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Case report

Intratesticular serous cystadenoma of borderline malignancy. A pathological, histochemical and DNA content study of a case with long-term follow-up

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Abstract. A 61-year-old man presented with a painless right testicular swelling of 6 months duration. A right orchiectomy was performed and pathological examination showed an intratesticular serous borderline tumour (SBT). Immunohistochemical staining was positive for carcinoembryonic antigen, LeuM1, B72.3, S100-protein, Ca125, cytokeratins AE1/AE3 and vimentin, suggesting a Müllerian origin or differentiation. DNA image analysis revealed an aneuploid histogram. The favorable outcome of the patient confirms that testicular SBTs behave as non-aggressive tumours, even when characterized by aneuploid DNA content.

Key words: Testis – Serous borderline tumour – Immunohistochemistry – DNA-analysis

Introduction

Testicular and paratesticular tumours of ovarian common epithelial type are very rare (Young and Scully 1986). The most frequent histological type is the serous. Seven testicular serous tumours have been reported in the literature (Table 1); six of them were serous borderline tumours (SBTs) and one was an SBT with foci of carcinomatous infiltration. The biological behaviour of these tumours, based on a short follow-up of five cases, does not seem aggressive. We present a case of intratesticular SBT showing morphological and histochemical evidence of Müllerian differentiation, characterized by an aneuploid DNA content and a favorable outcome after a long-term follow-up.

Case report

A 61-year-old Caucasian male was admitted to the hospital with a history of painless right scrotal swelling of 6 months duration. Physical examination revealed a testicular mass which appeared cystic on ultrasound examination. Laboratory tests were unremarkable. A right orchiectomy was performed. The patient, followed up periodically with clinical examinations, is alive and well 15 years after surgery.

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Materials and methods

The testis was cut and fixed in buffered formalin. Nine blocks of paraffin-embedded material were prepared; six samples were taken from the cyst, one from the surrounding testicular parenchyma, one from the epididymis and one from the spermatic cord. Sections were stained with haematoxylin and eosin, periodic acid-Schiff (PAS), and PAS after diastase predigestion (PAS-D).

Immunostaining was performed on formalin-fixed, paraffin-embedded material using the avidin-biotin-peroxidase complex (ABC) technique (Hsu et al. 1981), with an ABC kit (Vector, Burlingame, Calif., USA). Tissue serial sections were stained with primary antibodies to carcinoembryonic antigen (CEA, DakoPatts, Santa Barbara, Calif., USA; 1:1000), Leu-M1 (DakoPatts, 1:50), B 72.3 antigen (Nuclear Laser Medicine, Milan, Italy; 1:10), S100 protein (Ortho Diagnostic System, Raritan, N.J., USA; pre-diluted), placental alkaline phosphatase (PLAP, DakoPatts, 1:50), Ca-125 (CIS Diagnostici SPA, Vercelli, Italy; pre-diluted), cytokeratins AE1/AE3, (Ortho Diagnostic System, pre-diluted) and vimentin (DakoPatts, 1:10). Appropriate positive and negative controls for each antibody were carried out.

DNA content was measured on a Feulgen-stained section using a Leitz TAS image analyser based on a Leitz Orthoplan microscope (Leica, Wetzelar, Germany). One hundred non-overlapping nuclei were interactively measured together with 30 lymphocytes present in the same section and used to establish the DNA diploid reference value. The nuclear DNA content was expressed as a DNA histogram and classified according to the distribution of the DNA peaks in the different ploidy regions (De Nictolis et al. 1992).

