CASE REPORT

Diagnosis of Ovarian Yolk Sac Tumor on Intra-operative Cytology

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Abstract:

A 23-year-old female patient presented with chief complaints of painful discomfort in right lower abdomen and weakness. She was subjected to CT-scan of abdomen which revealed neoplastic lesion in the right adnexa. Cytological features from ovarian cystic fluid sample received intra-operatively from operation theatre showed features of yolk sac tumor (YST) which was later confirmed by histopathology examination. YST is a rare neoplasm, which mainly affects gonads of children and adolescents. When exfoliative cytology samples are examined, YSTs are most often identified in pleural, peritoneal or pericardial fluids. However, intraoperative ovarian cystic fluid aspirates have been rarely used for prompt cytological diagnosis. Rapid intraoperative diagnosis of the nature of the ovarian tumour in young woman avoids unnecessary removal of the contralateral ovary and helps in preservation of fertility. Sample obtained after aspiration could also be used for flow-cytometry and cytogenetic studies.

Keywords: Yolk sac tumor (YST), Ovarian germ cell tumor

Introduction:

Incidence of ovarian carcinoma in India was 5.6% in the year 2004[1]. Most of the ovarian carcinomas are usually detected when they have spread beyond the ovary. Gross examination and clinico-radiological impression cannot easily help to differentiate various types of ovarian tumors, needing further testing.

The cytological interpretation of ovarian neoplasm is both interesting and challenging[2]. Fine Needle Aspiration Cytology (FNAC) as a pre-operative investigation has been discouraged because deep location makes it relatively inaccessible for aspiration without image guidance. Further, this approach is controversial from safety point of view due to possibility of needle tract seeding and dissemination[3].

Intraoperative cytology should provide rapid diagnosis (within 20 minutes) without the fear of dissemination. Faster intra-operative diagnosis of the nature of the ovarian tumour avoids unnecessary removal of the contralateral ovary and helps in preservation of fertility. It can also be used for staging of malignancy, for postoperative follow-up and for recurrence[4]. In spite of all these advantages intra-operative cytology has been underutilized as a modality for primary diagnosis of ovarian carcinoma.

Case Report:

A 23-year-old young lady presented to the clinics with complaints of heaviness and discomfort in the right lower abdomen. In the past two years, she had recurrent episodes of abdominal pain. There was no family history of such complaints. Her menses were regular. She had generalised weakness and vomiting episodes for past three days. However, there was no fever or cough.

In the laboratory investigations, haemoglobin was 13.3 g/dl. Serum alphafetoprotein (AFP) level was markedly elevated to 2000 ng/ml. β-HCG was 1.20 mIU/ml

(normal), CA-125 was 114.9 U/ml(raised), CEA was 3.06 ng/ml (mildly raised) and LDH was 437.1 U/L (normal). Her liver function tests and renal function tests were normal. Random blood sugar levels were 100 mg/dl.

CT scan of abdomen showed a large well-defined rounded neoplastic mass which was partly cystic, partly solid of size 8.9 cm × 9.8 cm × 9.7 cm in the right adnexal region without ascites. The solid component was showing heterogeneous enhancement on post-contrast study. Other organs showed no abnormality. Sub-centimetre sized, small mesenteric lymphadenopathy was noted. Genitals were normal on examination.

The patient was subjected to right salpingo-oophorectomy surgery after consent. Intra-operatively, the cystic fluid from the right adnexal mass was aspirated by using a 22-G needle. Cytologist received 10 ml, hazy, reddish fluid with absence of coagulum.

Cytological smears (Figure 1) were highly cellular with malignant cells arranged in multilayered/ mono-layered sheets, papillae, clusters and loose aggregates. Tumor cells were seen surrounding hemorrhagic vascular spaces (Schiller Duval bodies). The peripheral cells lining the sheets showed rounding effect in hemorrhagic background. Individual tumor cells were round to oval with scant to moderate vacuolated cytoplasm with eccentric convoluted to bizarre nucleus, also round to oval hyperchromatic nucleus, coarse cuclear chromatin and inconspicuous nucleoli. No squamous cell component and lymphocytes were seen. Based on the cytological findings, a diagnosis of Yolk sac tumor (YST) was made.

Right cystic ovarian tumor mass with right fallopian tube was received for histopathology (Figure 2) examination. Gross examination showed right ovary measuring 11x10x4 cm. External surface was smooth, congested with an intact capsule. Cut section showed variegated appearance with solid-cystic tumor. Solid component showed papillary excrescences and gray-white tumor areas. Areas of haemorrhagic necrosis were noted. Cystic areas were filled with haemorrhagic fluid. Attached right fallopian tube (FT) was stretched over the ovarian surface.

