Cancer Management and Research

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CASE REPORT

Rare Giant Pure Yolk Sac Tumor Originating from Cryptorchidism in an Adult

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Abstract: Cryptorchidism is a well-established risk factor for testicular cancer. Among adult male patients, pure testicular yolk sac tumors (YSTs) are rare, and those arising from cryptorchidism in adult males are even less common. We report a case of a 35-year-old male with a giant YST originating from cryptorchidism, with no distant metastasis detected preoperatively. The initial treatment plan was radical orchiectomy combined with postoperative chemotherapy for curative intent, but direct surgery was extremely challenging due to the large tumor size. Therefore, we attempted neoadjuvant chemotherapy to facilitate surgical resection. To our knowledge, there are relatively few reports on the use of neoadjuvant chemotherapy to reduce tumor burden prior to testicular tumor resection. The patient received four cycles of neoadjuvant chemotherapy before surgery, after which the tumor volume decreased, and the levels of alpha-fetoprotein (AFP) and lactate dehydrogenase (LDH) also dropped. Unfortunately, Liver metastases were detected during the reexamination on the 28th post-operative day, and lung metastases were identified in another reexamination on the 85th post-operative day. Regrettably, the patient refused further treatment and discontinued it, and we eventually lost follow-up. Post-pubertal YSTs are highly aggressive, and early detection and intervention are crucial for patients suspected of having cryptorchidism. Neoadjuvant chemotherapy can be considered as an adjuvant therapeutic strategy for reducing tumor burden in testicular tumors.

Keywords: cryptorchidism, yolk sac tumor, testicular cancer, neoadjuvant chemotherapy

Introduction

Cryptorchidism, also known as undescended testis, is a consistent risk factor for testicular cancer. The undescended testis increases the risk of testicular tumor by 3.7–7.5 times.[1,2] Pure YST is typically found in infants and young children.[3] With regard to adult male patients, YSTs mainly present as components of mixed germ cell tumors (GCTs).[4] By contrast, pure YSTs of testis are fairly infrequent, occupying less than 1% of testicular GCTs, and pure YST originating from cryptorchidism is even rarer in adult male patients.[3,5–9] Upon conducting a search on PubMed (the biomedical literature database of the US National Library of Medicine), it was found that fewer than 40 cases of adult pure YSTs have been reported, and there were only 4 reported cases of YSTs originating from cryptorchidism.[3,6–11] Here, we present a case of an adult male patient with a pure YST over 15 cm in diameter originating from cryptorchidism, who developed tumor metastasis on the 28th day after tumor resection. This study provides a reference for the treatment of pure YSTs in adults by analyzing the patient's treatment methods and therapeutic effects.

Case Report

A 35-year-old unmarried man presented at The First People's Hospital of Qinzhou in January, 2022, complaining of abdomen pain for about 1 month and abdominal mass for 10 days. The general condition was good, and the patient had no other complaints of discomfort. Clinical examination revealed a round mass in his lower abdomen, measuring approximately 10 cm×15 cm×12 cm, with moderate consistency, ill-defined borders, a smooth surface, no obvious tenderness, and poor mobility. No enlarged lymph nodes were palpable in the bilateral inguinal regions. Testis and epididymis were found in left scrotal sac, but not in right scrotal sac or inguinal region. Laboratory tests including blood

Received: 18 July 2025
Accepted: 24 October 2025
Published: 11 November 2025

routine, liver function, renal function, coagulation function, electrolytes, and urine analysis showed no obvious abnormalities. Serum tumor makers were notably elevated, of which AFP was extremely high (37181 ng/mL) and LDH rose to 1033 U/L, the detection of beta-human chorionic gonadotropin (β-HCG) was not carried out. Abdominal CT revealed a huge solid mass in the abdominal cavity and pelvis cavity measuring 104 mm × 164 mm × 171 mm in size (Figure 1), several enlarged lymph nodes were shown beside the abdominal aorta, and the largest one was approximately 25 mm × 17 mm. No signs of metastasis to bone, lung, liver or other organs were found on single-photon emission-computed tomography supplemented with low dose-computed tomography (SPECT/CT) imaging. The patient underwent a biopsy

Figure 1 Transverse, coronal and sagittal sections of contrast-enhanced CT of abdomen and pelvis before neoadjuvant chemotherapy, the tumor measures approximately 104 mm × 164 mm × 171 mm.

