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Vulvar angiomyofibroblastoma – a case report of rare entity mimicking Bartholin cyst

Angiomiofibroblastoma sromu – opis rzadkiego guza naśladującego torbiel Bartholina

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Abstract

Vulvar angiomyofibroblastoma is rare tumor of obscure histological origin. Here a case of 49-year old woman is described with this intriguing benign vulvar entity. The tumor developed at left vulvar labia and clinically imitated Bartholin cyst with clinical complaints of regional discomfort without pain. A macroscopic evaluation revealed well separated, encapsulated tumor of 3,5cm in diameter. On cut surface the tumor was whitish, flesh, solid with myxoid appearance without any apparent cysts formation. There were alternating hypo- and hypercellular in the neoplasm. Microscopically the tumor comprised proliferation of small thin walled vessels that were surrounded with cuffs and islands of epithelioid, spindle and plasmacytoid cells with occasional vacuolization. Some aggregations of cells were quite dense and in such fields, vessels were compressed and ecstatic enough to mimic a bit haemangiopericytoma pattern. A production of myxoid intercellular matrix was seen in loose, hypocellular areas and was confirmed by positive pas –alcian blue stain that demonstrated prominent myxoid stroma and intracytoplasmatic globules of acid glicoproteins. The immunoprofile was remarkable enough to show strong expression of vimentin and desmin, while there was a lack of pan-keratin (CKAE1/3) and smooth muscle actin (SMA) immunoreactivities. Such an immunofentype is regarded to share some of myofibrolastic origin despite SMA negativity. Tumor cells seemed to sprout from perivascular regions giving an impression of accumulations strictly associated with neighbouring vascular branches. This configuration of cells is very often viewed as pericyte-like proliferation. Thus, our case of angiomyofibroblastoma is an example of tumor that probably derives from perivascular stem cells that acquire some of myoid features.

Key words: **angiomyofibroblastoma** / **Bartholin cyst** / **aggressive angiomyxoma** / / **differential diagnosis** / **vulva** /

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Streszczenie

Angiomyofibroblastoma sromu to rzadki guz o niejasnej histogenezie. Prezentujemy opis przypadku tego łagodnego guza u 49-letniej kobiety. Guz rozwinął się na lewych wargach sromowych i klinicznie imitował torbiel Bartholina dając uczucie miejscowego dyskomfortu bez dolegliwości bólowych. Badaniem makroskopowym stwierdzono dobrze odgraniczony otorebkowany guz śr. 3,5cm. Na przekroju guz był białawy, lity z nieco śluzowatym wejrzeniem bez wyraźnego tworzenia przestrzeni torbielowatych. Naprzemienne utkanie bogatokomórkowe i ubogokomórkowe tworzyło strukturę guza. W badaniu mikroskopowym rozrost małych, cienkościennych naczyń był otoczony przez wyspy złożone z epitelioidnych, wrzecionowatych i plazmocytoidnych komórek, niekiedy wykazujących wakuolizację. Niektóre skupienia komórkowe były całkiem gęste i w takich polach naczynia były nieco uciśnięte i łukowato poszerzone przypominając utkanie hemangiopericytoma. Produkcja międzykomórkowego śluzowatego podścieliska była widoczna w luźnych ubogokomórkowych obszarach i była potwierdzona dodatnim odczynem histochemicznym w barwieniu pas-alcian blue, które dowodziło obecności śluzowatego podścieliska i wewnątrzcytoplazmatycznych globul kwaśnych glikoprotein w komórkach nowotworowych. Immunoprofil guza charakteryzował się dodatnimi odczynami na wimentynę i desminę oraz ujemnymi odczynami na pancytokeratynę (CKAE1/3) i aktynę mięśni gładkich (SMA). Taki immunofenotyp częściowo przemawia za miofibroblastycznym pochodzeniem pomimo ujemnego odczynu na SMA. Komórki nowotworowe wydawały się wyrastać z okolic okołonaczyniowych stanowiąc masy ściśle związane z sąsiadującymi gałęziami naczyniowymi. Taki typ rozrostu przywodzi na myśl proliferację perycytów. Opisywany tu przypadek angiomiofibroblastoma stanowi przykład nowotworu wywodzącego się prawdopodobnie z okołonaczyniowych komórek macierzystych, które nabywają niektórych cech utkania pochodzenia mięśniowego.

