Case report

Immature Teratoma with Components of a Yolk-Sac Tumour – a Rare Combination of a Mixed Malignant Ovarian Germ Cell Tumour

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Abstract

Immature teratoma (IMT) is an ovarian germ cell tumour with high malignant potential. It is occasionally combined with other ovarian germ cell malignancies, but rarely just with yolk-sac tumour, which exhibits even more aggressive behaviour. We present a case of a young patient who presented with giant, atypical, steady growing tumour comprised of IMT with YST islets. Throughout adolescence the tumour grew to gigantic measures of 33 × 23 × 19 cm and weighed 7162 grams, without any symptoms, and secreting no significant quantities of alpha-fetoprotein (AFP), which is the major biomarker for YST. In spite of a huge abdominal tumour, giving her body contour characteristics of a late third trimester pregnancy, the disease was fortunately in FIGO Ia stage, enabling the patient to choose the conservative treatment of fertility sparing surgery alone. The recovery was complete, with defined frequent follow-up sessions, and her 5-year outcome is excellent. Given that almost all of mixed malignant ovarian germ cell tumours (MOGCTs) are highly chemo-sensitive, potential neo-adjuvant chemotherapy remains an alternative treatment if the signs of recurrence appear. Today's golden standard in chemotherapy for MOGCTs presents a BEP (bleomycine, etoposide, and cisplatin) regimen. After thorough search of recent literature we present a review of novel insights in aetiology, diagnostics and treatment options for this rare group of cancers.

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Introduction

Teratomas constitute the most common subtype of ovarian germ cell tumors, representing approximately 10–20% of ovarian malignancies in females under 20 years of age (1) and roughly 15% of all ovarian neoplasms across age groups (2). Historically misconceived as remnants of aborted embryos, these lesions were termed "teratomas," derived from the Greek teras ("monster") (1). They arise from totipotent ovarian germ cells capable of differentiating into tissues derived from ectoderm, mesoderm, and endoderm. Based on the degree of cellular maturation, teratomas are classified as mature or immature (IMTs). Multiple histological variants exist, comprising mature or immature germ layer–derived tissues (3).

Mature cystic teratomas are the most prevalent subtype and are typically composed of well-differentiated elements including ectodermal derivatives (e.g., epidermis, neural tissue), mesodermal components (e.g., adipose or muscle tissue), and endodermal epithelia (e.g., mucinous or ciliated epithelium) (4). In contrast, immature teratomas are characterized by variably developed, embryonic-type tissues from all three germ layers (3). IMTs usually manifest as solid or mixed solid–cystic masses containing serous or mucinous fluid, occasionally admixed with sebaceous or fatty material (4).

Mixed malignant ovarian germ cell tumors (MOGCTs), identified in approximately 8% of MOGCT cases, contain two or more malignant germ cell components (5). The most frequent combination includes dysgerminoma with a yolk sac tumor (6). Teratomas predominantly affect pediatric, adolescent, and young adult populations. While mature teratomas are benign—with the mature cystic variant ("dermoid cyst") being the most common benign ovarian germ cell tumor—immature teratomas account for <1% of ovarian neoplasms but possess significant malignant potential (7). The presence of a yolk sac tumor (YST) component further increases biological aggressiveness and warrants intensified therapeutic management.

IMTs primarily occur in the first two decades of life, with peak incidence between 15 and 19 years; postmenopausal presentation is exceedingly uncommon (4). Patient age demonstrates an inverse correlation with tumor malignancy, as younger individuals exhibit a higher likelihood of aggressive behavior. Mature teratomas are generally small (typically <10 cm) and bilateral in 15–25% of cases. Although benign, they may recur and rarely undergo malignant transformation (2). Conversely, immature teratomas are predominantly unilateral, occurring on one side in approximately 80% of patients (1). Their clinical course is notably aggressive, contributing to nearly 30% of ovarian cancer–related mortality among individuals aged 10–20 years.

