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Yolk Sac Tumor of the Ovary with Polyvesicular-Vitelline Pattern: Case Report of an Uncommon Tumor and a Brief Review of the Literature

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Abstract

Ovarian yolk sac tumors (YSTs) are rare malignant germ cell tumors (GCTs) that can present with nonspecific abdominal symptoms and pose a diagnostic challenge, particularly when classic histologic features are absent. We report a case of a 23-year-old female with no clinically significant medical history who presented with worsening abdominal distension and a palpable mass for four weeks. Associated symptoms included 11-pound unintentional weight loss, early satiety, and pelvic pain. Treatment with analgesics resulted in no improvement. Rapid enlargement and worsening of her abdominal distention warranted an urgent gynecological referral. Transvaginal ultrasonography revealed a large, complex adnexal mass measuring 18 x 15 x 14 centimeters. Computed tomography (CT) demonstrated a solid mass without calcifications, mild omental thickening, and mild ascites. Laboratory studies showed markedly elevated Alpha-fetoprotein (AFP) levels and mildly elevated beta-hCG and Lactate dehydrogenase (LDH). Considering the imaging and labs, a malignant germ cell tumor was suspected. The patient underwent a right unilateral salpingo-oophorectomy. Pathological examination revealed a unique polyvesicular-vitelline appearance, including multiple vesicles and cysts with no evidence of Schiller-Duval bodies. Immunohistochemistry (IHC) was positive for AFP and glypican-3, with cytoplasmic staining, confirming the diagnosis of yolk sac tumor. The patient completed adjuvant chemotherapy and underwent serial AFP monitoring. Three months after initial treatment, AFP was undetectable, and CT was unremarkable. The patient remained in complete remission three years after initial treatment. This case details a rare germ cell tumor with an uncommon histologic pattern, lacking the disease's classic hallmark. This case emphasizes the importance of keeping a broad differential diagnosis in patients with progressive abdominal complaints.

Keywords: Yolk sac tumor; Germ cell tumor; Polyvesicular-vitelline morphology; Immunohistochemistry; Chemotherapy.

1. Introduction

Ovarian YSTs are unusual but highly clinically significant neoplasms that belong to the malignant germ cell category. They have a predilection for young females in their second and third decades of life and exhibit primitive extra-embryonal differentiation. [1] They are very rare among ovarian malignancies. However, to achieve optimal treatment outcomes, their histological heterogeneity and aggressive course necessitate their recognition and differentiation from other types of ovarian neoplasms. [1] YSTs can present with multiple morphologic patterns, including

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reticular/microcystic, solid, and hepatoid growth; polyvesicular-vitelline is an uncommon variant that may complicate histopathological diagnosis and is characterized by characteristic cysticity. [2] [3]

The presence of numerous small vesicle-like spaces within a myxoid stroma, reminiscent of other cystic or glandular structures, is characteristic of the polyvesicular-vitelline pattern. It is a rare variant that depicts primitive yolk sac differentiation but must be recognized to avoid diagnostic pitfalls with benign cystic lesions or other malignant ovarian tumors. [2] [4] When this pattern is predominant, the morphologic findings should be correlated with IHC profiles to confirm the diagnosis of a YST. [3]

IHC markers such as AFP, glypican-3 (GPC3), and SALL4 are crucial to confirm the diagnosis of YSTs, especially in rare histologic subtypes. The germ cell marker SALL4 has been positive in yolk sac tumors and negative in epithelial tumors. Although not completely specific, glypican-3 is more sensitive than AFP for several patterns of YST, including polyvesicular-vitelline areas, underscoring the need for a combined IHC panel. [4] [5] This practice of including these markers in the diagnostic process enhances histopathologic diagnosis specificity and ensures optimal case management.

In this respect, a detailed study of ovarian yolk sac tumors with polyvesicular-vitelline morphology facilitates understanding of the pathologic features and diagnostic pitfalls of this rare variant. Enhancing recognition and reporting of such cases supports improved pathology precision and patient management.

2. Case presentation

2.1. Clinical presentation

A 23-year-old female presented to her primary care physician with complaints of progressive lower abdominal distension and a palpable mass for four weeks. The patient reported other symptoms during the last six weeks in the form of intermittent dull pelvic pain, early satiety, and unintentional weight loss of approximately 11 pounds.