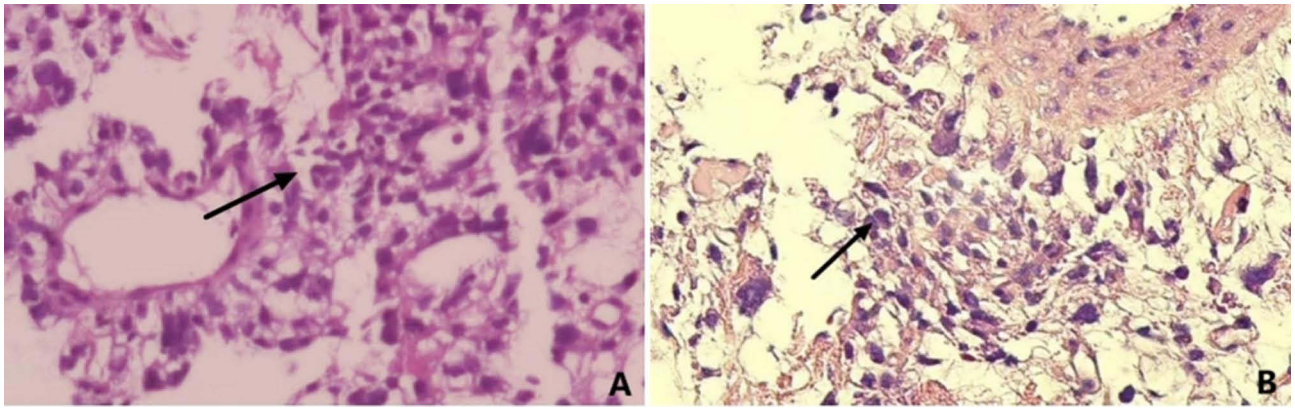

Figure 2 Schiller-Duval bodies (Black arrow) (**A**) (hematoxylin–eosin, 100× magnification). Yolk sac tumor cells (Black arrow) (**B**) (hematoxylin–eosin, 400× magnification).

of the abdominal mass, and histopathologic examination reported a pure YST originating from germ cells (Figure 2). Immunohistochemical staining revealed positive expressions of SALL4, CD117, GPC-3, pan-CK, and Ki-67 (with a positive index of approximately 80%), while PLAP, OCT4, D2-40, and CD30 were negative (Figure 3).

The patient was diagnosed with cryptorchidism and testicular YST. Based on the 8th edition of the TNM staging system by the Union for International Cancer Control (UICC), the tumor was staged as TxN2M0S3 (stage 3C). Given the extremely large size and advanced stage of the tumor, direct surgical resection was deemed challenging. Despite limited reports on neoadjuvant chemotherapy for reducing tumor burden prior to testicular tumor resection, we attempted this approach to downsize the tumor and facilitate subsequent surgery. The patient then received 4 cycles of neoadjuvant chemotherapy with the BEP regimen. The specific protocol was as follows: etoposide 0.15g, cisplatin 40mg, and bleomycin 15,000 U, all administered on Days 1–3 of each cycle, with an interval of 3 weeks between cycle. Post-chemotherapy, the abdominal mass shrank to 97mm × 131mm × 171mm (Figure 4), with AFP level showed an overall fluctuating trend of "first decreasing and then increasing": 37,181 ng/mL before the first cycle of chemotherapy, decreasing to 23,811 ng/mL before the second cycle, further dropping to 7793 ng/mL before the third cycle, then rising back to 17,696 ng/mL before the fourth cycle, and increasing to 29,694 ng/mL before the surgery, while the LDH level had dropped to 507 U/L. To further reduce the tumor burden, the patient underwent tumor resection. Intraoperatively, extensive adhesions were noted between the tumor and abdominal tissues, particularly the small intestine; thus, the tumor and adherent small intestine were resected en bloc (Figure 5). Due to significant intraoperative blood loss and prolonged operative time, retroperitoneal lymph node dissection was deferred to a second stage. Postoperative histopathology confirmed the preoperative biopsy findings, revealing a YST with extensive hemorrhage and necrosis. On day 7 post-surgery reexamination showed the AFP level was 4541 ng/mL; By day 12 post-surgery, the patient's condition improved and they were discharged. On the 28th day after surgery, the patient returned to the hospital for subsequent chemotherapy. At this time, a reexamination showed the AFP level was 486.43 ng/mL, and chest and abdominal CT indicated no lung metastases and residual tumor at the primary tumor site. Unfortunately, there were multiple liver metastases. Treatment involved salvage chemotherapy with paclitaxel 240 mg combined with nedaplatin 120 mg. On the 85th day after surgery, a reexamination showed that the AFP level had reached 37,305 ng/mL, and chest and abdominal CT further indicated newly developed lung metastases. On the 89th day after surgery, the patient developed symptoms of abdominal pain, abdominal distension, shortness of breath, fatigue, and anorexia, with the condition showing a progressive deterioration. Shortly thereafter, the patient declined further treatment, and subsequent follow-up was discontinued.