Paraffin fixed, formalin-embedded H&E sections (Figure 3) showed solid-cystic ovarian tumour comprising polygonal cells with moderate amount of clear to amphophilic cytoplasm and mitotically-active moderately pleomorphic vesicular nuclei. The tumor cells were arranged in reticular, micro-cystic, tubulo-papillary pattern with focal sheets. Schiller-Duval bodies were seen with numerous hyaline globules. Stroma was myxoid with foci of haemorrhagic necrosis. Right Fallopian tube was free of tumor. On histopathology, it was confirmed as YST. Patient was discharged on the seventh day after an uneventful postoperative course and advised follow-up after chemotherapy and testing for a recurrence.

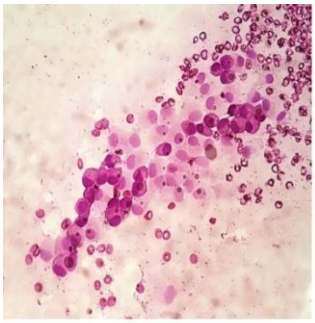

Fig. 1a

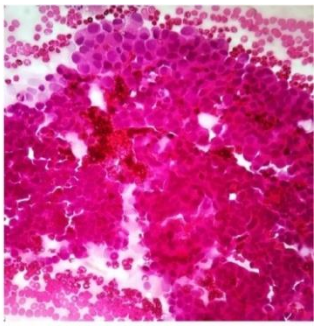

Fig. 1b

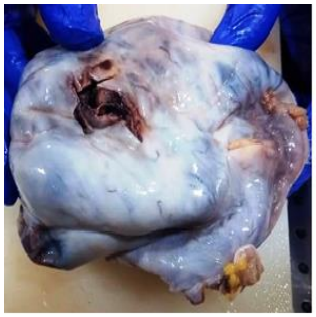

Fig. 2a

Fig. 2b

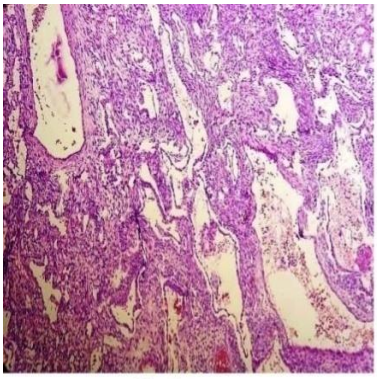
Fig.3a

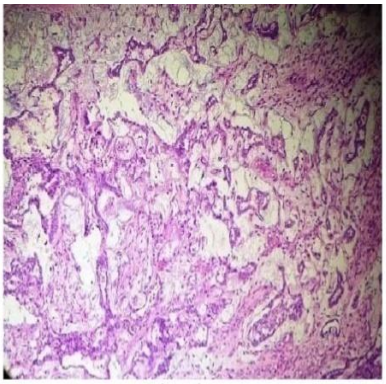
Fig.3b

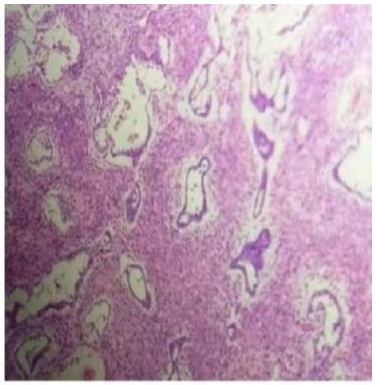
Fig.3c

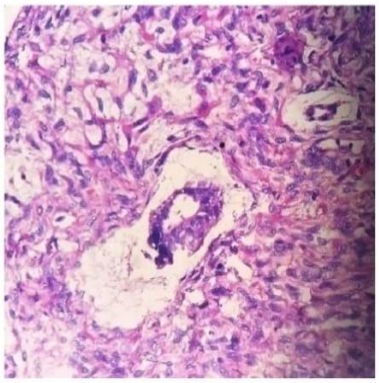
Fig.3d

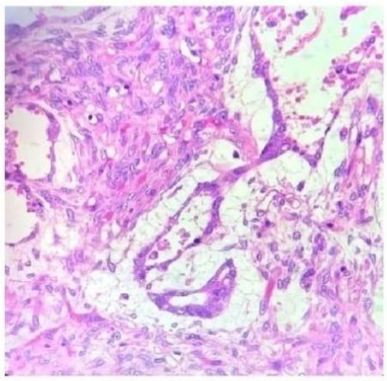
Fig.3e

Figure. 1: Cytological microphotograph of YST- 1a) shows small clusters of tumors cells with eccentric to pale nucleus, clear to vacuolated cytoplasm on a mucoid background (PAP, X100).1b) shows tumor cells surrounding irregular, hemorrhagic vascular spaces (Schiller Duval bodies/glomeruloid cell clusters). The peripheral cells lining the sheets show rounding effect (H&E, X400).

Figure. 2: Gross photograph of YST: **2a** shows right ovary measuring 11x10x4 cm with smooth, congested and intact capsule on external surface. **2b** shows cut section showing variegated appearance with solid-cystic tumor. Solid component showed papillary excrescences and gray-white tumor areas. Areas of haemorrhagic necrosis noted. Cystic areas were filled with haemorrhagic fluid.

