



Dysgerminoma with Syncytiotrophoblastic Giant Cells Associated with a Concurrent Ectopic Pregnancy

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Abstract

Background Dysgerminomas constitute around 1–2% of all germ cell tumours. It is very very rare to have dysgerminoma with concurrent pregnancy with an incidence of 0.2–1 per 100,000 pregnancies. It is extremely difficult to conceive with no assisted reproductive interventions and carry it till completion with no complications in a concurrent dysgerminoma. Dysgerminoma has a characteristic specific histomorphology and is easy to diagnose. However, occasionally, syncytiotrophoblastic differentiation can be seen in dysgerminoma although it is a rare histopathological finding. Also, the raised serum B-HCG levels due to the syncytiotrophoblast giant cells seen can lead to a diagnostic dilemma.

Clinical presentation Here we report a case of a 27-year-old 8-week pregnant female who came to the hospital with chief complaints of left-sided abdominal pain and a lump abdomen. Clinical and radiological examination revealed a left ovarian tumour of malignant aetiology with the presence of right ectopic pregnancy. A staging laparotomy with left salpingoophorectomy was performed and sent for histopathological examination. It was reported as dysgerminoma with syncytiotrophoblastic giant cells. The right fallopian tube showed products of conception. Finally, she was planned for adjuvant chemotherapy and serial B-HCG levels.

Summary This case is reported not only just for its rare histopathological finding but also for the diagnostic dilemma it causes both to the surgeon as well as the pathologist. There are various factors which can act as prognosticators such as early suspicion of a tumor, radiological findings, surgery, histopathological examination, and oncology team.

Keywords Dysgerminoma · Germ cell tumour · Syncytiotrophoblast · Giant cell

Introduction

Ovarian germ cell tumours (GCT) comprise of most common dysgerminomas, Yolk sac tumours, mixed germ cell tumors, embryonal carcinoma and teratomas respectively [1]. Dysgerminomas usually occur in the second to third decade of life and are usually unilateral, although bilateral cases are seen in around 15% [2]. It comprises 2% of all ovarian tumours [1, 2]. However, it is extremely rare to have dysgerminoma associated with pregnancy with an incidence

of approximately 0.2–1 per 100,000 pregnancies [3]. These tumours can be of variable size ranging from a few centimetres to huge size nearly filling the abdomen. Timely and accurate diagnosis is important because it is mainly found in females of reproductive age and responds well to treatment, avoiding complications like infertility and mortality at a younger age [1]. There are various factors which can act as prognosticators such as early suspicion of a tumour, radiological findings, surgery, histopathological examination, and oncology team. This case is reported not just for its rare histopathological finding but the diagnostic dilemma it causes both to the surgeon as well as the pathologist.

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Case presentation

A 27-year-old pregnant female presented with chief complaints of left-sided abdominal pain with a lump abdomen which was increasing in size for 2 months. It was

associated with nausea, vomiting and amenorrhea for 2 months. She also had a history of irregular menstrual bleeding but no other symptoms of bladder/bowel compression were seen.