Discussion

It's estimated that about 5% of men with testicular cancer have a history of cryptorchidism, and early surgical intervention can reduce the risk of developing malignancy in the cryptorchidic testis. Patients should undergo surgical intervention at 6 months of age. For patients who have missed early surgical treatment, surgical intervention should be performed at the time of diagnosis.[2,12–14] The most common testicular tumor in patients with cryptorchidism is

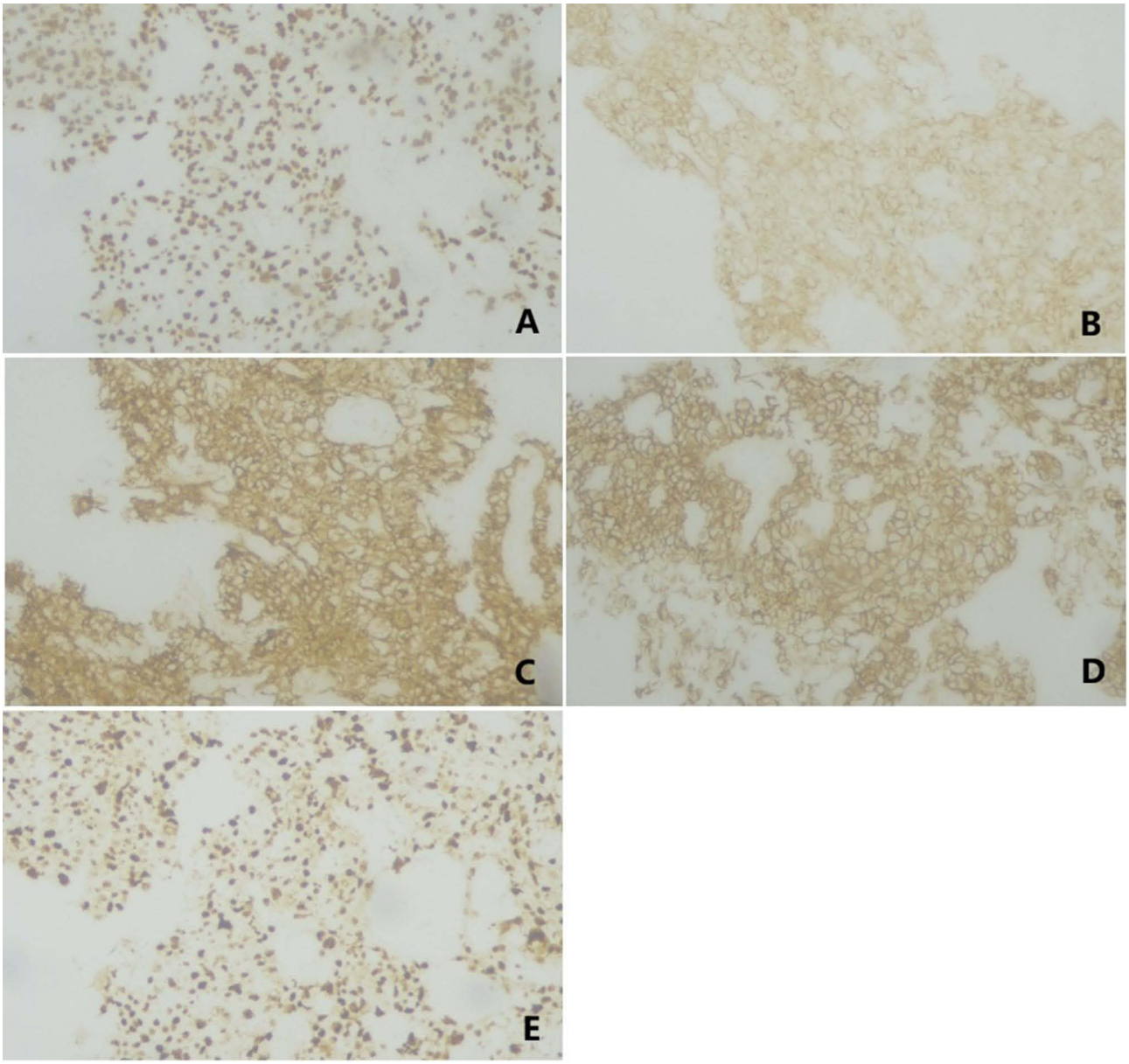

Figure 3 Immunohistochemistry results showed positive expression of SALL4 (**A**), CD117 (**B**), GPC-3 (**C**), pan-CK (**D**), and Ki-67 (**E**); all images were captured at 100× magnification.

seminoma, and seminoma is also the most common testicular tumor in adults, YSTs are very rare in adult patients with cryptorchidism.[15] In this case, the patient had a history of cryptorchidism for 35 years and did not undergo surgical intervention, eventually resulting in a huge testicular YST. YSTs of the testis are rare in after puberty, and it is extremely rare for cryptorchidism to induce pure YSTs after puberty.

YSTs of testis are aggressive malignant GCTs with early hematogenous metastases.[16] Simmi Patel et al[3] reported four cases of pure YSTs of testis after puberty, three of the cases had metastases at the time of diagnosis or after it, which confirming the aggressive nature of this rare neoplasm. Through a PubMed search, we found that among the four reported cases of pure YSTs induced by cryptorchidism, metastasis had been documented for two of them, the tumor recurred postoperatively in one patient, and he received a second surgical treatment.[6–9] It is worth noting that among the four patients, the oldest one was 46 years old and the youngest one was 24 years old, which was similar in age to the patient reported in this case, they were all post-pubertal patients. Three out of the four patients had not undergone any

Figure 4 Transverse, coronal and sagittal sections of contrast-enhanced CT of abdomen and pelvis after neoadjuvant chemotherapy, the tumor measures approximately 97mm × 131mm × 171mm.

Figure 5 Gross specimen of tumor.

