CASE REPORT

Hyperreactio luteinalis encountered during caesarean delivery of an uncomplicated spontaneous singleton pregnancy

Inês Sarmento Gonçalves, Sofia Malafaia, Helena Belchior, Pedro Tiago-Silva

Department of Gynaecology and Obstetrics, Hospital Pedro Hispano, Matosinhos, Portugal

Correspondence to

Pedro Tiago-Silva,
pedro.tiago@ulsm.min-saude.pt

Accepted 12 September 2015

SUMMARY

We report a rare case of hyperreactio luteinalis presenting as an incidental finding during caesarean section in an uncomplicated spontaneous singleton pregnancy. Caesarean section was performed due to failure to progress in labour, and delivered a healthy male neonate. The mother's analytical tests revealed a hyperandrogenic state without any other relevant alterations. Ovarian volume and testosterone serum concentration normalised in 2 months. The expectant management of this case permitted conservation of both ovaries in a young woman without adding morbidity.

BACKGROUND

Hyperreactio luteinalis is an uncommon benign adnexal condition specific to pregnancy.¹ The exact aetiology of hyperreactio luteinalis is unknown, but there is some evidence of genetic predisposition and a possibility for recurrence in future pregnancies.² This entity is characterised by bilateral ovarian enlargement due to theca-lutein cysts and excessive production of ovarian androgens during pregnancy, with spontaneous regression after delivery.³ Many patients have no symptoms or pregnancy complications.³ However, the enlarged ovaries may cause abdominal pain or acute abdomen due to ovarian torsion or haemorrhage, and pregnancy may be complicated by placental or hypertensive disorders.^{2,3}

We report a rare case of hyperreactio luteinalis presenting as an incidental finding during caesarean section in an uncomplicated spontaneous singleton pregnancy.

CASE PRESENTATION

We report a case of a 29-year-old primigravida woman with an unremarkable history and an uneventful pregnancy, under surveillance in a primary care unit. The three gestational ultrasounds (at 12, 20 and 32 weeks of gestation) were not performed at our institution. Those reports were normal, without reference to any adnexal pathology. At 39 weeks' gestation, a healthy male neonate (weight 2800 g; Apgar score 6–9) was delivered by caesarean section at our maternity unit, due to the mother's failure to progress in labour. During intraoperative abdominopelvic cavity inspection, incidental grossly enlarged polycystic ovaries were detected, the right ovary with a mean diameter of 15 cm and the left with a mean diameter of 8 cm. Subsequent analytical tests

revealed an elevation of total testosterone (1074 ng/dL), oestradiol (2420 pg/mL) and β subunit of human chorionic gonadotrophin (hCG; 3085 IU/mL), and a decrease of follicle-stimulating hormone (FSH; <0.05 mIU/mL) and luteinising hormone (LH; <0.02 mIU/mL), with normal values of haematocrit, liver and renal functions, ovarian cancer tumour marker (CA-125), thyroid-stimulating hormone and coagulation profiles. Apart from the hyperandrogenic state, maternal virilisation was not seen. When asked about specific signs or symptoms, the patient reported experiencing unusual aggressive behaviour (having little patience with family members, being easily irritated and always arguing with her husband) during the third trimester of pregnancy.

The patient's postoperative course was uneventful. MRI was performed by day 10 post partum revealing enlarged ovaries occupied by multiple cysts (figure 1). Ovarian volume decreased slowly (figure 2) and reached normal appearance in 6 months (figure 3). Testosterone concentration regularised faster, with a normal value of 21 ng/dL 2 months after delivery.

DIFFERENTIAL DIAGNOSIS

This entity is commonly mistaken for an ovarian neoplasm since the possibility of ovarian cancer should be taken into consideration in cases of rapid ovarian growth.^{1,4} However, hyperreactio luteinalis is often a bilateral ovarian enlargement with regular morphology and normal levels of ovarian tumour markers,⁴ as occurred in this case. MRI can

Figure 1 MRI at day 10 post partum showing enlarged cystic ovaries without solid components: the right ovary with a maximum diameter of 14 cm and the left with a maximum diameter of 8 cm.

