

Endometriosis in a mesothelial cyst of tunica vaginalis of the testis. Report of a case

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SUMMARY

A rare case of endometriosis occurring in paratesticular mesothelial cyst is presented. It was found in a 7 mm mesothelial inclusion cyst of tunica vaginalis in a 46-years-old man who underwent a radical orchiectomy for seminoma. It showed a typical histologic pattern with endometrioid cylindrical epithelium and cellular stroma. The lesion was immunohistochemically positive for estrogen receptors and progesterone receptors, in contrast with the adjacent mesothelium. However, rare endometrioid epithelial cells expressed mesothelial markers calretinin and cytokeratin 5/6. This immunohistochemical overlap with mesothelium and morphological transition between endometrioid epithelium and mesothelium favor metaplastic pathogenesis of the lesion. In differential diagnosis, it is important to distinguish paratesticular endometriosis from tissue of teratoma (especially when a germ cell tumor is present in the testis, as was seen in this case).

Keywords: endometriosis – mesothelial cyst – seminoma – testis – tunica vaginalis

Endometrióza v mezotelovej cyste tunica vaginalis testis. Kazuistika

SÚHRN

Prezentovaný je zriedkavý prípad endometriózy v paratestikulárnej mezotelovej cyste. Lézia bola v 7 mm-ovej inklúznej cyste tunica vaginalis u 46-ročného pacienta, u ktorého bola prevedená radikálna orchiektómia z dôvodu seminómu. Ložisko endometriózy malo typickú morfológiu, s endometrioidným kolumnárnym epitelom a celulárnou strómou. Imunohistochemicky bola lézia pozitívna na estrogénové a progesterónové receptory, na rozdiel od blízkeho mezotelu, ktorý bol negatívny. Niekoľko epitelových buniek endometriózy expri-movalo aj mezotelové markery kalretinín a cytokeratín 5/6. Tento nález spolu s morfológickým nálezom prechodu medzi endometrioidným epitelom a mezotelom svedčia pre metaplastickú patogenézu lézie. V diferenciálnej diagnóze paratestikulárnej endometriózy je dôležité odlíšenie od tkaniva teratómu (najmä ak testis obsahuje "germ cell" tumor, ako tomu bolo v prezentovanom prípade).

Kľúčové slová: endometrióza – mezotelová cysta – seminóm – semenník – tunica vaginalis

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Endometriosis in male patients is very rare, in contrast with its frequent occurrence in women. In the paratesticular region, only one case with typical morphology has been reported before, to the best of our knowledge (1). An additional recently published case of paratesticular endometriosis (2) represents only so-called stromal endometriosis, i.e. the lesion composed of endometrial stroma and lacking endometrioid-type glands. We would like to present briefly our case of endometriosis occurring in a paratesticular mesothelial cyst.

MATERIAL AND METHODS

The tissue was fixed in 10% formalin and processed routinely. The sections were stained with hematoxylin and eosin, and periodic acid-Schiff stain (PAS) with and without diastase digestion. For

immunohistochemistry, the following primary antibodies were used: estrogen receptor (ER) (clone 1D5, 1:40), progesterone receptor (PR) (clone PgR636, 1:100), CK7 (clone OV-TL12/30, 1:200), CK5/6 (clone D5/16B4, 1:50), EMA (clone E29, 1:700), placental alkaline phosphatase (PLAP) (clone 8A9, prediluted), CD119 (polyclonal, 1:150), (all from DAKO, Glostrup, Denmark), CD10 (clone 56C6, 1:50, Novocastra, Newcastle, UK), calretinin (5A5, 1:100, Novocastra, Newcastle, UK), OCT3/4 (polyclonal, 1:3200, Santa Cruz, Vienna, Austria), pancytokeratin (AE1/AE3/PCK26, prediluted, Ventana, Illkirch, France). Immunostaining was performed according to standard protocols using avidin-biotin complex labeled with peroxidase or alkaline phosphatase. Microwave antigen pretreatment was used for immunoreactions with CD10, ER, and PR. Appropriate positive and negative controls were applied.