surgical interventions before the onset of the disease, the only patient who did not experience metastasis and recurrence underwent orchiopexy at the age of 10 and developed a testicular YST at the age of 43. It can be seen from this that it is crucial to perform surgical interventions on patients with cryptorchidism at an early stage. We also found that there are similarities between our report and the case reported by Janugade H et al.[6] Both cases involve patients with cryptorchidism after puberty, the diameter of the tumor is greater than 10 cm, there are necrotic areas within the tumor, the tumor is adhered to multiple organs in the abdominal cavity, AFP is greater than 10000 nanograms per milliliter, histopathological diagnosis is pure YST, and there is a rapid progression of the disease after the surgery. We speculate that perhaps some of these characteristics may have a certain connection with the invasive properties of YSTs, and this requires confirmation by more cases. Previous studies showed that maximum tumor diameter and histological type were risk factors for poor prognosis in patients with YSTs of the testis.[17,18] The International Germ Cell Cancer Collaborative Group (IGCCCG, 1997) stated that patients with nonseminomatous GCTs can be classified as a high-risk group, indicating a poor prognosis, if they have any of the following conditions: primary mediastinal tumor, metastases to organs other than the lungs and lymph nodes, β-HCG > 50,000 mIU/mL, AFP > 10,000 ng/mL, or LDH > 10 × ULN.[19] A study by O'Shea et al[20] showed that all patients with YST stage I disease at their prepubertal age were cured by radical inguinal orchiectomy. Maoxian Li et al[21] reported that higher disease stage and relapse predicted a poor prognosis. Meanwhile, they inferred that age might be a risk factor for relapse, suggesting that older patients may have a higher relapse rate than younger patients. In our report, the patient had a history of cryptorchidism for 35 years. Nevertheless, early surgical intervention was not carried out, and the disease was not detected and treated in a timely manner. When the patient presented with symptoms and underwent examination, the cryptorchidism had developed into a large YST with a maximum diameter of 171 mm. The AFP level reached 37,181 ng/mL, the LDH level reached 1033 U/L, and there were suspicious metastases in the para-aortic lymph nodes. According to the IGCCCG (1997) criteria, the patient was classified as a high-risk group with a poor prognosis. Although the tumor was removed, liver and lung metastases occurred after surgery due to the highly malignant and aggressive nature of the tumor. So far, it has been suggested that early detection, timely diagnosis and surgical intervention are critical for cryptorchidism.

