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CASE REPORT

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Ovarian sertoliform endometrioid carcinoma

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Abstract Sertoliform endometrioid carcinoma (SEC) is a rare ovarian neoplasm occurring almost exclusively in post-menopausal patients. We studied a 71-year-old patient who underwent a total hysterectomy with bilateral salpingo-oophorectomy for a right ovarian mass measuring 25 cm in its maximal dimension. Histology revealed an SEC, featuring foci of typical endometrioid carcinoma and areas of clear cell differentiation. This particular type of ovarian neoplasm, already described in 21 reported cases in the literature, must be distinguished from Sertoli cell tumours and Sertoli-Leydig cell tumours which are encountered at a younger age. We discuss the elements of the differential diagnosis and insist upon the value of anti-epithelial membrane antigen in identifying an SEC.

Key words Ovary · Endometrioid carcinoma · Sertoli cell tumour

Introduction

Ovarian endometrioid carcinoma (EC) develops from the surface epithelium of the ovary and presents the microscopic characteristics of several typical forms of endometrial neoplasms [6]. This malignant tumour is reported to have an incidence of approximately 20% and is considered to be the second most frequent primary ovarian tumour after the serous cystadenocarcinoma [2, 4].

The histological appearance of the tumour varies according to the grade of its glandular and squamous components, and depending on the quantity of squamous cell and clear cell differentiation. Exceptionally, EC is characterized by prominent tubular structures mingled with solid areas and cord-like areas resembling Sertoli (SCT) and Sertoli-Leydig cell tumours (SLCT). Twenty-one tumours of this type have been reported in the literature [1, 4, 8]. Their denomination is purely descriptive: "ovarian endometrioid tumour mimicking Sertoli and Sertoli-Leydig cell tumors", "sertoliform variant of endometrioid carcinoma" (SEC) [4] and "ovarian endometrioid carcinomas resembling sex-cord stromal tumours" [1].

In this paper we describe another case of this uncommon SEC.

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Case report

A 71-year-old patient, gravida III, para III, consulted her gynaecologist for an onset of metrorrhagia associated with a sensation of pelvic "heaviness", following a post-menopausal interval of 19 years. Clinical examination revealed a voluminous mass extending from the pelvis to the right hypochondriac region, filling the right utero-vesical recessus. No indication of virilization was noted.

Abdominal CT-scanning clearly showed a heterogeneous cystic, partially solid mass, pressing back the intestinal loops and associated with pronounced ascites.

An assay of pre-operative blood serum yielded a CA125 value of 1010 u/l (normal<35 u/l). A total hysterectomy with bilateral salpingo-oophorectomy was performed. Complementary post-operative treatment consisted of five courses of chemotherapy (carboplatin), followed by normalization of the CA125 values. A year later, abdominal CT-scanning revealed pleural effusion, ascites and tumour infiltration of the omentum. A new course of chemotherapy (Taxol) was then initiated. Four months later radiographs confirmed regression of the epiploic tumour infiltration and resorption of the pleural effusion and the ascites.

Material and methods

Buffered formalin-fixed, paraffin-embedded tissue sections of surgically resected uterus, ovaries and fallopian tubes were stained with haematoxylin and eosin. Additional histochemical stains included periodic acid-Schiff (PAS), alcian blue and an argyrophilic type stain for intracytoplasmic granules using the Lars Grimelius technique. Immunohistochemical study was performed on paraffin sections employing the following monoclonal antibodies: anti-cytokeratins (CAM 5.2, AE-1/AE-3, CK13, CK20), monoclonal antibodies reactive with epithelial membrane antigen (EMA) and with carcinoembryonic antigen (CEA). Other antibodies included:

anti-vimentin, anti-S-100, anti-neuron-specific enolase (NSE), chromogranin A, synaptophysin, anti-human lysozyme, anti-alpha-chymotrypsin (ACT), anti-alpha-1-antitrypsin (A-1 AT) and anti-CA125.

The tissue sections were also tested for progesterone and oestrogen receptors. All slides were studied by light microscopy.

