
CASE REPORT**Diagnosis of Ovarian Yolk Sac Tumour on Intra-Operative Cytology**

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Abstract:

A 23-year-old female patient presented with chief complaints of discomfort in right lower abdomen and weakness. She was subjected to computerized tomography scan abdomen which revealed neoplastic lesion in right adnexa. Cytological features from ovarian cystic fluid sample received intra-operatively from Ovarian Tumour (OT) showed features of Yolk Sac Tumour (YST) which was later confirmed on histopathology. YST is a rare neoplasm, which mainly affects gonads of children and adolescents. When exfoliated cytological samples are considered, 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 OT in young woman avoids unnecessary removal of the contralateral ovary and helps in preservation of fertility. Aspirate sample obtained can also be used for flow-cytometry and cytogenetic studies.

Keywords: Yolk Sac Tumour, Ovarian Germ Cell Tumour, Fertility

Introduction:

Ovarian cancer is the seventh most commonly diagnosed cancer among women in the world. The highest age-adjusted incidence rates are observed in developed parts of the world with rates generally exceeding 8 per 100,000. Rates are lowest in Asia and Africa (≤ 3 per 100,000) [1]. In 2018, 4.4% of entire cancer-related mortality among worldly women was attributed to ovarian cancer [2]. Most

of the ovarian carcinomas are usually detected when they have spread beyond the ovary. Ovarian tumours cannot be easily distinguished from one another on the basis of their clinical and gross characteristics alone. 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 approach is controversial from safety point of view due to possibility of needle tract seeding and dissemination [3].

But intraoperative cytology will provide rapid diagnosis (within 20 minutes) without the fear of dissemination. Faster intraoperative 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 our clinic with complaints of heaviness and discomfort in the

right lower abdomen with tense on and off painful abdomen since the last two years. No family history noted of such complaints. Her menses were regular. She had generalized weakness and vomiting episodes for the previous three days. There was no fever or cough.

Her hemoglobin was 13.3 g/dl. Serum Alpha-fetoprotein (AFP) level was markedly elevated to 2000 ng/ml. Beta-Human Chorionic Gonadotropin (β -HCG) was 1.20 mIU/ml (normal), Cancer Antigen (CA)-125 was 114.9 U/ml (raised), Carcinoembryonic Antigen (CEA) was 3.06 ng/ml (mildly raised) and Lactic acid dehydrogenase (LDH) was 437.1 U/L (normal). Her liver function tests and renal function tests were normal. Random blood sugar level was 100 mg/dl.

Computerized Tomography (CT) abdomen showed a large well-defined rounded neoplastic mass which was partly cystic, partly solid of size 8.9 cm \times 9.8 cm \times 9.7 cm in the right adnexal region without ascites. The solid component was showing heterogenous enhancement on post-contrast study. Other organs showed no abnormality. Sub-centimeter sized, small mesenteric lymphadenopathy noted. Genitals were normal on examination. The patient was subjected to right salphingo-oophorectomy surgery after consent. Intra-operatively, the cystic fluid from the right adnexal mass was aspirated by using a 22-G needle. Cytologists received 10 ml, hazy, reddish fluid with absence of coagulum.

Cytological smears (Fig. 1) were highly cellular with malignant cells arranged in multilayered/mono-layered sheets, papillae, clusters, loose aggregates. Tumour cells were seen, surrounding hemorrhagic vascular spaces (Schiller Duval

bodies). The peripheral cells lining the sheets showed rounding effect in hemorrhagic background. Individual tumour cells were round to oval with scant to moderate vacuolated cytoplasm with eccentric convoluted to bizarre nucleus, also round to oval hyperchromatic nucleus, coarse chromatin, inconspicuous nucleoli. No squamous cell component and lymphocytes were seen. Based on the cytological findings, a diagnosis of Yolk Sac Tumour (YST) was made.

