



RESEARCH ARTICLE

Clinicopathological Evaluation Of Yolk Sac Tumor Of Testis: A Case Report

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ABSTRACT

Background: Yolk sac tumor (endodermal sinus tumor) is a malignant germ cell neoplasm and represents the most common malignant testicular germ cell tumor in infants and young children. It is characteristically associated with elevated serum alpha-fetoprotein (AFP) levels and demonstrates distinctive histopathological features that aid in diagnosis.

Case Presentation: A 2-year-old male child presented with a painless right scrotal swelling of three months' duration. Ultrasonography revealed a 5.2 × 4.6 × 4.1 cm heterogeneous solid intratesticular mass with prominent internal vascularity. Serum alpha-fetoprotein was markedly elevated at 18,650 ng/mL, while serum beta-human chorionic gonadotropin was <2 mIU/mL and lactate dehydrogenase was 286 U/L. The patient underwent right radical inguinal orchiectomy. Gross examination revealed a 5.0 cm yellowish, soft to mucoid tumor with focal hemorrhage and necrosis. Microscopic examination demonstrated a predominantly reticular/microcystic pattern with characteristic Schiller-Duval bodies. PAS staining demonstrated PAS-positive hyaline globules. Immunohistochemistry showed strong AFP, SALL4, and glypican-3 positivity, with negative OCT3/4 and CD30 expression. The findings confirmed the diagnosis of pure prepubertal-type yolk sac tumor.

Conclusion: Yolk sac tumor is an aggressive yet highly treatable malignancy in pediatric patients. Early diagnosis through correlation of clinical findings, age-adjusted serum AFP, imaging, histopathological examination, and immunohistochemistry is essential for appropriate management and favorable outcome. Recognition of Schiller-Duval bodies, reticular/microcystic architecture, and PAS-positive hyaline globules provides important diagnostic clues.

Keywords: Yolk sac tumor; endodermal sinus tumor; testis; pediatric testicular tumor; alpha-fetoprotein; Schiller-Duval body; PAS; SALL4; glypican-3

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INTRODUCTION

Testicular tumors are uncommon in children, accounting for approximately 1–2% of all solid childhood tumors, but they constitute an important group of pediatric genitourinary neoplasms. Their histological spectrum and biological behavior differ substantially from those of adult testicular tumors.[1] Pediatric testicular tumors can broadly be classified into germ cell and nongerml cell tumors. Germ cell tumors include seminomatous and non-seminomatous neoplasms, with teratoma, embryonal carcinoma, choriocarcinoma, and yolk sac tumor (YST) representing important entities in the pediatric population. [1-3] Although benign lesions are relatively frequent in prepubertal children, malignant testicular tumors typically present as painless, progressively enlarging solid masses and require prompt evaluation.[2,3]

Yolk sac tumor, also known as endodermal sinus tumor, is a malignant germ cell neoplasm characterized by differentiation toward extraembryonic yolk sac structures. It represents the predominant malignant testicular germ cell tumor in infants and young children and has a characteristic peak incidence during early childhood,

particularly around two years of age.[4,5] In the current World Health Organization classification, prepubertal-type YST is included among germ cell tumors unrelated to germ cell neoplasia in situ, reflecting its distinct biological characteristics from postpubertal germ cell tumors.[6] Pediatric YST predominantly affects infants and young children, with published clinicopathological series demonstrating a marked predominance in this age group.[4,5]

The usual clinical presentation is a painless unilateral testicular or scrotal swelling, which may be overlooked because of the absence of pain.[5,7] Ultrasonography is the primary imaging modality for evaluating pediatric testicular masses and generally demonstrates a predominantly solid intratesticular lesion, often with heterogeneous echogenicity and increased vascularity on color Doppler examination. [5,9] Serum alpha-fetoprotein (AFP) is particularly valuable in pediatric YST because tumor cells characteristically produce AFP. Markedly elevated AFP supports the diagnosis and serial postoperative measurements are useful for assessing treatment response and detecting persistent or recurrent disease.[7,8] Interpretation, however,

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requires age-adjusted reference values because AFP is physiologically elevated during infancy.[7]

