

CASE REPORT

Clinical characterization and surgical-pathological findings of immature ovarian teratoma: case report and literature review

Caracterización clínica y hallazgos quirúrgico-patológicos del teratoma inmaduro de ovario: reporte de caso y revisión de la literatura

Julián Yañez-Hartmann¹, Laura Estefanía Giraldo-Guzmán², Claudia Marcela Guarín-Villamizar²,
Jeiry Gabriela Gamarra-Paternina², Breinny Natalia Escalante-Parra², Angélica María Duque-Leal³,
Luz Patricia Cruz-Mojica⁴

¹ Gynecologic Oncology, Hospital Universitario Erasmo Meoz, Cúcuta, Colombia.

² Undergraduate medical student, Universidad de Pamplona, Cúcuta, Colombia.

³ Oncofem IPS, Cúcuta, Colombia.

⁴ Association of Pathologists (ASOPAT), Cúcuta, Colombia.

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Conflicts of interest

The authors declare no conflicts of interest.

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Corresponding author

Laura Estefanía Giraldo Guzmán
Undergraduate medical student, Universidad de Pamplona, Cúcuta, Colombia.

Email:

lg300302@gmail.com

Resumen

Los tumores de células germinales de ovario constituyen un grupo heterogéneo de neoplasias que representan alrededor del 25% de los tumores ováricos, donde solo un 5% son malignos. Dentro de estos, el teratoma inmaduro representa menos del 1% de todos los casos de cáncer de ovario. Su presentación clínica es inespecífica y puede simular otras patologías, por lo que la evaluación clínica e imagenológica inicial orienta el abordaje diagnóstico; sin embargo, la histopatología posterior a la resección quirúrgica determinará su diagnóstico confirmatorio. Se presenta el caso de paciente femenina de 21 años con dolor abdominopélvico, con ecografía que reportó ovario derecho no evaluable ocupado por gran masa, marcadores tumorales elevados y resección quirúrgica, consistente con teratoma quístico inmaduro grado 3, según informe de patología. El reporte de este caso se realiza con el fin de aportar evidencia adicional para realizar una aproximación clínica e imagenológica de este infrecuente tumor ovárico.

Palabras clave: neoplasias de células germinales y embrionarias; teratoma; neoplasias ováricas; biomarcadores de tumor; procedimientos quirúrgicos operativos; patología.

Abstract

Ovarian germ cell tumors are a heterogeneous group of neoplasms that make up about 25% of ovarian tumors, with only 5% being malignant. Within this group, immature teratomas account for less than 1% of all ovarian cancer cases. Their clinical presentation is nonspecific and can mimic other pathologies; therefore, initial clinical and imaging evaluation guides the diagnostic approach. However, histopathology after surgical resection will ultimately determine the final diagnosis. We present the case of a 21-year-old female patient with abdominopelvic pain, with an ultrasound showing an unevaluable right ovary occupied by a large mass, elevated tumor markers, and surgical resection, consistent with a grade 3 immature cystic teratoma, according to the pathology report. This case report aims to provide additional evidence for the clinical and imaging approach to this rare ovarian tumor.

Keywords: neoplasms, germ cell and embryonal; teratoma; ovarian neoplasms; biomarkers, tumor; surgical procedures, operative; pathology.

Introduction

Ovarian tumors include a range of benign and malignant tumors, such as germ cell tumors (GCTs), epithelial stromal tumors, sex cord-stromal tumors, and other miscellaneous tumors. Although GCTs are relatively rare and most are benign in adult women, they are the most common type of ovarian neoplasm, with one-third being malignant. According to the World Health Organization definition, the histological subtypes of ovarian GCTs include teratoma (mature, immature, or monodermal), dysgerminoma, yolk sac tumor, embryonal carcinoma, polyembryoma, non-gestational choriocarcinoma, and mixed GCT (1).

Ovarian GCTs form a heterogeneous group of neoplasms originating from primordial germ cells of the ovary. Although these tumors account for about 20% to 30% of all ovarian neoplasms, only 5% are malignant (immature teratoma, dysgerminoma, and yolk sac tumor), emphasizing the importance of their study in clinical practice (2). Additionally, immature teratomas are the least common, representing less than 1% of all ovarian tumor cases, and typically affect young women (3).