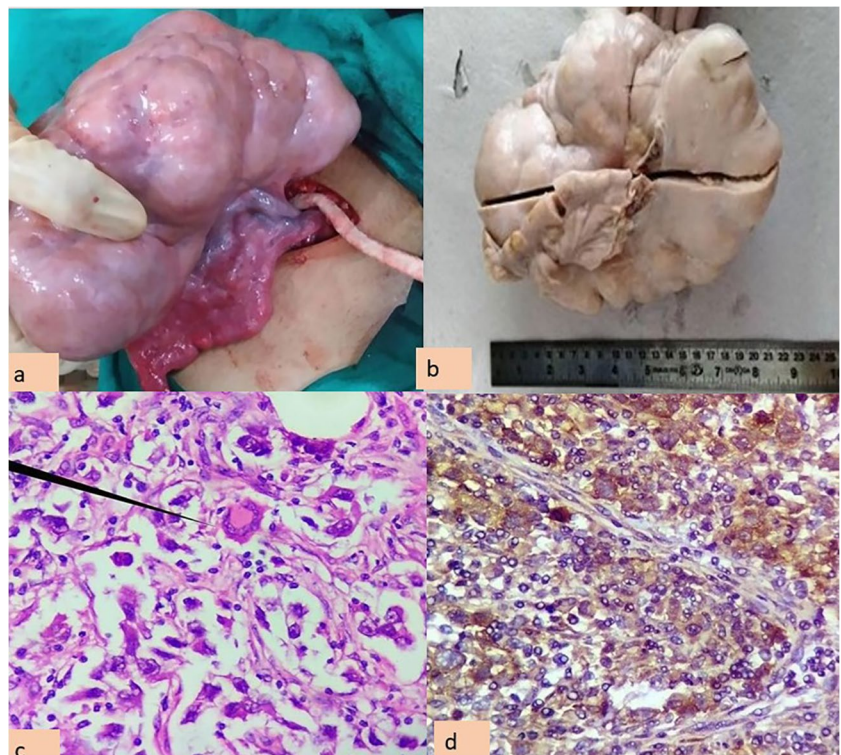
On clinical examination, vitals were stable. Abdominal examination revealed a firm, irregular, non-tender, mobile mass in the left adnexa, approximately 28 weeks in size of the pregnant uterus. It was non-adherent to the skin. Therefore, radiological examination was advised which on ultrasonography of the abdomen showed a large hypoechoic mass in the pelvis measuring $17 \times 15 \times 10$ cm arising from the left adnexa and reaching up to the epigastrium. Also seen was an ectopic pregnancy in the right fallopian tube. There was 50 ml of ascitic fluid found. Further, a computed tomography (CT) scan revealed a hyperechoic irregular mass arising from the left adnexa measuring $18.5 \times 14.3 \times 9$ cm suggestive of a neoplastic germ cell tumour.

The patient was investigated for routine investigations and was within limits. Alkaline phosphatase (ALP) 325 IU/l, beta-HCG 435 mIU/ml, alpha-fetoprotein 65 ng/ml, and CA-125 49 U/ml. Raised serum B-HCG was suspected to be due to concurrent pregnancy.

The patient was taken up for exploratory laparotomy with left salpingo-oophorectomy and right salpingectomy and the specimen was sent for histopathological

examination. The gross examination of the specimen received showed a left ovarian tumour measuring $19 \times 14 \times 8$ cm. The outer surface was encapsulated, greyish tan, bosselated with congested areas. The cut section showed cystic, solid and hemorrhagic areas (Fig. 1a,b). Multiple sections were given from representative areas for microscopic examination. H&E stained sections from the tumour showed nests of round to polyhedral cells divided by fibrous septa infiltrated by lymphocytes (Fig. 1c). These tumour cells had clear cytoplasm, vesicular chromatin and prominent nucleoli along with diffusely scattered multinucleated giant cells, reminiscent of syncytiotrophoblasts. There was no component of any other germ cell tumour like yolk sac/teratoma/embryonal carcinoma or choriocarcinoma histologically observed in the multiple sections. There was no extracapsular invasion of the tumour. The fallopian tubes, omentum, lymph nodes and peritoneal washings were free of tumours. Therefore, a diagnosis of dysgerminoma with syncytiotrophoblastic giant cells was suggested and further immunohistochemical markers were advised for confirmation. The tumour cells showed positivity for PLAP, CD117 (Fig. 1d), and SALL4 and were negative for cytokeratin, CD30, B-HCG and AFP. Thus a final diagnosis of dysgerminoma, left ovary was rendered. The patient was advised neoadjuvant chemotherapy and was

Fig. 1 a,b Gross examination shows an encapsulated grey tan tumour with bosselated outer surface (a). The cut section showed a firm tan-coloured fleshy appearance with areas of haemorrhage and cystic change. a-intact ovary, b,c-cut section of tumour (b). c H&E stained section shows tumour cells arranged in the nest and separated by fibrous septa along with many Syncytiotrophoblastic giant cells in the background of tumour cells (arrow). (H&E stain, 40X). d The section examined shows tumour cells positive for Immunohistochemistry CD-117 (IHC CD117, 40 X)



followed up with a reduction in serial B-HCG and is recovering well.