Radical orchidectomy combined with postoperative adjuvant chemotherapy is a treatment strategy for testicular YSTs.[22] Some studies have shown that postoperative adjuvant chemoradiotherapy can effectively reduce the recurrence rate of testicular tumors,[23,24] which is a common therapy for testicular tumors.[25,26] Neoadjuvant chemotherapy refers to systemic chemotherapy administered before local treatment. At present, neoadjuvant chemotherapy has been widely applied to the adjuvant treatment of tumors such as breast cancer, cervical cancer, ovarian cancer, esophageal cancer, gastric cancer and rectal cancer, and has achieved very good therapeutic effects.[27–32] In urologic cancers, neoadjuvant chemotherapy is commonly used for the adjuvant treatment of bladder cancer.[33,34] There are still relatively few reports on the use of

neoadjuvant chemotherapy to reduce the tumor burden before the resection of testicular tumors.[35,36] When tumors are relatively large and locally advanced, neoadjuvant chemotherapy may reduce tumor burden and downstage tumor, facilitating achieving the purpose of surgical resection and improving the outcomes of surgery.[37–40] Cisplatin-based chemotherapy has been highly effective in the treatment of GCTs for a long time. Through the combination of surgery and cisplatin-based chemotherapy, the cure rate for patients with testicular tumors has exceeded 90%.[41] Shoukry et al[42] and Thompson et al[43] reported two cases where patients experienced significant tumor shrinkage after receiving 3–4 cycles of cisplatin-based neoadjuvant chemotherapy. In this case, after the patient received four cycles of cisplatin-based neoadjuvant chemotherapy, the tumor shrank compared to before, which enabled the patient who was originally deemed ineligible for direct surgery to obtain the opportunity for surgical intervention. By reducing tumor volume and creating conditions for surgery, neoadjuvant chemotherapy may be regarded as an adjuvant therapeutic option for alleviating tumor burden in testicular tumors. However, in this case, the AFP level showed a "first decreasing and then increasing" trend during neoadjuvant chemotherapy. This change suggests that the tumor may have developed drug resistance during the chemotherapy process; this may explain why the tumor volume shrank after chemotherapy but failed to achieve the expected effect. Therefore, the issue of tumor drug resistance in neoadjuvant chemotherapy cannot be ignored.

This case report has certain limitations: first, β-HCG levels were not routinely measured before each chemotherapy cycle, which may have affected the comprehensive assessment of the tumor's response to treatment; second, baseline evaluations of pulmonary function and hearing were not completed prior to chemotherapy initiation, making it impossible to provide a fundamental reference basis for monitoring treatment safety; Finally, the preoperative assessment of metastatic lesions relied solely on chest and abdominal CT scans, and no repeat SPECT/CT scan was performed after neoadjuvant chemotherapy to screen for potential metastases in other sites, resulting in an insufficient scope of metastatic evaluation.

Conclusion

The case presented in this paper had a huge pure YST originating from cryptorchid testis, which is extremely rare. For those suspected of having cryptorchidism, detecting the condition early, making a timely diagnosis, and performing surgical intervention are essential. Neoadjuvant chemotherapy can be used as an adjuvant treatment option for lighten the tumor load of testicular tumors.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics Statement

This study was approved by Ethics Committee of the First People's Hospital of Qinzhou, and publishing the detailed information of this case does not require additional institutional approval.

Patient Consent for Publication

Written informed consent was obtained from the patient for the publication of the present study and for processing their medical data.

Author Contributions

All authors have made significant contributions to the work reported in this study, including contributions to the conception of the study, study implementation, provision of professional knowledge interpretation and images; participation in the drafting, revision, or critical review of the manuscript; final approval of the version to be published; agreement on the journal to which the manuscript has been submitted; and agreement to be accountable for all aspects of the work.

Funding

This work was supported by the No funding to declare.

Disclosure

The authors declare that they have no competing interests.

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