

Vaginal myofibroblastoma with glands expressing mammary and prostatic antigens

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SUMMARY

A case of unusual vaginal myofibroblastoma containing glands which expressed mammary and prostatic markers is described. The tumor occurred in 70-year-old woman in the proximal third of the vagina. It showed morphology and immunophenotype typical of so-called cervicovaginal myofibroblastoma. The peripheral zone of the lesion contained a few groups of glands suggesting vaginal adenosis or prostatic-type glands on initial examination. The glands showed a surprising simultaneous expression of mammary markers mammaglobin and GCDFP-15 and prostatic markers prostate-specific antigen (PSA) and prostate-specific acid phosphatase (PSAP). Immunostains for alpha-smooth muscle actin, p63 and CD10 highlighted the myoepithelial cell layer of the glands. The finding indicates that simultaneous use of both mammary and prostatic markers for examination of unusual glandular lesions in the vulvovaginal location can be helpful for an exact diagnosis, and can contribute to better understanding of prostatic and mammary differentiations in the female lower genital tract.

Keywords: vagina – myofibroblastoma – mammary glands – prostatic glands – immunohistochemistry

Vaginálny myofibroblastóm so žľazkami exprimujúcimi mamárne a prostatické antigény

SÚHRN

Popísaný je prípad vaginálneho myofibroblastómu, ktorý obsahoval žľazky pozitívne imunohistochemicky na mamárne a prostatické markery. Jednalo sa o tumor zistený u 70-ročnej pacientky v proximálnej tretine vagíny. Morfológia a imunofenotyp lézie boli typické pre cervikovaginálny myofibroblastóm. Periférna subepitelová zóna tumoru obsahovala niekoľko skupín žľazok, u ktorých bola predpokladaná pri prvom vyšetrení diagnóza vaginálnej adenózy alebo prostatických žľazok. Imunohistochemia ukázala prekvapujúcu pozitívnosť týchto žľazok na prostatické i mamárne markery súčasne (prostatický špecifický antigén, prostatická kyselá fosfatáza, mamaglobín, GCDFP-15). Myoepitel žľazok exprimoval hladkosvalový aktín, p63 a CD10. Nález ukazuje, že pri vyšetrení glandulárnych lézií dolného genitálneho traktu ženy môže simultánne vyšetrenie na prostatické a mamárne antigény byť prínosom pre diagnózu i pre ďalšie poznanie mamárnej a prostatickej diferenciácie v tejto lokalizácii.

Kľúčové slová: myofibroblastóm – vagina – mamárna žľaza – prostata – imunohistochemia

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Cervicovaginal myofibroblastoma (myofibroblastoma of the lower genital tract) is one of the distinct mesenchymal genital tract tumors that have been described only recently (1–3). Additional unusual lesions of the lower genital tract which have been recently described are mammary type tumors with the corresponding mammary immunophenotype (4–6) and prostatic type glandular lesions expressing prostatic antigens such as prostate-specific antigen (PSA) and prostate-specific acid phosphatase (PSAP) (7–11).

Here, we present an interesting vaginal tumor that showed features of myofibroblastoma containing in its superficial zone sev-

eral unusual bland-appearing glands. These glands expressed mammary and prostatic antigens simultaneously. To the best of our knowledge, a similar finding has not been reported before.

MATERIAL AND METHODS

The tissue was fixed in 4% formalin and processed routinely. The sections were stained with hematoxylin and eosin, periodic acid-Schiff stain (PAS) with and without diastase digestion, mucicarmine, and alcian blue at pH 2.5. For immunohistochemistry, the following primary antibodies were used: alpha-smooth muscle actin (clone 1A4), desmin (clone D33), S100 (polyclonal), estrogen receptor (ER) (clone 1D5), progesterone receptor (PR) (clone PgR636), androgen receptor (AR)(ER441), mammaglobin (304-1A5), prostate-specific antigen (PSA) (polyclonal), high-molecular weight cytokeratin K903 (34BE12), p63 (4A4) (all from DAKO, Glostrup, Denmark), GCDFP-15 (EP1582Y, Ventana Medical Systems, Tuscon, USA), prostate-specific acid phosphatase (PSAP) (PASE/4LJ, Ventana Medical Systems, Tuscon, USA), CD10 (clone

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56C6, Novocastra, Newcastle, UK), and CD34 (clone Qbend/10, NeoMarkers, Westinghouse, CA, USA).

