oksuzoglu OB. Isolated ovarian metastasis of gastric cancer: Krukenberg tumor. Contemp Oncol (Pozn). 2013;17(6):515-9. https://doi.org/10.5114/wo.2013.37542

[8] O'Reilly DA, Malde DJ, Duncan T, Rao M, Filobbos R. Review of the diagnosis, classification and management of autoimmune pancreatitis. World J Gastrointest Pathophysiol. 2014 May 15;5(2):71-81. https://doi.org/10.4291/wjgp.v5.i2.71

[9] Kazemi F, Nahidi F, Kariman N. Disorders Affecting Quality of Life During Pregnancy: A Qualitative Study. J Clin Diagn Res. 2017 Apr;11(4):QC06-QC10. https://doi.org/10.7860/JCDR/2017/23703.9560

[10] Ercan CM, Sakinci M, Dede M, et al. Tumor markers in normal pregnancy. Arch Gynecol Obstet. 2011;284(3):635-8.

[11] Han SN, Lotgerink A, Gziri MM, Van Calsteren K, Hanssens M, Amant F. Physiologic variations of serum tumor markers in gynecological malignancies during pregnancy: a systematic review. BMC Med. 2012 Aug 8;10:86. https://doi.org/10.1186/1741-7015-10-86

[12] Zhang Y, Du H, Li T, Li H, Deng Y, Wu R. Krukenberg Tumor of Gastric Origin in Pregnant Women with Preeclampsia. Case Rep Oncol. 2023;16(1):718-27. https://doi.org/10.1159/000531991

[13] Dłuski D, Szamatowicz J, Szamatowicz M. Krukenberg Progression of Gastric Carcinoma in Pregnancy: Is Early Diagnosis Possible? J Clin Med. 2023;12(16):5397. https://doi.org/10.3390/jcm12165397