Pathological findings

The right ovarian mass weighed 1650 g and measured 25×13×9 cm in its maximal dimensions. On cut section the tumour was beige in colour, predominantly solid with several cystic cavities which varied in diameter up to 5 cm and contained a yellow fluid; multiple foci of necrosis and oedema were also conspicuous (Fig. 1). Macroscopically, tumour infiltration extended beyond the capsule of the ovary and invaded the lumen of the right fallopian tube.

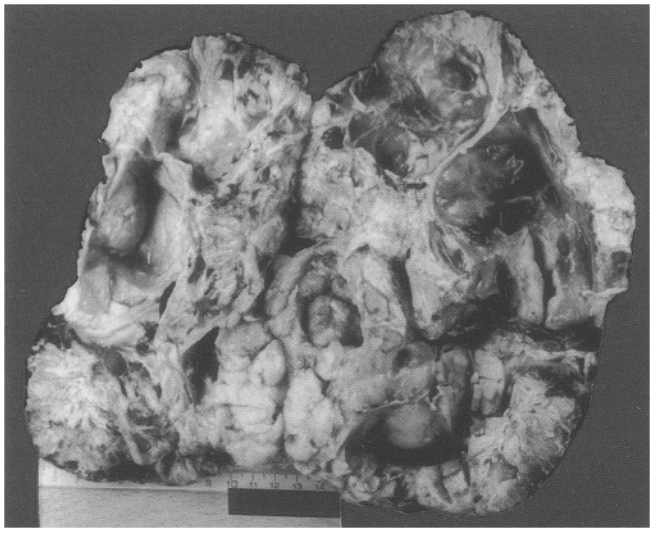

Fig. 1 Macroscopy. Medial cut section of right ovarian mass (25×13×9 cm) depicting multiple cystic cavities in a solid, beige, necrotic and oedematous parenchyma

The uterus weighed 130 g and measured 9×5×4 cm in its greatest dimensions, the endometrium measured 0.2 cm in thickness and was macroscopically devoid of tumour invasion.

The left ovary measured 4.5×2.2×0.8 cm and presented a beige, nodular, superficial lesion measuring about 1.5 cm in diameter. The left fallopian tube was unremarkable.

The histological features of the right ovarian mass disclosed prismatic cells with abundant eosinophilic, focally vacuolated cytoplasm and round or oval atypical nuclei showing numerous mitoses; cell membranes were indistinct. The predominating pattern depicted tubular glands lined by pseudostratified epithelial cells and separated one from another by thin strands of connective tissue (Fig. 2).

Less frequently, anastomosing cord-like structures of tumour cells resembling SCT were conspicuous (Fig. 3). Rarer foci of clear cell differentiation, without squamous elements, were also observed (Fig. 4). The stroma was often oedematous and did not contain luteinized cells. The tumour infiltration of the right fallopian tube was microscopically similar to the ovarian tumour.

The histological appearance of the left ovarian nodule was clearly an SEC displaying multiple foci of clear cell differentiation and areas of endometrioid carcinoma of the usual type. The left fallopian tube was histologically unremarkable.

The cytoplasmic vacuoles were distinctly demonstrated after staining with PAS, whereas only the apex of the tumour cells was positive with alcian blue. Neither the