Słowa kluczowe: **angiomiofibroblastoma** / **torbiel Bartholina** / / **naczyniakośluzak agresywny** / **diagnostyka różnicowa** / **srom** /

Background

Angiomyofibroblastoma (AMF) was first described by Fletcher et al. [1]. The novel entity was primarily characterized in comparison to aggressive angiomyxoma. In opposition to that tumor, angiomyofibroblastoma is well circumscribed and gives no recurrence after surgical removal. Smooth, ovoid shape and well defined borders of AMF cause clinical suspicions that this tumor is a cystic mass and it is usually regarded as Bartholin gland cyst until verified histopathologically to be solid tumor [2]. Although a cyst is a quite common finding in such a site, it should also be mentioned that Bartholin gland could very seldom be involved with primary carcinoma [3]. Besides squamous cell carcinoma which is the most common vulvar cancer, other very aggressive malignancies as Merkel cell carcinoma and malignant melanoma are rarely described in vulvar location [4]. The differential diagnosis of angiomyofibroblastoma also includes aggressive angiomyxoma and lipoma [5]. AMF could reach up to 23 cm in diameter and weight of over 4kg as reported in 48 old woman[6]. Such huge dimensions could be achieved because of lack of any clinical complaints of affected patients thanks to compressive mode of growth of AMF [6]. This tumor biology is quite different from infiltrating and recurrent manner of spread of angiomyxoma, that requires more urgent and earlier surgical intervention [6]. Angiomyofibroblastoma has no metastatic potential [7]. Very rarely angiomyofibroblastoma could undergo malignant transformation into high grade sarcoma of myxoid malignant fibrous histiocytoma type [8]. The tumor is found usually in perimenopausal period [9]. However, the range of age can be very wide in case of occurrence of angiomyofibroblastoma as it was reported in even 16 year old patient or pregnant woman whose tumor was devoid of estrogen and progesterone receptor [10, 11]. Vulva and vagina are the most common locations for angiomyofibroblastoma [12]. The hallmarks of histological architecture is a mixture of hypercellular and hypocellular fields, rich vasculature of mainly the capillary type with thin walled vessels [1]. Although there is no hyalinization of vessels of AMF, hyalinized collagen mats with "amianthoid-like fibers" were reported to draw comparison to histology of myofibroblastomas in case of so called polypoid angiomyofibroblastoma-like tumor in oral cavity from 15 year old patient [13]. Spindle, plump spindled, and oval stromal cells of epithelioid and plasmacytoid appearance were accumulated around the blood vessels to consolidate in dense focal areas or to be scattered in myxoid stroma with presence of pas-alcian blue positive stromal mucin.

Case description

49-year old woman was referred to hospital due to vulvar mass. Clinically, slightly elevated non polypoid tumor was localized at left major vulvar labia and imitated Bartholin cyst due to its convex and smooth appearance (Fig.1 A,B). Macroscopic evaluation revealed well separated tumor mass that measured 3,5cm in maximum dimension. On cut surface tumor was whitish, flesh, solid with evident myxoid appearance without cysts formation (Fig. 1A). External surface was covered by smooth mesenchymal tissue /(Fig. 1B). Microscopic evaluation revealed proliferation of small thin walled vessels with abundant perivascular proliferation of small round epithelioid cells with occasional vacuolization of the cytoplasm some of them and produce myxoid, intercellular matrix. Architectural picture of vascular proliferation was similar to acinar like form (Fig. 1C), but the essence of this neoplasm is presence of small perivascular cells (Fig. 2A). These cells morphologically were round to oval with central and eccentrically located nuclei like plasma cells and with eosinophilic cytoplasm (Fig 2A). In same cells we observed intracytoplasmatic vacuoles localized mainly in perinuclear region. Pas- alcian blue -stain demonstrated prominent myxoid stroma and intracytoplasmatic globules of acid glicoproteins which corresponded to vacuoles in H&E stain (Fig 2B).

