Primary extragonadal pure yolk sac tumor in a post-menopausal female

Dear Editor,

Yolk sac tumor is a primitive malignant germ cell tumor. Some of the histological patterns of yolk sac tumor recapitulate the various phases in the development of normal yolk sac. The usual age group affected is children and young adults. Yolk sac tumor in post-menopausal age group is rare and the histogenesis of the tumor in this age, whether somatic or germ cell origin, is not clear. Still rarer is the occurrence in an extra gonadal site in this group.

A 52-year-old female presented with abdominal distention and backache of 1 month duration. Examination revealed a large mass filling the abdomen. Imaging showed lobulated mass with heterogeneous enhancement in the right inframesocolic compartment of peritoneal cavity measuring 14 cm × 12 cm and multiple small mass lesions in gastro hepatic ligament. Left ovary was cystically enlarged measuring 7 cm × 6 cm × 4 cm. Right ovary was normal. CA125 level was 28 International Units.

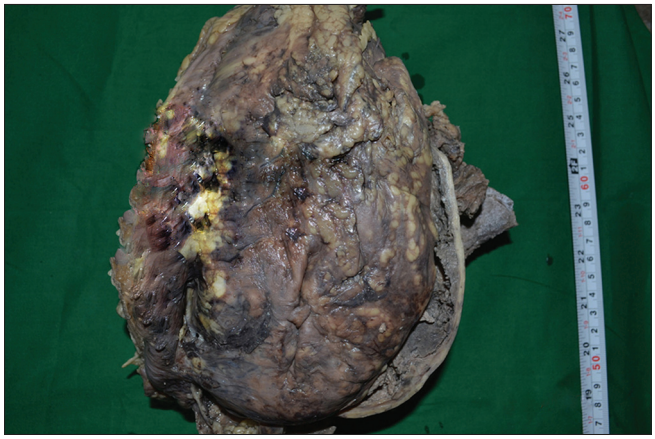

Figure 1: Gross appearance showing large mass with adherent colon

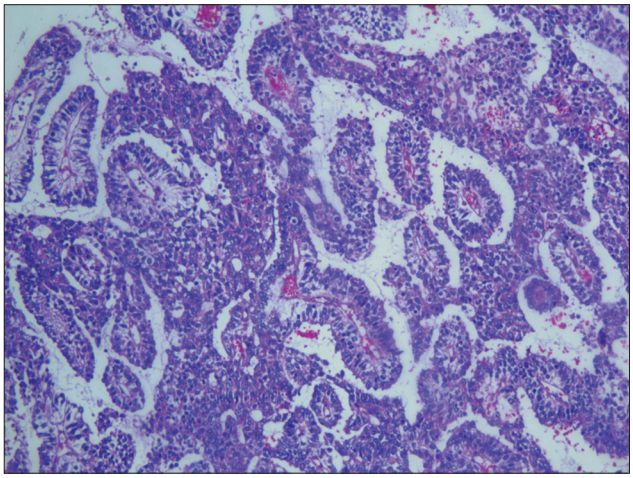

Figure 3: Cells arranged in papillary pattern (H and E, ×100)

Repeated biopsies yielded necrotic material only. With the clinical impression of retroperitoneal sarcoma, exploratory laparotomy was carried out. Macroscopic examination showed a large mass measuring 18 cm × 12 cm × 11 cm with adherent colon [Figure 1]. Cut section was necrotic and hemorrhagic with grey white areas in the periphery. Microscopy showed a neoplasm with extensive areas of necrosis and hemorrhage. Neoplastic cells were arranged in reticular [Figure 2] and papillary patterns [Figure 3]. Glomeruloid structures and many Schiller Duval bodies [Figure 4] were seen. Alpha fetoprotein (AFP) immunostain showed diffuse positivity [Figure 5]. Left ovarian cyst measured 8 cm × 5 cm × 4 cm. Microscopic examination showed serous cystadenoma. After the histology diagnosis, serum germ cell markers were checked. Serum AFP was markedly elevated while other markers were within normal range.

Germ cell tumors are classified as extra gonadal if there is no evidence of primary tumor in the testis or ovary. Extra gonadal germ cell tumors (EGCT) are rare and constitute 2-5% of all germ cell tumors. In children, benign and malignant EGCT occur equally in both sexes. In adults, only

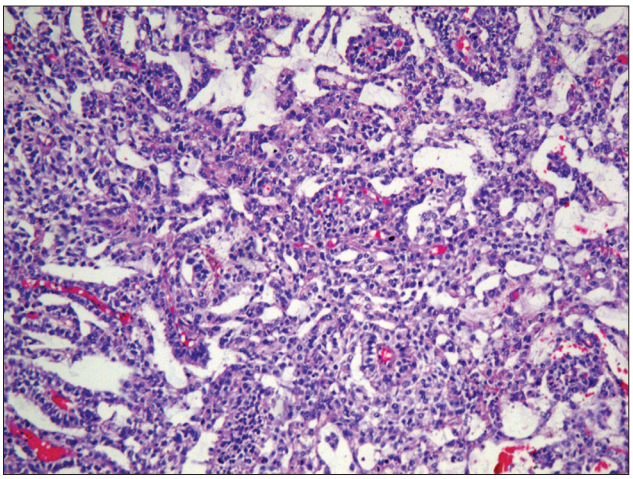

Figure 2: Tumor cells arranged in reticular pattern (H and E, ×100)

