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CASE REPORT

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Primary signet-ring stromal tumor of the testis

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Abstract We present, in a 47-year-old man, the first case of the signet-ring stromal tumor of the testis. The tumor was located beneath the tunica albuginea surrounded by the testicular tubules and rete testis. It was sharply circumscribed by a thin and irregular fibrous capsule. Histologically, it was composed of cells with a widespread signet-ring cell change separated by fibrous stroma. In some places, the signet-ring cells formed vague Indian files, thus resembling metastatic carcinomas with signet-ring cell morphology. Under high magnification, most of the cytoplasm of the tumor cells was seen to be replaced by an empty clear vacuole which pushed the nuclei to the periphery of the cells. Some of the nuclei were indented by the cytoplasmic vacuoles, others were without indentation. Only in a small area did the tumor show cells without a signet-ring cell change. They looked like epithelioid fibroblasts forming abortive and vaguely tubular structures. Mitoses and necroses were absent. Mucicarmine and PAS stains were negative. Immunohistochemically, the tumor was vimentin positive and it was negative with antibodies to cytokeratins, inhibin, prostatic acid phosphatase, prostate-specific antigen, smooth muscle actin, S-100 protein, EMA and calretinin. The signet-ring stromal tumor of the testis is thus similar morphologically and immunohistochemically to the signet-ring stromal tumor of the ovary. The patient was free of recurrence and metastasis 3 years after the excision.

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Introduction

Signet-ring stromal tumor is a rare type of ovarian tumor and it has never before been described in the testis. Microscopically, this ovarian neoplasm is characterized by a proliferation of stromal spindle-shaped cells merged with rounded cells containing eccentric nuclei and single vacuoles, resembling signet-ring cells [1, 3, 7–10, 12]. The signet-ring cells may either be diffuse or represent only a focal change in an otherwise typical fibroma. We present a case of signet-ring stromal tumor of the testis identical to that of the ovary. To the best of our knowledge, this is the first case of signet-ring stromal tumor of the testis ever to be published.

Materials and methods

Tissue was fixed in 4% formaldehyde and paraffin embedded. Sections (5 μm thick) were stained using routine staining methods.

The case was examined by means of immunohistochemistry on the formaldehyde-fixed, paraffin-embedded material. As a detection system, we employed the avidin–biotin complex or streptavidin–biotin complex labeled with peroxidase or alkaline phosphatase (DakoCytomation). We used microwave antigen pretreatment prior to the application of the primary antibodies. Automated immunostaining employing Lab Vision autostainer was used. Antibodies against cytokeratins (CAM 5.2, Becton-Dickinson), AE1–AE3 (Boehringer), epithelial membrane antigen (EMA; E29, DakoCytomation), S-100 protein (polyclonal, DakoCytomation), neuron specific enolase (NSE; polyclonal, DakoCytomation), prostate specific antigen (polyclonal, DakoCytomation), prostate acid phosphatase (polyclonal, DakoCytomation), glial fibrillary acidic protein (polyclonal, DakoCytomation), CD 34 (QBEnd 10, DakoCytomation), calretinin (DC8, Zymed), vimentin (V9,

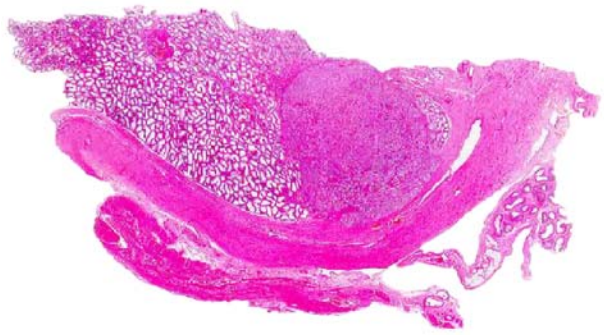

Fig. 1 A low-power view showing that the tumor lies beneath the tunica albuginea surrounded by the testicular tubules and rete testis

DakoCytomation), smooth muscle actin (1A6, DakoCytomation), desmin (D33, DakoCytomation), placental alkaline phosphatase (8B6, DakoCytomation), melanosome (HMB45, DakoCytomation), estrogen and progesterone receptors (Immunotech), androgen receptors (AR 441 DakoCytomation) and Ki67 (MIB1, Immunotech) were used.