Right cystic ovarian tumour mass with right fallopian tube was received in histopathology (Fig. 2). Gross examination showed right ovary measuring 11 \times 10 \times 4 cm. External surface is smooth, congested with an intact capsule. Cut section shows variegated appearance with solid-cystic tumour. Solid component showed papillary excrescences and gray-white tumour areas. Areas of haemorrhagic necrosis noted. Cystic areas were filled with haemorrhagic fluid. Attached Fallopian Tube (FT) was stretched over the ovarian surface. Paraffin fixed, formalin-embedded H&E sections (Fig. 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 tumour 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 FT was free of tumour. On histopathology, it was confirmed as YST. Patient was discharged on the seventh day after an uneventful postoperative course and advised follow-up for chemotherapy and testing for recurrence.

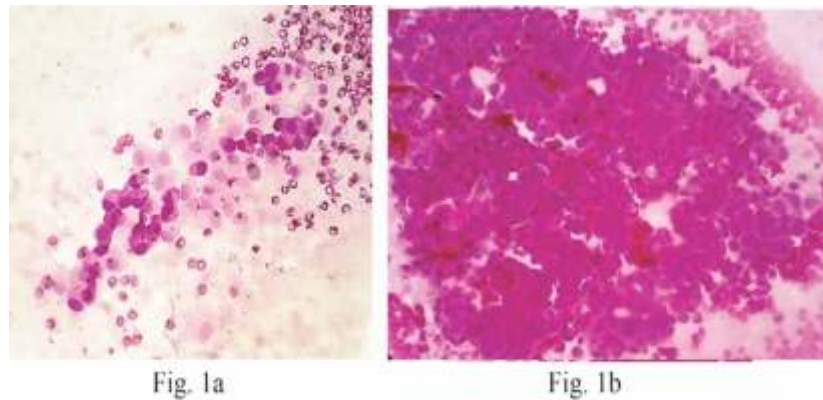


Fig. 1: Cytological Microphotograph of YST: Shows small clusters of tumours cells with eccentric, pale nucleus, clear to vacuolated cytoplasm on a mucoid background (PAP, $\times 400$). Fig. 1b shows tumour cells that surround the irregular, hemorrhagic vascular spaces (Schiller Duval bodies/ glomeruloid cell clusters). The peripheral cells lining the sheets show rounding effect (H&E, X100).

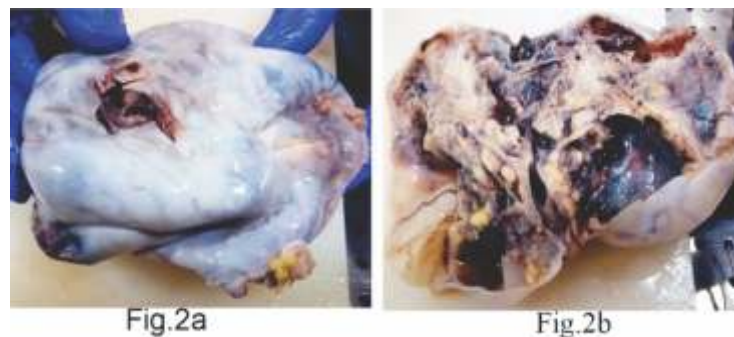


Fig. 2: Gross Photograph of YST: Shows right ovary measuring 11x10x4 cm with smooth, congested and intact capsule on external surface. Fig. 2b shows ovarian cut section showing variegated appearance with solid-cystic tumour. Solid component showed papillary excrescences and gray-white tumour areas. Areas of hemorrhagic tumour necrosis noted. Cystic areas were filled with hemorrhagic fluid.

