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Case Report

CASE REPORT

Virilization of a postmenopausal woman by a mucinous cystoadenoma

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Abstract

Objective: To describe the case of the most hyperandrogenaemic ovarian mucinous cystadenoma reported to date.
Methods: We present the clinical, laboratory and radiologic findings in a patient with an unusual diagnosis according to age and the clinical behaviour of the tumour, as well as a review of relevant literature.
Results: A 77-year-old women came to our consult because of fronto-parietal alopecia and an augmentation of the abdominal perimeter since 1 year ago. Clitoromegaly was observed during the physical examination. Hormonal analysis showed elevated testosterone and dehydroepiandrostenerone-sulphate levels (659 ng/dL and 1950 ng/ml, respectively), and imaging examination described an andexal cystic mass dependent on the right ovary. Pathological diagnosis was "mucinous cystoadenoma". After surgery, clinical and analytical alterations were normalized.
Conclusion: Although ovarian mucinous cystadenomas are classically classified as "nonfunctional" tumours, they exceptionally can act as functional, and produce testosterone levels as high as directly secreting hormones or germ cell tumours.

CASE REPORT

A 77-year-old woman was evaluated in our outpatient endocrinology clinic because of alopecia. She reported a 1-year history of frontal and parietal alopecia and progressive abdominal swelling. She had not noticed the development of hirsutism, deepening of her voice, increased muscle mass or menorrhagia. No other diseases of interest were known and no treatment had been followed. About her obstetric history, she referred menarche at 17 years, with regular cycles. She had two healthy children and no miscarriages. Menopause was diagnosed at age 52. She had never been checked by a gynaecologist. On physical examination, the following findings were recorded: blood pressure: 125/80 mmHg, pulse: 88 bpm, height: 1.74 m, weight: 53 kg, body mass index: 24.5 kg/m^2 and waist circumference: 99 cm. She showed a male-baldness pattern (Ludwig score: II-2/III). She had no hirsutism (modified Ferriman–Gallwey score: 3). She presented a significant abdominal wall distension, with a big palpable mass on the right hemiabdomen. A pelvic examination revealed female external genitalia with clitoromegaly. No other findings were found.

Virilization of recent onset and rapid progression suggested an androgen-secreting tumour. We simultaneously ordered an androgen profile, tumour markers and a transvaginal

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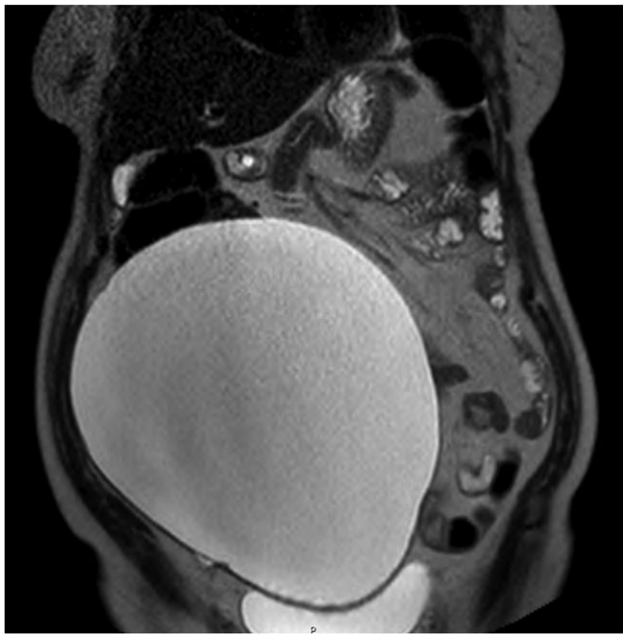

Figure 1: Abdomino-pelvic magnetic nuclear resonance. Voluminous mass, with a cystic appearance, dependent on pelvic structures

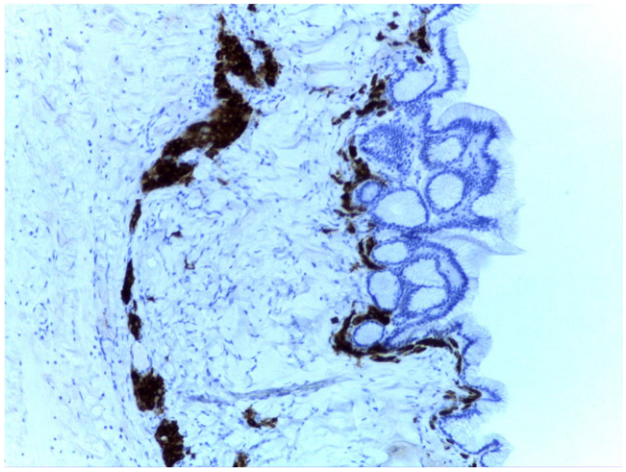

Figure 2: Histopathologic examination, ovarian cells with a positive inhibin staining, which makes us believe in the presence of luteinized stromal cells that are polygonal shaped and have enlarged pale eosinophilic cytoplasm

