Unilateral ovarian agenesis and clear cell type epithelioid leiomyoma of uterus mimicking ovarian malignancy

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Abstract
A case of unilateral absent ovary together with clear cell type epithelioid leiomyoma of uterus mimicking ovarian malignancy discovered during laparotomy is presented. Unilateral absence of an ovary is an extremely rare finding. Although the exact pathophysiological mechanism is not known, it could result from a defect in embryological development or asymptomatic torsion of ovary. Clear cell type epithelioid leiomyoma of uterus is also a rare variant, composed of round or polygonal 'clear' cells rather than typical spindle-shaped cells and ultra structurally differs from non-uterine counterparts.
Keywords: Ovarian agenesis, Clear cell epithelioid leiomyoma.

Introduction

Developmental abnormalities have been observed at all points along the female reproductive tract, including the external genitalia, vagina, cervix, uterus, fallopian tubes, and ovaries. Abnormalities including organs which originate from the Mullerian ducts were most commonly observed. These occur in 0.5% of women.[1] Complex anomalies involving the urinary system, fallopian tubes, ovaries and vagina occur less frequently.[2] Unilateral absence of an ovary is an extremely rare finding and describes the absence of one ovary, with or without the absence of the fallopian tube.1 The incidence has been suggested to be approximately 1in 11240 women.[3] Although the exact pathophysiological mechanism is not known it could result from a defect in embryological development. Asymptomatic torsion of ovary during prenatal and postnatal period is another proposed mechanism.[4]
While epithelioid smooth-muscle tumours of the gastrointestinal tract have been well studied similar tumours of the uterus have been reported very rarely.[5] Clear cell type epithelioid leiomyoma of uterus is also a rare variant which ultrastructurally differs from nonuterine counterparts.[5,6] In this case the occurrence of these extremely uncommon conditions in the same patient along with the difficulty in differential diagnosis from an ovarian malignancy was reported.To the best of our knowledge, this is the first report of such a confluence of these conditions. Patient consent form and IRB approval were obtained.

Case Report

A 48 year old woman, gravida 3, para 2, was admitted to emergency service with the complaint of pelvic pain, nausea and vomiting for two days. Gynaecologic history was not significant. She had no past surgical history, regular monthly menses and no complaints of dysmenorrhoea or dyspareunia. The patient was born to unrelated parents and was the product of a full-term uneventful pregnancy. Her growth pattern during childhood and adolescence was normal. There was no history of maternal drug use, exposure to toxic materials in utero or any unusual childhood illness. A general physical

examination was normal. Since our preoperative diagnosis was ovarian malignancy and all the clinical and laboratory findings were also in favour of ovarian malignancy, MRI was not done to differentiate between normal smooth muscles of uterus and clear cell type Epithelioid Leiomyoma. Bimanual examination revealed a tender solid mass in the right adnexal region extending to the umbilicus. Laboratory workup revealed low Hb 9.4 g/dl. CA-125 was 38.8 U/mL (upper limit 21 U/mL). Transvaginal ultrasonographic examination demonstrated 150x120x110 mm solid mass with irregular borders and cystic dilatations in the right ovary and ascites. No significant pathology was reported regarding left ovary and uterus. Doppler values of the mass were compatible with a benign mass (RI 0.54). Pelvic computerized tomography examination, in accordance with ultrasonographic examination, showed a 150x80x70 mm solid mass with multiple cystic dilatations resembling ovarian malignancy. Colonoscopy was normal.

Explorative laparotomy was planned with the presumed diagnosis of pelvic mass. Two liters of haemorrhagic ascites fluid was drained and sent for cytological examination. A 150x100 mm solid mass with irregular borders and containing haemorrhagic degenerative regions originating from right cornual region of uterus was observed. Uterus, left ovary, and bilateral fallopian tubes were normal in appearance. The right ovary was absent (Figure: a-b).

