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CASE REPORT

# A rare case of an androgen-secreting mucinous borderline ovarian tumour in a perimenopausal woman

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## Introduction

Virilising ovarian tumours account for less than 0.2% of cases of hyperandrogenism. To date, only two cases of functional mucinous borderline ovarian tumours have been reported.

This article presents the case of a 50-year-old woman who presented with a 1-year history of abdominal distension, oligomenorrhea and severe facial acne. There was no hirsutism, loss of female body contours, increased muscle mass or clitoromegaly. A computed tomography scan showed a large multiloculated cystic mass arising from the right adnexa, with multiple enhancing internal septations and an enhancing mural nodule. Initial investigations revealed an elevated serum total testosterone level of 5.2 nmol/litre and a serum androstendione level of 9 ng/ml. The patient underwent total abdominal hysterectomy and bilateral salpino-oopherectomy with omentectomy. Histology of the

### Case report

A 50-year-old woman initially presented to the gynaecologist with a 1-year history of abdominal discomfort and distension, initially attributed to gastro-oesophageal reflux, with no improvement with anti-acids. She also had an associated 1-year history of severe facial acne that did not improve with topical treatments. Before this, her last flare-up of acne had been during her previous pregnancies, the last one being 13 years ago, with complete spontaneous remission a few months postpartum. She had not had any further acne since then. She denied any change in voice, hirsutism or temporal balding, but complained of oligomenorrhoea over the past year. She had a previously normal menstrual history, with menarche at 14 years of age. On examination, she had severe facial nodular acne and gross abdominal distension. There was no hirsutism, loss of female body contours, increased muscle mass or clitoromegaly.

A transvaginal ultrasound was performed, showing a large right cystic ovarian lesion. This raised the suspicion of an androgen-secreting tumour. A computed tomography scan of the abdomen and pelvis showed a large multiloculated cystic mass arising from the right adnexa measuring 20 cm x 18.7 cm x 15.4 cm with multiple enhancing internal septations and an enhancing mural nodule (Figure 1). Magnetic resonance imaging of the abdomen and pelvis showed normal adrenal glands and confirmed the presence of the previously described large ovarian tumour.

Initial investigations revealed an elevated serum total testosterone level of 5.2 nmol/litre and serum androstendione level of 9 ng/ml. Follicle-stimulating hormone and luteinising hormone levels were normal. An overnight dexamethasone suppression test showed appropriate cortisol suppression, which indicated the likely possibility of an androgen-secreting ovarian mass. The rest of the investigations are shown in Table 1.

The patient underwent total abdominal hysterectomy and bilateral salpino-oopherectomy with omentectomy. A right, smooth-surfaced ovarian mass and greenish mucoid peritoneal fluid were noted. Histology of the right ovary showed a borderline mucinous ovarian tumour of intestinal type, with atypia (Figures 2a and b). On immunohistochemistry, tumour cells stained positive for CK7 and partially positive for CDX2, and negative for CK20, WT-1, PAX-8, p53. Mucinous tumour cells were also present in cell block ascitic fluid. The left ovary was normal.

At a follow-up visit 4 weeks postoperatively, there was significant improvement in the patient's facial acne. Repeat hormone levels showed normalisation of serum total testosterone and serum androstenedione (Table 1), confirming that the increased steroid hormone synthesis was of ovarian origin.

