Case Report

Testicular teratoma demanded in-depth pathological exploration to rule out malignancy: A pediatric case report

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Abbreviations & Acronyms
AFP = alpha-fetoprotein
CT = computed tomography
hCG = human chorionic gonadotropin
US = ultrasound
YST = yolk sac tumor

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Introduction: Prepubertal testicular tumors can be both benign and malignant. Although most testicular teratomas are benign, some immature cases include malignant transformation or the mixed type with yolk sac tumor and, occasionally, it is challenging to rule out malignancy.
Case presentation: We present a case of immature testicular teratoma in a 7-month-old infant, whose alpha-fetoprotein level was sequentially elevated following orchidectomy. Since malignancy could not be ruled out, we performed whole body imaging and in-depth pathological exploration. GLYPICAN3, OCT3/4, and SOX2 staining revealed no evidence of malignancy. The patient was finally diagnosed with benign immature teratoma, and has been free from recurrence for 3 years.
Conclusion: Here, we describe the case report, as well as all the comprehensive diagnostic tests that we performed in order to rule out the malignant component.

Key words: alpha-fetoprotein, testicular teratoma, yolk sac tumor.

Keynote message

Pediatric testicular teratoma includes some cases in which the malignant components cannot be ruled out from the clinical course. In those cases, in-depth exploration for malignancy is mandatory. Here, we describe a case report of pediatric testicular teratoma, as well as all the diagnostic tests that we chose toward ruling out the malignant component.

Introduction

Pediatric testicular tumors are rare and large-scale data have not fully been accumulated. Although mostly benign, testicular immature teratoma sometimes contains malignant components, such as YST. Although AFP is a relevant marker in YST, ruling out YST is sometimes challenging because normal AFP levels should not be expected in infants aged <1 year.[1] Our patient was a 7-month-old infant whose postoperative AFP level consecutively elevated, partly suggesting malignant metastatic YST.

Case presentation

A 7-month-old boy was referred to our hospital because of a right testicular solid mass without any symptoms. Preoperative serum AFP and hCG levels were 24.7 ng/mL and <0.1 mIU/mL, respectively. Scrotal US revealed a heterogeneous composition with calcifications in the tumor (Fig. 1) and CT revealed no metastatic site. Total orchidectomy was performed and the tumor extracted was 4.1 × 2.6 × 2.2 cm in size. Pathologically, the tumor was composed of a mixture of three germ layers plus primitive neural tubes (Fig. 2a–e) and was diagnosed as an immature teratoma without any evidence of malignancy. However, the AFP level after surgery was elevated twice to 40.7 ng/mL and then 48.0 ng/mL. We could not completely rule out a

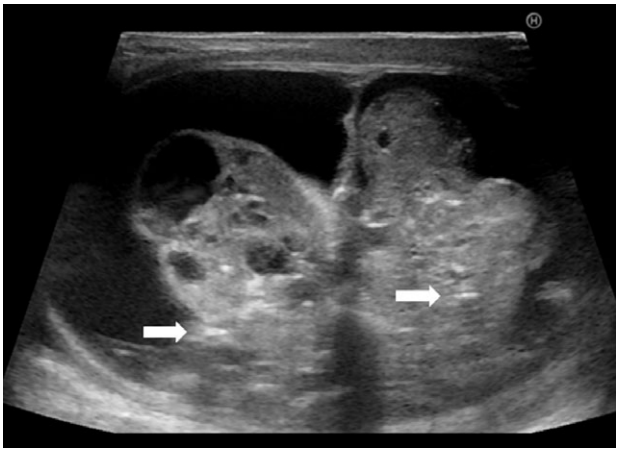

Fig. 1 US revealed calcifications (arrow) in the tumor.

hidden contamination of YSTs. We suspected a rare form of YST and performed bone marrow aspiration and bone scintigraphy; however, we found no evidence of malignancy. The in-depth pathological exploration of AFP and GLYPICAN3 revealed no evidence of YST or malignant teratomas (Fig. 2f). We therefore observed the natural course and found that the AFP level decreased gradually to a normal level (Fig. 3). Presently, the patient has been free from recurrence since 3 years.

Discussion

Pediatric testicular tumors are rare, comprising only 1% of all pediatric solid tumors, with an annual incidence of 0.5–2.0 per 100 000 boys.[2] Most prepubertal testicular tumors are teratomas or pure YSTs. The initial clinical suspicion of benign *vs* malignant is critical because it will influence the decision as to whether the child has to undergo a testicular-preservation surgery or radical orchidectomy.[2] Radical orchidectomy was chosen in our case because the pre-surgical US did not show a normal testicular component.

The tumor pathology indicated an immature teratoma, and the postoperative high AFP level was thought to be compatible with physiological elevation, because AFP in infants is above the normal range until 8 months of age.[3] However, postoperative sequential increase in the AFP level suggested a malignant disease, and we proceeded to the next exploration to distinguish YST from immature teratoma concomitant with physiological AFP elevation.

One study that sought to distinguish teratomas from YSTs by means of serum AFP level[3] showed that, in all patients with teratoma aged older than 6 months, the AFP level is <100 ng/mL (sensitivity 100%), implying that ours was a case of pure teratoma. However, there are two reasons that we still could not rule out malignant diseases. First, the study only included mature teratomas (not immature ones) and was too small for concluding outcomes, because the study included approximately 60 patients. Second, another report showed that as many as 44% of immature testicular teratomas include yolk sac components in patients aged <4 years.[4] Hence, in this case, we could not totally rule out the YST component and we performed additional pathological study.