As a control group for examination of mammaglobin and GCDFP-15 in prostatic tissue, five consecutive cases of prostatic transurethral resection specimens were used. All cases showed clinical and histological features of prostatic nodular hyperplasia.

Immunostaining was performed according to standard protocols using an avidin-biotin complex labeled with peroxidase or alkaline phosphatase. Microwave antigen pretreatment was used for immunoreactions with CD10, CD34, ER, and PR. Appropriate positive and negative controls were applied.

CASE REPORT

A small polypoid nodule was found in the posterior wall of the proximal third of the vagina in a 70-year-old para 3 gravida 3 patient during a routine examination. It was excised and sent for histologic examination. The patient underwent conization 25 years ago for chronic cervicitis. In addition, 17 years ago she underwent a mastectomy for medullary carcinoma of the right breast, and had the same surgery for medullary carcinoma of the contralateral breast one year ago. Both mammary carcinomas were limited to the breast and were without metastasis. The patient was treated further with radiotherapy and chemotherapy. A hormonal therapy was not administered. The remaining medical history of the patient was unremarkable. The patient has no history of diethylstilbestrol exposure.

Grossly, the removed nodule measured 1.2 cm in diameter, and had the macroscopic appearance of a fibroma. Histologically, it was well-circumscribed and unencapsulated. A well developed Grenz zone was seen focally between the lesion and the vaginal epithelium (Fig. 1). The tumor was composed of bland-appearing

spindle cells arranged haphazardly or in vague wavy fascicles (Fig. 1). A zoning phenomenon with increased cellularity in the marginal zone was seen in only one lateral margin of the lesion. The nuclei were ovoid and elongated with mostly invisible nucleoli, and mitotic figures were very rare. Among the tumor cells, the collagen was either hyalinized or it had a fine fibrillary appearance (Fig. 1). The lesion contained numerous vessels without hyalinization of their thin walls. The peripheral zone below the vaginal epithelium contained a few small groups of glands (Fig. 2) resembling prostatic-type glands similar to those seen in tubulosquamous polyps (7,8) or in a prostatic metaplasia of the uterine cervix (9,10). These groups were composed of mildly dilated ducts and associated small glands. The epithelium was cuboidal to cylindrical, with eosinophilic or clear cytoplasm. Focally, a squamous metaplasia or apocrine-like cytoplasmic protrusions were seen (Fig. 2C). The epithelium in the ducts created a few small papillary proliferations or true small papillae with fibrovascular stroma. Already in HE stained sections, a basal cell layer was clearly discernible especially in the small acini. The vaginal epithelium was hyperplastic, and in rare foci found in only some sections, projections of the epithelium suggested that the glands had probably originated from the surface epithelium (Fig. 1A), although a fully obvious continuity between the surface epithelium and the glandular lesion was not found.

PAS stain with diastase digestion showed positivity of cytoplasm in the apocrine-like cells of the glands. Alcian blue and mucicarmine stains were negative.

Immunohistochemically (Fig. 3), the spindle cells strongly expressed desmin (Fig. 3A), ER, PR, AR, and they were negative for actin, S100 protein, CD34, CD10, cytokeratins, and p63. The glands showed actin, K903, p63 and CD10 expressions in myoepithelial cells (Figs. 3B–D). In addition, the p63 stained rare foci of squamous differentiation of the glandular epithelium (Fig. 3C).