Discussion

Dysgerminoma is a rare malignant ovarian tumour comprising less than 5% of all ovarian malignancies [2]. These lesions are most commonly found in adolescents and young females with approximately 2/3rd of cases in less than 20 years of age [3]. It is rare to have concurrent pregnancy with dysgerminoma [4]. Zhang et al. report a viable pregnancy with ovarian dysgerminoma in a 25-year-old pregnant woman [4]. Chen et al. reported a case of a 23-year-old pregnant female with dysgerminoma of the right ovary with simultaneous abdominal desmoid tumour [3]. Reda et al. diagnosed a case of dysgerminoma of the right ovary with a viable intrauterine pregnancy at 10 weeks [5]. Natural conception is possible in females with dysgerminoma but it can be difficult in most cases with variable prognosis of mother, fetus and the tumour [5]. The pregnancies occurring in such cases can be ectopic and can lead to complications like rupture and ovarian torsion. It can also lead to diagnostic dilemmas for the clinician. The ideal treatment for the mother can be compromised due to the ongoing pregnancy.

It usually presents with nonspecific findings such as abdominal distention, mass or abdominal pain. Some patients have menstrual abnormalities or compression symptoms [6]. Radiological examination can give a clue to malignant aetiology. However, a CT scan of the abdomen and pelvis may pose an increased risk to the developing fetus, although not very significant [5].

MRI is a sensitive test with an accuracy of 98% for diagnosing ovarian tumours. However, it has been mistaken for fibroid, especially when cystic change is seen [7]. A high titre of B-HCG results sometimes may have clinical features similar to either ectopic pregnancy or hydatiform mole [8]. Serial B-HCG titre should be performed to follow such patients as around 3% of patients with a pure dysgerminoma ovary may have an increased amount of B-HCG in the blood, secreted by syncytiotrophoblastic cells within the tumour tissue [9].

Histopathology can help solve such diagnostic dilemmas. On gross examination, the tumour has a smooth capsule, although it may have a nodular appearance. On microscopy, the tumour cells are large round to polygonal with vesicular nuclei containing one or more nucleoli, clear to granular cytoplasm. Lymphocytic infiltrates are seen within the fibrous septae, which is a characteristic histological finding [9]. In around 5% of dysgerminomas, syncytiotrophoblastic giant cells, the source of increased levels of gonadotrophin are seen [9]. There are a few cases reported of dysgerminoma with syncytiotrophoblast giant cells which are summarized in Table 1. Rarely, dysgerminomas may have syncytiotrophoblastic giant cells infiltrating tumour cells which produce B-HCG. Therefore, it is empirical to have a pre-operative evaluation of these markers in cases of suspected ovarian dysgerminomas.

Immunohistochemical stains are needed to confirm the diagnosis of pure dysgerminoma with the exclusion of other associated mixed germ cell tumour components. The tumour cells are positive for PLAP, CD117, SALL4, D2-40, OCT-4, and NANOG and negative for CD30, CK, B-HCG, EMA, ER and PR [9].

Although this is a highly malignant tumour but it responds well to treatment. These tumours are radio-sensitive with a good prognosis if treated timely. Factors like the large size of the tumour and the advanced stage at presentation of the tumour are bad prognostic indicators [5]. Unilateral oophorectomy and surgical staging are the minimal surgeries prescribed in cases of ovarian germ cell tumours and dysgerminomas as fertility preservation in younger age group females is the main issue [6].