The clinical signs of GCTs are often nonspecific, with symptoms like acute abdominal pain, which may be mistaken for appendicitis; increased abdominal size due to ascites, the tumor itself, or both; early puberty; and other

signs such as vaginal bleeding. Sometimes, they are found incidentally during imaging studies (4).

The diagnostic approach includes a comprehensive medical history, a targeted physical examination of the abdomen and gynecological area, and laboratory tests such as tumor markers. Given their high sensitivity, these tests should be supplemented with imaging methods, such as abdominal and pelvic ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI), to enhance characterization. Diagnosis is confirmed by histological analysis after surgical excision (2, 4). The relevant tumor marker is alpha-fetoprotein (AFP), with elevated serum levels found in 33% to 65% of patients with immature teratoma (1, 5). On ultrasound, immature teratomas appear as large, oval or irregularly shaped ovarian masses, well or poorly defined, averaging 9.7 cm in size, and are heterogeneous, solid or cystic, and unilateral. In addition, the solid components may contain extensive echogenic calcifications, sebum appearing as multiple hyperechoic regions, and might display absent or minimal vascularity on Doppler ultrasound. On CT, observable intratumoral fat is rare or absent, and the sebaceous fluid contains less fat than in mature teratomas, resulting in higher attenuation. Additionally, CT can detect calcifications, fat, and possible hemorrhage within the solid component. Cross-sectional imaging also reveals peritoneal gliomatosis, seen as omental thickening and peritoneal soft-tissue masses.

On MRI, in addition to the characteristic findings of an ovarian mass, peritoneal gliomatosis appears as hyperintense lesions on T2-weighted sequences, which may be focal, multinodular, or show diffuse nodular thickening of the peritoneum. Thus, key features such as marked heterogeneity, predominance of the solid component, minimal or absent visible fat, and the potential presence of peritoneal gliomatosis can raise suspicion of immature teratoma in studies using this technique (6). However, if the immature nerve cell components that represent the immature teratoma are scarce, it is generally difficult to diagnose the tumor as such using imaging modalities such as CT or MRI (7). In this context, the identification of an adnexal mass on imaging, combined with elevated tumor markers, significantly improves preoperative diagnosis (5, 7).

Regarding histological findings, microscopically, immature teratomas contain tissues from all three germ layers—endoderm, mesoderm, and ectoderm—in varying degrees of immaturity. The most common and easily recognizable immature element used for classification and prognosis is neuroepithelium, which is of neuroectodermal origin, composed mainly of small blue neuroblasts, primitive neuroepithelial rosettes, and tubules lined by columnar cells with stratified hyperchromatic nuclei. These cells have a high nucleus-to-cytoplasm ratio, numerous mitotic figures, and apoptotic bodies. The presence of other immature components, such as cartilage, bone, skeletal muscle, and immature glandular structures or other embryonic elements, is not sufficient to diagnose an immature teratoma. Typically, endodermal tissues are less extensive than ectodermal or mesodermal tissues in this type of teratoma. The classification system for immature teratomas classifies them from grade 1 to grade 3 based on the amount of immature neural tissue present (8).

This case report presents a clinical and imaging approach to an infrequent, low-incidence malignant ovarian tumor, for which there are few reports in the literature, with the aim of providing additional evidence to support clinical suspicion and timely treatment.

Clinical case description

A 21-year-old female patient with a gynecological and obstetric history of two pregnancies, no deliveries, two cesarean sections, two live births, and no stillbirths was admitted to the emergency department with a three-day history of nonspecific abdominopelvic pain and increasing distension. She experienced nausea, vomiting, and a sensation of a large abdominal mass, along with signs suggestive of peritoneal irritation. She reported no sexual activity, used a subdermal implant for contraception, and her last period occurred in the same month as the consultation. Based on her reproductive history, it appeared her fertility needs had been met. On examination, a solid abdominal mass was palpable, occupying much of the abdominal area. The abdomen was distended, globular, and painful, with a pain level of 9/10.

A transvaginal ultrasound revealed that the right ovary was not visible or assessable, occupied by a large, heterogeneous mass measuring 20 cm × 18 cm × 15 cm, with color Doppler flow and significant ascites. Tumor markers CA-125 (80.980 IU/ml) and AFP (1,005.65 ng/ml) were elevated, suggestive of a germ cell tumor, leading to the decision to perform a priority surgical procedure.