Results

On gross examination the upper portion of the testis was enlarged, while the tunica vaginalis was normal. On cut surface, a unilocular cyst measuring 2.5 cm in diameter and containing a dense fluid was identified within the testicular parenchyma, in the superior-medial portion of the testis. The cyst was separated from the

Table 1. Testicular tumours of ovarian serous type

Authors	Age	Diagnosis	Treatment	Follow-up
Herschman and Ross 1974	56	Papillary cystadenoma	Orchiectomy	Died after 3 weeks, of lung cancer. Autopsy showed no evidence of testicular tumour spread
Young and Scully 1986	18	Serous surface papilloma of borderline malignancy	Orchiectomy	Alive and well 3 years
Young and Scully 1986	59	Serous papillary cystadenoma of borderline malignancy	Orchiectomy	Alive and well 3 years
Axiotis 1988	51	Serous papillary cystadenoma of low malignant potential	Orchiectomy	Alive and well 1.5 years
Meister et al. 1990	54	Cystadenoma of borderline malignancy	Orchiectomy	Unknown
Meister et al. 1990	44	Serous cystadenoma of borderline malignancy	Orchiectomy	Unknown
Remmele et al. 1992	59	Serous papillary cystadenoma of borderline malignancy with foci of cystadenocarcinoma	Orchiectomy	Alive and well 1 year
Present case 1993	61	Serous cystadenoma of borderline malignancy	Orchiectomy	Alive and well 15 years

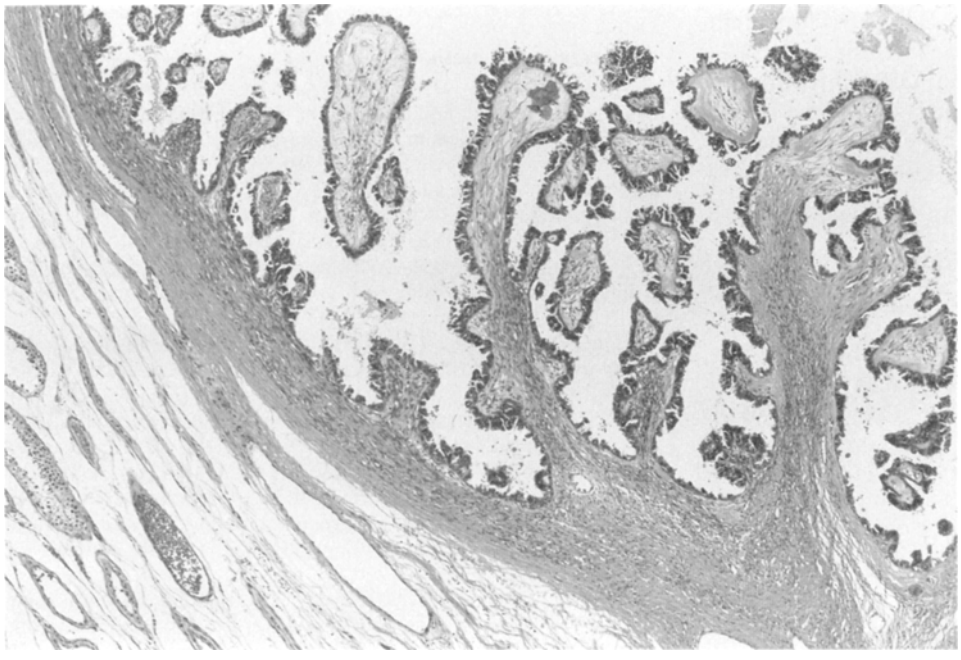

Fig. 1. Testicular serous borderline tumour (SBT). The inner surface of the cyst wall shows papillae lined by low columnar epithelial cells. ×63

Table 2. Results of immunohistochemistry

Determinants	Positive cells (%)	Type of positivity
CEA	10	Cytoplasmic
Leu M1	50	Membranous
B72.3	30	Cytoplasmic Membranous
S100	40	Cytoplasmic
PLAP	0	–
Ca 125	20	Membranous
Cytokeratins	100	Cytoplasmic
Vimentin	10	Cytoplasmic

surrounding parenchyma by a thin fibrous capsule; the internal lining of the cyst was largely smooth with areas of granular, gray tissue.