Her menstrual period was regular during that time, but she noted progressive dysmenorrhea. The patient's management included symptomatic treatment with analgesics, assuming the diagnosis of a benign ovarian cyst. Her primary physician decided to refer her to an urgent gynecological evaluation due to rapid abdominal enlargement accompanied by a sensation of abdominal fullness and new episodes of nausea. A Transvaginal ultrasonography was performed and showed a large, complex adnexal mass, and it was decided to transfer the patient to a gynecologic oncology center for comprehensive evaluation and management.

2.2. History and physical examination

The patient's personal history revealed menarche at age 12 with regular menstrual cycles. She was nulligravid with no history of infertility, pelvic inflammatory disease, endometriosis, or previous ovarian pathology. She denied tobacco, recreational drug use, and drank alcohol socially. Her medical and surgical histories were unremarkable. The family history was significant of breast cancer in her mother at the age of 52 and a paternal grandmother who had colon cancer, but no family history of ovarian cancer, endometrial cancer, or other gynecologic malignancies. The patient denied any known genetic cancer syndromes in the family.

Physical examination indicated a young female who was in slight distress due to abdominal heaviness and pain. Vital signs were normal. Abdominal palpation revealed apparent distension with a firm, smooth, movable mass that continues all the way to the pelvis and about 4 centimeters above the umbilicus. The mass was non-tender to palpation, devoid of any peritoneal findings, and there was no hepatomegaly or splenomegaly. A dullness changes implied minimal ascites. Pelvic exam revealed a large, irregular right adnexal mass with a smooth surface, localized in the pelvis and lower abdomen. The mass showed only limited mobility. The left adnexa was unremarkable. No cervical lesions and no vaginal discharge abnormalities were observed. Inguinal lymph nodes were not palpable bilaterally. Cardiopulmonary examination was insignificant—no axillary or supraclavicular lymphadenopathy. The rest of the physical examination was normal.

2.3. Radiographic studies

Transvaginal ultrasonography showed a large, solid cystic, right ovarian mass measuring 18 x 15 x 14 centimeters with scattered multiple cystic structures, internal septations, and papillary projections. Color Doppler showed increased vascularity with low-resistance blood flow patterns. A low amount of free pelvic fluid was detected. The left ovary had a normal appearance and normal size.

A contrast-enhanced computerized tomography (CT) of the abdomen and pelvis demonstrated a large, heterogeneous, solid cystic right adnexal mass. The solid regions were moderately enhancing, and the cystic spaces showed varying attenuation, indicating different fluid contents. No calcifications were identified. There were also minimal ascites and mild omental thickening. Retroperitoneal and pelvic lymph nodes were also identified, with the largest being less than 1 centimeter. There was no evidence of peritoneal carcinomatosis or metastasis to any organ.

MTI imaging demonstrated a mass with T1 hypointense-to-isointense solid components and heterogeneous T2 signal intensity. There were several small cystic areas with different T1 and T2 signal characteristics. The solid components were found to have restrictive diffusion. No fat or calcification was found, making mature teratoma unlikely.

Imaging studies suggested that a malignant GCT was the most likely diagnosis, including dysgerminoma, immature teratoma, and YST, with the possibility of a mixed germ cell tumor. An alternate diagnosis was epithelial ovarian malignancy, especially serous or mucinous carcinoma. The imaging features and the demographics of the patient were less likely to have sex cord-stromal tumors.

2.4. Tumor board meeting to discuss the management

The tumor board, headed by the multidisciplinary team, reviewed the clinical, laboratory, and radiographic results. Alpha-fetoprotein (AFP) serum level was markedly elevated to 8,450 ng/mL, strongly indicating a component of yolk sac tumor. Beta-hCG and LDH were slightly elevated, whereas CA-125 was normal. The tumor characteristics and imaging features were suggestive of a malignant germ cell tumor. The board debated whether tissue diagnosis could be performed by core needle biopsy or by direct surgical excision. Considering the patient's young age, the high suspicion for a chemotherapy-sensitive germ cell malignancy, and possible complications with percutaneous biopsy, the consensus favored primary surgical excision without preoperative biopsy. It was decided to carry out fertility-preserving surgery, unilateral right salpingo-oophorectomy, with total surgical staging, peritoneal washings, omentectomy, lymph node sampling, and examination of every peritoneal surface. A frozen section would be used during surgery to guide the operation.