It was complemented with a contrast-enhanced CT scan to assess the extent of the disease in the abdominal and retroperitoneal cavity. The scan showed an abdominopelvic mass measuring 20.5 cm × 13.8 cm × 23.9 cm, likely originating from the right ovary. The mass was predominantly solid, with heterogeneous enhancement and cystic/necrotic areas, without apparent infiltration. It caused a mass effect on adjacent structures, compressing the inferior vena cava and the iliac venous axis, without obvious thrombosis, leading to bilateral pyelocaliceal dilation due to extrinsic pressure on both ureters. Additionally, the scan revealed multiple retroperitoneal and mesenteric lymph nodes, splenomegaly, and ascitic fluid (Figure 1).

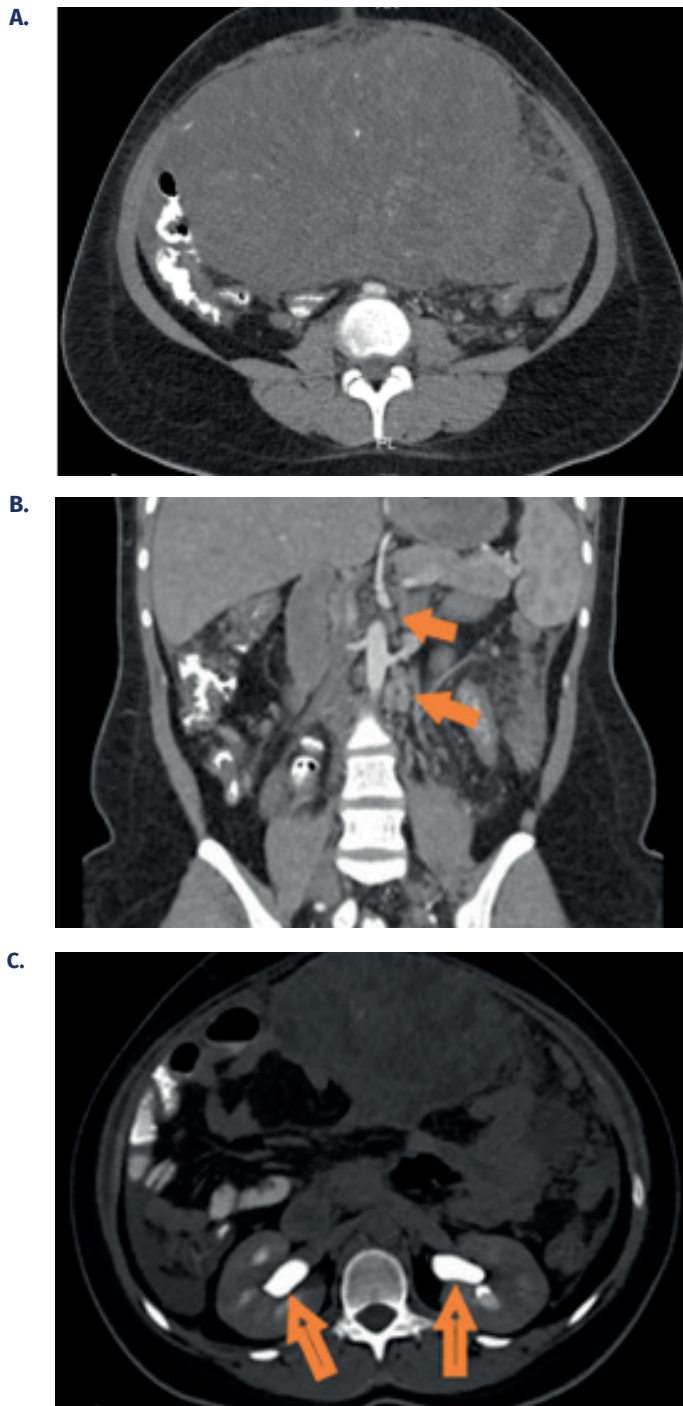


Figure 1. Computed tomography of the abdomen and pelvis. **A.** Large, predominantly solid abdominopelvic mass with heterogeneous enhancement and cystic/necrotic areas, measuring 20.5 cm × 13.8 cm × 23.9 cm, causing mass effect on adjacent structures and showing evidence of free fluid. **B.** Diffuse decrease in density related to steatosis. The inferior vena cava and the iliac venous axis appear compressed by extrinsic pressure, without obvious thrombosis. Both kidneys look normal in shape, size, and density. **C.** Mild bilateral pyelocaliceal ectasia likely caused by extrinsic compression of the mid-ureters. Homogeneous splenomegaly with a maximum longitudinal diameter of 13.9 cm.

