Case report

Hyperreactio luteinalis of the ovary

N D Ranathunge , K C K Wasalaarachchi , K A M S Karunaratna , I S H Liyanage , A P Ginige

Introduction

A rare case of Hyperreactio luteinalis occurring in a spontaneously conceived pregnancy is reported and the importance of differentiating it from malignancy and other cystic lesions of the ovary occurring during pregnancy is highlighted.

Case report

A 24 year old female with one living child in her second pregnancy was found to have bilateral multiloculated ovarian cysts on a routine ultrasound scan at 20 weeks. A follow up scan revealed further enlargement of these cysts. There was no history of ovarian induction or other complicating factors. Her previous pregnancy was uneventful. On examination there were bilateral palpable masses.

At exploratory laparotomy she was found to have bilateral malignant looking ovarian cysts. The cystic parts were removed and part of the left ovary was reconstructed.

Right and left ovarian masses received separately revealed enlarged ovaries with lobulated surfaces. The right and left ovaries measured 13.0 x 7.0 x 4.0 cm and 10.0 x 7.0 x 4.0 cm respectively. Cut sections revealed ovaries containing multiple thin-walled cysts within the cortex, filled with haemorrhagic fluid. The cysts ranged from 1.0 cm to 4.0 cm in diameter. Solid areas were not seen (Fig. 1).

Histological examination of both ovarian masses revealed multiple large follicular cysts within the ovarian cortex, lined by inner layers of granulosa cells and outer layers of theca interna cells. Both cell layers showed prominent luteinisation. Occasional granulosa cells showed bizarre nuclei. The theca layer and the inter-

Department of Pathology, Colombo South Teaching Hospital, Kalubowila, Sri Lanka

Correspondence: ND Ranathunge, e mail- nilukaranathunge@gmail.com

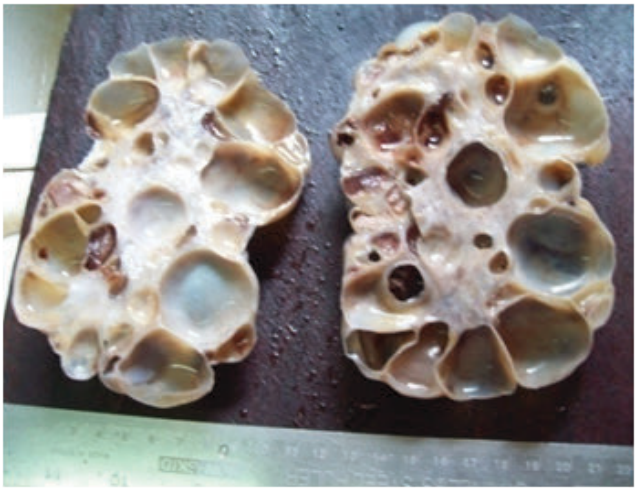

Fig. 1- Macroscopic appearance of the cystic ovaries

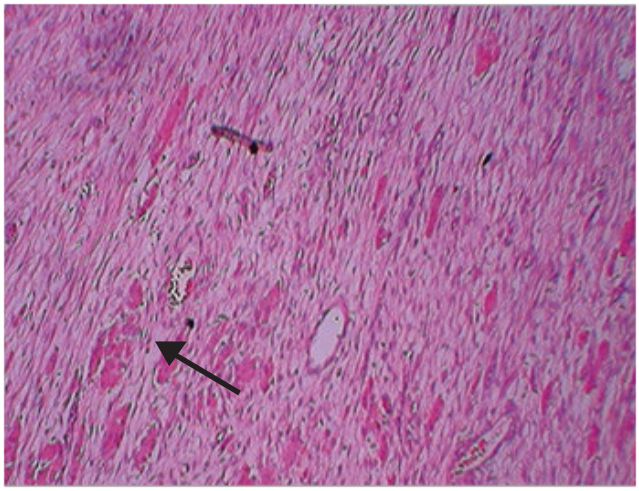

Fig. 2 – Clusters of luteinized cells in oedematous stroma - arrow (H & Ex400)

vening stroma showed marked oedema. Nests of luteinized cells devoid of atypia were present in the ovarian stroma (Fig. 2).