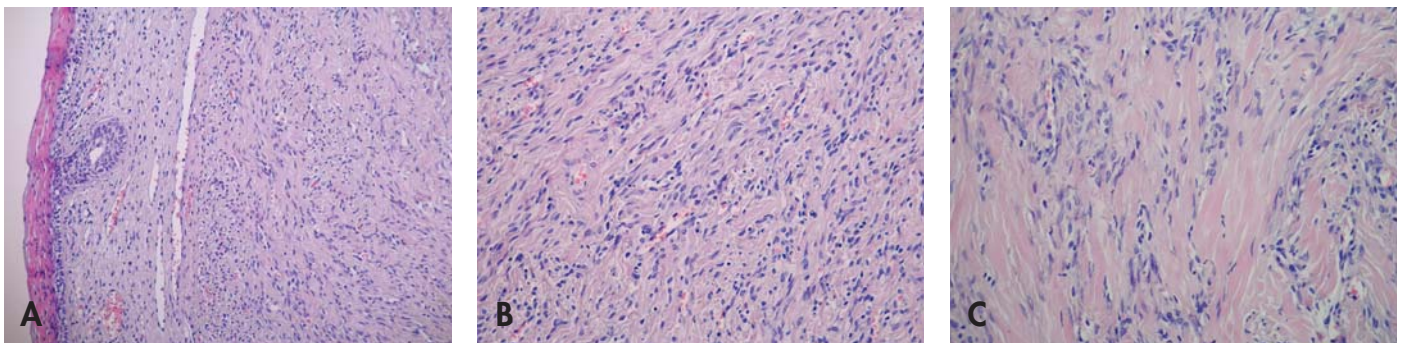


Fig. 1. Histological features of vaginal myofibroblastoma: (A) sharp circumscription with subepithelial Grenz zone, one duct-like cell proliferation of the surface epithelium is also seen; (B) bland spindle cells arranged in vague fascicles; (C) an area with focal hyalinization (HE, original magnifications x100, x200, and x400, respectively).

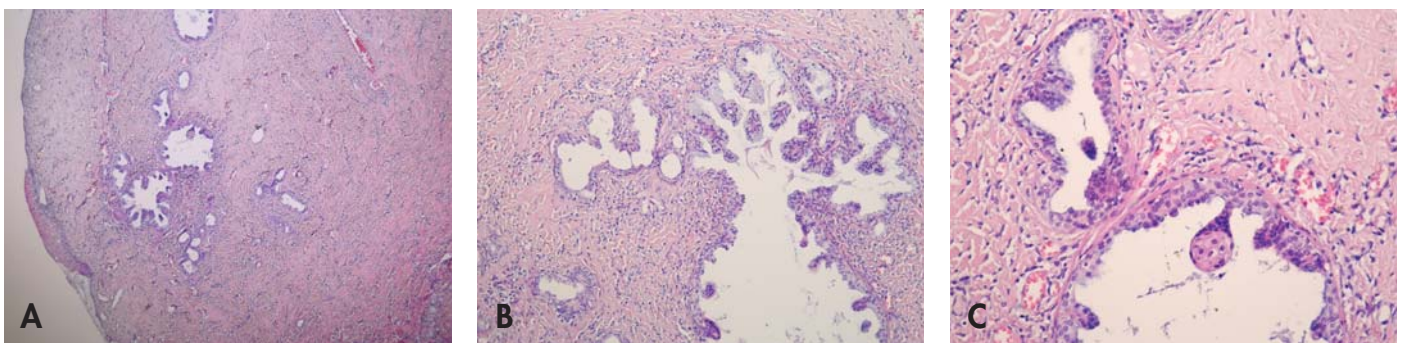


Fig. 2. Vaginal myofibroblastoma with glands expressing mammary and prostatic antigens. Histological features of the glandular component: (A, B) glandular lesion in the peripheral zone of myofibroblastoma shows mildly dilated duct-like glands with associated small acini; (C) apocrine-like snouts and squamous metaplasia were seen focally. Myoepithelial/basal cell layer can be suggested at this high power magnification (HE, original magnifications x40, x100, and x400, respectively).