During the surgical procedure, a large mass was identified that involved the entire pelvic and abdominal cavity. It originated from the right adnexa and was closely related to and firmly attached to other pelvic structures: the uterus, left adnexa, omentum, and large, suspicious lymphadenopathies. Given that the patient was a young mother of two and there were intraoperative and imaging suspicions of advanced disease, it was necessary to conclude the surgical procedure with a hysterectomy and contralateral salpingo-oophorectomy, along with cytorreduction of the suspicious lymphadenopathies (Figure 2). Additionally, abundant, unquantified ascites were observed during the examination.

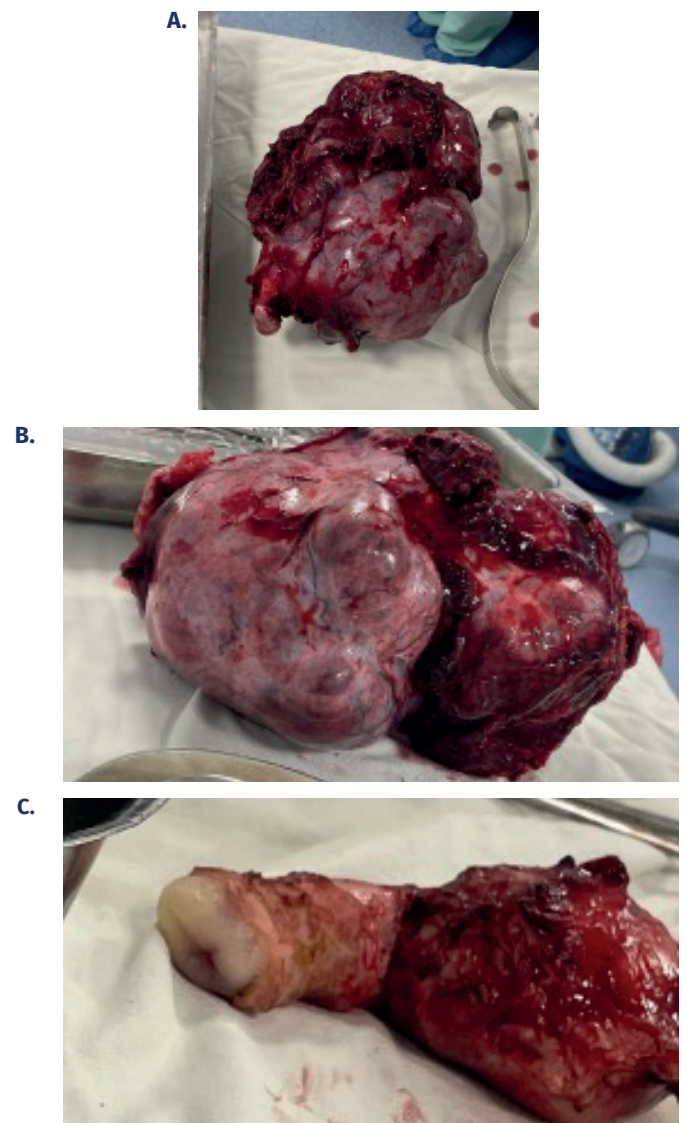


Figure 2. Right abdominopelvic tumor involving the uterus, omentum, left pelvic lymph nodes, and peritoneal adhesions. **A and B.** Abdominopelvic tumor resection. **C.** Hysterectomy with bilateral salpingo-oophorectomy.

The pathological examination included a detailed macroscopic description of the tissue and lesions observed during the procedure. An ovoid fragment of tissue, labeled “right pelvic tumor,” weighing 3,600 grams and measuring 22 cm × 22 cm × 8 cm, was reported. It presented as a multilobulated structure of soft consistency, with an encapsulated fluid observed. Upon sectioning, the tumor mass showed a fleshy appearance with cystic areas containing greenish-yellow and mucinous fluid. Regarding microscopic findings,

the multifocal tumor lesion was composed primarily of immature hyaline cartilage, occasional bony trabeculae, along with areas of mucus-producing respiratory epithelium resting on a myxoid stroma with evidence of necrosis. Endometrial sections showed no evidence of tumor involvement, exhibiting only mild inflammatory changes and proliferative phases. The pelvic lymph nodes were free of malignancy and showed hyperplasia without sinusoidal histiocytosis ([Figure 3](#)).