Histologically, the granular tissue consisted of papillae of variable size (Fig. 1) lined by low columnar and focally ciliated epithelial cells exhibiting discontinuous tufting (Fig. 2). Detached clusters of epithelial cells were present in the eosinophilic fluid of the cyst. Nuclear atypia was moderate and only a few mitotic figures were observed. The cell brush borders and the intracystic fluid stained with PAS-D, indicating the presence of neutral mucins. The non-papillary portion of the cyst was also

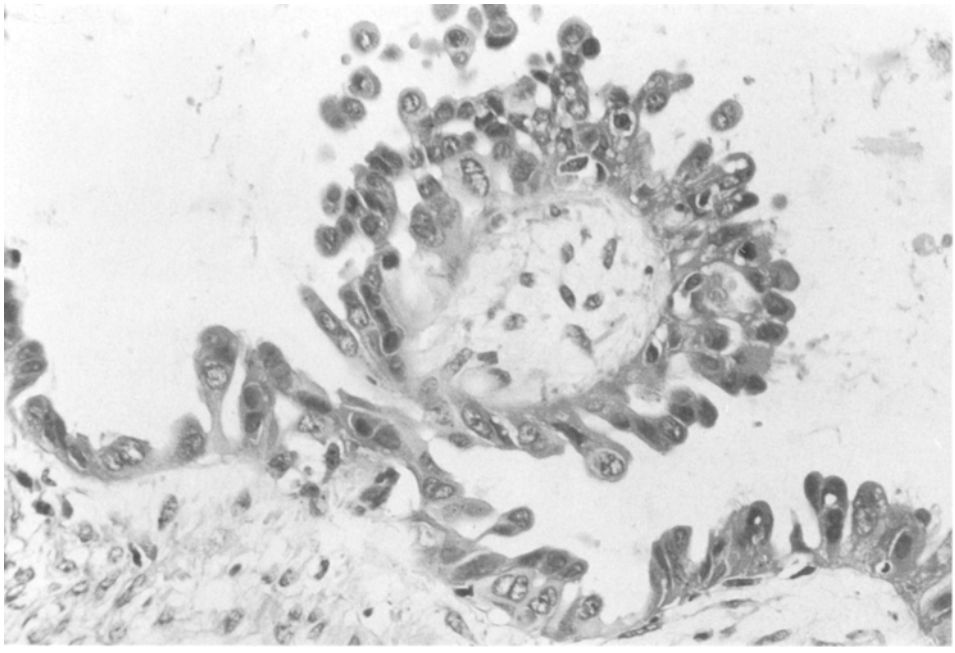

Fig. 2. Testicular SBT. Atypical columnar cells, sometimes ciliated, showing irregular stratification. ×400