Histopathological examination remains the definitive diagnostic modality. YST demonstrates considerable morphological diversity, including reticular/microcystic, solid, glandular, papillary, macrocystic, myxomatous, and hepatoid patterns.[4,10] Schiller-Duval bodies, although sometimes focal, are highly characteristic of YST, while PAS-positive hyaline globules provide additional morphological support.[4,10] Immunohistochemical expression of AFP, glypican-3, and SALL4 can further confirm yolk sac differentiation, particularly in morphologically challenging cases.[11-13]

We present a case of testicular yolk sac tumor in a two-year-old boy, emphasizing the clinical presentation, serum AFP elevation, radiological findings, gross morphology, characteristic histopathological features, PAS staining, and immunohistochemical confirmation.

CASE PRESENTATION

A 2-year-old male child was brought by his parents with a history of painless swelling of the right side of the scrotum for approximately three months. According to the parents, the swelling had gradually increased in size. There was no history of acute scrotal pain, fever, trauma, vomiting, urinary complaints, weight loss, anorexia, or night sweats. There was no significant past medical history. The child had no history of previous scrotal surgery or testicular trauma. There was no documented history of cryptorchidism. His developmental milestones were appropriate for age.

On physical examination, the child was conscious, alert, and clinically stable. His weight was 12.1 kg and height was 87 cm. The pulse rate was 104/min, respiratory rate was 24/min, and temperature was 36.7°C.

Local examination revealed enlargement of the right hemiscrotum. The right testis was enlarged, firm, and non-tender, measuring approximately 6 × 5 cm clinically. The overlying scrotal skin was normal without erythema, ulceration, or venous prominence. The left testis was normally positioned and clinically unremarkable. No palpable inguinal or supraclavicular lymphadenopathy was present.

The clinical findings raised suspicion of a testicular neoplasm, and serum tumor markers and scrotal ultrasonography were performed.

Investigations

Serum Tumor Markers

- The initial laboratory evaluation showed

The serum AFP level of 18,650 ng/mL was markedly elevated for a child of two years of age. In the clinical setting of a solid intratesticular mass, this finding strongly suggested a yolk sac tumor. The serum β-hCG was not elevated, making β-hCG-producing germ cell tumors less likely.

Ultrasonography

High-resolution ultrasonography of the scrotum revealed a markedly enlarged right testis measuring approximately 6.1 × 4.8 × 4.6 cm.

Table 1: Initial Laboratory Evaluation and Serum Tumor Marker Profile

Investigation	Result	Reference/Interpretation
Alpha-fetoprotein	18,650 ng/mL	Markedly elevated for age
β-hCG	<2 mIU/mL	Not elevated
LDH	286 U/L	Within laboratory reference range
Hemoglobin	11.4 g/dL	Within expected range
Total leukocyte count	8,900/μL	Normal
Platelet count	3.24 × 10 ⁵ /μL	Normal
Serum creatinine	0.4 mg/dL	Normal
Liver function tests	Within normal limits	Normal

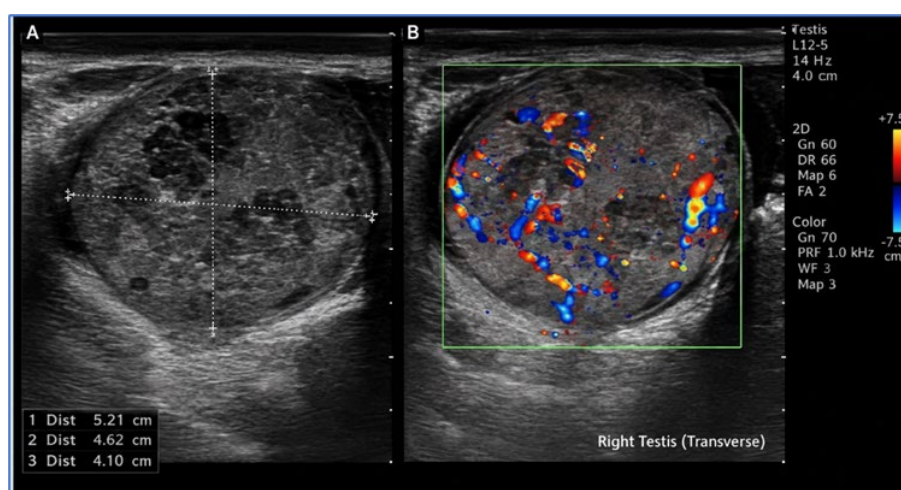


Figure 1: Ultrasonographic image demonstrating a heterogeneous predominantly solid intratesticular mass with prominent internal vascularity.