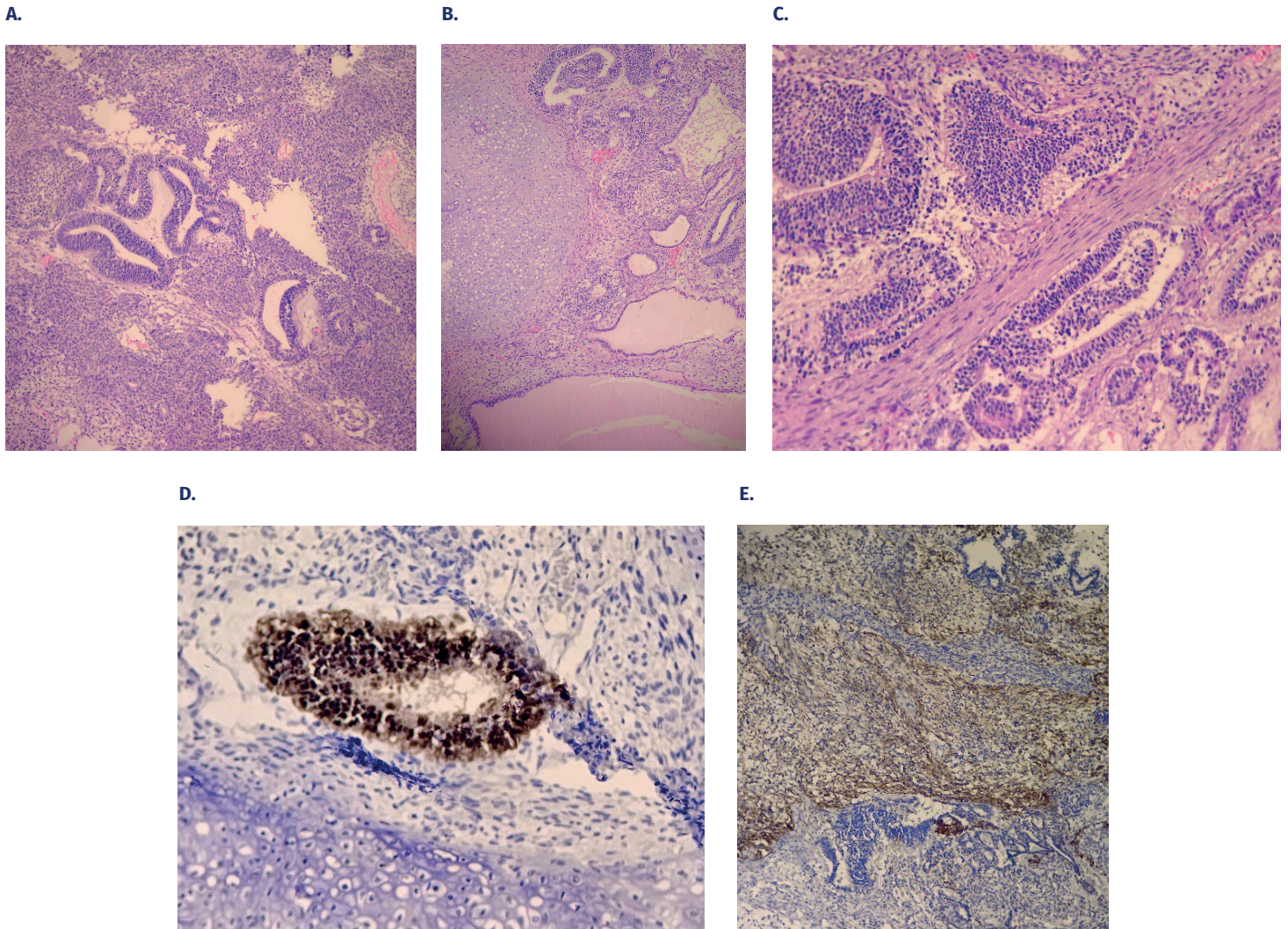


Figure 3. Immunohistochemistry of the abdominopelvic tumor. **A.** Primitive neuronal component with pseudorosette formation and spindle cells. **B.** Immature neuroepithelium forming rosettes and fetal cartilage. **C.** Higher magnification showing areas of primitive immature morphology and rosette formation. **D.** Positive OCT-4 expression in immature neuralgia tissue. **E.** Positive glial fibrillary acidic protein (GFAP) expression in the immature component.