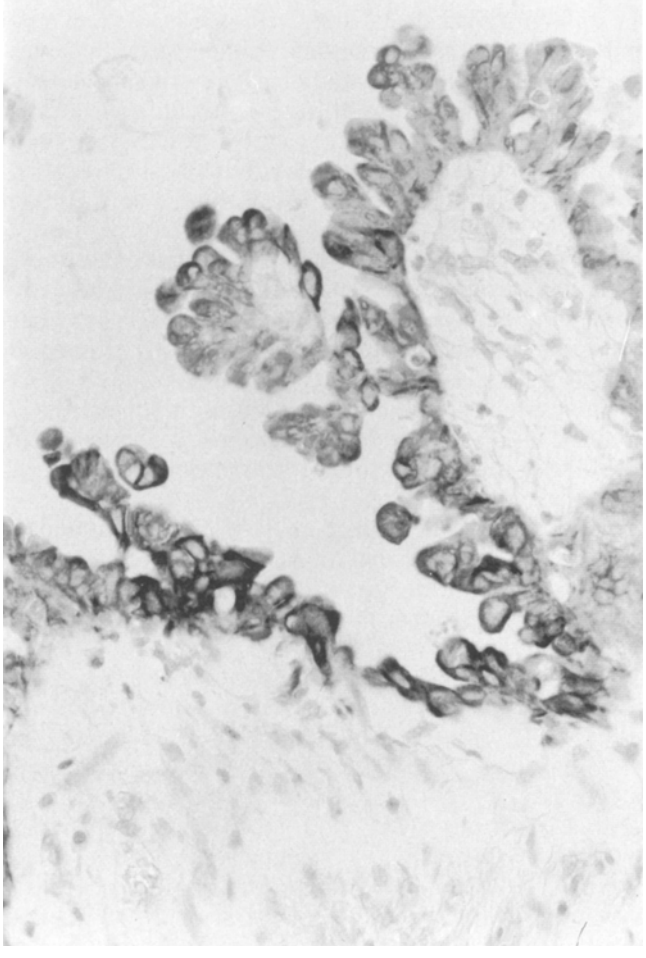

Fig. 3. Testicular SBT. Immunoreactivity for carcinoembryonic antigen is present in the cell cytoplasm. ×400

lined by low columnar and focally ciliated cells with mild nuclear atypia and focal stratification. The adjacent seminiferous tubules showed focal atrophic changes; the rete testis, epididymis and spermatic cord were unremarkable. A diagnosis of serous cystadenoma of borderline malignancy was made.

The results of the immunohistochemically study are summarized in Table 2. Cytoplasmic staining for CEA is illustrated in Fig. 3, whereas membranous staining for CA-125 is shown in Fig. 4.

DNA image analysis revealed an aneuploid histogram (Fig. 5).

Discussion

The occurrence in the testis and paratesticular tissues of neoplasms indistinguishable from ovarian tumours of common epithelial type is unusual: the first reported series included only four cases, all seen in consultation (Young and Scully 1986). SBTs accounted for the majority of these neoplasms (Herschman and Ross 1974; Young and Scully 1986; Axiotis 1988; Meister et al. 1990).

Both the gross and microscopic features of our case were identical to those of ovarian SBTs. Nevertheless, in considering the site of origin of the tumour, the most relevant differential diagnosis should be with well-differentiated mesothelioma arising from the tunica vaginalis (Antman et al. 1984; Grove et al. 1989). The intratesticular location of our tumour and its lack of connection with the tunica vaginalis argue against the diagnosis of mesothelioma. Moreover, histologically the cells of mesothelioma are more uniform than those of SBT, and

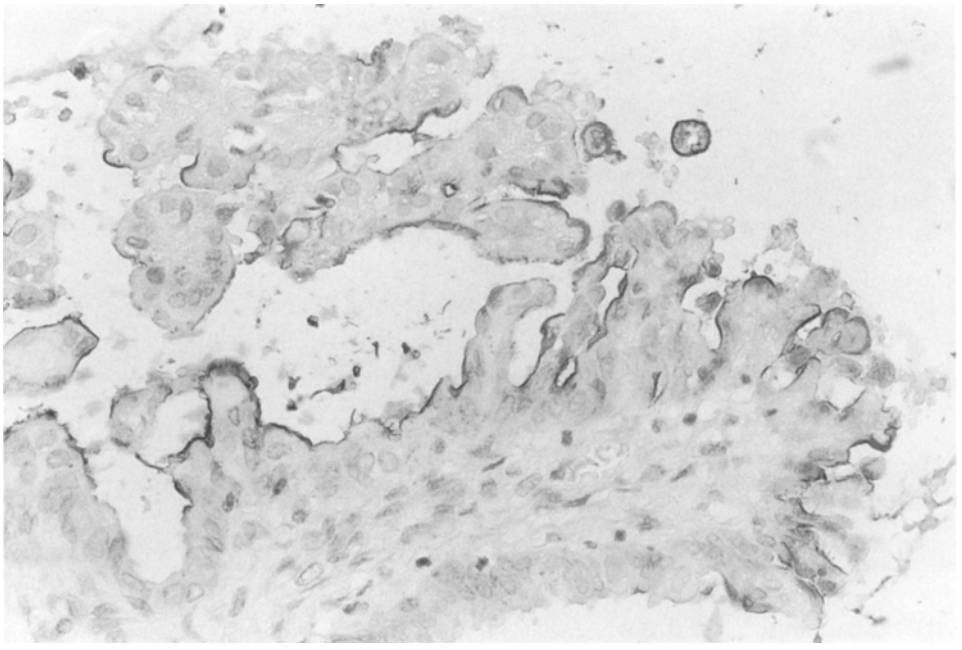

Fig. 4. Testicular SBT. Immunoreactivity for Ca-125 is mainly observed on the luminal border of the tumour cells. ×400