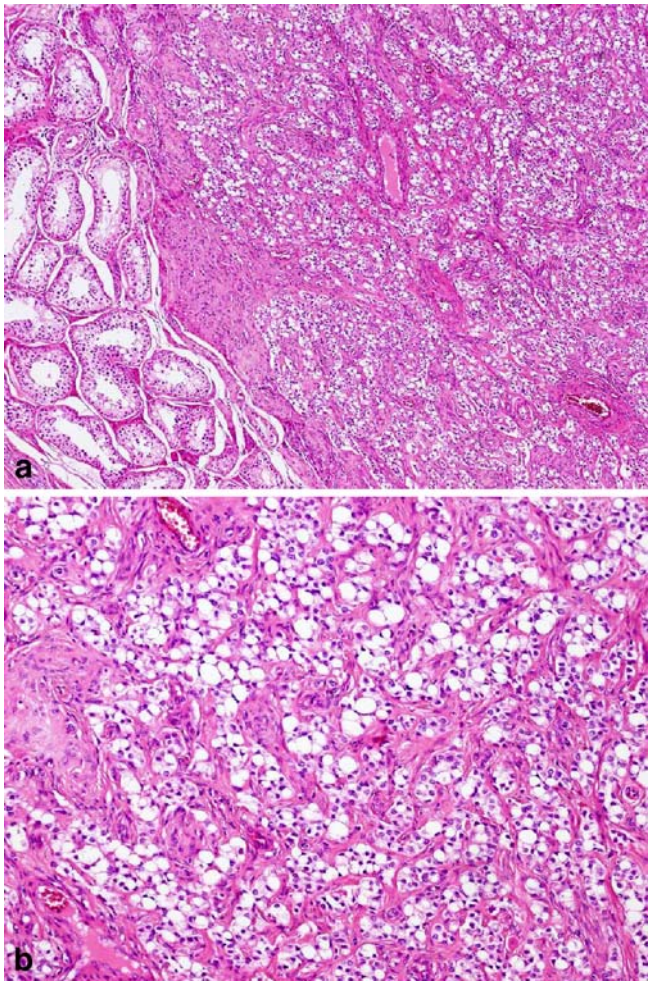

Fig. 2 The tumor is well circumscribed (**a**) and is formed by cells with widespread signet-ring cell change separated by fibrous stroma (**b**)

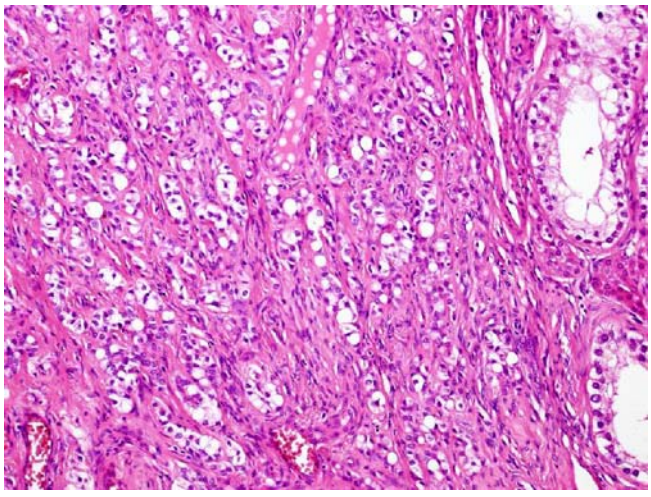

Fig. 3 In some places, the signet-ring cells form vague Indian files, thus having a resemblance to metastatic signet-ring cell carcinomas

Tissue material for ultrastructural examination was not available.

Results

Case report

A 47-year-old patient was found to have a round-shaped tumor 1 cm in largest diameter in the right testis. The tumor was surgically removed. Grossly it was white in color and hard in consistency. The patient is without signs of recurrence and metastasis 3 years after the excision.

The tumor was located beneath the tunica albuginea surrounded by the testicular tubules and rete testis. It was sharply circumscribed by a thin and irregular fibrous capsule (Fig. 1). Histologically, it was composed of irregular and variously shaped trabeculae of cells with a widespread

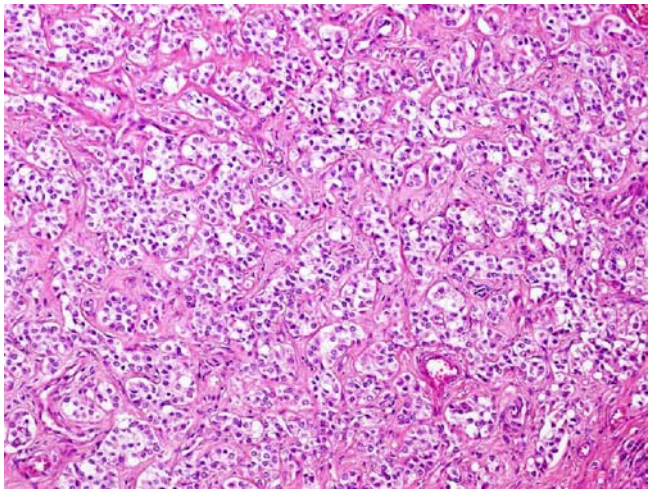

Fig. 4 The tumor cells in this area have the appearance of epithelioid fibroblasts