Additionally, the complementary immunohistochemical study revealed an immunophenotypic profile compatible with GCT. The neoplastic cells were positive for SALL4, PGP9.5, neuron-specific enolase, CK AE1/AE3, and CK7, findings supporting a germ cell origin with neuroectodermal and epithelial differentiation. Furthermore, focal positivity was observed for glial fibrillary acidic protein (GFAP), Glypican-3, and OCT-4, markers associated with immature component and neuroectodermal differentiation, while CK20 and AFP were negative.

The pathological diagnosis determined that the tumor lesion in the right ovary was an immature, grade 3 (high-grade), encapsulated cystic teratoma with necrosis in about 10% of the tumor and no evidence of lymphovascular invasion. The uterus and other tissues showed no signs of malignancy, confirming a high-grade immature teratoma stage IA, and with indication for adjuvant chemotherapy, leading to the decision to refer the patient to an oncology center for further management.

Discussion

Ovarian tumors are occasionally diagnosed in patients under 20 years old. The most common type of ovarian tumor in this age group is GCT, of which >40% are malignant. Malignant GCTs account for about two-thirds of ovarian cancers in the first two decades of life; moreover, they form a histologically diverse group of neoplasms with a common origin in the primitive germ cell, which can exhibit features from primordial germ cells (germinomas) to differentiation into embryonic structures (non-germinomas, such as teratoma) (9-10).

There are two types of ovarian teratomas based on their histology: mature and immature. Mature teratomas, also known as dermoid cysts, are benign and account for 95% of all teratomas; they consist of well-differentiated derivatives from at least two of the three germ cells (ectoderm, mesoderm, and endoderm). Conversely, in immature and malignant teratomas, the presence of neuroectodermal tissue determines the degree of malignancy and is the primary unfavorable factor (11-12).

Immature teratomas are rare and may account for 1% to 3% of malignant ovarian tumors. They tend to be aggressive, grow quickly, and have an unfavorable prognosis when

poorly differentiated neuroepithelium is present, which is why clinical suspicion is essential for timely study and treatment of this condition (11).

Because it is a germ cell and poorly differentiated disease, it typically presents with elevated tumor markers characteristic of this histological type, such as AFP, chorionic gonadotropin, carcinoembryonic antigen, and, depending on peritoneal involvement, CA-125. Diagnostic imaging may suggest malignant lesions due to infiltration of other organs or increased vascularization, although these are not pathognomonic of this disease. The clinical presentation is nonspecific, characterized by increased abdominal girth due to the rapid growth of an intraabdominal lesion. This presentation can worsen if rupture, torsion, or superinfection occurs, thereby complicating preoperative diagnosis (10, 12).

Almost a third of immature teratomas express tumor markers, with AFP and CA-125 being the most common (13-14). AFP levels are typically elevated but usually do not exceed 1,000 ng/mL; however, in this case report, the patient had an AFP level of 1,005.65 ng/mL, and CA-125 was elevated to 80.980 IU/mL. These values were initially interpreted as indicating peritoneal involvement; however, this was later excluded by pathology (10, 15).

Unlike mature teratomas, where calcifications, areas of fat, and a classic disease pattern can be visualized, the images are less specific in the case of an immature teratoma. However, given the infiltrative presence of neighboring organs, the increased vascularization documented by Doppler, and the hemorrhagic areas suggestive of necrosis, these signs, along with clinical manifestations and biomarkers, can inform therapeutic decision-making (6, 8, 15).

It is the clinician's priority to suspect this aggressive disease and to obtain a timely diagnosis and definitive tumor staging, which will be done exclusively through pathology (12, 15).

