Malays J Pathol 2020; 42(2): 301 – 305

CASE REPORT

Primary extragonadal vaginal yolk sac tumour: A case report

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Abstract

Introduction: Yolk sac tumour (YST) or endodermal sinus tumour is rare and typically seen in gonads. *Case Report:* We described a case of extragonadal vaginal YST in a one year and seven months old girl who presented with vaginal discharge and bleeding, and discuss its differential diagnosis and potential pitfalls in immunohistochemistry. She was found to have a suprapubic mass on examination. The serum alpha fetoprotein was 11919.4 ng/mL. Computed tomography of the pelvis revealed a large 6.4 cm heterogenous pelvic mass. Colposcopic examination of the pelvis showed a fungating vaginal mass that was subsequently confirmed as a yolk sac tumour. Immunohistochemically, the malignant cells were positive toward CKAE1/AE3, AFP and glypican-3, as well as CD117. *Discussion:* Solid pattern extragonadal vaginal YST may morphologically resemble dysgerminoma that is also CD117 positive, while the glandular pattern YST may have clear cytoplasm and is positive for cytokeratin; hence, may resemble clear cell carcinoma. Being mindful of these potential diagnostic caveats is necessary to prevent misdiagnosis.

Keywords: CD117, children, extragonadal, immunohistochemistry, yolk sac tumour

INTRODUCTION

Primary extragonadal yolk sac tumour (YST) constitutes less than 5% of all germ cell tumours (GCT) in children.[1] YSTs represent a multifaceted group of neoplasms with the capacity to differentiate into various extraembryonal and somatic cell types. These tumours could develop into primitive endoderm and mesenchyme, with different histological patterns.[2] Sites of extragonadal YST include perineal, retroperitoneum, sacral region, mediastinum and pineal region. It has variable immunohistochemical staining. Only alpha fetoprotein and glypican-3 are the two most reliable marker but these have variable staining on YST. Here, we described a case of extragonadal vaginal YST in a one year and seven months old girl who presented with vaginal discharge, with discussion of its differential diagnosis and the potential pitfalls in immunohistochemistry.

CASE REPORT

A one year and seven months old girl presented to our hospital with a 2-month history of vaginal discharge, vaginal bleeding, fever, and difficulty in passing urine and motion. There was no history of weight loss. She was on breast feed exclusively until 6 months of age. There was no family history of malignancy. All her siblings were healthy. On physical examination, a mobile suprapubic mass with smooth surface was noted. The abdomen was soft and there was no hepatosplenomegaly. The serum alpha fetoprotein (AFP) was 11919.4 ng/ml. The ultrasonography of pelvis showed an intravaginal heterogenous mass. On colposcopic examination, a fungating vaginal mass was noted and the cervix was unable to visualise. The clinical diagnosis was a vaginal mass, likely neoplastic in nature. Computer tomography of pelvis revealed a large heterogenous pelvic mass measured 6.4 x 4.9 cm with central hypodensity, consistent with central necrosis. A biopsy of the vaginal mass was obtained.

Histopathological examination of vaginal mass showed malignant cells arranged in reticular and solid patterns. These cells have large, pleomorphic and hyperchromatic nuclei, open chromatin, few with prominent nucleoli, high

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nucleo-cytoplasmic ratio and scanty eosinophilic cytoplasm. Mitoses were frequently observed, with up to 15 mitoses in 10 high power fields. Large areas of necrosis were seen. Hyaline globules were noted. Immunohistochemically, these cells were positive toward Cytokeratin AE1/AE3, CD117 (patchy), AFP (focal) and glypican-3 (focal), and were negative for CD30 and β-hCG (Fig. 1). This finding was consistent with extragonadal yolk sac tumour.

She was given chemotherapy (IV etoposide on day 1, 2 and 3, IV carboplatin on day 2 and IV bleomycin on day 3) for 6 cycles. Post-treatment magnetic resonance imaging showed good chemo-response with reduction in size of the vaginal mass, measured 3.0 x 1.6 x 1.5 cm. The serum AFP was reduced to 7.07 ng/ml. However, 5 months later she again had vaginal bleeding with loss of appetite. The serum AFP was again increased to 1505.5 ng/ml. The ultrasonography