CASE REPORT

A focus of endometriosis was found in mesothelial inclusion cyst of tunica vaginalis in a 46-years-old man who underwent a radical right-sided orchiectomy for seminoma. Nine years ago, he had surgery for deviation of the septum nasi. His other medical history was unremarkable. The patient is currently obese, with body mass index 31. He has no gynecomastia or other high estrogen

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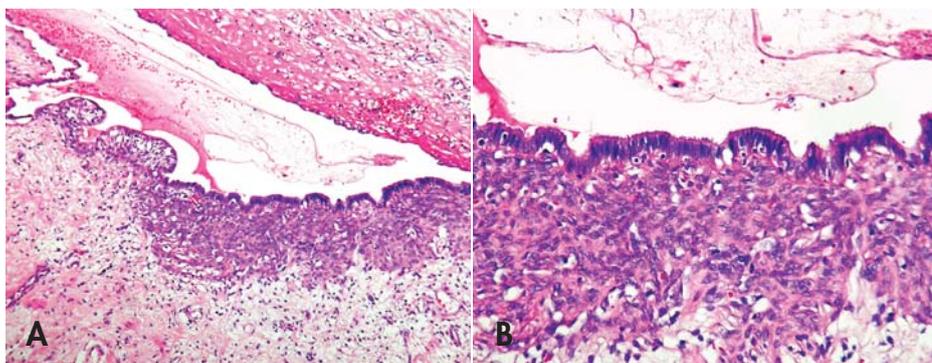


Fig. 1. A: A focus of endometriosis in the mesothelial cyst. The endometrioid epithelium with cellular stroma (on the center and on the right), and a flat mesothelium with fibrous stroma (on the left and on the top) are seen. **B:** Columnar endometrioid epithelium with cellular stroma (HE, magnifications x100 and x200, respectively).

symptoms such as infertility, erectile dysfunction or muscle/bone loss, and clinical examinations did not find any abnormality of the genitourinary tract. The patient denied any use of steroids. **Grossly**, a radical right-sided orchiectomy specimen showed a 10 cm seminoma which filled up the testis completely. On the medial side of the mediastinum testis, a slightly thickened tunica albuginea with a 0.7 cm cyst was seen. The cyst was serous and it was grossly suggestive of a mesothelial inclusion cyst of the tunica vaginalis. The visceral lamina of the tunica vaginalis was otherwise opaque and without gross features of tumor penetration. The tumor grew into the rete testis and epididymis. In addition, a 1.5 cm metastatic nodule was found in the spermatic cord in a 4 cm distance from the epididymis. **Histologically** (Fig. 1), the 7 mm cyst was of the mesothelial type. It was located in fibrous stroma immediately below the mesothelium of the tunica vaginalis. In part of the cyst wall, a 4 mm focus of endometriosis was found. In this focus, the mesothelium showed transition into the columnar epithelium of endometrial type. The stroma below this epithelium was cellular and of an endometrioid appearance, contrasting with fibrous paucicellular

stroma below the mesothelium. In the fibrous non-endometrioid stroma, a few scattered mesothelial cells were seen (Fig. 2F), as found commonly in a mesothelial inclusion cyst (3). The tumor was an anaplastic seminoma with a typical morphology and immunophenotype (CD119+/PLAP+/OCT4+/EMA-/CK-). It grew into the rete testis and epididymis. A complete penetration through the tunica albuginea was not found. The metastasis in the spermatic cord was identical to the primary tumor. No structure of testicular or epididymal appendages was found in the resectate. **Immunohistochemically** (Fig. 2), endometrioid epithelium expressed strongly estrogen receptors (ER), progesterone receptors (PR), cytokeratin 7, epithelial membrane antigen (EMA), and some of its cells were positive for mesothelial markers calretinin and cytokeratin 5/6 (4). Stromal endometrial cells were positive for PR, and some of them expressed calretinin and endometrial stromal marker CD10 (4). The mesothelium was negative for EMA and sex-steroid receptors, and it expressed strongly CK7 and mesothelial markers CK5/6 and calretinin. A fibrous stroma below the mesothelium contained some CK5/6+/calretinin+/CK7+ mesothelial cells.