2.5. Tissue diagnosis

The histopathologic specimen was a right ovary that was 20 x 16 x 15 centimeters with a weight of 1,850 grams. Its exterior was plain, undamaged, and bosselated. Sectioning showed that the tumor was mostly solid with a soft and friable cut surface that was interspersed with numerous small cystic spaces of between 0.2 and 1.5 centimeters. The cystic spaces had clear to mucinous fluid. About 30 percent of the tumor volume had necrosis and hemorrhage. The fallopian tube was grossly unremarkable.

Microscopic examination revealed the unique polyvesicular-vitelline appearance of yolk sac tumor, with multiple vesicles and cysts lined with flattened to cuboidal epithelium. The vesicles were of different sizes with loose mesenchymal stroma. The pattern resembled extraembryonic structures of the secondary yolk sac. Large eosinophilic intraluminal material was found in many vesicles. Scattered areas displayed focal areas of reticular and solid growth patterns. Scattered areas with prominent nuclear atypia, increased mitotic activity, and focal necrosis were identified. Schiller-Duval bodies were not identified. (Figure 1 A, B, C, D)

The typical morphology of the yolk sac and AFP positivity ruled out a diagnosis of clear cell carcinoma. Dysgerminoma is not structurally complex and displays a unique immunoprofile. Juvenile granulosa cell tumor exhibits variable growth patterns and lacks AFP expression. Immunohistochemistry (IHC) was essential for establishing the diagnosis. The tumor cells were strongly and diffusely positive for AFP, Cytokeratin (AE1/AE3), and glypican-3 with cytoplasmic staining. They were also strongly positive with nuclear staining for SALL4. OCT3/4 was negative, which ruled out embryonal carcinoma. In addition, EMA, inhibin, and calretinin were negative. (Figure 2 A, B, C, D)

Next-generation sequencing identified wild-type TP53. Chromosome 12p abnormalities consistent with isochromosome 12p were detected by FISH analysis, supporting the germ cell origin. The tumor was diagnosed as a Yolk Sac Tumor of the Ovary with predominantly Polyvesicular-Vitelline Pattern.

2.6. Treatment, outcome, follow-up, and status at three years

Because of intraoperative rupture of the capsule, the tumor was staged as IC2 yolk sac tumor. The patient was referred to medical oncology to initiate adjuvant chemotherapy with four cycles of Bleomycin, etoposide, and cisplatin (BEP) as per the standard protocols. Serum AFP levels were monitored during treatment and returned to normal following the second cycle. The patient also responded well to chemotherapy, with anticipated side effects such as myelosuppression,

nausea, alopecia, and minor peripheral neuropathy medically managed. Pulmonary function tests did not change during the period of taking Bleomycin.

The surveillance after chemotherapy consisted of clinical check-ups, serum tumor markers (AFP, beta-hCG, LDH), and imaging tests performed at defined intervals. Three months later, AFP was undetectable, and CT was negative. The patient's menstrual cycles returned 6 months after chemotherapy. At one-year post-diagnosis, she remained disease-free with normal tumor markers and unremarkable surveillance imaging. Two years later, the left ovary had been spared, and a normal level of anti-Mullerian hormone and normal menstrual cycles confirmed its preserved function.