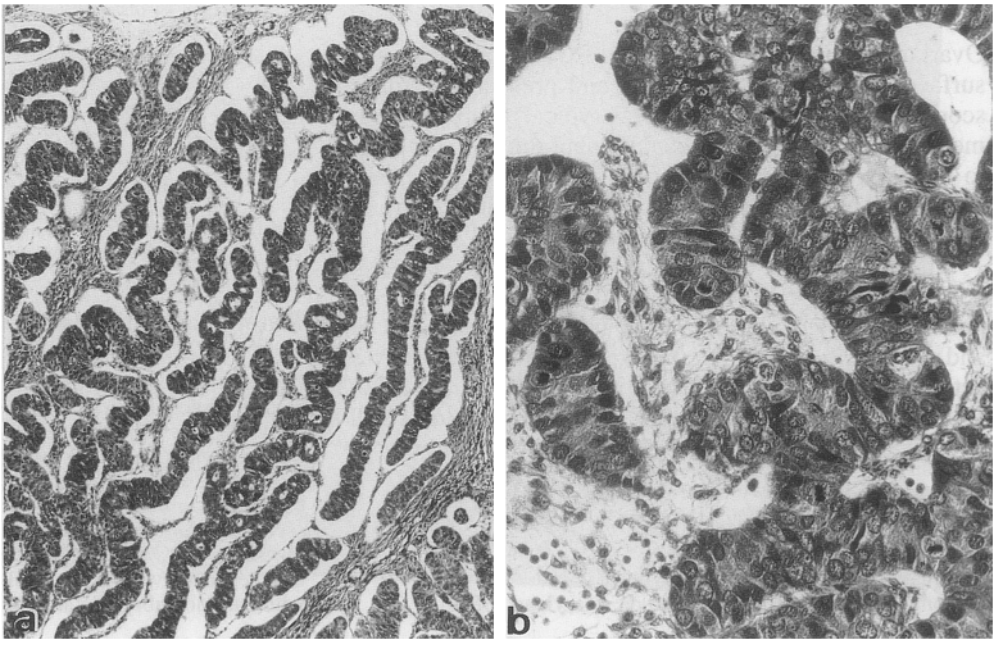

Fig. 2a, b Predominating pattern is of tortuous tubular glands lined by pseudostratified epithelial cells and separated by thin strands of connective tissue. [Haematoxylin and eosin, ×150 (**a**) and ×300 (**b**)]

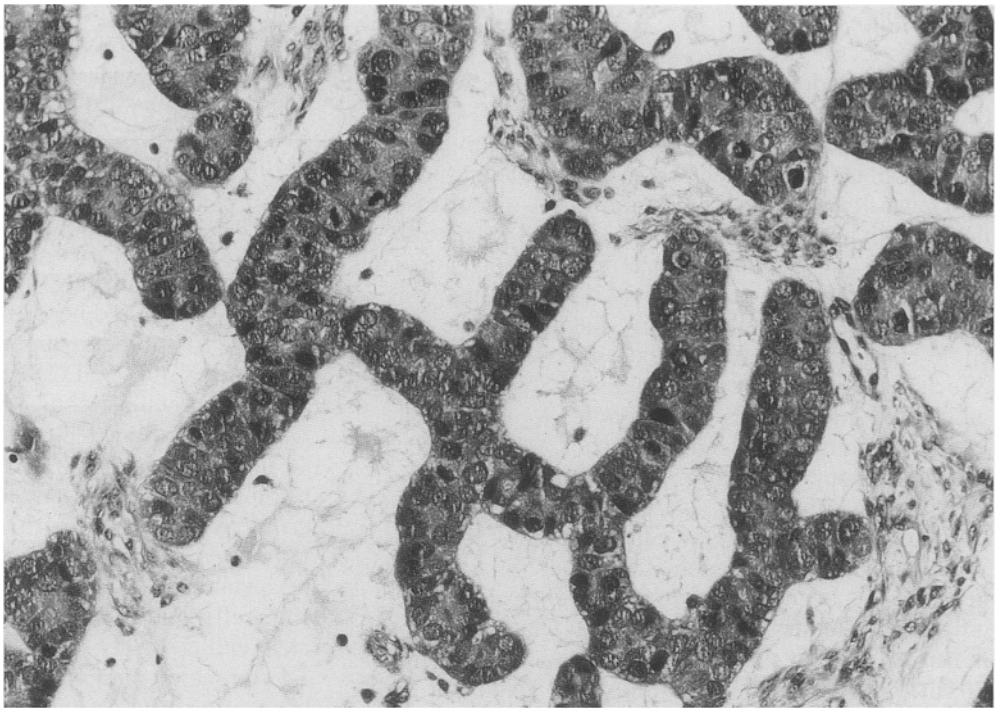

Fig. 3 Anastomosing cord-like structures of tumour cells resembling a Sertoli cell tumour. (Haematoxylin and eosin, ×300)

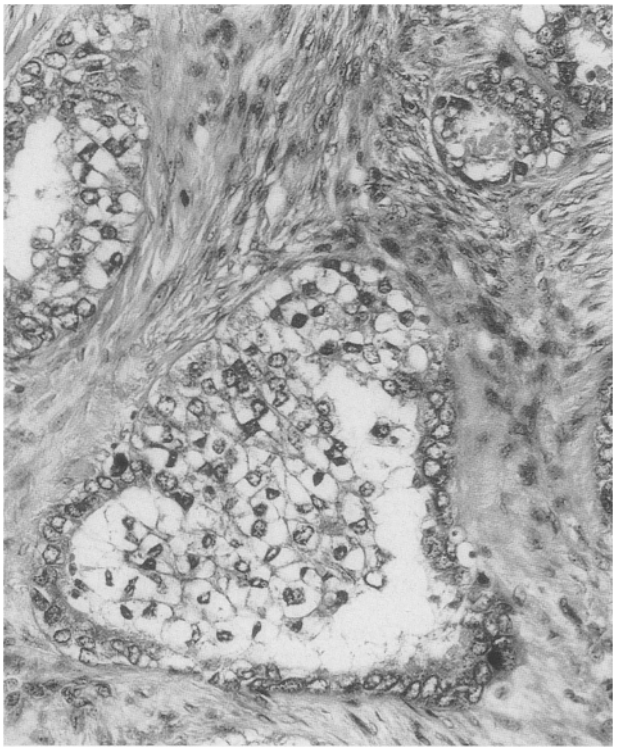

Fig. 4 Rare foci of clear cell differentiation. (Haematoxylin and eosin, ×300)

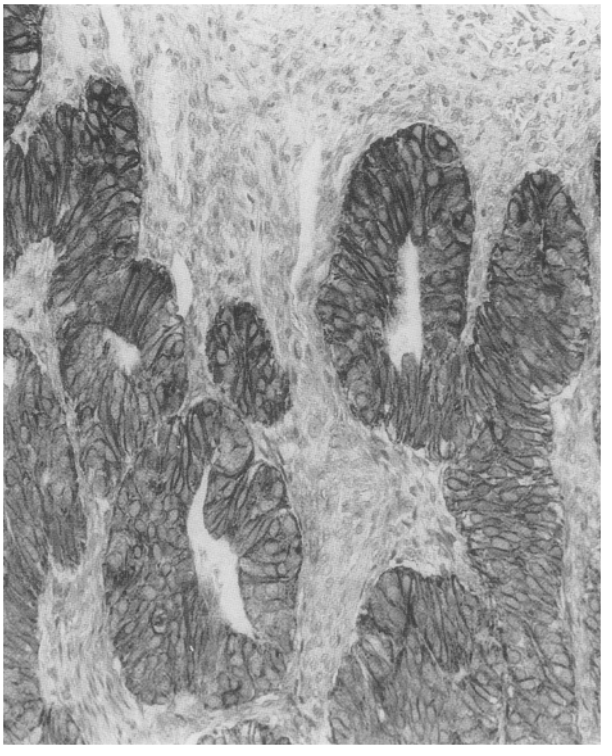

Fig. 5 Positive immunoreactivity in the tumour cells for epithelial membrane antigen. (×300)

Lars Grimelius technique nor immunohistochemical stains (chromogranin A, synaptophysin, NSE) demonstrated intracytoplasmic secretory granules.

Immunoreactivity was detected in the tumour cells only for EMA (Fig. 5), CAM 5.2, A-1 AT and ACT antibodies. The nuclei of the Sertoli-like tumour cells demonstrated a positive reaction for receptors for progesterone but not for oestrogen.

The endometrium showed foci of atypical complex hyperplasia. The peritoneal washings were positive for carcinoma cells.