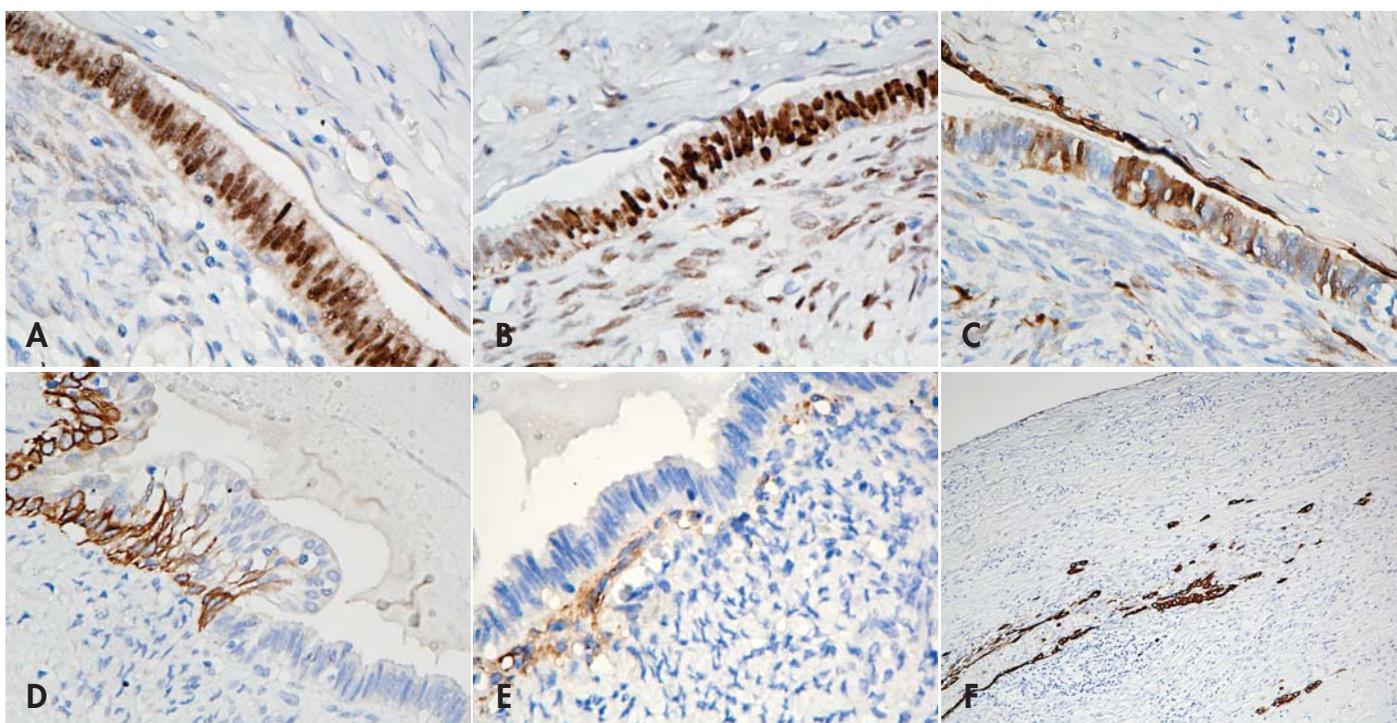


Fig. 2. Immunohistochemical findings. A: ER positivity in endometrioid epithelium contrasts with nuclear negativity of a flat mesothelium. **B:** PR is positive in endometrioid epithelium and stroma, and it is negative in mesothelium. **C:** Calretinin highlights the mesothelium and it is positive also in some cells of endometriosis. **D:** CK5/6 in a zone of transition between mesothelial (left) and endometrioid (right) cells. **E:** CD10 is positive in some cells beneath the endometrioid epithelium. **F:** CK7 highlights also the mesothelial cells in the stroma (in addition to the cells which line the inner surface of the cyst). Superficial and very flat mesothelium of the tunica vaginalis is seen on the above and left (SABC technique, magnifications x400 (A–E), and x100 (F), respectively).

DISCUSSION

Our finding has a typical morphology and immunophenotype of endometriosis (1,5–8) found in the mesothelial cyst.