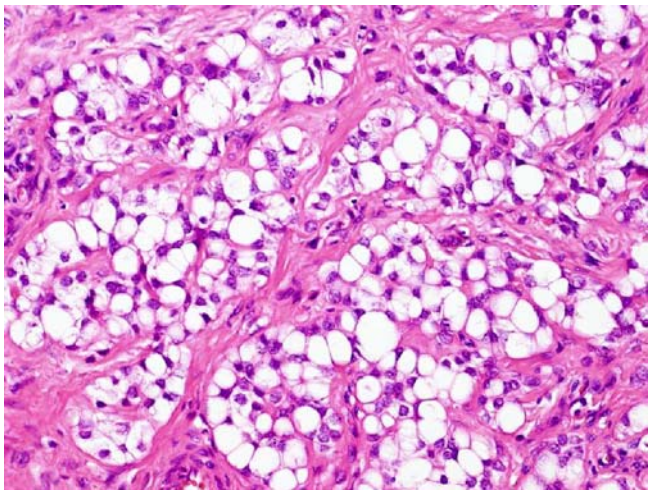

Fig. 5 Under high magnification, most of the cytoplasm is shown to be replaced by an empty clear vacuole that has pushed the nucleus to the periphery of the cell. Some of the nuclei are indented by the cytoplasmic vacuoles, while others are not

signet-ring cell change separated by fibrous stroma (Fig. 2). In some places the signet-ring cells formed vague Indian files, thus resembling metastatic signet-ring cell carcinomas (Fig. 3). Only in a small area were there cells without signet-ring cell change. The tumor cells in this area had the appearance of epithelioid fibroblasts arranged in abortive and vaguely microalveolar structures (Fig. 4). Under high magnification, most of the cytoplasm of the majority of the tumor cells was seen to be replaced by an empty clear vacuole which pushed the nucleus to the periphery of the cell. Some of the nuclei were indented by the cytoplasmic vacuoles, others were without sign of indentation (Fig. 5). Mucicarmine and PAS stains were negative. Mitoses and necroses were absent.

Immunohistochemically, the tumor cells reacted strongly with antibody to vimentin; and all other antibodies—including those against MIB1 and estrogen, progesterone and androgen receptors—reacted negatively.

Discussion

Benign fibrous tumors of the testis are quite unusual. Most of these tumors within this category are paratesticular and they have been considered variants of fibrous pseudotumor [11]. Jones et al. [4] coined the term "fibroma of gonadal stromal origin" for a group of rare testicular tumors in order to delineate these neoplasms from all other types of testicular lesions for which the term "fibroma" was used. However, in none of the cases of testicular fibromas of gonadal stromal origin was the observation of a signet-ring cell change ever published [2, 4].

Our case seems to have many similarities to the rare ovarian neoplasm called "signet-ring stromal tumors of the ovary" (SSTO). SSTO shown a spindle cell fibroblastic component which merges imperceptibly with rounded cells containing eccentric nuclei and large vacuoles resembling signet-ring cells. Ultrastructural examination showed that in some cases of SSTO the vacuoles result from generalized edema of the cytoplasmic matrix, from a swelling of mitochondria or from cytoplasmic pseudoinclusions of an edematous extracellular matrix [3]. Similar to this tumor, our case revealed a fibroblastic component without signet-ring vacuoles, which merged with PAS and mucicarmine negative signet-ring cells [3]. In addition, immunohistochemical vimentin positivity and immunohistochemical negativity with antibodies to cytokeratins, inhibin, smooth muscle actin, S-100 protein, EMA, and calretinin confirm that the immunoprofile of our case was identical to that of SSTO [3, 12]. Absence of mitoses, necroses, immunohistochemical negativity with MIB1 antibody and sharp circumscription of the lesion point to the benign nature of signet-ring stromal tumor of the testis.

There are very few lesions from which signet-ring stromal tumor of the testis should be differentiated. In contrast to the ovary, metastasis of gastric adenocarcinoma (Krukenberg tumor) with signet-ring cell morphology is an extremely rare event in the testis [5, 6]. Sharp circumscription, lack of mitoses, PAS, mucicarmine negativity and immunohistochemical negativity with antibodies to MIB1, EMA and cytokeratins clearly distinguish the visceral metastases with signet-ring cell morphology from the primary signet-ring stromal tumor of the testis. The authors are not aware of any other primary testicular tumor with so widespread a signet-ring cell morphology.

In summary, we describe the first example of the signet-ring stromal tumor of the testis, which had similar features to the SSTO. It is different from any other known primary testicular neoplasm and it can easily be differentiated by morphology and by immunohistochemical means from visceral metastatic carcinomas with signet-ring cell morphology.

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