Clinical manifestations are nonspecific and commonly include abdominal or pelvic pain, distension, and detection of a palpable adnexal mass. Despite extensive research, imaging modalities have limited accuracy in reliably distinguishing mature from immature teratomas. Ultrasonography, MRI, and radiography generally reveal that IMTs are substantially larger than their mature counterparts, with reported sizes ranging from 14 to 25 cm, compared with <7.5 cm in mature cystic teratomas. Additionally, IMTs frequently contain a dominant solid intratumoral component (3).

Case report

A 24-year-old nulligravid woman (G0P0) presented for routine contraceptive counseling. Her prior gynecologic evaluations during adolescence had been unremarkable, with no symptoms requiring investigation or treatment. She reported regular menstrual cycles without dysmenorrhea or additional complaints; menarche occurred at age 12. Since adolescence, she had perceived a persistent firmness in the lower abdomen but denied pelvic pain, urinary disturbances, or gastrointestinal symptoms. Gradual abdominal enlargement during her teenage years was attributed to familial obesity and presumed accumulation of subcutaneous adipose tissue.

During the current pelvic examination, a large abdominal mass was palpated, prompting referral for pelvic ultrasonography. Imaging revealed a heterogeneous lesion occupying the pelvis and extending into the upper abdomen. Multislice computed tomography (MSCT) demonstrated a well-circumscribed, mixed-density mass arising from the left ovary, with no radiologic indicators of lymphadenopathy. Externally, the abdominal contour resembled that of a 32–36-week gestation (Figure 1), and MSCT estimated the tumor volume at approximately 7.5 liters.

Figure 1. Patient´s profile photography, demonstrating enlarged abdominal contour due to an ovarian mass

With informed consent and in accordance with CARE guidelines, an extended midline laparotomy and left adnexectomy were performed (Figure 2). The resected mass contained cystic and solid components with fatty and soft tissue material; coarse calcifications were predominantly located in the cranial capsule. The uterus and contralateral ovary appeared normal and were preserved. The specimen measured 33 × 23 × 19 cm and weighed 7162 g (Figure 3). There was no intraoperative evidence of invasive growth, metastatic deposits, or suspicious lymphadenopathy. Peritoneal lavage samples were obtained for cytologic assessment.

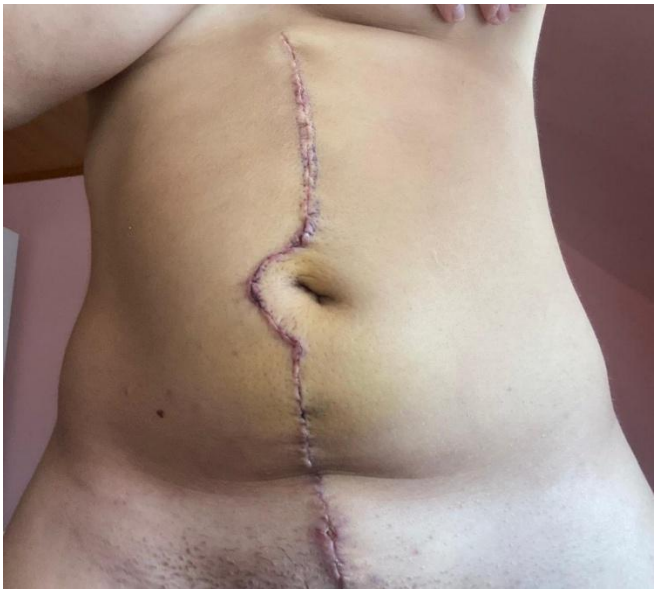

Figure 2. Patients anterior abdominal aspect in late healing phase after medial laparotomy incision

Histopathological analysis established a diagnosis of high-grade immature teratoma, classified according to the 2020 WHO 5th edition criteria, with focal yolk sac tumor (YST) differentiation. Peritoneal cytology showed no atypical cells, and immunohistochemical staining for membrane-bound markers was negative.