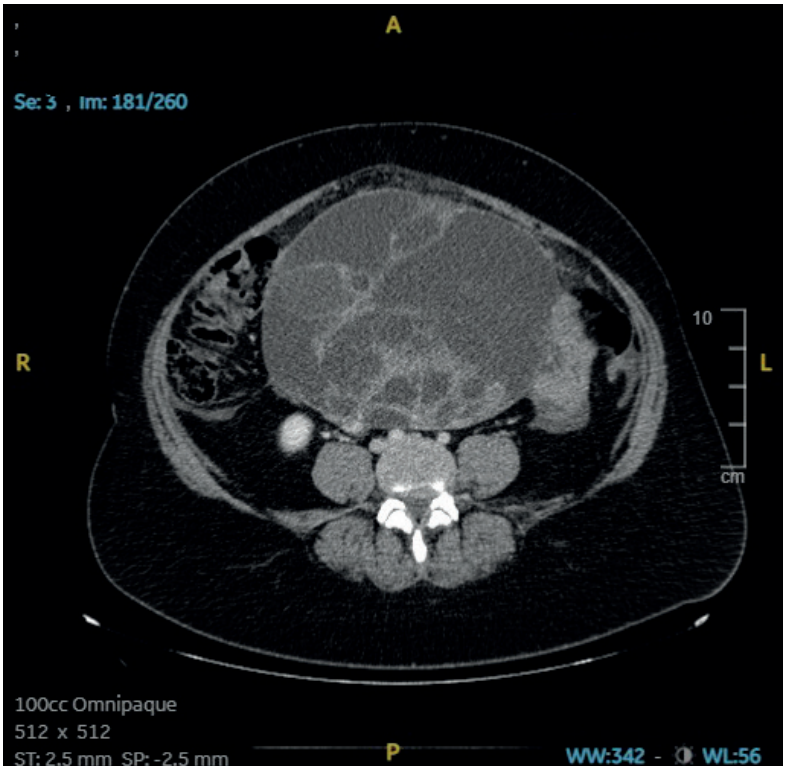


**Figure 1.** Computed tomography scan of the abdomen and pelvis, showing a large multiloculated cystic mass arising from the right adnexa with multiple enhanced internal septations, measuring 20 x 18.7 x 15.4 cm.

**Table 1. Hormone profile: preoperative and 4 weeks postoperative**

| Hormone (unit) | Preoperative level | Postoperative level | Reference range (premenopausal) |
|---|---|---|---|
| Testosterone (nmol/litre) | 5.2 | <0.69 | 0–2.53 |
| Androstendione (ng/ml) | 9 | 1.5 | Follicular phase 0.75–3.1; luteal phase 0.94–3.2 |
| Dehydroepiandrosterone (µmol/litre) | 4.53 | 1.77 | 0.95–11.67 |
| 17-hydroxyprogesterone (ng/ml) | 6.9 | Not repeated | Follicular phase 0.2–1.3; luteal phase 1.0–4.5 |
| Luteinising hormone (U/litre) | 4.6 | 21.4 | Follicular phase 1.1–11.6; midcycle phase 17–77; luteal phase 0–14.7 |
| Follicle-stimulating hormone (U/litre) | 7.6 | 41.7 | Follicular phase 2.8–11.3; midcycle phase 5.8–21; luteal phase 1.2–9 |
| Oestradiol (pmol/litre) | 248 | 89 | Follicular phase 71.6–529; midcycle phase 234–1309; luteal phase 205–786 |
| Anti-Müllerian hormone (pmol/litre) | 0.42 | <0.30 | <19.3 |
| Prolactin (mIU/litre) | 235 | 225 | 59–619 |
| Inhibin B (ng/litre) | 19.5 | Not repeated | 10–185 |
| Ca125 (U/ml) | 46.7 | Not repeated | 0–30.2 |
| Alphafetoprotein (IU/ml) | 2.70 | Not repeated | 0–6.64 |
| Human chorionic gonadotropin (mIU/ml) | <1.0 | Not repeated | 0–2.7 |