Within the right testis, there was a $5.2 \times 4.6 \times 4.1$ cm heterogeneous predominantly solid mass. The lesion demonstrated mixed echogenicity with relatively hypoechoic and mildly hyperechoic areas. Multiple small internal cystic spaces were noted.

Color Doppler examination demonstrated prominent internal and peripheral vascularity.

Small areas of internal hemorrhage and necrosis were suspected.

The epididymis was not separately visualized from the mass but showed no definite focal abnormality. A minimal right hydrocele was present. The left testis was normal in size and echotexture, with preserved vascularity and no focal lesion.

Ultrasonographic impression

Large heterogeneous solid vascular intratesticular mass of the right testis, suspicious for a malignant testicular germ cell tumor. In view of the patient's age and markedly elevated AFP, yolk sac tumor was favored.

Staging Evaluation

Contrast-enhanced computed tomography of the abdomen and pelvis demonstrated an enlarged right testis containing a heterogeneous enhancing mass corresponding to the sonographic abnormality.

There was no radiological evidence of retroperitoneal lymphadenopathy. The para-aortic and paracaval lymph nodes were not enlarged.

The liver, spleen, pancreas, kidneys, and adrenal glands were unremarkable.

Contrast-enhanced CT of the chest showed no pulmonary nodules or evidence of thoracic metastatic disease.

There was no radiological evidence of distant metastatic disease.

Based on the clinical and radiological assessment, the lesion was considered localized disease.

Surgical Management

Considering the patient's age, painless progressive testicular swelling, solid intratesticular mass, and markedly elevated serum AFP, a malignant germ cell tumor, particularly yolk sac tumor, was strongly suspected.

The patient underwent right radical inguinal orchiectomy.

The postoperative period was uneventful. The child tolerated oral feeds and was discharged on the fourth postoperative day.

The orchiectomy specimen was submitted for detailed gross and histopathological examination.

Gross Pathological Examination

The specimen consisted of a right orchiectomy specimen measuring $7.2 \times 5.6 \times 4.9$ cm, with an attached spermatic cord measuring 4.8 cm in length.

The external surface of the testis was smooth and intact. The tunica vaginalis was unremarkable.

On serial sectioning, a $5.0 \times 4.5 \times 4.0$ cm predominantly yellowish-gray, soft to mucoid tumor was identified.

The cut surface was predominantly yellowish and gelatinous with a mucoid appearance. Multiple irregular areas of hemorrhage and necrosis were present, involving



Figure 2: Gross photograph of the orchietomy specimen showing a yellowish, soft to mucoid intratesticular tumor with focal areas of hemorrhage and necrosis.

approximately 10% of the tumor.

The tumor was predominantly confined to the testicular parenchyma. The rete testis was focally approached but showed no definite gross invasion. The epididymis and spermatic cord appeared grossly uninvolved. The spermatic cord resection margin was grossly free of tumor.

Representative sections were submitted from the tumor, areas of hemorrhage and necrosis, tumor-testis interface, rete testis, epididymis, tunica, and spermatic cord margin.

Histopathological Examination

Sections stained with hematoxylin and eosin demonstrated

a malignant germ cell neoplasm arranged predominantly in a reticular/microcystic pattern.

The tumor consisted of loosely arranged malignant cells forming anastomosing cords and delicate cellular networks surrounding irregular microcystic spaces. The overall appearance resembled a lace-like or reticular architecture.

The tumor cells were predominantly round to oval, with moderate amounts of pale to eosinophilic cytoplasm. The nuclei were vesicular with finely dispersed chromatin and variably prominent nucleoli. Mild to moderate nuclear pleomorphism was present.

Mitotic figures were readily identified, averaging approximately 4-5 mitoses per 10 high-power fields.

Foci of hemorrhage and necrosis were present.

Several characteristic Schiller-Duval bodies were identified. These showed a central fibrovascular core surrounded by tumor cells and projecting into a surrounding cystic space, producing a characteristic glomeruloid appearance. Scattered hyaline globules were also identified within the tumor cells and extracellularly.