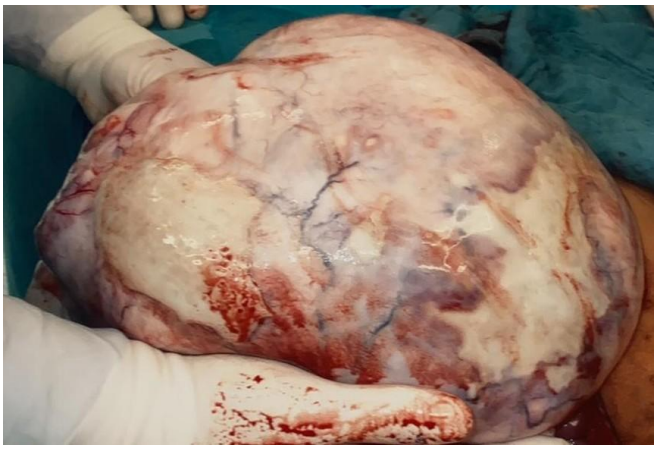

Figure 3. Operative specimen- ovarian tumour estimated to 7162 g, that was removed without opening of its capsule

Additional immunohistochemistry revealed strong nuclear SALL-4 expression in regions suggestive of YST, while Glypican-3 displayed weak, granular positivity in isolated cell clusters.

These findings supported a final diagnosis of mixed malignant ovarian germ cell tumor, composed predominantly of immature teratoma with minor multifocal YST components.

Given the patient's age and the presumed early stage of disease, a fertility-sparing management strategy was prioritized. A second-stage laparoscopic procedure was recommended, including infragastric omentectomy, targeted peritoneal biopsies, and ipsilateral pelvic lymphadenectomy. Histopathological evaluation of all subsequently excised tissues revealed no residual malignancy. Final staging was pT1a N0 (0/1) L0 V0 Pn0 R0 according to TNM criteria, consistent with FIGO stage IA.

Following surgical treatment and diagnostic workup, quarterly gynecologic evaluations and semiannual abdominal MSCT monitoring were advised. In consideration of the patient's fertility wishes and the absence of residual disease, adjuvant chemotherapy was deferred. The postoperative course was uneventful, and the patient has remained disease-free for five years while adhering to the prescribed surveillance protocol.

Discussion

Immature teratomas (IMT) represent the third most common subtype of malignant ovarian germ cell tumors (MOGCT), following dysgerminoma and yolk sac tumor (YST) (8). Multiregional whole-exome sequencing conducted by Heskett et al. demonstrated that diverse meiotic errors may generate genetically distinct IMTs characterized by extensive allelic imbalance, a low somatic mutational burden, and multiple copy-number variations. Importantly, IMTs, mature teratomas, and YST components within the same mixed neoplasm share identical genome-wide loss-of-heterozygosity patterns, indicating a shared clonal origin. These findings suggest that copy-neutral loss of heterozygosity resulting from meiotic disruption is sufficient for the development of ovarian IMTs from germ cells (9).

Although ovarian and testicular teratomas derive from primordial germ cells, their biological behavior diverges: ovarian and prepubertal testicular teratomas originate from benign germline clones, whereas postpubertal testicular teratomas emerge from malignant precursors and represent differentiation within an existing non-teratomatous neoplasm (10). MOGCTs may appear as pure or mixed tumors, with immature neuroepithelium being the most frequent immature component. IMTs are graded from 1 to 3 based on cytological atypia, mitotic activity, and the quantity of immature elements (10). The presence of immature tissues correlates with aggressive clinical behavior, and IMTs account for approximately 30% of ovarian cancer–related deaths in patients aged 10–20 years (1).