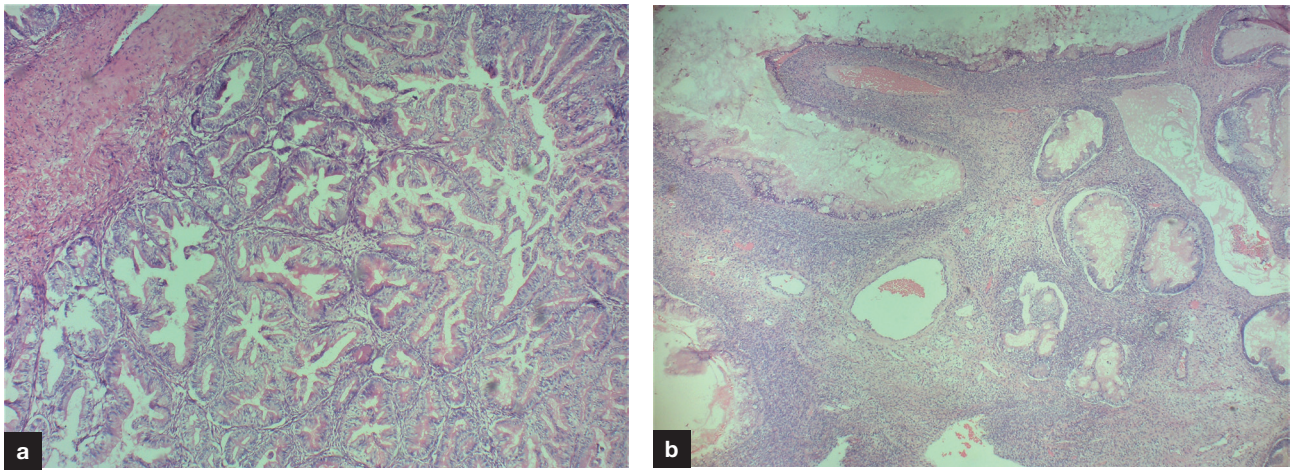


**Figure 2.** a. Histology of the right ovarian tumour mass showing mucinous borderline tumour. Stain haematoxylin and eosin, magnification x100. b. On immunohistochemistry, the cells are CK7 positive, CDX2 focally positive, and CK20, WT-1, PAX-8, p53 negative. Some areas show complex papillae, pseudocribriforming and minor foci of necrosis. There is no evidence of stromal invasion or capsular breaching.

right ovary showed a borderline mucinous ovarian tumour of intestinal type, with atypia. At follow up, there was significant improvement in the patient's facial acne with normalisation of serum levels of total testosterone and androstenedione.

## Discussion

Hyperandrogenism in women can have various causes, both cancerous and non-cancerous. A good clinical history and a baseline androgen level may provide clues to the probable diagnosis. Sudden onset and rapidly progressing symptoms with virilisation, together with very high levels of testosterone, as in this case, are highly suggestive of cancerous causes of hyperandrogenism (Markopoulos et al, 2015). Figure 3 summarises the differential diagnosis and work-up of postmenopausal hyperandrogenism.