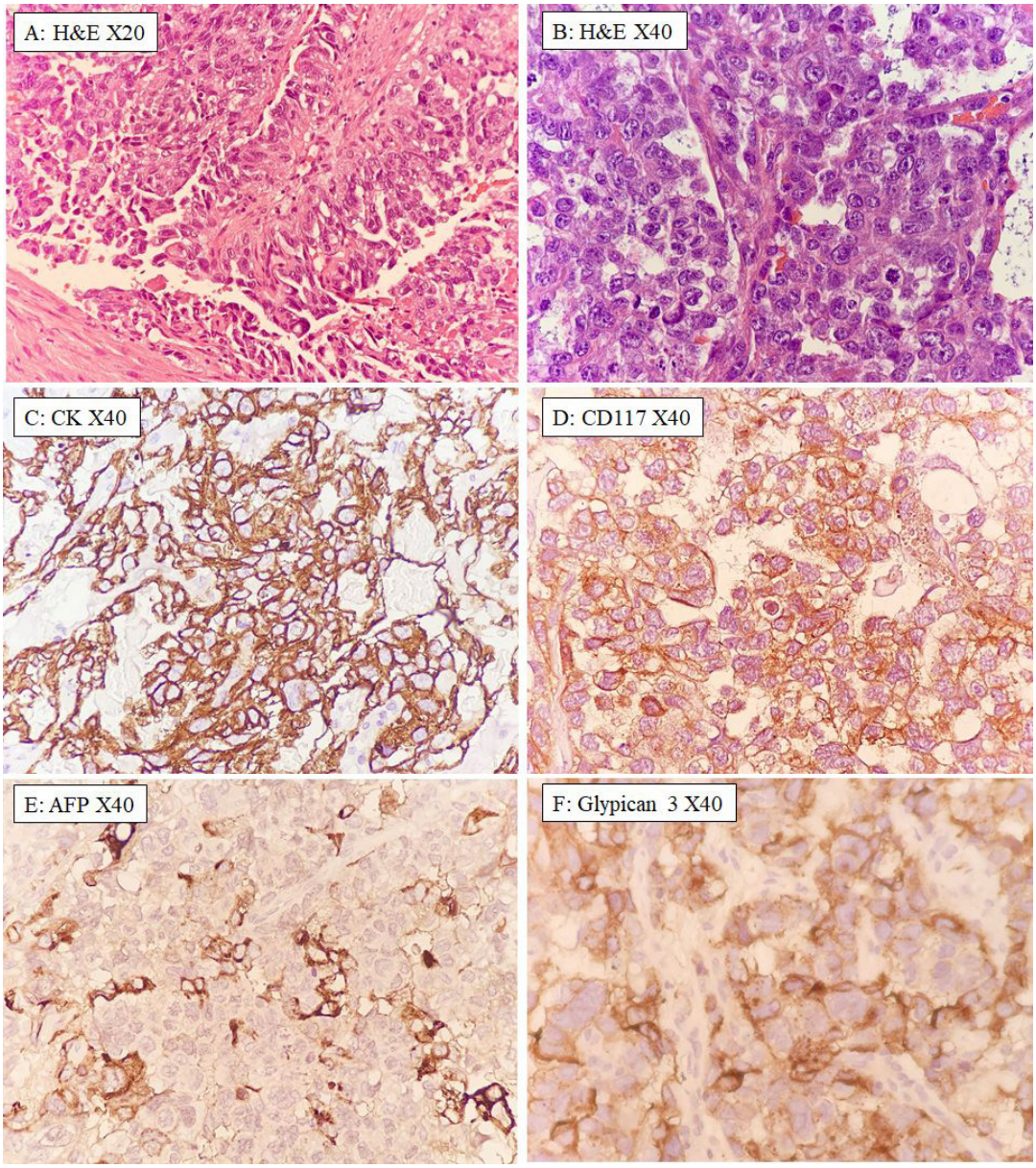

FIG. 1: Yolk sac tumour. (A) Schiller-Duval body (X20). (B) Solid pattern with neoplastic cells demonstrating pleomorphic nuclei, prominent nucleoli and eosinophilic cytoplasm (X40). Neoplastic cells with diffuse CK AE1/AE3 positivity (C, X40), patchy membranous and cytoplasmic CD117 positivity (D, X40), focal AFP positivity (E, X40) and focal glypican-3 positivity (F, X40).

TABLE 1: Immunohistochemical profiles of yolk sac tumour, dysgerminoma and cervical clear cell carcinoma

	Age distribution/ Morphological patterns/ Immunohistochemistry	Yolk sac tumour	Dysgerminoma	Cervical clear cell carcinoma
1	Age of presentation	Bimodal (<4 years and 10-30 years)	Children and young adult, rare >50 years	Bimodal (17-37 years and 44-88 years) [9]
2	Morphological patterns	Microcystic/reticular, glandular, solid, papillary and hepatoid	Solid sheets and nests, may grow as cords, microcysts, tubules, pseudoglandular spaces or trabeculae [10]	Tubulocystic, papillary and solid
3	CD117	Usually negative but can be variable (positive in 60% of solid pattern)	Positive, diffuse	NA
4	AFP	Variable, often focal, may be absent in some cases	Negative	Negative[11]
5	Glypican-3	Positive in most cases, may be patchy	Negative	NA
6	CK AE1/AE3	Positive	Usually negative, can be focal and weak	Positive
7	SALL4	Positive (positive in most germ cell tumour)	Positive	NA
8	OCT3/4	Negative	Positive	NA
9	LIN28	Positive [12]	Positive	NA
10	PLAP	Negative	Positive	NA
11	Podoplanin (D2-40)	Rarely positive	Positive	NA
12	CD30	Very rarely positive, focal	Negative	NA
13	CK7	Variable [8,13]	Variable [14]	Positive
14	CK20	Variable, rare cells [8]	Negative [14]	Negative [11]
15	CDX2	Positive [15]	Positive in minority of cases	Negative [11]
16	GATA3	Positive in minority of cases, weak [15]	Negative	Negative [11]
17	DOG1	Negative [15]	Negative	NA
18	P63	Negative [13]	Negative	P40-Negative [11]
19	B-hCG	Variable [13]	Variable	NA
20	Inhibin	Negative [13]	Negative	NA