Mixed ovarian germ cell tumors most commonly include dysgerminoma (80%), YST (70%), IMT (53%), choriocarcinoma (20%), and embryonal carcinoma (16%) (3). The most typical combination is dysgerminoma with YST (6). The coexistence of predominant IMT with only focal YST, as in our case, is extremely rare. No published reports describing mixed tumors composed exclusively of IMT and YST without embryonal carcinoma were identified. Rare mixed tumors comprising IMT, YST, and embryonal carcinoma—historically termed polyembryoma due to their resemblance to early embryonic structures—have been documented (11). YST, formerly known as endodermal sinus tumor, is considered the most aggressive ovarian germ cell malignancy (12). Histologically, YST typically displays solid, tubular, papillary, and sinusoidal patterns with characteristic Schiller–Duval bodies and frequent mitoses (12).

Prognosis is strongly influenced by tumor composition: neoplasms >10 cm with >33% YST, those containing choriocarcinoma, or grade 3 IMT exhibit poorer outcomes. Bilateral MOGCTs tend to present at more advanced stages with unfavorable histology and worse survival (6). Ethnic variation is notable, with incidence approximately five times higher among Asian, Pacific Islander, and Hispanic populations

compared to Caucasians and African Americans (13).

Pain and a rapidly enlarging abdominal mass are the most frequent presenting symptoms, often facilitating diagnosis. However, patients lacking pain or exhibiting slow tumor growth, such as in our case, pose diagnostic challenges (8). IMTs do not reliably secrete tumor markers. AFP is elevated in >90% of YSTs (14), though our patient exhibited normal AFP levels despite histological YST foci. Clinicians should maintain suspicion for malignancy in cases of pelvic masses with pain, prompting early tumor marker assessment and urgent referral to gynecologic oncology (12). Nonspecific symptoms frequently lead to delayed diagnosis, and many patients present with advanced disease manifesting abdominal distension, pain, irregular bleeding, fever, or leukocytosis, mimicking inflammatory or gastrointestinal conditions (8).

In adolescents, >60% of ovarian neoplasms arise from germ cells, and one-third are malignant with potential for local invasion and vascular or lymphatic metastasis (6). Unilateral presentation and early FIGO stage in >90% of patients allow for fertility-sparing treatment. Five-year disease-free survival for mixed germ cell tumors is approximately 86% (13). For IMT, stage I survival approaches 90–95%, while advanced-stage survival drops to ~50% for grade 1–2 and to ≤25% for grade 3 tumors (3). Owing to rapid tumor doubling time and potential dissemination to the peritoneum, lungs, liver, and brain, expedited evaluation is crucial (8).

Diagnostic imaging modalities—ultrasonography, CT, MRI, and radiography—each have limitations. Sonographically, IMTs appear as solid hyperechoic masses with fibrotic foci and small cysts, with low to moderate vascularization (11). CT and MRI typically reveal large solid components with coarse calcifications and fat deposits (5). However, radiological differentiation from other malignant ovarian tumors remains difficult (14). Any suspicion of MOGCT warrants immediate surgical exploration due to the tumor's aggressive nature (15). In cases of disseminated disease, PET/CT using 18F-FDG has shown utility in detecting primary and metastatic lesions when conventional imaging is inconclusive (7); similar considerations apply to gallium-67 scintigraphy.

Therapeutic decision-making in MOGCTs is multifactorial (17). Chemotherapy responsiveness is generally high, and platinum-based regimens—particularly BEP (bleomycin, etoposide, cisplatin)—remain standard therapy with excellent curative potential (18). Cytoreduction improves chemotherapy effectiveness; thus, initial surgery often includes adnexectomy or tumor debulking. For young patients, fertility preservation must be carefully balanced against oncologic safety. Stage I, grade 1 IMTs may be managed with surgery alone, though recurrence has been reported in up to 50% of cases, with most successfully salvaged using chemotherapy (1). Fertility-sparing surgery followed by surveillance is considered safe in selected early-stage cases (19), though chemotherapy may impair ovarian function through cortical fibrosis, follicular depletion, and maturation arrest. Radiotherapy offers no additional benefit (1). Chemotherapy is recommended for grade ≥2 or stage >Ia tumors (3).