In a still controversial pathogenesis of endometriosis, the main proposed mechanisms are the following: cell proliferation in müllerian embryonic rests, retrograde menstruation, and coelomic metaplasia (6–8). In our case, we did not find any congenital müllerian abnormality (including persistent müllerian duct remnants such as appendix testis and paradidymis) which could support embryonic rest theory. Retrograde menstruation is of course excluded, because the patient is male. The endometrial type epithelium showed continuity with a mesothelial cell layer. This continuity strongly supports a metaplastic genesis of the endometriosis in the present case. The epithelium, although a typical endometrioid with an ER+/PR+/EMA+ phenotype, retained in some cells an expression of mesothelial markers CK5/6 and calretinin. We think that this finding can be interpreted as a residual mesothelial phenotype (as metaplasia is a gradual process), and that it further supports an origin from the mesothelium.

In males, endometriosis was described in bladder, prostate, seminal vesicles, retroperitoneum, epididymis, and paratesticular tissue (1,2,5). It usually occurs in patients with a high estrogen serum level due to estrogen therapy for prostatic carcinoma. The

hormone probably induced a development of steroid receptors in the tissue, and this led to its endometrial differentiation. In our case, the patient was not treated with estrogens, and he also denied other steroid use. We did not find high estrogen symptoms such as gynecomastia, infertility, erectile dysfunction or muscle/bone loss. The patient has obesity which is sometimes associated with a high estrogen level (9), but this symptom is not specific. Thus, a pathogenetic "trigger" in the present case remains unknown. Possibly, a local effect of seminoma and/or of a tumor-associated inflammatory fibrous process that led also to the formation of a mesothelial inclusion cyst, could have a role in our case.

From the viewpoint of differential diagnosis, paratesticular endometriosis must be distinguished from tissue of teratoma, especially when seminoma is present in the testis, like in our case. Bland biphasic morphology with typical epithelium and cellular stroma, location in the mesothelial layer, and distinct immunophenotype indicated endometriosis.

In conclusion, we have described a rare case of endometriosis arising in a mesothelial cyst of tunica vaginalis adjacent to seminoma. No persistent embryonic müllerian remnants and no congenital anomalies were found in the patient. Our findings suggest that endometriosis in this case arose through metaplasia of the mesothelium.

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MONITOR

aneb nemělo by vám uniknout, že ...

■ PATOLOGIE ORL OBLASTI

... že byl upřesněn mikroskopický popis juvenilního trabekulárního osifikujícího fibromu

Juvenilní trabekulární osifikující fibrom (JTOF) je nedávno popsanou variantou osifikujícího fibromu, který společně s fibrózní dysplázií a oseální dysplázií patří mezi tzv. maxilofaciální fibro-oseální léze. Jak již název napovídá, JTOF se vyskytuje především u dětí a adolescentů a v důsledku svého rychlého růstu, způsobujícího často výrazné zvětšení a deformaci čelisti, je nezdědkou klinicky mylně diagnostikován jako zhoubný nádor. Prognóza nádoru je dobrá a většina lokálních recidiv je způsobena opětovným růstem nádorové tkáně ponechané *in situ* při nepřilži radikální chirurgické léčbě (excize, kyretáž).

Mikroskopicky JTOF sestává z bohatě buněčné vazivové tkáně s osteoidem a s trámečky nezralé kosti, které obsahují osteocyty a na jejichž povrchu jsou četné osteoblasty. Nápadná je vysoká mitotická ak-

tivita nádorových buněk, výraznější cytologické atypie však nejsou přítomny. V nedávno uveřejněném článku upozorňuje P. J. Sloomweg na doposud nezmiňované mikroskopické nálezy, které považuje za velmi charakteristické a doporučuje je zahrnout do definice JTOF v příštím vydání WHO klasifikace. Jedná se o přítomnost obrovských mnohojaderných buněk, krvácení a pseudocystické degenerace stromatu, přičemž tyto změny se v nádoru nevyskytují nahodile, nýbrž v pruzích, které jsou dokonce viditelné makroskopicky při přikrajování (v článku obrazově doloženo). Autor považuje tyto nálezy za přínosné i v diferenciální diagnostice JTOF, která zahrnuje zejména fibrózní dysplázií a osteosarkom, u kterých tyto změny nepozoroval.

Zdroj:

Sloomweg PJ. Juvenile trabecular ossifying fibroma: an update. *Virchows Arch* 2012; 461(6): 699–703.

– J. Laco –