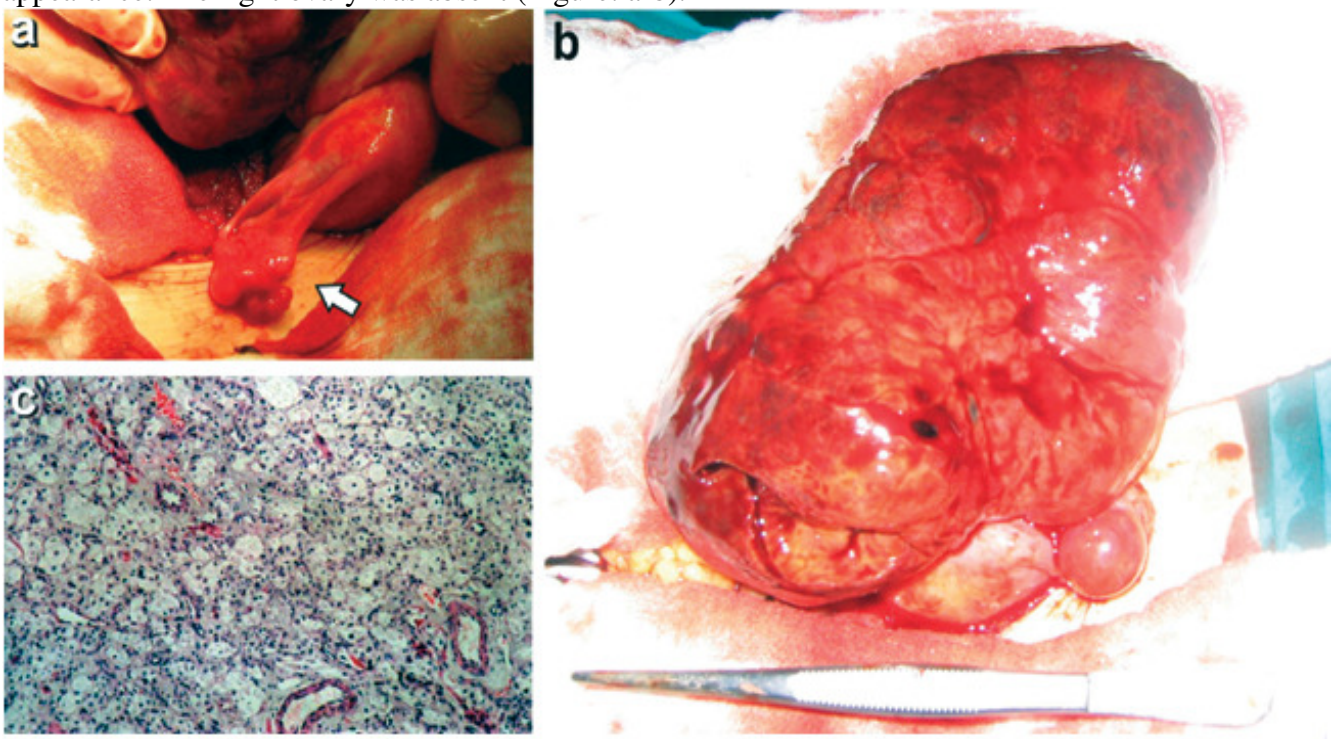

Figure: (a) Right fallopian tube without ovary (b). Epithelioid leiomyoma with uterine pedicle. (c). Tumour cells have a round shape and artifactually clear cytoplasm (HE X100).

Despite an attentive search, no ovarian remnant, pedicle or utero-ovarian ligament was identified. Also any acute finding of torsion or necrosis was not observed at location of right ovary.

No tumour infiltration was observed in the other abdominal organs. Frozen section gave no result about the nature of the mass. So total abdominal hysterectomy, bilateral salpingectomy and left oophorectomy, omentectomy, pelvic and paraaortic lymph node dissection were performed. Frozen sections of lymph nodes were negative.

Final pathological examination of mass was reported as epithelioid (clear cell) leiomyoma of uterus (Figure: c). Among the histologically normal smooth muscle fibers neoplastic epithelial tumour cells was observed in the oedematous stroma. These moderately atypical epithelial cells had vesicular nuclei with mild pleomorphism, prominent nucleolus, wide clear cytoplasm and regular cell membrane

contours. Two-three mitotic figures per ten HPF (high-power fields) were present.
Immunohistochemistry was done; tumour cells were reactive only with vimentin and smooth muscle actin; however no reaction was seen with keratin, desmin, CD10 and HMB45. No mucin staining was observed histochemically.
Postoperative recovery was uneventful. CA-125 level returned to normal. Intravenous pyelography which was performed to detect associated urinary abnormalities was normal.