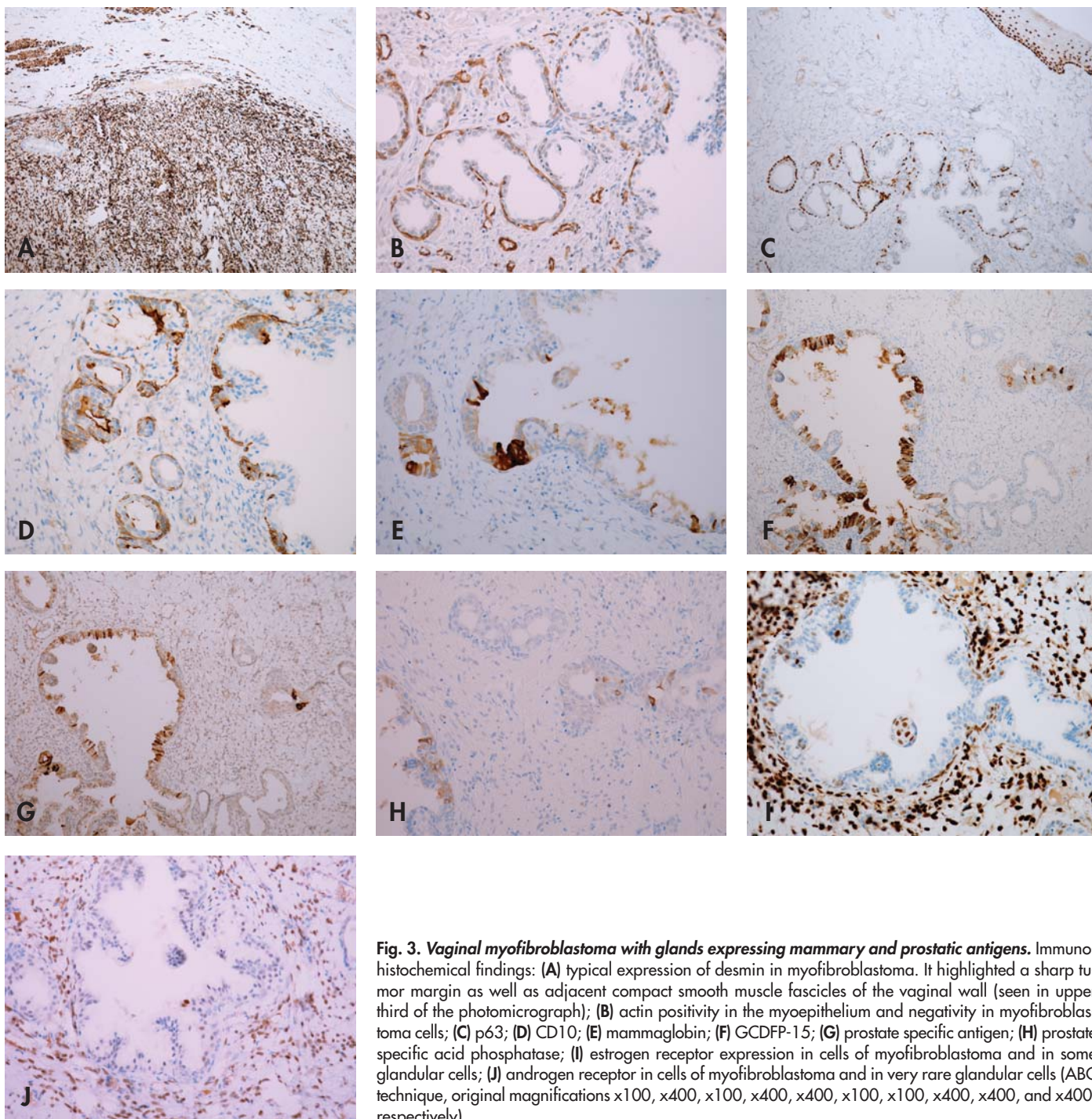


Fig. 3. Vaginal myofibroblastoma with glands expressing mammary and prostatic antigens. Immunohistochemical findings: (A) typical expression of desmin in myofibroblastoma. It highlighted a sharp tumor margin as well as adjacent compact smooth muscle fascicles of the vaginal wall (seen in upper third of the photomicrograph); (B) actin positivity in the myoepithelium and negativity in myofibroblastoma cells; (C) p63; (D) CD10; (E) mammaglobin; (F) GCDFP-15; (G) prostate specific antigen; (H) prostate specific acid phosphatase; (I) estrogen receptor expression in cells of myofibroblastoma and in some glandular cells; (J) androgen receptor in cells of myofibroblastoma and in very rare glandular cells (ABC technique, original magnifications x100, x400, x100, x400, x400, x100, x100, x400, x400, and x400, respectively).

CD10 also stained some luminal borders of the glandular cells (Fig. 3D). Many cells were positive for mammary marker mammaglobin (13,14) and GCDFP15 (15), as well as for prostatic markers PSA and PSAP (Figs. 3E–H). Co-expression of mammary and prostatic markers was seen in many glands. On the other hand, some glands expressed only myoepithelial markers and were negative for mammaglobin, GCDFP15, PSA and PSAP. ER was positive in some glandular cells, AR in very rare epithelial cells, and PR was negative in the epithelium (Figs. 3I and 3J).