ultrasonography. Laboratory findings showed a total testosterone (by radioimmunoassay) of 659 ng/dl (10–70 ng/dl), dehydroepiandrosterone-sulphate of 1950 ng/ml (170–900 ng/ml), FSH of 75 IU/l, LH of 28 IU/l and estradiol of 25 pg/ml. Biochemical tumour markers studied including human chorionic gonadotropin (β-HCG), alpha-fetoprotein, carcinoembryonic antigen, CA-125, CA19-9, lactate dehydrogenase were all negative and other biochemical parameters were normal as well.

Transvaginal sonography revealed a 22 cm × 16 cm right adnexal cystic mass. An ulterior abdomino-pelvic magnetic resonance imaging confirmed a huge 20 cm × 14 cm × 22 cm cystic lesion dependent of pelvic structures (Fig. 1). Both, radiologic and laboratory, data agreed with an ovarian neoplasm. A hysterectomy with double oophorectomy was indicated and performed with no surgical complications.

Neoplasm histopathology showed a 24 cm × 9 cm × 11 cm large cystic tumour of 3.5 kg of weight originated from the right ovary. It had a whitish-grey coloration and a cystic membranous appearance within a yellowish serous content. Its microscopic examination showed nests of luteinized cells in the cyst wall (Fig. 2) with a final diagnosis of 'mucinous cystadenoma with stromal luteinization'. Three months after surgery, the patient had a normal serum total testosterone of 36 ng/dl.

DISCUSSION

The present clinical case exemplifies how many times postmenopausal hyperandrogenism becomes in a diagnostic challenge. Postmenopausal virilization may be associated to adrenal or ovarian androgen-secreting tumours or to benign conditions. A detailed clinical history is critical to make out between the mild phenotype that characterizes benign causes from the rapid progression and severe hyperandrogenism, including virilization, of androgen-secreting tumours. When symptoms clearly develop after menopause, hyperandrogenism is severe, progression is rapid and virilization or defeminization is present, adrenal and ovarian imaging must be immediately ruled out. Postmenopausal virilization may result from adrenal tumours, including androgen-secreting carcinomas and adenomas; from ovarian tumours, including Sertoli–Leydig cell tumours (androblastoma, arrhenoblastoma), granulosa-theca cell tumours and hilus cell tumours; or from benign ovarian conditions such as ovarian stromal hyperplasia and hyperthecosis [1]. Rare causes, such as transfer of testosterone from a male partner using testosterone gels, have been also described.

Ovarian mucinous cystadenomas are classically considered as 'non-functional' tumours. This neoplasm represents around 8–25% of all ovarian tumours. It is more prevalent from the third to fifth decades of life, being exceptional before puberty and after menopause. Very few cases of postmenopausal women with an androgen-producing mucinous cystadenoma had been reported, most of them in pregnant women [2–5]. Anecdotically, this tumour is diagnosed in adolescents [6], and to the best of our knowledge, only two cases have been reported in postmenopausal women [7, 8]. Only three of them had severe hyperandrogenemia [3, 7, 8]. In our patient, circulating total testosterone levels were on male range, a feature associated to other androgen-secreting neoplasms and germ cell tumours [9].

The reason why those epithelial tumours can secrete androgens as a functional one is not well known. Some authors have proposed that tumour cells may synthesize several stimulus for proliferation and differentiation into hormone-producing cells including gonadotropins or β-hCG [10]. In conceptual agreement, most of these tumours are diagnosed during pregnancy. In our case, FSH was normal for postmenopausal range, LH was mildly suppressed according to androgen levels and β-HCG was normal. Lastly, another hypothesis is the presence of a mechanical effect, so that, the amount of hormone production would be due to a direct contact between neoplastic epithelial and stromal cells surfaces [2–5].

We would like to emphasize that these kinds of tumours appear to present with higher testosterone levels in postmenopausal women than in younger patients, a fact to be considered in future studies.

In conclusion, we report an unusual case of a postmenopausal woman with an androgen-producing ovarian mucinous cystadenoma, which is a very rare diagnosis according to its behaviour as a functional neoplasm, especially in that range of

age. This case shows that stromal cells-derived tumours are able to induce severe hyperandrogenism and virilization, and they have to be included in the differential diagnosis of a postmenopausal women with hyperandrogenism.

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CONFLICT OF INTEREST STATEMENT

None declared.

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