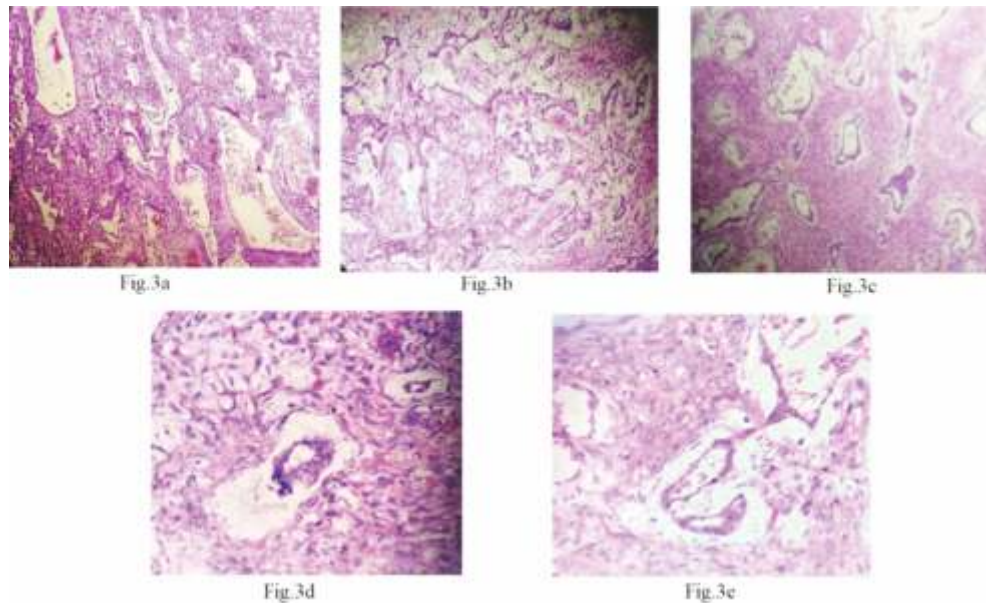


Fig. 3: Histological Microphotograph of YST: Tumour cells arranged in reticular (3a), micro-cystic with myxoid areas (3b), tubulo-papillary pattern (3c), Schiller Duval bodies (3d), Tubular pattern (3e) (H&E, X400).

Discussion:

Ovarian germinal neoplasms differ from adenocarcinomas: 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 tumour markers (AFP in YST) [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 sometimes lead to urgent surgery especially in case of ovarian torsion. Other symptoms could include: pelvic mass, metrorrhagia, ascites, fever, symptoms related to infection or rupture of tumour mass [5].

Radiological investigations are first-line investigations supplemented by cytology. Histopathology is gold-standard for YST diagnosis. Malignant germ cell tumours account for about 3% of pediatric malignancies, with the commonest being YST (Endodermal Sinus Tumour). Teilum in 1960 described this tumour in the testes of young children and in the ovaries [6]. Apart from gonadal sites, some extra-gonadal YST sites such as the vulva, vagina, broad ligament, prostate, cervix, sacro-coccygeal 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

vitalize, 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 tumour is seen in elderly women with an aggressive course.

The tumour 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, with cytoplasmic glycogen vacuoles and a large pleomorphic and hyperchromatic nucleus with lymphocytes/ plasma cells in a tigroid background.

Cytological characteristics of YST may be confused with clear cell carcinoma of the ovary. Cytologically, clear cell carcinoma shows more marked cohesiveness of tumour cells with less marked pleomorphism, well-preserved cell borders, fine vesicular cytoplasm, evenly thickened nuclear membrane, fewer nucleoli and multinucleated giant cells. Cells with large cytoplasmic vacuolation were infrequent and few hobnail shaped tumour cells [7]. On the other hand, YST showed more dyscohesive cells with marked cellular pleomorphism, usually faint cell borders, no thickening of nuclear membrane. Numerous nucleoli and multinucleated giant cells are 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].

YST 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 tumour that shows good response to surgery and chemotherapy [7-8].

Serum AFP seen in pure YST is always more than 1000 ng/ml. AFP in YST can be demonstrated 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 in patients who achieved complete clinical response, a surveillance of AFP every 2 to 4 months during two years. To detect eventual recurrence, imaging could be considered since many case reports suggest that patients who have received chemotherapy for germ cell tumours may later present with growing teratoma syndrome [10].

Conclusion:

A rapid and specific diagnosis of ovarian neoplasm can be made by an intra-operative FNAC. It is extremely beneficial, cost-effective and spares the patient from a host of diagnostic procedures. Intra-operative FNAC can successfully aid in planning definitive therapy which include chemotherapy and radiotherapy, in addition to the extent of surgical resection.

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