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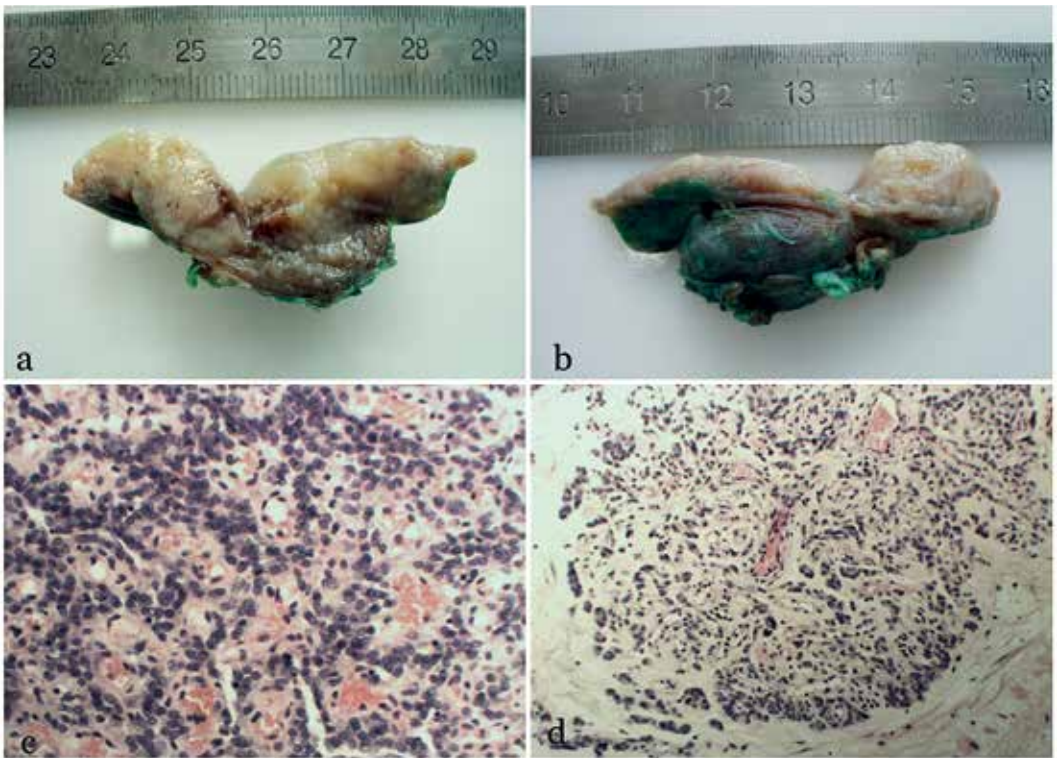

Figure 1. A – Cut surface of solid whitish tumor with prominent myxoid appearance. **B** – External surface of tumor with easy visible intact fibrous capsule (green inked margin). **C** – Prominent vascular and perivascular proliferation: Highly vascularized area of increased cellularity that contains densely distributed vessels of postcapillary venule type. In the background, plenty of small cells form perivascular cuffs (H&E stain Magnification 100x). **D** – Lobular appearance of hyperplastic vessels and perivascular cells: Acinus-like aggregation of perivascular cells within focal accumulation of sprouting of vessels (H&E stain Magnification 40x).