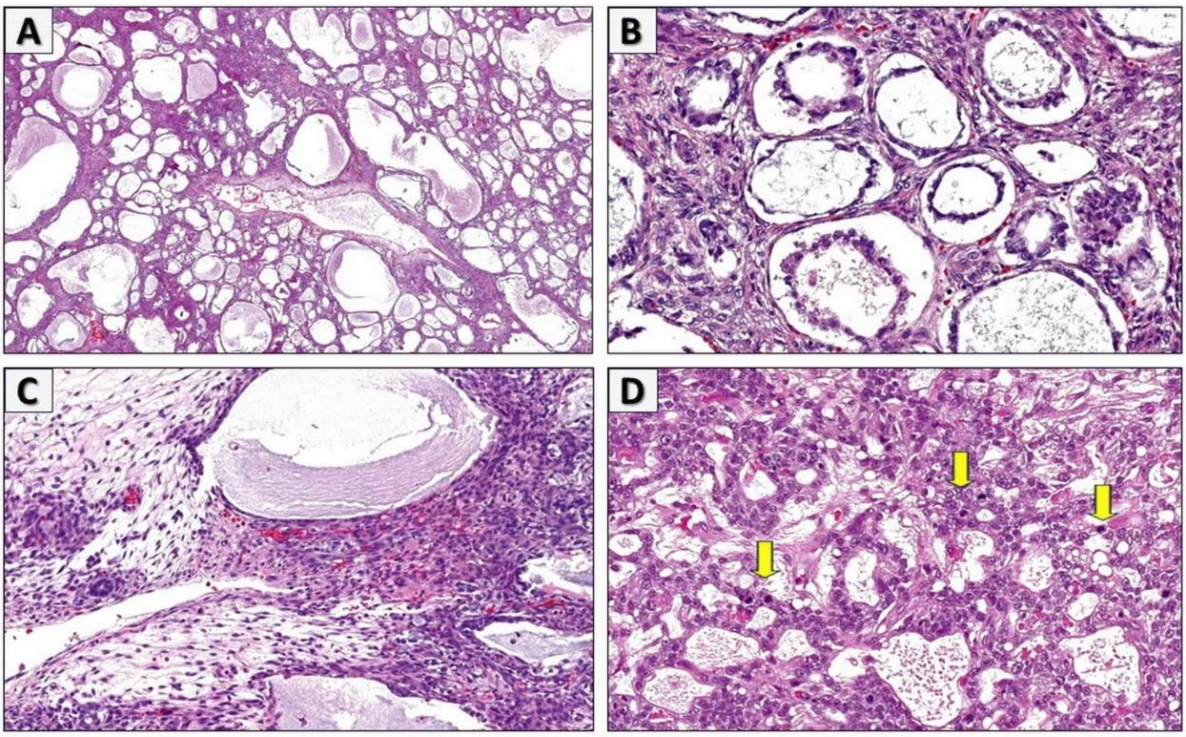

Figure 1 Histomorphology of the Yolk Sac Tumor with Polyvesicular-Vitelline Pattern

1A Low power view showing the unique polyvesicular-vitelline appearance of yolk sac tumor, with multiple vesicles and cysts lined with flattened to cuboidal epithelium (H&E stain X20).; 1B High power view showing atypical cells lining the cysts and vesicles (H&E stain X60); 1C Intermediate power view showing myxoid stroma (H&E stain X40); 1D High power view showing areas displaying foci of reticular and solid growth patterns with prominent nuclear atypia and increased mitotic activity (yellow arrows) (H&E stain X60)

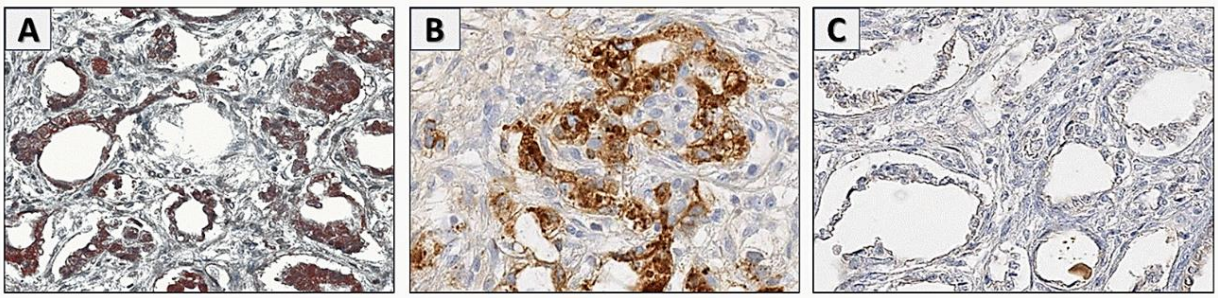

Figure 2 Immunohistochemistry studies on yolk sac tumor

2A Tumor cells positive for AFP; 2B Tumor cells positive for Glypican 3 ; 2C Tumor cells are negative for EMA

Three years later, the patient remained in complete remission, with stable AFP levels and negative surveillance imaging. She had completed her graduate studies and was undergoing counseling on how she could save her fertility before she could conceive a baby. Her prognosis remained excellent given the chemotherapy-sensitive nature of yolk sac tumors and her sustained remission.