To cite: Sarmento Gonçalves I, Malafaia S, Belchior H, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211349

Figure 2 Ultrasonography at 2 months post partum showing a reduction of the ovaries ((A) right ovary 6.4×2.8×5 cm; (B) left ovary 5.8×2.8×4.1 cm) with multiple small follicles.

be used to help differentiate this entity from ovarian malignancies,¹ revealing the classic ‘spoke wheel’ appearance that is characteristic of theca-lutein cysts without solid components.

The imaging appearance mimics ovarian hyperstimulation syndrome. However, this is a well-known complication in the first trimester of pregnancy, typically diagnosed in patients who undergo ovulation induction, or spontaneously in patients with hypothyroidism, polycystic ovarian syndrome, increase in FSH levels due to FSH-secreting adenoma, or mutation of the FSH or LH receptors,¹ which was not the case with our patient. Besides, ovarian hyperstimulation syndrome is associated with more severe symptoms involving acute fluid imbalances such as ascites, pleural effusion and haemoconcentration.^{4 5}

OUTCOME AND FOLLOW-UP

Currently, the patient has completed 1 year of follow-up without any other relevant findings or symptoms. The child is now 22 months old with appropriate development for a child of that age.

DISCUSSION

Hyperreactio luteinalis is thought to be an exaggerated ovarian luteinisation due to increased levels of circulating hCG or to abnormal ovarian response to hCG.^{1 2} Hyperreactio luteinalis has been described as complicating pregnancies with elevated placental hCG (multiple pregnancies, gestational trophoblastic disease)^{6 7} and decreased clearance of hCG due to renal dysfunction⁸; but it has also been observed in normal singleton pregnancies,⁴⁻⁶ as occurred in the present case, with levels of hCG not abnormally elevated. We assume that the hyperreactio luteinalis in this case was due to an abnormal ovarian hypersensitivity of unknown aetiology.

Hyperreactio luteinalis is usually found in Caucasian first-time mothers,⁹ as occurred in this case. Fifty-four percent of cases are diagnosed later in pregnancy (third trimester or puerperium) and 16% are diagnosed in the first trimester. Approximately 37% of cases are diagnosed during caesarean delivery, since its

typical presentation consists of bilateral enlargement of the ovaries without other symptoms and spontaneous involution after delivery,^{1 5} as happened in this case. In this case, a thorough assessment of the ovaries during third trimester ultrasound could have allowed earlier diagnosis.

Clinical symptoms include maternal abdominal pain or acute abdomen due to ovarian torsion or haemorrhage.^{1 2} Virilisation is seen in 15–25%^{4 10} of patients, but hyperandrogenaemia is more frequent.⁴ Placental aromatisation of testosterone in hyperreactio luteinalis prevents fetal virilisation, unlike that seen in masculinising ovarian tumours,⁹ however, a case of a female virilised fetus has been described.¹¹ In the present case, hyperandrogenaemia was confirmed but maternal virilisation features were not seen. Nevertheless, the patient reported experiencing particularly aggressive behaviour during the third trimester of pregnancy, which can be explained by a hyperandrogenic state from that gestational time onward.¹² The male neonate had normal sexual phenotypical characteristics.

Elevated levels of hCG produced by the trophoblast in the first trimester in otherwise normal pregnancies may be a sign of abnormal placental development.¹³ Besides, hormonal changes in hyperreactio luteinalis may contribute to alterations in coagulation factors and predispose the patient to thromboembolic complications.¹⁴ These factors explain the association that has been made between hyperreactio luteinalis and some pregnancy complications such as preeclampsia, hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, severe fetal growth restriction and preterm delivery.^{2 10 13 15} In this case, the hCG level was not abnormally elevated and no such complications occurred.

Labour dystocia may be associated with this entity as well as other ovary-expanding pathologies,⁴ thus leading to caesarean delivery, as occurred in this case.

MRI has been suggested as the preferred method for imaging enlarged ovaries,¹ however, in this case, it added no further information to the data drawn by careful clinical and ultrasonographic surveillance.