Discussion

Unilateral absence of an ovary in a multiparous woman is an extremely rare condition.[3]
Embryologically 3 sources which were mesodermal (coelemic) epithelium (lining the posterior abdominal wall), underlying mesenchyme (embryonic connective tissue) and primordial germ cells contribute to the development of ovaries. The genital (gonadal) ridge is created by proliferation of epithelium and mesenchyme. Primordial germ cells arising from the caudal portion of yolk sac migrate along the dorsal mesentery of the hindgut to the genital ridge.[7] Paramesonephric (Müllerian) ducts develop into uterine tubes, uterus and superior part of vagina.[4] Urogenital organs such as uterus, fallopian tubes, kidneys, and ureters may be abnormal in paramesonephric duct defects.[8]
Torsion in the prenatal or postnatal life and embryological agenesis were proposed to explain this clinical entity.[4] Congenital absence of ovary may arise from underdevelopment of primitive gonad due to failure of migration of germ cells. Also it may be present in patients with abnormal karyotypes.[3]
Etiology of congenital absence of the ovary or adnexa may be a vascular accident occuring in utero resulting in complete absence of that ovary.[9]
In the congenital cases, one would expect to observe one sided ovarian agenesis together with uterine or urinary tract abnormalities.[3] In our case uterus, bilateral fallopian tubes and urinary tract are normal, therefore developmental anomaly is unlikely. If it is a developmental anomaly, it is postulated that during the developmental phase, local blood supply to the adnexa might be compromised. So complete absence of that ovary and/or a developmental failure of fallopian tube may be seen.[4]
Adnexial torsion can be responsible for the absence of ovary when torsion occurs during adult life or childhood. Usually severe abdominal pain, nausea, and vomiting are present.[2] Sometimes these symptoms may be minimal or even absent. Thus lack of any classic history of symptoms does not preclude the diagnosis of torsion.[3,4] Passive congestion during menstruation and pregnancy would result in increasing rotation and torsion.[4] Especially during pregnancy no symptoms are observed when torsion and subsequent absorption takes place.[4] However, our case had no past history of classic symptoms of torsion. But on the other hand patient had the symptoms of torsion; probably these symptoms could be due to the parasitic leiomyoma as well. Although literature supports the belief that obstetric performance may be impaired in the presence of Müllerian and ovarian agenesis, this case demonstrates that fertility may not be impaired.[10]
Epithelioid leiomyoma of uterus is a rare variant of leiomyoma composed of round or polygonal 'clear' cells rather than typical spindle-shaped cells. Prognostic factors of epithelioid leiomyoma of uterus have not been well established. It may further be divided into: leiomyoblastoma, clear cell leiomyoma, plexyform leiomyoma. Clear cell type of this epithelioid leiomyoma is thought to be an ultrastructurally unique lesion that is different from nonuterine clear cell leiomyomas.[6] Combination of significant nuclear atypia, mitotic activity, and tumour cell necrosis suggest malignancy which metastasize infrequently.[5] Immunohistochemistry was done; tumour cells were reactive only with vimentin and smooth muscle actin; however no reaction was seen with keratin, desmin, CD10 and HMB45. No mucin staining was observed histochemically. In this case, a broad differential diagnosis

of carcinoma, endometrial stromal tumour and PEComa were made histopathologically. Also the main differential diagnosis was made with their malign counterpart (clear cell leiomyosarcoma). Although it has got a large tumour size; the lack of moderate to severe cytologic atypia and tumour cell necrosis, elevated mitotic rate, predominace of clear cells with circumscribed margins pointed to benign behaviour.

To best of our knowledge this is the first report related with unilateral ovarian agenesis together with epithelioid leiomyoma, clear cell type. This case illustrates the significance of occurrence of these two extremely rare conditions and highlights the potential pitfalls for diagnosis when they occur together because the diagnostic difficulty preoperatively they cause is obvious.

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