No mature cartilage, bone, glandular epithelium, neural tissue, seminomatous component, embryonal carcinoma, choriocarcinoma, or other distinct germ cell tumor component was identified in the extensively sampled sections.

Lymphovascular invasion was not identified

The epididymis was free of tumor. The spermatic cord was free of tumor, and the resection margin was negative.

The overall morphological findings were strongly suggestive of pure yolk sac tumor.

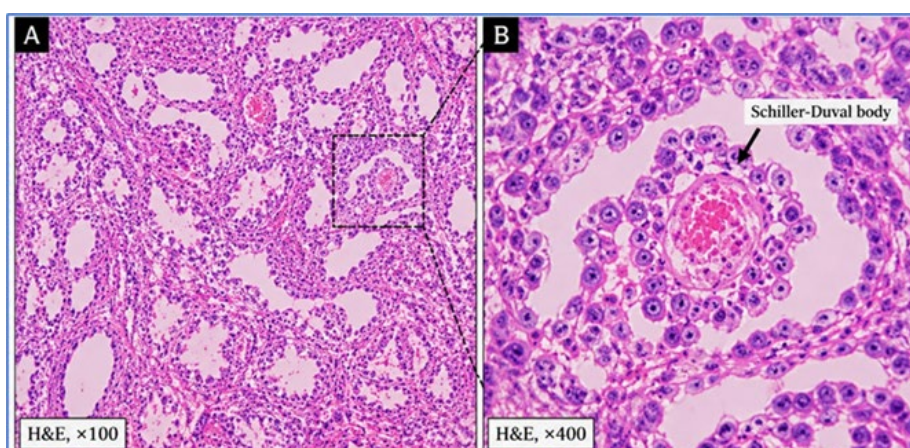


Figure 3: Histopathological examination showing the characteristic reticular/microcystic pattern with a Schiller-Duval body (H&E, ×100/×400).

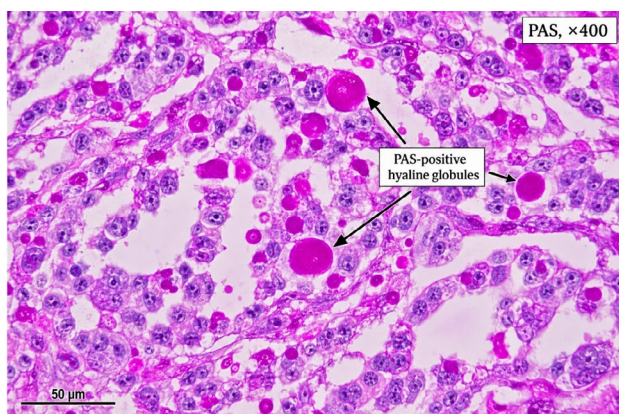


Figure 4: PAS-stained section demonstrating PAS-positive hyaline globules within the tumor (PAS, ×400).

Special Staining

Periodic Acid-Schiff Staining

PAS staining was performed for further evaluation of the hyaline globules. The tumor demonstrated multiple PAS-positive hyaline globules, both intracellularly and extracellularly. The globules appeared as rounded, intensely magenta-staining structures within the tumor.

The presence of PAS-positive hyaline globules, together with the characteristic reticular/microcystic architecture and Schiller-Duval bodies, provided additional support for the diagnosis of yolk sac tumor.

Immunohistochemistry

Immunohistochemical examination was performed to

Table 2: Immunohistochemical Profile of the Tumor and Diagnostic Interpretation

Marker	Result	Interpretation
AFP	Strong diffuse positive	Supports yolk sac differentiation
SALL4	Strong nuclear positive	Supports germ cell differentiation/YST
Glypican-3	Strong positive	Supports yolk sac differentiation
Cytokeratin	Positive	Compatible with YST
OCT3/4	Negative	Against seminoma/embryonal carcinoma
CD30	Negative	Against embryonal carcinoma
β-hCG	Negative	No evidence of choriocarcinomatous differentiation

confirm the diagnosis and exclude other malignant germ cell tumors. The tumor cells demonstrated strong and diffuse cytoplasmic AFP positivity. Strong nuclear positivity for SALL4 was also observed. Glypican-3 showed strong diffuse cytoplasmic/membranous positivity. The tumor was negative for OCT3/4 and CD30. β-hCG was negative.