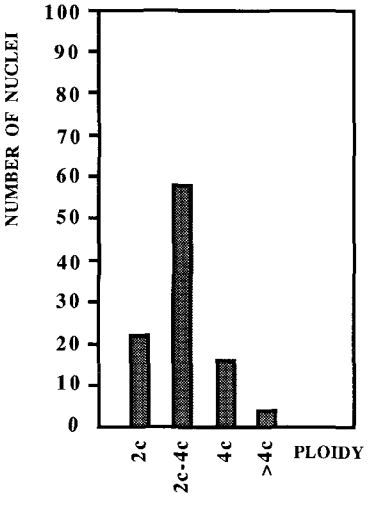

Fig. 5. Aneuploid DNA histogram of a testicular SBT showing a high proportion of nuclei between 2c and 4c

cilia are characteristically absent (Young and Scully 1986). Immunohistochemistry may be of additional help in differentiating SBT from mesothelioma. Although the rate of positive cells varied, immunoreaction for CEA, LeuM1, B72.3, S100 and Ca125 was obtained in our case. Although none of these immunohistochemical markers is completely specific for Müllerian neoplasms, their simultaneous detection is consistent with the Müllerian nature of our tumour (Wick et al. 1986); moreover, CEA, B72.3 and LeuM1 positivities may be considered sufficient evidence to exclude the diagnosis of mesothelioma (Khoury et al. 1990; Clement and Young 1993). Cytokeratins and vimentin were co-expressed by many tumour cells; this is in agreement with the results obtained in ovarian SBTs (Viale et al. 1988), and it underlines the probable common origin of these tumours, whether they arise from the ovary or testis.

Other uncommon tumours that may be included in the differential diagnosis are carcinoma of the rete testis and metastatic adenocarcinoma to the testis. Unlike testicular SBTs, rete testis carcinomas are grossly solid and histologically show areas of transition within the normal rete testis. Although metastatic carcinoma, may theoretically be included in the differential diagnosis, identification of a primary tumour should produce a correct diagnosis.

The histogenesis of testicular SBTs and of testicular Müllerian tumours in general has been discussed by Young and Scully (1986); intratesticular SBTs may derive from mesothelium present within the testicular parenchyma. Possibly, remnants of Müllerian ducts or vaginal mesothelium are entrapped during testicular development; co-expression of cytokeratins and vimentin by the tumour cells would support this hypothesis (Miettinen et al. 1983).

In our case, DNA image analysis showed an aneuploid DNA content. Using flow and static cytometry, several investigators have reported primary ovarian SBTs to be diploid in some cases and aneuploid in others (Fu et al. 1986; Klemi et al. 1988; De Nictolis et al. 1992; Padberg et al. 1992). Some investigators have suggested an association between aneuploidy of ovarian SBTs and unfavorable outcome (Fu et al. 1986; Padberg et al. 1992), whereas others have failed to detect a correlation between ovarian SBT ploidy and prognosis (Klemi et al. 1988; De Nictolis et al. 1992). Moreover, other investigators have indicated that prognosis in ovarian SBTs, depends mainly upon the presence and type of peritoneal implants (Bell et al. 1988; De Nictolis et al. 1992). Our patient and five others reported in the literature had unilateral testicular SBTs without extragonadal spread. All of them had a favorable outcome after orchiectomy,

including the patient whose SBT contained foci of infiltrating carcinoma. These findings support the view that testicular SBTs are unilateral, non-aggressive tumours that can be cured by orchiectomy or probably by cystectomy in selected cases. Furthermore, the favorable outcome of our case, characterized by aneuploid DNA content, does not support an independent correlation between DNA ploidy and prognosis in testicular SBTs. However, a larger number of cases must be studied before more precise conclusions on the biological behaviour of these tumours can be drawn.

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