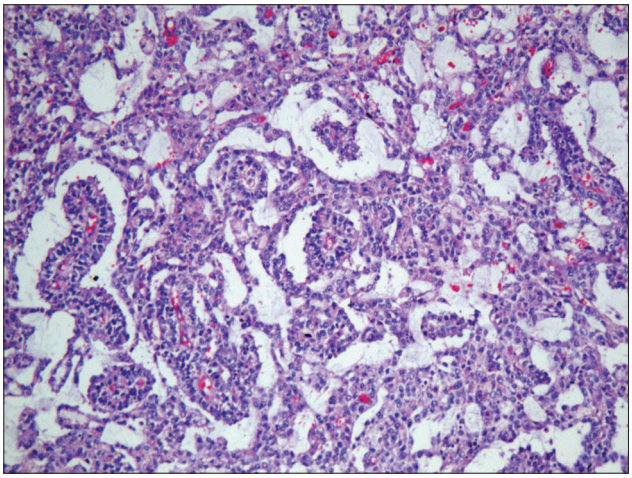

Figure 4: Photomicrograph showing Schiller Duval bodies (H and E, ×100)

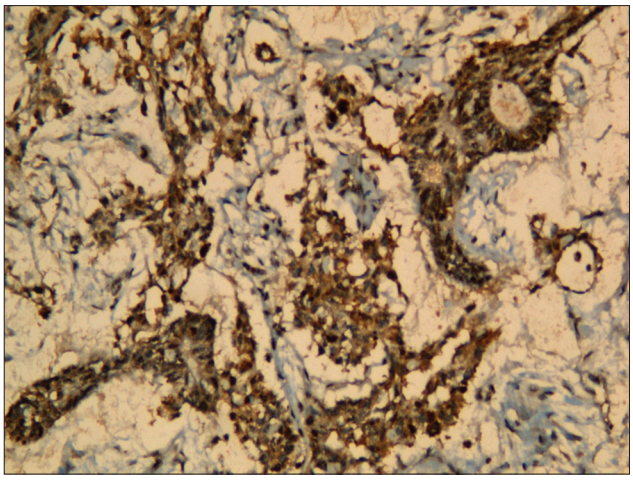

Figure 5: Immunostaining showing alpha fetoprotein positivity (IHC, ×200)

benign EGCT (teratomas) occur at equal frequency in both sexes. More than 90% of malignant EGCT in adults occur in males and most are considered to be metastasis from testicular germ cell tumors.[1,2] The occurrence of malignant EGCT in post-menopausal age group is distinctly uncommon.

EGCT occur mainly in the midline of the body-mediastinum, retroperitoneum and pineal gland. Majority of adult EGCT occur in males.[2] The only risk factor identified is Klinefelter syndrome, which is associated with non-seminomatous germ cell tumors.[3] There is no clear explanation regarding the pathogenesis of EGCT. According to the widely accepted theory, EGCT arise from malignant transformation of misplaced primordial germ cells. From the 4th to 6th week of embryogenesis the germ cells migrate through the mid-line dorsal mesentery. A remnant of tissue anywhere along the migration course can be the site of EGCT in future.[4] An alternative explanation for EGCT is the presence of metastasis from primary gonadal tumors.[1] The differentiation of metastatic gonadal tumor from a primary EGCT depends on adequate gonadal examination both clinically and radiologically. It may be difficult to distinguish true EGCT from metastatic tumors in which the primary gonadal tumor has regressed.

Retroperitoneal tumors usually present in late stages when the tumors become large enough to cause pressure symptoms. These large tumors can produce encasement, displacement, and compression of abdominal vessels. The imaging characteristics of retroperitoneal germ cell tumors are nonspecific and radiological examination cannot distinguish germ cell tumors from lymphoma, retroperitoneal metastasis, and retroperitoneal soft-tissue sarcoma.[5] Serum tumor marker human chorionic gonadotropin (beta hCG) will be elevated in choriocarcinoma, embryonal carcinoma and in 10% of cases of seminoma. Levels of AFP will be elevated in yolk sac tumor and embryonal carcinoma.[5]

Yolk sac tumors constitute 20% of all malignant germ cell tumors of the ovary. Most of the yolk sac tumors are diagnosed between 7 months and 3 years of age. There have been limited case reports of post-menopausal women diagnosed with pure yolk sac tumor of the ovary.[6,7] Although the histogenesis of the yolk sac tumor in a post-menopausal woman is unclear, a likely explanation is that it originates from the surface epithelium by a process of neoplastic dedifferentiation or transformation and therefore the histogenesis is totally different from that of germ cell neoplasms.[6,8] Rare cases of mixed yolk sac tumor within endometriosis, endometrioid carcinoma or mucinous cystadenoma of the ovary have been reported.[9,10] These cases also challenge the theory that yolk sac tumors originate only from germ cells, and present the possibility that they may originate from somatic mesodermal cells, a sort of retro differentiation or neometaplastic process.[6,8,9] Hybrid tumors with yolk sac component tend to be aggressive neoplasms with poor response to therapy.[10]

The majority of adult EGCT present with advanced local disease and distant metastasis. Since pure gonadal yolk sac tumor in a postmenopausal age is uncommon, exceptionally rare is its occurrence in an extra gonadal site in this age group. The histogenesis of post-menopausal yolk sac tumor is quite different from that of germ cell neoplasm in young female and thought to have a somatic rather than germ cell origin. When this tumor occurs in an unusual site in an extremely rare age group, a preoperative diagnosis is often missed. Serum markers are usually not checked. Extra gonadal non-seminomatous germ cell tumors are highly sensitive to cisplatin based chemotherapy regimens.[11] Serum tumor markers – serum AFP and/beta hCG are elevated in extra gonadal non-seminomatous germ cell tumors and provide diagnostic, staging, and prognostic information.

Renu Sukumaran, Thara Somanathan, Anitha Mathews, Jayasree Kattoor

Department of Pathology, Regional Cancer Centre, Trivandrum, Kerala, India

Correspondence to: Dr. Renu Sukumaran,

E-mail: renu.sukumaran@gmail.com

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