NA – Not available

of the pelvis showed an increased in size of the vaginal tumour, measured 3.9 x 2.3 x 1.6 cm. Biopsy confirmed a recurrent tumour.

DISCUSSION

In 1970s, yolk sac tumour was referred to as orchioblastoma in the testis of young boys. It has the same histological features as ovarian tumour in young girls, which Teilum (1971)[3] referred to as endodermal sinus tumour, while those tumours that were in the mediastinum was known as mesoblastoma vitellinum.[4]

Primordial germ cells are recognizable at 24 days after fertilization in the endodermal layer of the yolk sac which subsequently exit from the yolk sac and migrate across the dorsal mesentery to eventually reach the gonads. Dorsal mesentery spans between pharynx and anus that facilitates intestinal mobility.[5] Extragonadal GCTs (GCT) arise from misplaced primordial germ cells during their migration through the midline dorsal mesentery in the 4th to 6th week of embryogenesis.[1] If these cells do not degenerate but remain viable, they may transform into tumours along this path, include the perineal, retroperitoneum, sacral region, mediastinum, and pineal region. GCT has been reported in the penile shaft, urachus, stomach, liver, lungs, heart, thyroid, nasal region, vulva, vagina, endometrium, retroperitoneum, prostate, pericardium, diaphragm, mesentery, mouth, ears, omentum, eyes, subcutaneous region and cranial base.[6]

A large study by Shah *et al*. (2008)[7] showed yolk sac tumour has a bimodal distribution, at the first four years of life and the 2nd to 4th decade of life. The male to female ratio is 1.3. Pure or mixed YSTs have been seen to occur in extragonadal sites. Klinefelter's is a predisposing factor.[1] Tang *et al*. (2014)[8] described 8 cases of primary vaginal GCT and found that half of them were pure yolk sac tumour, while the other 4 cases were mixed GCTs of which all have yolk sac tumour component. The other components in the mixed GCTs include embryonal carcinoma and dysgerminoma. Of these 8 cases, one had recurrence and two had metastasis.

YST has variable morphological features: microcystic/reticular, glandular and solid are the more common patterns, while papillary and hepatoid are less common patterns. Mixed histologic pattern was present in two-third of the cases. Schiller-Duval bodies were seen in one-fifth cases.[9] In solid pattern, the neoplastic cells usually have mostly pale to clear abundant cytoplasm, frequently had intercellular basement membrane deposits, rare microcysts, nuclear pleomorphism and hyaline globules.

YST with glandular pattern and clear cytoplasm could be misdiagnosed as clear cell carcinoma as it will be positive for cytokeratin (CK AE1/AE3). Immunohistochemical markers that may be positive in yolk sac tumour include SALL4, AFP, Glypican-3, CDX2, CK7, CK20, PAX8 and CD117.[9,10] SALL4 is an antibody for pluripotent cells and is consistently positive in yolk sac tumour; therefore, it is helpful in differential diagnosis.[2] However, as SALL4 is a pluripotent marker, other GCT like dysgerminoma will also be positive. Similarly, LIN28, a pluripotent marker is also positive in YST. Other markers such as Octamer binding transcription factor (OCT) 3/4, placental-like alkaline phosphatase (PLAP) and CD30 (may be very rare and focal) are negative in YST. Table 1 shows the age distribution, morphological patterns and immunohistochemical profile of YST, dysgerminoma and cervical clear cell carcinoma.[11-17] CD117 is an immunohistochemical marker for dysgerminoma. However, it is also positive in about two-third of YST.[10] In situation where morphological distinction between solid-pattern YST and dysgerminoma may be difficult, CD117 is not a reliable marker.

In conclusion, solid pattern extragonadal vaginal YST may morphologically resemble dysgerminoma and CD117 positive, while the glandular pattern YST may have clear cytoplasm and is positive for cytokeratin; hence, may resemble clear cell carcinoma. Being mindful of the potential caveats in immunohistochemistry is necessary to prevent misdiagnosis.

Acknowledgement: We would like to express our sincere thanks to the Faculty of Medicine, Universiti Kebangsaan Malaysia (FF-2019-002) for providing the research fund for this study.

Conflicts of Interest: The authors declare they have no conflict of interest.

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