As we did not find in the literature any study on mammaglobin and GCDFP-15 expressions in prostatic tissue, we performed these immunostains in a series of five transurethral resection specimens in consecutive cases of prostatic nodular hyperplasia. All five cases were negative for both markers.

DISCUSSION

The present mesenchymal lesion shows features typical of cervicovaginal myofibroblastoma (1,2) such as sharp circumscription, bland and myoid appearing spindle cells arranged haphazardly or in vague fascicles, fibrillary to hyalinized stroma, and immunohistochemical expression of desmin and sex steroid receptors with negativity for actin and CD34. An interesting feature of the tumor is the presence of glands which appear entrapped beneath the surface of the vaginal epithelium in the peripheral zone of the myofibroblastoma. In HE stained sections, we supposed that these glands represented either vaginal adenosis or prostatic-type glands similar to those described recently in tubulosquamous polyp (7,8) and in uterine cervix (9–11). The positivity for PSA and PSAP strongly suggested the prostatic nature of the glands.

However, the glands surprisingly expressed mammary markers mammaglobin and GCDFP15 (13,14), and they also showed an actin-positive myoepithelial cell layer, like in a normal mammary gland. Therefore, we suggest that they are mammary-type glands with an unusual expression of prostatic antigens. Namely, the positivity for PSA was reported already in normal mammary glands (16), and thus it does not contradict a mammary phenotype. Regarding PSAP, it is rather nonspecific being reported in various lesions such as neuroendocrine and salivary gland tumors, adenocarcinoma of the bladder, cloacogenic carcinoma and malignant lymphoma (17). The finding of a myoepithelial cell layer further favors the mammary nature of the glands, although actin positive myoepithelial/basal cells can also be seen very rarely in the prostate, in so-called sclerosing adenosis (18,19). However, the present glands were different from those of prostatic sclerosing adenosis as they were mildly dilated and ductal-appearing, and did not show pseudoinfiltrative small acini with a distorted shape as typically seen in sclerosing adenosis. In addition, reactivity for mammaglobin or GCDFP15 has not been described in the prostate until now, and our small control series of non-neoplastic prostatic tissue samples showed no reactivity for these antigens in any case.

Mammary-type glands can occur rarely in the anogenital region (4–6), but, to the best of our knowledge, they have not been observed in the proximal part of the vagina as seen in our case. We are also not aware of any report of a vulvar/vaginal lesion with glands expressing mammary and prostatic antigens simultaneously. However, the reason could be in that the lesions with a morphology suggesting mammary or prostatic phenotype have never been examined simultaneously for both mammary and prostatic antigens. The histogenesis of the present lesion is difficult to explain. Possibly, the myofibroblasts of the mesenchymal tumor induced epithelial cell proliferation of this unusual type. Because the glands seems to be

of a mammary-type, in analogy to them the myofibroblastoma could be regarded as myofibroblastoma of the mammary-type as well. Mammary-type myofibroblastomas in extramammary locations were described recently by McMenamin and his co-workers (20). Their series included even one case occurring in the vagina. We think, however, that this vaginal case pictured in Fig. 2 of that paper was very similar, if not identical, to cervicovaginal myofibroblastoma as described by Laskin et al. or Ganesan et al. (1,2). The difference between mammary-type myofibroblastoma and cervicovaginal myofibroblastoma seems to us to be very subtle, with great overlap between both entities. According to current limited knowledge, mammary-type myofibroblastoma in comparison with cervicovaginal myofibroblastoma can contain (but only in some cases) adipocytes in addition to myofibroblasts, shows more pronounced hyalinization, and is more often CD34 and actin positive. We suppose that further studies will show whether any difference exists between cervicovaginal myofibroblastoma and mammary-type myofibroblastoma occurring in the cervicovaginal location.

In conclusion, we described an additional case of cervicovaginal myofibroblastoma (myofibroblastoma of the lower female genital tract) which represents a recently described entity. In addition, the lesion was interesting in that it contained unusual glands which expressed mammary and prostatic antigens simultaneously. We suggest that these glands are of the mammary-type with aberrant expression of prostatic antigens. Our case shows that by examination of unusual glandular lesions of the lower genital tract (including cases of vaginal adenosis), a simultaneous use of both mammary and prostatic markers can be helpful, especially when prostatic glands are considered in the differential diagnosis. Further study of cases similar to our case can contribute to better knowledge of prostatic and mammary differentiations in the lesions of the lower female genital tract.

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