3. Discussion

3.1. Background (History, epidemiology, risk factors, and WHO classification):

Roth and Panganiban initially reported the polyvesicular-vitelline pattern of ovarian YST in 1976 as a rare histologic variation different from the more prevalent endodermal sinus pattern of the tumor, rather than as a distinct diagnostic entity. [6] Subsequent clinicopathologic studies have upheld this interpretation. Mostly affecting children, adolescents, and young adults, ovarian yolk sac tumors are rare malignant germ cell neoplasms. With a mean age of 21.5 years, about 75% of patients in the largest current series of ovarian YSTs presented in their second and third decades of life, and less than 1% of cases occur after age 50. [6] Although it was noticeable in only about half of these cases, the polyvesicular-vitelline pattern was found in approximately 25% of tumors in this cohort; its actual incidence remains unknown. [2] [6]

Clinically, ovarian YSTs usually manifest as large, quickly growing unilateral adnexal masses; 95–96% of cases are reported to have unilateral involvement. [2] [7] The polyvesicular-vitelline pattern is distinguished histologically by numerous cystic spaces of varying sizes, creating a honeycomb-like appearance that may partially or completely efface the stroma. [2] Although YSTs are malignant, there are few reports of long-term disease-free survival, and scant evidence indicates that tumors with a predominant polyvesicular-vitelline pattern may have a more indolent clinical course. [2] [8]

From a biological perspective, germ cell tumors are believed to result from early developmental events and show signs of genetic susceptibility as opposed to inherited cancer syndromes. [9] While TP53 mutations are comparatively rare, molecular studies of yolk sac tumors have revealed recurrent somatic alterations involving KRAS, KIT, and genes within the PI3K/AKT pathway, as well as distinctive copy-number changes. [10] Although epidemiologic studies have suggested associations with prenatal and environmental factors, including parental occupational exposures, no specific causative agents have been consistently identified, and most cases appear sporadic; however, subtype-specific risk factors for ovarian YSTs remain unknown. [11]

3.2. Pathogenesis, Pathophysiology

Yolk sac tumors (YSTs) of the ovary are malignant germ cell neoplasms originating in the ovary. They originate from primordial germ cells of the embryonic gonad that do not develop properly [12] They usually affect women in their 20s and 30s and have a good prognosis. because they respond well to chemotherapy. [12] The most typical symptoms of the disease are abdominal pain and distension.

YST is thought to be caused by mutations in primitive germ cells, which can be hereditary or somatic. Primitive germ cells move from the yolk sac to the vaginal ridge through the hindgut and mesentery, where they become gonads. [13] KIT and KRAS are the two genes that are most frequently identified as mutated. In YST, genes in the WNT/Beta-catenin and TGF-beta/BMP pathways are overexpressed. [10]

3.3. Comparative analysis of our case with the existing literature

Our case involved a large, heterogeneous tumor. CT imaging revealed a complex mass, which MRI further characterized as having both solid and cystic components, a presentation typical of YSTs. [14] While initial assessment strongly suggested a malignant GCT, definitive diagnosis awaited histopathological examination.

Microscopic evaluation showed a polyvesicular-vitelline pattern; however, no Schiller-Duval bodies were identified. This absence is not uncommon, as a literature review of over 150 ovarian YSTs notes that these classic structures are present in only about one-third of cases. [22] This underscores the polymorphic nature of YSTs, which can exhibit a wide spectrum of histological appearances. In our case, the tumor was predominantly solid and focally soft with a friable surface, interspersed with cystic spaces.

IHC studies were consistent with the literature, showing positivity for AFP, glypican-3, SALL4, and Cytokeratin (AE1/AE3). Negativity for OCT3/4 ruled out embryonal carcinoma, while negative stains for EMA, inhibin, and calretinin helped exclude other malignancies. [3] The combination of typical microscopic features and markedly elevated AFP levels confirmed the diagnosis of a YST, ruling out clear cell carcinoma.

Molecular analysis revealed a wild-type TP53 via next-generation sequencing, while FISH identified chromosome 12p anomalies. Although the specific constellation of markers in our case has not been widely reported, it further illustrates the biological variability of YSTs. [17] A retrospective study of 10 YST cases found targetable oncogenic mutations

(*in* KRAS*,* KIT*, and* ARID1A) in only a subset of tumors, with most demonstrating microsatellite stability and a low tumor mutational burden. [17] While no pathognomonic mutation has been established, molecular profiling may guide future therapy for patients who do not respond to first-line treatment.

YSTs carry the worst prognosis among malignant ovarian GCTs, necessitating aggressive treatment regardless of stage. The standard first-line regimen is BEP chemotherapy (Bleomycin, Etoposide, and Cisplatin), which was offered to our patient. Given the high risk of swift recurrence, rigorous follow-up is imperative. [18] This involves close monitoring of serum AFP levels and surveillance imaging. Fertility-sparing surgery is often considered, as it was in this case. [18] The patient underwent a unilateral right salpingo-oophorectomy with comprehensive surgical staging, including peritoneal washings, omentectomy, and lymph node sampling. The procedure was uncomplicated, and the excised tissue provided ample material for definitive diagnosis.