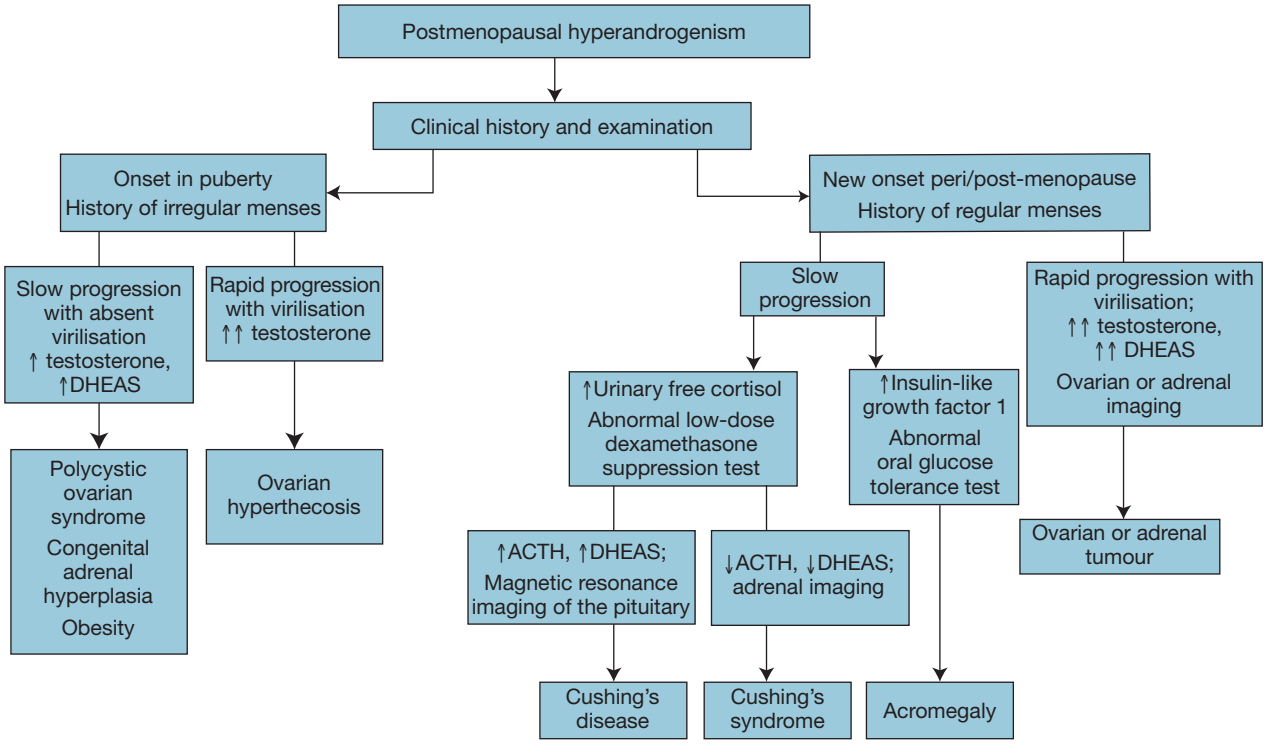


**Figure 3.** Work-up of patient with postmenopausal hyperandrogenism. ACTH = adrenocorticotrophic hormone; DHEAS = dehydroepiandrosterone.

## Learning points

- Hyperandrogenism in women can be secondary to various causes, so a thorough clinical history and examination provides vital clues to the probable diagnosis.
- Onset and progression of symptoms can help pinpoint the likely diagnosis and thus choose the appropriate investigations.
- Although functional mucinous borderline ovarian tumours are extremely rare, they should be considered as a possible cause of virilisation in women.

Virilising ovarian tumours account for less than 0.2% of cases of hyperandrogenism. The majority of these tumours arise from the sex-cord cells surrounding the oocytes or, rarely, from the stroma. The typical androgen-secreting ovarian tumours include Sertoli-Leydig cell tumours, granulosa cell tumours, steroid cell tumours and thecal cell tumours. These sex cord-stromal tumours only account for 5–8% of all ovarian tumours and fewer than half are androgen secreting (Cohen et al, 2015).

Surface ovarian epithelial cells account for 65% of ovarian tumours and are classically considered as non-functional (Alonso Díaz et al, 2018). Borderline ovarian tumours account for about 15–20% of all epithelial ovarian tumours. The majority of borderline ovarian tumours are serous tumours (53%), followed by mucinous tumours (42.5%), and less common histotypes (<5%). Mucinous borderline ovarian tumours can be of two types: the intestinal type (85%) and the endocervical type (15%). Mucinous borderline ovarian tumours are described as a separate category of mucinous cystadenoma (benign) and mucinous carcinoma (malignant). Prognosis of mucinous borderline tumour is usually good, with a 10-year survival rate of approximately 94% (Kozawa et al, 2019).

To date, only two cases of functional mucinous borderline ovarian tumours have been reported during pregnancy, resulting in virilisation of the mothers (Pather et al, 2007; Fanara et al, 2008). In one case, the patient developed severe pre-eclampsia, requiring caesarean section at 33 weeks of gestation (Fanara et al, 2008). In a few other published case reports, hyperandrogenism secondary to mucinous ovarian tumours was histologically either benign mucinous cystadenomas or mucinous carcinomas (Nezhat et al, 2002; Antoniou et al, 2003; Bolat et al, 2011; Kucur et al, 2016; Alonso Díaz et al, 2018).

Most mucinous borderline ovarian tumours appear as a large unilateral, multiloculated cystic mass with thick septations on computed tomography or magnetic resonance imaging, as seen in this case (Kozawa et al, 2019). The characteristics of the ovarian lesion on imaging and the normal levels of inhibin B and anti-Müllerian hormone made the diagnosis of typical androgen-secreting sex-cord ovarian tumours less likely in this patient.

There are various proposed hypotheses that explain the mechanism behind the secretion of androgens from epithelial cell tumours. Some authors proposed that this is the response of stimuli, such as gonadotrophins and beta-human chorionic gonadotropin produced from the tumour cells leading to differentiation into hormone producing cells. Another theory suggests that the mechanical pressure of the tumour on the stromal cells may stimulate androgen secretion (Antoniou et al, 2003; Bolat et al, 2011).

This article reports a rare case of hyperandrogenism in a perimenopausal woman secondary to a functional mucinous borderline ovarian tumour. Despite the fact that these tumours are usually non-functional, they should be considered as a possible cause of virilisation in women.

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