Figure 3 Ultrasonography at 6 months post partum with normal ovaries ((A) right ovary 4.1×2.1×2.5 cm; (B) left ovary 3.1×1×2 cm).

Learning points

- ▶ Hyperreactio luteinalis is a rare reversible ovarian enlargement condition due to increased ovarian sensitivity to human chorionic gonadotrophin.
- ▶ The diagnosis of ovarian abnormalities should not be an incidental finding during caesarean delivery but should, instead, be diagnosed prenatally by using ultrasound and looking at the ovaries in every pregnant patient at every stage of gestation.
- ▶ Diagnosis of hyperreactio luteinalis during pregnancy should prompt careful obstetric surveillance in order to identify and plan adequate strategies to prevent and manage possible disease-related complications, such as fetal growth restriction and hypertensive disorders.
- ▶ With the expanding use of ultrasonography in pregnancy, this entity is expected to be encountered more frequently. Therefore, it is important to be familiar with this extremely rare self-limiting pregnancy condition in normal singleton pregnancies in order to differentiate it from other malignant mimics, thus avoiding unnecessary oophorectomy in women of reproductive age.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Chiang G, Levine D. Imaging of adnexal masses in pregnancy. *J Ultrasound Med* 2004;23:805–19.
- 2 Cavoretto P, Giorgione V, Sigismondi C, *et al.* Hyperreactio luteinalis: timely diagnosis minimizes the risk of oophorectomy and alerts clinicians to the associated risk of placental insufficiency. *Eur J Obstet Gynecol Reprod Biol* 2014;176:10–16.
- 3 Phelan N, Conway GS. Management of ovarian disease in pregnancy. *Best Pract Res Clin Endocrinol Metab* 2011;25:985–92.
- 4 Haimov-Kochman R, Yanai N, Yagel S, *et al.* Spontaneous ovarian hyperstimulation syndrome and hyperreactio luteinalis are entities in continuum. *Ultrasound Obstet Gynecol* 2004;24:675–8.
- 5 Abe T, Ono S, Igarashi M, *et al.* Conservative management of hyperreactio luteinalis: a case report. *J Nippon Med Sch* 2011;78:241–5.
- 6 Page SM, O'Brien J. Hyperreactio luteinalis with clitoromegaly in a twin pregnancy. *Rev Obstet Gynecol* 2009;2:3–4.
- 7 Al-Ramahi M, Leader A. Hyperreactio luteinalis associated with chronic renal failure. *Hum Reprod* 1999;14:416–18.
- 8 Skandhan AK, Ravi V. Hyperreactio luteinalis: an often mistaken diagnosis. *Indian J Radiol Imaging* 2014;24:84–6.
- 9 Kaňová N, Bičíková M. Hyperandrogenic states in pregnancy. *Physiol Res* 2011;60:243–52.
- 10 Lynn KN, Steinkeler JA, Wilkins-Haug LE *et al.* Hyperreactio luteinalis (enlarged ovaries) during the second and third trimesters of pregnancy: common clinical associations. *J Ultrasound Med* 2013;32:1285–9.
- 11 Simsek Y, Celen S, Ustun Y, *et al.* Severe preeclampsia and fetal virilization in a spontaneous singleton pregnancy complicated by hyperreactio luteinalis. *Eur Rev Med Pharmacol Sci* 2012;16:118–21.
- 12 Rohr UD. The impact of testosterone imbalance on depression and women's health. *Maturitas* 2002;41:25–46.
- 13 Atis A, Cifci F, Aydin Y, *et al.* Hyperreactio luteinalis with preeclampsia. *J Emerg Trauma Shock* 2010;3:298.
- 14 Saisto T, Tiitinen A, Ulander VM, *et al.* Clinical cure of severe, early onset preeclampsia with low molecular weight heparin therapy in primigravida with hyperreactio luteinalis and thrombophilia. *Hum Reprod* 2004;19:725–8.
- 15 Haq AN, Sher Z, Naz S. Hyperreactio luteinalis associated with pregnancy induced hypertension. *J Coll Physicians Surg Pak* 2010;20:137–9.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow