SHORT REPORT

Mixed epithelial and stromal tumour of the kidney with luteinised ovarian stroma

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We report a case of a 9-cm mixed epithelial and stromal tumour of the kidney in an obese 70-year-old woman with diabetes. The ovarian-type stroma had a spindle cell component that was positive for progesterone receptors and had the hitherto unreported presence of abundant foci of luteinised stromal cells with characteristic immunohistochemical positivity to α -inhibin, calretinin, aromatase and gonadotropin-releasing hormone (GnRH) receptors. We conclude that the stromal component is identical to ovarian cortical stroma. We believe that ovarian-type stroma occurs in extragenital tumours as a result of an epithelial–stromal interaction in an environment of hormonal hyperstimulation.

Mixed epithelial and stromal tumours (MESTs) of the kidney¹ are rare benign composite cystic neoplasms of stroma and epithelium, which occur in women under oestrogen stimulation and unusually in men undergoing oestrogenic treatment. The stroma of these tumours is remarkable, resembling that of the ovary. The presence of isolated smooth muscle differentiation and oestrogen and progesterone receptors in these tumours suggests an ovarian phenotype,¹ although, to date, more specific immunohistochemical markers for ovarian stroma have not been reported in MESTs.² We report a case of MEST in which ovarian-type stroma (OTS) had luteinised stromal cells with a characteristic immunohistochemical ovarian profile. We also review the occurrence of heterotopic ovarian stroma and ovarian cell types in different tumours and organs.

CASE REPORT

A 70-year-old woman, menopausal since age 52, with a history of hypertension, obesity (body mass index 34.24) and type 2 diabetes, experienced an episode of metrorrhagia due to an endometrial polyp. She had been diagnosed with a 3-cm infiltrating ductal carcinoma of the breast. She underwent treatment with chemotherapy and radiotherapy and regular administration of anastrozol, a non-steroidal aromatase inhibitor. An abdominal computerised axial tomography scan carried out 3 months after mastectomy showed marked hepatic fatty change and, as an incidental finding, a right renal cystic multilocular mass. Gynaecological examination showed atrophic uterus and ovaries. A right nephrectomy was carried out. Six months later, the patient is alive and well.

Pathology

The 9-cm well-circumscribed tumour was situated in the renal hilum and was composed of multiple cysts ranging from 1 to 3 cm, with a smooth inner surface and serous contents (fig 1). The septal areas were white with some yellow streaks.

Microscopically, the cysts were lined by a cuboidal epithelium. In the septa there were small, narrow tubuli. The stroma showed richly cellular areas with packed spindle cells forming

wavy or whorled patterns with the “blue” appearance of ovarian stroma (fig 2A), and contained isolated clusters of cells, which had large polygonal, clear, foamy cytoplasm and central, round, regular nuclei (fig 2B). They were considered to be luteinised cells. Some broad fibrous patches resembling ovarian albuginea were also found.

The endometrial polyp removed 2 years previously had a typical histology, with isolated mitoses in its epithelial component and a 10% Ki-67 proliferation index, much higher than would be expected in a woman 18 years after menopause. Furthermore, a vaginal smear carried out before nephrectomy had shown an increase in the karyopyknotic index as a response to oestrogen stimulation.

Immunohistochemically (all antibodies from Master Diagnostica, Granada, Spain, except for monoclonal aromatase antibody SM1671P, from Acris, Germany, at 1:100 dilution), the cytoplasm of the luteinised stromal cells was CD68 and cytokeratin negative, but was strongly positive for vimentin, α -inhibin, calretinin and aromatase (fig 2C–E). The background OTS showed positive oestrogen, progesterone (fig 2F) and GnRH receptors. Isolated cytoplasmic positivity for smooth muscle actin and desmin was seen in some fusiform cells.

DISCUSSION

MESTs are a distinctive category of cystic renal tumours, different from cystic nephroblastomas, which have a biphasic proliferation of benign epithelium and stroma. MESTs occur predominantly in adult women and are associated with various hyperoestrogenic conditions. Indeed, this case is an obese patient with diabetes, probably resulting in peripheral oestrogen conversion by aromatisation, a situation that may have

Figure 1 Multicystic tumour present in the renal hilum.

Abbreviations: GnRH, gonadotropin-releasing hormone; MEST, mixed epithelial and stromal tumour; OTS, ovarian-type stroma

contributed to the presence of proliferative features in the endometrial polyp and the vaginal epithelium, as well as the concomitant breast cancer.

A striking feature of the stromal component of MESTs lies in its resemblance to ovarian stromal cortical tissue.³ Analogous stroma (OTS) has been reported in cystic mixed epithelial stromal tumours of extragenital locations such as pancreas and the hepatobiliary system.⁴⁻⁶ Apart from these neoplasms, ovarian stroma can be found in the adrenal gland of menopausal or oophorectomised patients,⁷ where it is unrelated to any epithelial component. A last feature, and unrelated to any of the above situations, is the presence of ovarian-type luteinised cells, which even display oestrogenic activity⁸ in some uterine sex-cord-like tumours, a type of neoplasm of uncertain histogenesis.

Microscopically, ovarian-type stroma of MESTs is composed of fusiform cells with scanty cytoplasm, which have a characteristic basophilic histology with a whorled, interlaced pattern. This case not only shows this component but also has a hitherto unreported feature: nests of luteinised cells, analogous to those found in ovarian hyperthecosis, which further emphasises its similarity to ovarian stroma. In a previous report,⁹ similar cells have been shown in the OTS of pancreatic cystadenomas, where they were positive for α -inhibin⁶ and progesterone receptors. These findings, however, have not been reported in MESTs and, indeed, a recent and extensive series of

these renal neoplasms² failed to show the presence of α -inhibin positivity in their tumours. We report for the first time in MESTs the presence of luteinised ovarian-type cells, whose identity is supported by the positivity of highly specific immunohistochemical markers such as α -inhibin, calretinin,¹⁰ aromatase and GnRH receptors.¹¹ Thus, we can conclude that this tissue is identical to ovarian stroma.

The histogenesis of OTS in MESTs was first explained by an embryological proximity between the urinary and genital systems,³ conforming with hypothetical displaced embryological rests (hamartoma).^{2,6} Such embryological theories are difficult to sustain for kidney tumours, as the developmental pathways of the ovary and kidney are different. The proposed terminology of "müllerian-like stroma"³ is a misnomer, because ovarian stroma is not related to the paramesonephric (müllerian) duct. Furthermore, these embryological explanations do not apply to the occurrence of OTS in tumours of pancreatic or hepatobiliary locations, as these organs arise from a different germ layer.

A more likely hypothesis to be considered is that of an epithelial-stromal interaction in a status of hormonal hyperstimulation.^{1,4,12} This possibility is partly supported by the recent finding, in pancreatic mucinous cystadenomas with OTS, of overexpression of genes associated with oestrogen metabolism.¹³ This may represent a mechanism similar to that occurring in the adrenals, where the unopposed high levels of

Figure 2 Mixed tumour with cystic dilations lined by a cuboidal epithelium (A). The stroma is of ovarian type and shows luteinised cells (arrows) (B) positive to calretinin (C), α -inhibin (D) and aromatase (E). The spindle cell component is positive to progesterone receptors (F).

pituitary gonadotropins of oophorectomised or menopausal patients⁷ are believed to be responsible for the occurrence of ectopic OTS. Both adrenals and ovary, however, share a very close developmental relationship that makes this phenomenon easier to understand in this particular location.

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Informed consent has been received for publication of this information

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