First, we confirmed some primitive tissues based on positive staining for AFP. We, then, co-stained the tissue for GLYPICAN3 because its sensitivity against YST is 100%.[5,6] However, the staining revealed no GLYPICAN3-positive cells in any of the AFP-positive populations, strongly suggesting that AFP-positive cells are not YSTs (Fig. 2f). Next, we co-stained the tissue for OCT3/4 and SOX2, based on the report that OCT3/4-positive cells and SOX2-negative cells in immature elements lead to the progression toward YST,[5] and that OCT3/4 is a typical marker of undifferentiated states, such as induced pluripotent stem cells, embryonic stem cells, or embryonal carcinomas. The result showed that immature elements harbored OCT3/4-negative but SOX2-positive cells, suggesting the possibility that these elements did not include those YST stem cells (Fig. 4).

All these studies indicated that the testicular tumor did not include malignant populations, and serum AFP elevation was

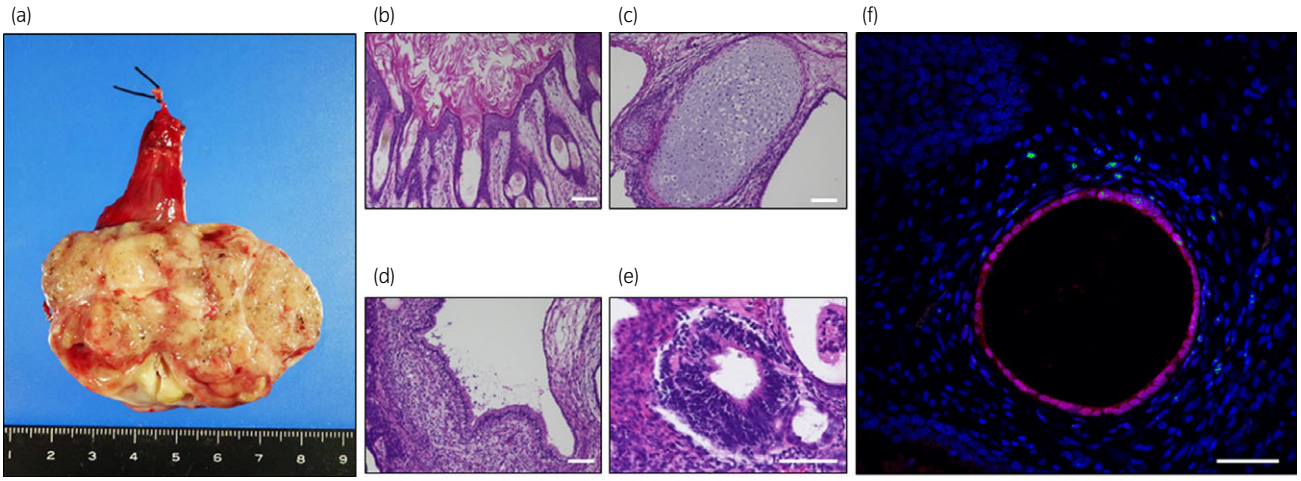

Fig. 2 (a) Tumor contained calcifications without any liquid component. (b–e) All three germ layers (b; hair root, ectoderm, c; cartilage, mesoderm, d; respiratory epithelium, endoderm) as well as primitive neural tubes (e) were seen in the tumor. Scale bar shows 100 μm. (f) AFP-positive cells were not co-stained for GLYPICAN3. AFP, GLYPICAN3, and DAPI were stained with red, green, and blue respectively. Scale bar shows 100 μm.

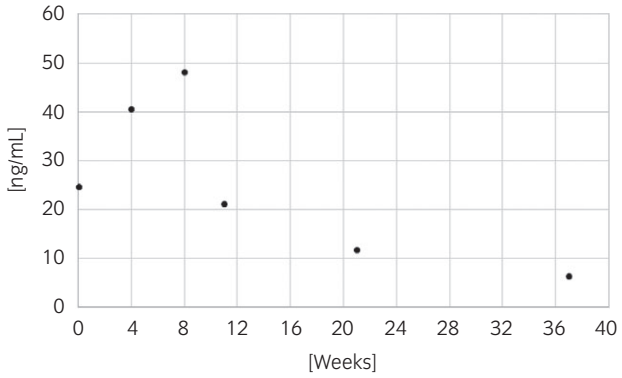

Fig. 3 Time course of serum AFP level.

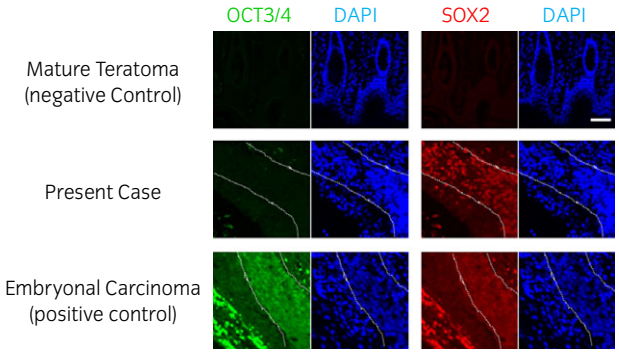

Fig. 4 OCT3/4-positive, but SOX2-negative cells were detected in the section. OCT4 and SOX2 were stained with green and red, respectively. Scale bar shows 100 μm.

within the physiological range. We followed up the AFP level, which decreased to normal values 8 months after surgery. Presently, the patient has been free from recurrence for 3 years.

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Conflict of interest

The authors declare no conflict of interest.

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