Immunohistochemical Findings

The immunohistochemical profile was consistent with yolk sac tumor. SALL4 is a highly sensitive germ cell tumor marker and demonstrates strong expression in yolk sac tumors.[11,12] Glypican-3 is also a useful marker for yolk sac differentiation and can demonstrate high sensitivity across different histological patterns.[13]

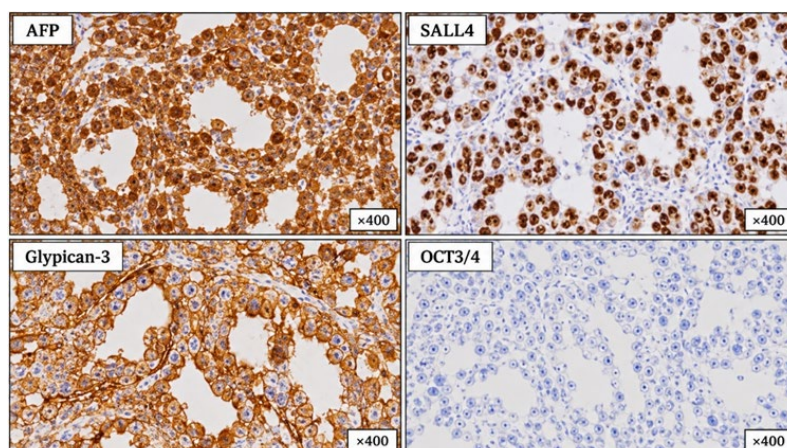


Figure 5: Immunohistochemical examination showing strong tumor-cell positivity for AFP, SALL4, and glypican-3.

Final Histopathological Diagnosis

Based on the clinical presentation, markedly elevated serum AFP, radiological findings, gross examination, histomorphology, PAS staining, and immunohistochemical profile, the final diagnosis was: Pure yolk sac tumor, prepubertal type, of the right testis

Pathological features

- Tumor size: $5.0 \times 4.5 \times 4.0$ cm
- Predominant reticular/microcystic pattern
- Schiller-Duval bodies present
- PAS-positive hyaline globules present
- Focal hemorrhage and necrosis
- Lymphovascular invasion absent
- Epididymis uninvolved
- Spermatic cord uninvolved
- Surgical margin negative
- No additional germ cell tumor component identified

DISCUSSION

Yolk sac tumor is an important malignant germ cell tumor of early childhood. The present case illustrates a classic pediatric testicular yolk sac tumor in a two-year-old child, with the characteristic combination of painless scrotal swelling, markedly elevated serum alpha-fetoprotein (AFP), solid intratesticular mass, reticular/microcystic histology, Schiller-Duval bodies, PAS-positive hyaline globules, and supportive immunohistochemistry. Prepubertal yolk sac tumor has a characteristic age distribution, with a strong predilection for infancy and early childhood. [4,5] Cornejo et al. evaluated 33 pure testicular yolk sac tumors in infants and children and reported an age range of five to 71 months, with a mean age of 20.7 months.[4] The age of two years in the present case therefore falls within the typical age range. Wei et al. similarly reported that pediatric yolk sac tumor predominantly affects very young children in their series of 61 cases.[5] The distinction between prepubertal and postpubertal yolk sac tumor is important, as prepubertal-type yolk sac tumor is not typically associated with germ cell neoplasia in situ and has distinct biological characteristics.[6]

The most common presentation of pediatric yolk sac tumor is a painless testicular or scrotal mass.[5,7] The present child had a three-month history of painless right scrotal swelling. The absence of pain is characteristic but can result in delayed presentation because parents may not consider a painless swelling to be urgent. In the series reported by Wei et al., painless scrotal swelling was the presenting complaint in the pediatric patients studied.[5] A

progressively enlarging unilateral testicular swelling should therefore be evaluated promptly with ultrasonography and serum tumor markers.