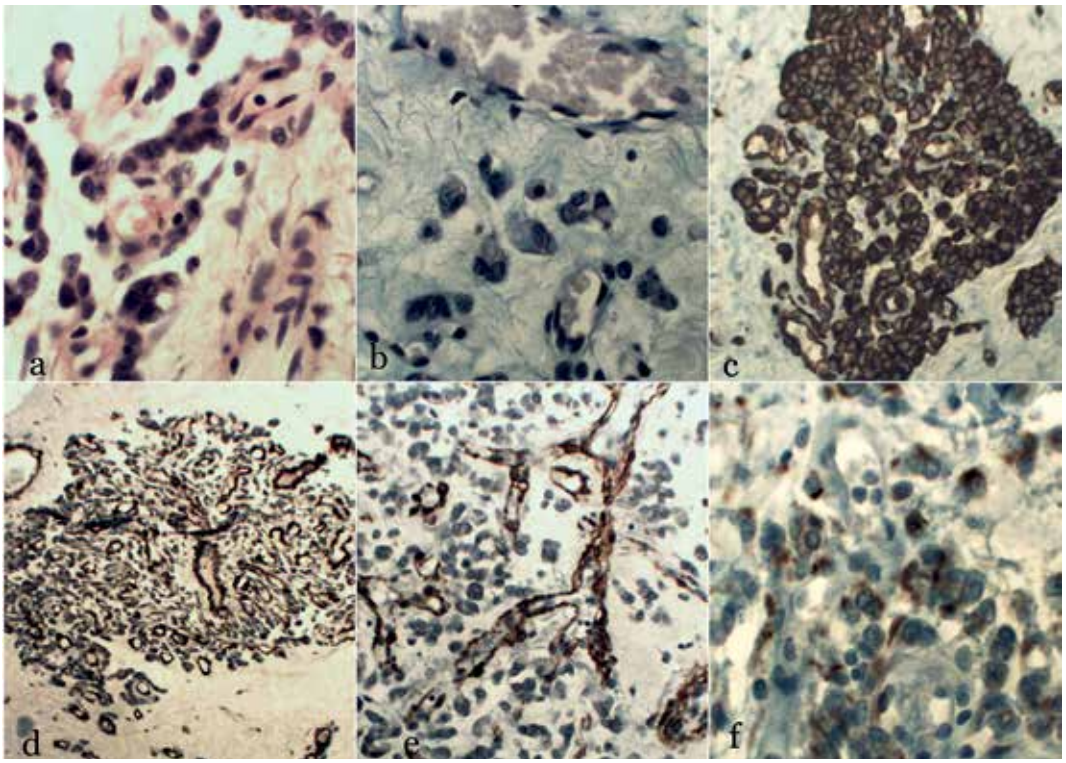

Figure 2. A – High magnification of perivascular cells with plasmocytoid and epithelioid appearance in small groups and rows crowded in perivascular area; some of cells are binucleated and there is a sparse addition of inflammatory cells (H&E stain, Magnification 400x). **B** – High magnification of myxoid oedematous matrix and vacuolised perivascular cells with drops of acid mucopolisacharydes with evident Alcian blue positivity (Alcian-PaS stain, Magnification 400x). **C** – Strong vimentin immunoreactivity of tumor cells arranged in lobular like aggregation (Magnification x100). **D** – CD34 staining shows contours of thin-walled vessels (Magnification x200). **E** – SMA staining highlights branching framework of capillaries (note -lack of SMA in neoplastic cells. (Magnification 200x). **F** – IHC stain for desmin shows typical cytoplasmatic and perinuclear inlocation of immunoreactivity in neoplastic cells (Magnification 400x).

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Immunohistochemistry showed strong expression of vimentin and desmin (Fig 2 C, F) and neither pan-keratin (CKAE1/3) nor smooth muscle actin (SMA) immunoreaction. Abundant vasculature was demonstrated with CD34 and SMA positive stains limited only to vascular network (Fig2 D, 3E).

Discussion

Although smooth ovoid borders of angiomyofibroblastoma could evoke suspicion of Bartholin cyst, it should be stressed that AMF never undergoes inflammatory change. In opposition to Bartholin duct cyst that can transform into reddened and tender abscesses after bacterial colonization of intracystic fluid and accumulation of neutrophils [14]. The origin of angiomyofibroblastoma is not clearly defined so far. Some answers are provided by immunoprofile of the tumor. AMF cells are positive for vimentin and desmin, and no immunoreaction for cytokeratin is present as in our case report [1]. Muscle-specific actin, alpha-smooth muscle actin, or S-100 protein were also reported to be negative[1]. Therefore, the tumor cells are believed to demonstrate a certain myoid features which are different from both myocytes and myofibroblasts [15].

Neoplastic cells of angiomyofibroblastoma were found to produce basic fibroblast-growth factor (bFGF), vascular-endothelial-growth factor (VEGF), and stem-cell factor (SCF), which are all potent drivers of angiogenesis [16]. Well developed network of vasculature seems to be a result of activities of such agents [16]. Furthermore, high mobility group I-C (HMGI-C) transcripts play a pivotal role in the molecular background of this tumor as well [16]. The development of AMF could potentially be influenced by sex hormones interplay because this tumor was reported to express both estrogen and progesterone receptors [7]. An idea of hormonal imbalance becomes more convincing in the light of the fact that AMF occurs in middle aged women who are about to enter a menopause period [7].