The 2014 International Federation of Gynecology and Obstetrics (FIGO) classification for malignant ovarian tumors, also used for GCTs such as immature teratoma, establishes the following stages: stage I: tumor limited to the ovaries (IA: one ovary, intact capsule, no tumor on surface or positive ascites; IB: both ovaries in the same condition; IC: tumor limited to one or both ovaries with

capsule rupture, tumor on surface, or malignant cells in ascites or peritoneal washings); stage II: pelvic extension (to the uterus or Fallopian tubes); stage III: peritoneal metastases beyond the pelvis or positive retroperitoneal lymph nodes (IIIA1: lymph nodes only; IIIA2-C: extrapelvic microscopic or macroscopic implants); stage IV: distant metastases (IVA: pleural effusion with positive cytology; IVB: parenchymal metastases or metastasis to extra-abdominal lymph nodes) (16).

Regarding the histological classification of immature teratoma, the guidelines of the European organizations: European Society For Medical Oncology, European Society of Gynaecological Oncology, and European Society for Paediatric Oncology (ESMO-ESGO-SIOPE) and of the National Comprehensive Cancer Network (NCCN) adopt the Norris and O'Connor system, which grades the amount of immature neuroectodermal tissue: grade 1: scarce presence that occupies less than one low magnification view (40x) per field; grade 2: between one and three views per low magnification field; grade 3: more than three fields with immature neuroectodermal tissue. This grading is prognostic and determining for adjuvant management (17-18).

Treating immature teratomas involves surgery with curative intent and comprehensive staging, with an emphasis on preserving fertility whenever possible. Collecting adequate samples of resected tissue is crucial for accurate diagnosis and classification of immature teratomas (19).

The ESMO-ESGO-SIOPE and NCCN guidelines recommend that patients with stage IA grade 1 (G1) disease, complete resection, and normal markers do not require chemotherapy and should instead undergo active surveillance, including clinical follow-up, marker monitoring, and imaging. Conversely, patients with stage IA G2 or G3, IB-IC, or more advanced disease should receive adjuvant platinum-based chemotherapy, with the standard regimen being bleomycin, etoposide, and cisplatin (BEP) for three cycles if resection is complete, or three or four cycles if residual disease remains. Bleomycin can be replaced or discontinued in older patients or those with pulmonary risk factors, and alternatives like the etoposide-cisplatin (EP) or carboplatin-paclitaxel regimen can be considered based on comorbidities. The patient of this case report had a diagnosis of a stage IA G3 malignant tumor; therefore, according to gynecologic oncology guidelines, adjuvant chemotherapy was prescribed (17, 20-21).

The immunohistochemical findings most often reported in the literature and referenced in the ESMO-ESGO-SIOPE and NCCN guidelines for immature teratomas correspond primarily to the characterization of their immature neuroectodermal components. These tumors typically test positive for SALL4, a sensitive marker of germ cell origin, though less focally than in other malignant germ cell tumors; they can also express SOX2, which is associated with neuroectodermal differentiation and aids in identifying primitive neuroepithelial-like areas. The glial components of the tumor generally show positivity for GFAP, and the epithelial components express cytokeratins (AE1/AE3). Typically, the common markers of other malignant GCTs (such as OCT3/4, PLAP, and CD30) are negative in pure immature teratomas, which helps differentiate them from embryonal carcinoma or dysgerminoma. Likewise, AFP may only be positive if there are associated foci of yolk sac tumor. In this case report, immunohistochemistry revealed positivity for SALL4, CKAE1AE3, and OCT-4, and negative results for AFP. These immunohistochemical profiles confirmed the diagnosis, indicated tissue maturity, and excluded other mixed germ cell tumors (17, 20-21).

Five-year survival rates are nearly 100% for early-stage disease and at least 75% for advanced-stage disease (5, 21).

Conclusions

This report underscores the importance of promptly diagnosing and treating immature ovarian teratomas, which are rare malignant tumors mainly affecting young women. Combining clinical history, imaging studies, and tumor markers helped form a suspected diagnosis, guided appropriate surgical intervention, and ensured complete tumor resection, allowing histopathology to confirm the diagnosis. Although this condition is uncommon, it is essential to raise awareness among patients and healthcare professionals about its risks and the importance of early detection. This report contributes to the understanding of this tumor type and serves as a useful reference for specialists and student trainees, thereby promoting early detection and improved treatment outcomes.

Ethical considerations and data confidentiality

The patient's consent was obtained to acquire and present the images for academic purposes. No personal data that could identify them is disclosed in this document.

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