Conclusion

Dysgerminoma ovary is an aggressive neoplasm occurring in young females. It is extremely rare to have concurrent pregnancy associated with dysgerminoma and it leads to additional complications like torsion ovary. Thus, a timely intervention and fertility-sparing surgery are required in such cases. It has a characteristic histopathological finding

Table 1 Reported cases of dysgerminoma with syncytiotrophoblastic giant cells

Author(s)	Year	Title	Clinical presentation	Serum markers
Song et al. [8]	2007	Dysgerminoma of the ovary with precocious puberty: A case report	A 6-year-old girl contracted ovarian Dysgerminoma with precocious puberty	β -human chorionic gonadotropin, α -fetoprotein and estradiol were high
Chakrabarti et al. [10]	2009	Fine needle aspiration diagnosis of bilateral dysgerminoma with syncytiotrophoblastic giant cells	A 34-year-old woman presenting with an abdominal lump, ascites, and abdominal pain bilateral ovarian mass	Elevated urinary and serum hCG levels
Rozenholc et al. [11]	2012	A pelvic mass on ultrasonography and high human chorionic gonadotropin level: not always an ectopic pregnancy	A 24-year-old patient with 7-week amenorrhoea was consulted for vaginal bleeding without abdominal pain	The serum β -hCG level was 11 998 IU/l
Kohmanee et al. [12]	2015	Pure gonadal dysgenesis (46 XX type) with a familial pattern	A 13-year-old girl mentioned no secondary sexual characteristics	LH and FSH were normal, and β -hCG was not done
Morimura et al. [13]	1998	Dysgerminoma with syncytiotrophoblastic giant cells arising from 46, xx pure gonadal dysgenesis	An 18-year-old phenotypic female of normal height without somatic anomalies with nonfunctional ovaries with a right ovarian tumour and left streak gonad	Serum hCG was elevated
Brettell et al. [14]	1984	Dysgerminoma with syncytiotrophoblastic giant cells presenting as a hydatidiform mole	Case series of 11 cases all in stage Ia with unilateral salpingo-oophorectomy, and the Stage IC reported, present as a hydatidiform mole	Raise hCG level; highest ever reported preoperative beta-hCG
Kaplan et al. [15]	1981	Dysgerminoma with giant cells. A case report with immunoperoxidase	A 15-year-old female with a positive pregnancy test was found to have a large ovarian tumour	HCG was demonstrated within and confined to the giant cells. alpha-fetoprotein were negative
Zarabi et al. [16]	1984	Human chorionic gonadotropin-secreting pure dysgerminoma	A young woman with a preoperative diagnosis of molar pregnancy with pure dysgerminoma in the right ovary	HCG was positive

but sometimes may have syncytiotrophoblastic giant cells along with tumour cells.

Abbreviations B- HCG-Beta: Human chorionic gonadotrophin; AFP: Alpha feto protein; IHC: Immunohistochemistry; USG: Ultrasound; CT: Computed tomography

Author Contribution Dr. Durre was responsible for the literature search and drafting of the manuscript. Dr. Noora was involved in the drafting of the manuscript and diagnosis. Dr. Sadaf was involved in reviewing, editing the manuscript and interpreting of smears. Dr. Mahboob was involved in reviewing and overall approval of the article.

Data Availability We declare if data is being shared, we shall provide the data.

Declarations

Ethics Approval All authors state that they contributed to this publication according to the guidelines of the journal and that no part of this manuscript was plagiarized.

1. This material is the author's original work, which has not been previously published elsewhere.
2. The paper is not currently being considered for publication elsewhere.
3. The paper reflects the authors' research and analysis truthfully and completely.
4. The paper properly credits the meaningful contributions of co-authors and co-researchers.
5. The results are appropriately placed in the context of prior and existing research.
6. All sources used are properly disclosed (correct citation). Copying of text must be indicated as such by using quotation marks and giving proper reference.

Consent for Publication The patient has given consent to publish the article, and she has no issue.

Conflict of Interest The authors declare no competing interests.

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