Figure. 3: Histological microphotograph of YST-Tumor cells arranged in reticular **(3a)**, micro-cystic with myxoid areas **(3b)**, tubulo-papillary pattern **(3c)**, Schiller Duval bodies **(3d)**. tubular pattern **(3e)** (H&E, X400).

Discussion:

Ovarian germinal neoplasms differ from adenocarcinomas in following ways: occurrence at younger age (women of 18 to 24 years old), a diagnosis in an earlier stage (70 to 80 at stage I), a better prognosis, a high chemo-sensitivity, possibility of fertility sparing surgery rather than radical one and presence of specific tumor markers (AFP in yolk sac tumors)[5]. YST is a non-dysgerminoma malignancy arising from endodermal sinus, most often unilateral with a diameter of 5-50 cm. The typical clinical presentation is a rapid abdomino-pelvic distension. Pain is the main revealing symptom and could require urgent surgical intervention, especially in case of ovarian torsion. Other symptoms could include: pelvic mass, metrorrhagia, ascites, fever and symptoms related to infection or rupture of tumor mass[5].

Radiological investigations are first-line investigations supplemented by cytology. Histopathology is gold-standard for YST diagnosis. Malignant germ cell tumors account for about 3% of paediatric malignancies, with the commonest being YST (Endodermal Sinus Tumour).

Teilum in 1960 described this tumor in the testes and ovaries of young children.[6]Apart from gonadal sites, some extra-gonadal YST sites such as the vulva, vagina, broad ligament, prostate, cervix, saccro-coc-cygeal and retroperitoneum region have also been documented[6].

The cytological findings of the YST reveals clusters of cells in a glandular appearance with large pleomorphic cells, vacuolated cytoplasm and PAS positive, diastase-resistant hyaline globules[7].

YST has a variable histological pattern like reticular, solid, pseudo-papillary and poly-vesicular vitelline, which reflects toward extra-embryonic yolk sac structure. The differential diagnoses of YST are poorly-differentiated adenocarcinoma, dysgerminoma and embryonal carcinoma. YST mixed with other germ cell tumor is seen in elderly women with an aggressive course.

The tumor cells of embryonal carcinoma show marked nuclear pleomorphism and blurred nuclear membranes, cellular cohesion with severe overlapping with branching capillaries whereas, dysgerminoma shows cells in dyscohesive groups or singly arranged. The dysgerminoma tumor cells in a tigroid background show cytoplasmic glycogenic vacuolation with a large hyperchromatic, pleomorphic nucleus and lymphocytes/ plasma cells.

Cytological characteristics of YST may be confused with clear cell carcinoma of the ovary. Cytologically, clear cell carcinoma show more marked cohesiveness of tumor cells with less marked pleomorphism, well-preserved cell borders, fine vesicular cytoplasm, evenly thickened nuclear membrane, fewer nucleoli and multinucleated giant cells. In our examination, cells with large cytoplasmic vacuolation were infrequent and few hobnail shaped tumor cells were observed in the cases examined[7]. On the other hand, YST showed more dyscohesive cells with marked cellular pleomorphism, usually faint cell borders and no thickening of nuclear membrane. Numerous nucleoli and multinucleated giant cells were frequently found with marked cellular and nuclear atypia. These findings indicate that detailed cytological examination can provide a means for differential diagnosis of clear cell carcinoma and YST, supplementing other clinical information[7].

Yolk sac tumor tends to recur locally and also have a high incidence of metastatic disease at the time of presentation[6]. Complete excision should be attempted in a malignant lesion[7-8]. Adjuvant chemotherapy has been most extensively used in YST. Metastatic lesions may require palliative treatment with local radiation. Early detection and therapy are important because it is highly aggressive tumor that shows good response to surgery and chemotherapy[7,8].

Serum AFP seen in pure YST is always more than 1000ng/ml. AFP in yolk sac tumour can be detected in serum, tumour and ascitic fluid. AFP levels are directly proportional to the bulk of YST. In the follow up, serum AFP levels start increasing 8-29 weeks prior to

clinical recurrence[9].The national comprehensive cancer network (2016) recommends surveillance of AFP every 2-4 months for over two years' in patients who achieve complete clinical response. To detect eventual recurrence, imaging could be considered since many case reports suggest that patients who have received chemotherapy for germ cell tumors may later present with growing teratoma syndrome[10].

Conclusion:

Ovarian yolk sac tumor is the second germinal malignancy after dysgerminoma. Every ovarian mass should be assessed with serum tumor markers to distinguish epithelial and nonepithelial malignancies in order to allow fertility sparing surgery. The standard of care is a fertility sparing surgery with adjuvant chemotherapy. A rapid and specific diagnosis of ovarian neoplasm can be made by an intra-operative FNAC which may be extremely beneficial, cost-effective and spare the patient a host of diagnostic procedures and aid in planning definitive therapy, which may include chemotherapy and radiotherapy, in addition to the extent of surgical resection.

Conflict of Interests-Nil
Sources of Support- Nil

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