The prognosis and prognostic factors of BEP-treated YST were analyzed in two studies, including 84 and 32 cases, respectively. The five-year survival rates of BEP-treated YST patients were 75-100% at Stage I and 63-75% at Stages II-IV. [19] [20] Another study included 20 YST patients treated with high-dose BEP; after a median follow-up of 70 months, the overall survival rate was 90%. [21]

Surgical strategy is an area of evolving discussion. A 2024 retrospective analysis of 40 patients found no difference in survival between primary debulking surgery and neoadjuvant chemotherapy (NACT) followed by interval surgery. Notably, NACT was associated with higher rates of optimal tumor resection, fewer surgical complications, and lower morbidity. The pronounced chemosensitivity of YSTs can be leveraged preoperatively, and response to NACT may itself be a prognostic factor in advanced disease. [22]

For our patient, given her young age, the suspected chemosensitive nature of the tumor, and the potential risks of biopsy, primary surgical excision was selected. This approach was supported by imaging demonstrating a single mass with minimal omental involvement, scant ascitic fluid, and no significant lymphadenopathy. The patient went on to receive four cycles of adjuvant BEP chemotherapy. She has remained in complete remission for three years, with consistent normalization of AFP and surveillance imaging, and continues to have an excellent prognosis.

This was a standard case of ovarian yolk sac tumor managed with fertility-sparing primary surgery followed by adjuvant BEP chemotherapy, the established protocol. However, literature suggests that for advanced or metastatic disease, neoadjuvant chemotherapy followed by interval debulking should be strongly considered, as it may improve resectability and reduce surgical morbidity. [22] While our patient has a good prognosis, the rapidly progressive potential of YST mandates lifelong, scheduled surveillance with AFP levels and imaging.

4. What have we learned from this case?

This case highlights the critical importance of integrating clinical, radiographic, and pathological data to diagnose rare histological variants of GCTs. We learned that while the polyvesicular-vitelline pattern of YST is uncommon, its clinical and biochemical profile, specifically the marked elevation of AFP, remains a reliable diagnostic marker.

This case emphasizes the importance of maintaining a high index of suspicion for malignant germ cell tumors (GCTs), especially in young women who present with rapidly progressive adnexal masses. It provides evidence that when alpha-fetoprotein (AFP) levels are very high, yolk sac tumor (YST) should be considered strongly in the differential diagnosis. This supports the view that, even without a biopsy, early surgical intervention and full oncologic treatment are necessary. From a diagnostic perspective, the polyvesicular-vitelline (PVV) pattern poses a significant challenge because its cystic architecture can mimic benign ovarian cysts and malignant entities, including clear cell carcinoma. Specifically, IHC for SALL4 and Glypican-3 is crucial.

The patient's sustained remission at three years and recovered ovarian function validate current methods of therapy and highlight the importance of multidisciplinary tumor boards in the management of uncommon histological variations. Finally, the case underscores the necessity of long-term surveillance, as sustained remission beyond two years is a strong indicator of a favorable prognosis in these chemotherapy-sensitive malignancies.

Abbreviations: Ovarian yolk sac tumors (YSTs); Germ cell tumors (GCTs); Immunohistochemistry (IHC); Neoadjuvant chemotherapy (NACT)

5. Conclusion

We report this case of a yolk sac tumor with a predominantly polyvesicular-vitelline pattern to expand the clinical and pathological understanding of this rare entity. By documenting the successful management and 3-year disease-free survival of a Stage IC2 tumor, this report provides valuable evidence to the medical community regarding the PVV variant's chemosensitivity and excellent prognosis. It emphasizes that standard germ cell tumor protocols remain highly effective for this subtype. Furthermore, this case serves as a reminder to clinicians and pathologists to maintain a high index of suspicion for YST in young patients with complex adnexal masses and elevated AFP, ensuring that even rare morphological patterns are recognized and treated promptly to optimize oncological and reproductive outcomes.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors make the following declarations:

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Statement of ethical approval

Ethical review and approval were not required for this study involving human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

Statement of informed consent

Consent for the publication of this case was obtained from the patient.

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