Discussion

Sertoliform endometrioid carcinoma is an extremely rare tumour which may simulate SCT and SLCT. Only three articles describing cases encountered with this uncommon neoplasm have been reported in the literature [1, 4, 8]. Generally, the tumour occurs in post-menopausal patients, with an average age of 68 years [8], whereas SCT and SLCT are usually encountered in younger patients, with an average age of 28 years [5]. Our patient was 71-years-old when her tumour was diagnosed. She presented no characteristics of virilization; however, androgenic effects have been reported in about 75% of the patients with SCT and SLCT [5].

The tumour was voluminous and on cut section was beige in colour, contrasting with SCT and SLCT which are typically smaller in size (8 cm in maximum dimension) and usually yellow on cut section [5].

Like the classic endometrioid carcinoma, bilateral masses have been observed in 15% of ovarian SEC [1]; however bilaterality of SCT and SLCT has been reported in less than 5% of the cases [5].

Histologically the epithelium of the glandular, tubular and cord-like areas was mainly pseudostratified. This feature is rarely observed in SCT and SLCT in which the epithelium is generally formed by a single layer of columnar cells [4].

In our case, the stroma was densely fibrous or oedematous. Luteinized stromal cells resembling steroid-producing cells were not observed. These cells have been described in SEC [4, 8], their presence making the differential diagnosis with SCT and SLCT more difficult.

Squamous and ciliated elements may rarely be observed in SEC [4, 8], but have never been described in SCT and SLCT [5]. These distinctive features, when present, are of great value in confirming the endometrioid nature of the tumour. In our case, neither squamous nor ciliated differentiation was noted, but foci of clear cell carcinoma were prominent. This finding has been described in 24% of the classic ovarian EC [2], but has never been reported in SEC [1, 4, 8].

Immunohistochemical studies proved to be very helpful in the differential diagnosis. In our case, the tumour demonstrated strong positive immunoreactivity with the anti-cytokeratin (CAM 5.2) and with EMA; antibodies CK 20, CK 13, AE 1/AE 3, anti-S-100 and anti-vimentin were not immunoreactive. As they originate from the ovarian epithelium, and not from the sex-cord stroma, the Sertoli-like cells lack the endocrine properties observed in real Sertoli cells.

In an immunohistochemical study of 17 cases of EC resembling sex cord-stromal tumours (ECSCS), Aguirre et al. [1] insisted on the diagnostic value of EMA and OM-1 antibodies to distinguish ECSCS from SCT and SLCT: positive immunoreactivity was displayed in 17 of 17 and 15 of 17 of the former tumours, respectively, and in only 1 of the 14 cases of SCT and SLCT was there positive immunoreactivity to both antibodies. Furthermore, the opinion of the same authors is that the antibodies directed against the cytokeratins, vimentin, lysozyme and S-100, are devoid of interest of differential diagnosis. The presence of progesterone receptors is in favour of the endometrioid nature of this neoplasm, since a study by Kühnel et al. demonstrated progesterone receptor positivity in 50% of the cases of ovarian EC but no positivity was detected in SLCT [3].

Before establishing a diagnosis of SEC, two other possibilities should be eliminated: carcinoid tumours and tubular Krukenberg tumours. Carcinoid tumours can simulate SCT and SLCT [5, 7, 8]. Agyrophilic intracytoplasmic granules can be demonstrated by the Lars Grimelius staining technique.

In case of doubt synaptophysin, chromogranin and serotonin antibodies, as well as subsequent electron microscopy study will permit correct identification of the tumour. A diagnosis of tubular Krukenberg tumour can be invalidated in the absence of mucin-containing signet ring cells, and in the presence of foci of typical EC and clear cell elements.

The majority of SEC described in the literature have been originally misdiagnosed as SCT and SCLT [4, 8]. Consequently, in our opinion, before establishing a diagnosis of SCT or SCLT, especially in post-menopausal patients, it is mandatory to make extensive sampling of the surgical specimen and to search for foci of typical EC and squamous or clear cell elements. To eradicate doubt, the diagnosis can be confirmed by immunohistochemical study with the anti-EMA antibody.

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