The preferred surgical approach aims to preserve fertility when oncologically safe (20). Standard procedures include unilateral oophorectomy, peritoneal washings, omental biopsy, and excision of enlarged lymph nodes; systematic lymphadenectomy is not recommended. Laparoscopic removal is acceptable for tumors that can be extracted intact. For women who completed childbearing, hysterectomy with bilateral salpingo-oophorectomy may be appropriate. Patients with stage Ic/IIa or higher disease often require neoadjuvant chemotherapy to reduce tumor burden and facilitate fertility-sparing surgery (21). Combined fertility-sparing surgery and BEP chemotherapy yields 5-year survival rates up to 94% (22). Standard BEP duration is three cycles for completely resected disease and four cycles for residual disease. Use of growth factors helps maintain chemotherapy dose intensity (13).

Oncofertility strategies are increasingly incorporated into MOGCT management (1). Despite gonadotoxicity risks, many patients regain normal reproductive function after treatment (12). In bilateral disease, conservative approaches such as partial oophorectomy plus chemotherapy may maintain fertility potential (23). Assisted reproductive technologies, including frozen oocytes and donor eggs, have enabled successful pregnancies after bilateral MOGCT treatment (1). Pre-treatment measures such as GnRH analogues may help reduce ovarian injury (23,25).

Follow-up must be intensive, particularly within the first year, when ~75% of recurrences occur. Surveillance includes tumor markers at each visit and chest radiographs every 2 months for 2 years, then every 3–6 months for an additional 3 years. Abdominal and pelvic CT scans are recommended at 3 months post-chemotherapy and subsequently as indicated (18). Long-term monitoring should also address cardiopulmonary and gastrointestinal complications (6), as well as psychosocial and psychosexual sequelae (14).

For patients with refractory or platinum-resistant MOGCT, salvage surgery may be considered, though novel therapies are urgently needed (11). Recent studies have explored molecular alterations—including mutations in KRAS, ARID1A, and KIT—and microsatellite instability as potential markers of chemoresistance (26,27). Targeted therapies, particularly EGFR-directed agents, may hold future promise given occasional EGFR expression in GCTs (7). Glypican-3, expressed in fetal tissues and in YST, represents another emerging immunotherapeutic target (28).

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Nezreli teratom s komponentama tumora žumanjčane vreće – rijetka kombinacija malignog tumora zametnih stanica

Sažetak

Nezreli teratom (IMT) je tumor zametnih stanica jajnika sa izrazitim malignim potencijalom. Obično dolazi u kombinaciji sa drugim tumorima zametnih stanica. U kombinaciji sa tumorom žumanjčane vreće (YST) nađe se izuzetno rijetko, kada pokazuje odlike izuzetno agresivnog tumora. Prikazujemo slučaj mlade pacijentice sa sporo rastućim golemim tumorom jajnika koji se histološki sastojao predominantno od IMT sa otočićima YST. Kroz adolescenciju, zahvaljujući sporom rastu, tumor je narastao do gigantske mjere od 33 × 23 × 19 cm i mase od 7162 grama, bez ikakve siptomatologije, kao i bez sekrecije značajnijih količina alfa-fetoproteina (AFP), glavnog biomarkera za YST. Uprkos golemom abdominalnoj masi, koja je njezinoj figure davala privid trudnoće u kasnom trećem trimestru, tumor je, na sreću, bio u FIGO Ia stadiju, što je omogućilo liječenje konzervativnijim pristupom – isključivo kirurškom terapijom kojom se čuva plodnost. Petogodišnji ishod liječenja pacijentice pokazuje odlične rezultate.

Ključne riječi: nezreli teratom, maligni tumor zametnih stanica, MOGCT, tumor žumanjčane vreće, endodermalni sinusni tumor