Serum AFP is one of the most important diagnostic markers in pediatric yolk sac tumor. [7,8] Yolk sac tumor cells characteristically produce AFP, and marked serum elevation is frequently present. In the present case, the AFP concentration was 18,650 ng/mL, substantially above the expected level for a two-year-old child. The patient's age is important because AFP is physiologically elevated in newborns and decreases progressively during infancy.[7] Consequently, AFP should not be interpreted using adult reference ranges in very young children. The combination of a markedly elevated AFP and a solid intratesticular mass in a two-year-old child is highly suggestive of yolk sac tumor. AFP also provides a valuable means of monitoring treatment response. Following complete surgical excision, the serum concentration should progressively decline. [7,8] In the present case, AFP decreased from 18,650 ng/mL preoperatively to 820 ng/mL at one month and 4.2 ng/mL at six months, providing biochemical evidence of successful tumor removal.

Ultrasonography represents the primary imaging modality for evaluation of a pediatric scrotal mass. [7,9] In the present case, ultrasound demonstrated a $5.2 \times 4.6 \times 4.1$ cm heterogeneous predominantly solid intratesticular lesion with prominent vascularity. These findings are compatible with the typical imaging appearance of pediatric yolk sac tumor. Wei et al. reported prominent vascularity in a substantial proportion of pediatric yolk sac tumors, supporting the observation that increased blood flow may be a useful imaging characteristic.[5] The presence of internal cystic spaces in the present case also corresponds with the histological microcystic architecture identified microscopically.

The tumor in this case measured 5.0 cm and demonstrated a yellowish, soft, mucoid cut surface with focal hemorrhage and necrosis. These features are consistent with previously described gross appearances of pediatric yolk sac tumor.[4] Cornejo et al. reported that pediatric testicular yolk sac tumors are generally nonencapsulated and have a gray-to-yellow, often mucoid cut surface.[4] Gross examination should document tumor size, appearance, extent, relationship to the tunica, rete testis, epididymis, and spermatic cord, and the presence or absence of hemorrhage and necrosis. Adequate sampling is essential because yolk sac tumor may display considerable

morphological heterogeneity and may coexist with other germ cell tumor components. [4,10]

The histological appearance of yolk sac tumor is variable, and multiple patterns may occur within the same tumor. [4,10] The present tumor demonstrated a predominantly reticular/microcystic pattern. This pattern is characterized by delicate anastomosing cords of tumor cells surrounding irregular spaces, creating a lace-like appearance. The identification of Schiller-Duval bodies was particularly important in establishing the diagnosis. Schiller-Duval bodies consist of a central fibrovascular core surrounded by tumor cells and projecting into a cystic or sinusoidal space. They are highly characteristic of yolk sac tumor. [4,10] However, Schiller-Duval bodies may be focal, and their absence in a biopsy or limited specimen does not exclude yolk sac tumor. The extensive sampling of the present orchiectomy specimen allowed identification of several well-formed Schiller-Duval bodies and excluded other germ cell tumor components.

PAS-positive hyaline globules are a recognized feature of yolk sac tumor.[10] In the present case, multiple PAS-positive hyaline globules were identified within the tumor. These structures provided additional support for the diagnosis. Although individual histological features should not be interpreted in isolation, the combination of PAS-positive hyaline globules, Schiller-Duval bodies, reticular architecture, and elevated AFP is highly supportive of yolk sac tumor.

The present tumor demonstrated strong AFP positivity, supporting the biochemical evidence of yolk sac differentiation. SALL4 showed strong nuclear expression. SALL4 is a sensitive marker of germ cell differentiation and has demonstrated high sensitivity in yolk sac tumors. [11,12] Cao et al. demonstrated the usefulness of SALL4 as a diagnostic marker in testicular germ cell tumors.[11] Subsequently, Wu et al. reported strong SALL4 expression in pediatric yolk sac tumors, supporting its application in this age group.[12] Glypican-3 was also strongly positive in the present case. Zynger et al. demonstrated high sensitivity of glypican-3 in testicular and ovarian yolk sac tumors and reported that it may show greater sensitivity than AFP in some cases.[13] The negative OCT3/4 and CD30 staining helped exclude embryonal carcinoma and seminomatous differentiation. Therefore, the immunohistochemical profile was concordant with the morphological diagnosis.