Discussion

This is one of the few reports of Hyperreactio luteinalis occurring in a spontaneously conceived pregnancy. Hyperreactio luteinalis (HL) and spontaneous ovarian hyperstimulation syndrome (OHSS) have similar macroscopic and microscopic appearances but different clinical presentations.

OHSS is almost exclusively associated with ovulation induction with exogenous gonadotropins. However, OHSS can rarely occur with spontaneous ovulatory cycles, especially in multiple gestations, hypothyroidism (1,2), molar pregnancy (3), in subjects with hyperandrogenism and polycystic ovary syndrome as well as in normal singleton pregnancy (4). Typically, iatrogenic OHSS is diagnosed immediately following conception, but the time of diagnosis is more variable with spontaneously occurring OHSS.

HL is believed to be an exaggerated ovarian luteinization due to hyperstimulation by or hypersensitivity to human chorionic gonadotrophins (hCG). HL may accompany conditions with elevated placental hCG, but more than half of the cases occurred with normal singleton pregnancies. Endogenous hCG is secreted by the trophoblasts 7–8 days after fertilization. In a normal singleton pregnancy hCG concentration in the maternal serum reaches a peak level of 100,000 IU/L between 8–10 weeks of gestation, and declines to 40 000 IU/L from 20 weeks until delivery. If beta hCG levels are high at the end of the first trimester, it could serve as the trigger to HL.

Many putative mediators have been cited as inducers of ovarian hyperstimulation including vascular endothelial growth factor (VEGF), various cytokines, prostaglandins, histamine, estrogen, prolactin and renin. VEGF was also shown to be triggered by hCG in vitro and in vivo. However, the blood level of VEGF does not always parallel the clinical course (5). Therefore, the finding of low serum VEGF concentration when hCG levels are maximal does not fully rule out the diagnosis, nor distinguish between OHSS and HL Some disparities between spontaneous OHSS and HL do exist; HL may occur unilaterally and its clinical course is more indolent and may be more prone to misdiagnosis as an ovarian tumor and unnecessary oophorectomy (6).

The diagnosis is often made incidentally and later in pregnancy, as in this patient. HL occurs in any trimester of pregnancy and rarely during pueperium. It is usually asymptomatic, but may present as a palpable pelvic mass or with acute abdominal symptoms related to hemorrhage, torsion, or rupture. In HL virilisation is seen in 25% of patients and hyperandrogenism is even more frequent. Probably the more indolent course of HL allows the changes in secondary sexual characteristics to develop over time.

The ‘spoke wheel’ sign of these large simple thin-walled cysts, along with the intensely compressed stroma and physiological vasculature, is regarded as the key feature on ultra sound examination in Hyperreactio luteinalis. This patient’s ultrasound scan did not show this characteristic appearance. Therefore exclusion of malignancy was difficult on ultra sound scanning.

The cysts regress following delivery but occasionally regression is incomplete until six months. Exceptionally the cysts regress spontaneously during pregnancy. Sometimes cysts persist but conservative treatment is warranted. Surgery is needed to remove infarcted tissue, to control haemorrhage or to reduce ovarian size in order to diminish androgen production in virilised patients. Rarely Hypereactio luteinalis can occur in subsequent pregnancies (2).

Both HL and OHSS share similar underlying risk factors, clinical presentations, sonographic appearances and non-surgical expectant management, and thus can be viewed as entities in continuum (7,8).

The presence of large multicystic ovaries and ascites during pregnancy is uncommon. There are multiple benign ovarian lesions including HL, pregnancy luteomas and Granulosa cell proliferations of pregnancy that can mimic ovarian neoplasms. Accordingly, it is important to differentiate these via a wedge biopsy and frozen section in order to avoid unnecessary surgical excision. HL shows multiple, usually bilateral, thin- walled cysts within the cortex filled with clear or haemorrhagic fluid (2), in contrast to an ovarian malignancy.

In conclusion, (i) spontaneous OHSS and HL are related entities that share risk factors, symptoms, and similar pathogenesis; (ii) both should be managed conservatively after ovarian malignancy is ruled out; (iii) serial ultrasound scans may be the preferable method of follow-up of ovaries with a multicystic appearance during pregnancy; and (iv) consideration of entities such as HL and spontaneous OHSS prevent unnecessary surgical intervention.

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