The differential diagnosis of a testicular mass in a prepubertal child includes mature teratoma, yolk sac tumor, mixed germ cell tumor, juvenile granulosa cell tumor,

Sertoli cell tumor, and other less common lesions. [2,3] Mature teratoma is an important differential diagnosis in prepubertal boys and may be benign.[2,3] Histologically, mature teratoma contains differentiated tissues derived from one or more germ layers. A pure mature teratoma does not usually produce markedly elevated serum AFP. The markedly elevated AFP and characteristic Schiller-Duval bodies in the present case strongly favored yolk sac tumor. Embryonal carcinoma is extremely uncommon as a pure tumor in very young children. It may demonstrate solid, glandular, or papillary architecture and may occasionally overlap morphologically with yolk sac tumor. Embryonal carcinoma typically expresses OCT3/4 and CD30, whereas yolk sac tumor generally demonstrates AFP, SALL4, and glypican-3 expression. [10-13] The negative OCT3/4 and CD30 results in the present case therefore supported yolk sac tumor.

A mixed germ cell tumor must also be excluded through adequate sampling because yolk sac tumor may occur together with teratoma, embryonal carcinoma, seminoma, or other germ cell components. No additional germ cell tumor component was identified in the extensively sampled specimen in the present case.

Management of pediatric testicular tumors is dependent on histological type, serum AFP, disease stage, and response to treatment.[7] Radical inguinal orchiectomy provides definitive local treatment and establishes the histological diagnosis. In appropriately selected prepubertal patients with localized yolk sac tumor, surveillance following complete tumor excision may be considered, whereas patients with metastatic or recurrent disease require systemic chemotherapy. [7,14] The present patient had localized disease, complete tumor excision, negative surgical margins, no lymphovascular invasion, and a favorable postoperative AFP trajectory. He was therefore followed under a structured surveillance protocol.

The prognosis of pediatric testicular yolk sac tumor is generally favorable, particularly when disease is localized. [7,14,15] Kaplan et al. reported excellent outcomes among children with stage I prepubertal yolk sac tumors.[14] More recent series have also demonstrated high survival rates among children with testicular yolk sac tumor, particularly when appropriate treatment is instituted early.[15] Postoperative AFP kinetics provide valuable prognostic and surveillance information. Persistent elevation may indicate residual disease, while normalization supports successful treatment. [7,15] In the present case, AFP normalized progressively following orchiectomy and remained within

the age-appropriate range during follow-up. No evidence of recurrence was identified at 12 months.

This case demonstrates the importance of integrating clinical, biochemical, radiological, and pathological findings in the diagnosis of pediatric yolk sac tumor. The diagnostic sequence in this patient can be summarized as painless scrotal swelling → solid intratesticular mass → markedly elevated AFP → radical orchiectomy → reticular/microcystic histology → Schiller-Duval bodies → PAS-positive hyaline globules → AFP/SALL4/glypican-3 positivity → definitive diagnosis of yolk sac tumor. The case also emphasizes the importance of age-adjusted interpretation of AFP and adequate pathological sampling. Recognition of the characteristic histological features can facilitate diagnosis even in cases where immunohistochemistry is limited. Conversely, immunohistochemistry can provide valuable confirmation when the morphology is heterogeneous or when Schiller-Duval bodies are not readily identified.

when the morphology is heterogeneous or when Schiller-Duval bodies are not readily identified.

CONCLUSIONS

Yolk sac tumor is the most important malignant testicular germ cell tumor of early childhood and should be considered in any young child presenting with a painless scrotal swelling.

In this case, the combination of a progressively enlarging painless scrotal swelling, solid vascular intratesticular mass, markedly elevated serum AFP, and characteristic histopathological findings led to the diagnosis of pure prepubertal-type yolk sac tumor.

The reticular/microcystic pattern and Schiller-Duval bodies represented the principal morphological findings, while PAS-positive hyaline globules provided additional histological support. Strong AFP, SALL4, and glypican-3 immunoreactivity confirmed yolk sac differentiation.

The case highlights the importance of a multidisciplinary approach involving clinical examination, serum tumor markers, ultrasonography, surgical management, histopathology, and immunohistochemistry.

Early diagnosis and appropriate stage-directed management are associated with excellent outcomes in children with localized disease. Serial monitoring of serum AFP remains an important component of postoperative surveillance.

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