Anyway ER and PR positivity aids nothing to differential diagnosis because it is shared by not only aggressive angiomyxoma (AAM) but also other neoplasms and tumor like conditions (fibroepithelial polyps, nerve sheath and smooth muscle tumors or pelvic myxoma) and even adjacent non neoplastic interstitium like fibroblasts of vulvar skin, as well [17]. AMF and AAM express different levels of hyaluronate receptor CD44 with much abundant presence of this marker in in glycosaminoglycan rich stroma of AAM [18]. CD44 is probably responsible for frequent recurrences in clinical course of AAM, because CD44 mediates movements of tumor cells in myxomatous matrix of AAM [18]. Besides spindled, plasmacytoid, or epithelioid mononuclear cells there are also some binucleated and multinucleated tumor cells [19]. In accordance to findings in our case report, vessels of angiomyofibroblastoma may be branched and accompanied by some mast cells, that could be source of VEGF and bFGF in tumor environment [19].

Currently it is still believed that AMF originates from perivascular stem cells which could undergo myofibroblastic or even lipomatous differentiation, as lipomatous variant of AMF was also described [20]. Our case report is a fine example of angiofibroblastoma that shows immunohistochemically confirmed myoid features and presents a classical and representative appearance of this distinct but rare entity.

Final notes: Sampling, tissue processing and all laboratory procedures took place in Niepubliczny Zakład Opieki Zdrowotnej Zakład Patologii Spółka z o.o. in Kielce.

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References:

1. Fletcher CD, Tsang WY, Fisher C, [et al.]. Angiomyofibroblastoma of the vulva. A benign neoplasm distinct from aggressive angiomyxoma. *Am J Surg Pathol.* 1992, 16, 373-382.
2. Kairi-Vassilatou E, Dastamani C, Vouza E, [et al.]. Angiomyofibroblastoma of the vulva: a clinicopathological and immunohistochemical analysis of a rare benign mesenchymal tumor. *Eur J Gynaecol Oncol.* 2011, 32, 353-355.
3. Ng SM, Nunns D, Lamb M. Bartholin's gland squamous cell carcinoma. *J Obstet Gynaecol.* 2012, 32, 318-319.
4. Jońska-Gmyrek J, Bobkiewicz P, Gmyrek L, [et al.]. Merkel cell carcinoma of the vulva - case report and the literature review. *Ginekol Pol.* 2013, 84, 385-389.
5. Sims SM, Stinson K, McLean FW, [et al.]. Angiomyofibroblastoma of the vulva: a case report of a pedunculated variant and review of the literature. *J Low Genit Tract Dis.* 2012, 16, 149-154.
6. Nagai K, Aadachi K, Saito H. Huge pedunculated angiomyofibroblastoma of the vulva. *Int J Clin Oncol.* 2010, 15, 201-205.
7. Van der Griend MD, Burda P, Ferrier AJ. Angiomyofibroblastoma of the vulva. *Gynecol Oncol.* 1994, 54, 389-392.
8. Nielsen GP, Young RH, Dickersin GR, Rosenberg AE. Angiomyofibroblastoma of the vulva with sarcomatous transformation („angiomyofibrosarcoma"). *Am J Surg Pathol.* 1997, 21, 1104-1108.
9. Wang J, Sheng W, Tu X, [et al.]. Clinicopathologic analysis of angiomyofibroblastoma of the female genital tract. *Chin Med J* (Engl). 2000, 113, 1036-1039.
10. Montella F, Giana M, Vigone A, [et al.]. Angiomyofibroblastoma of the vulva: report of a case. *Eur J Gynaecol Oncol.* 2004, 25, 253-254.
11. Cetinkaya K, Al RA, Gursan N. Angiomyofibroblastoma of the vulva during pregnancy. *J Obstet Gynaecol Res.* 2011, 37, 1162-1165.
12. Nielsen GP, Rosenberg AE, Young RH, [et al.]. Angiomyofibroblastoma of the vulva and vagina. *Mod Pathol.* 1996, 9, 284-291.
13. Magro G, Greco P, Alaggio R, [et al.]. Polypoid angiomyofibroblastoma-like tumor of the oral cavity: a hitherto unreported soft tissue tumor mimicking embryonal rhabdomyosarcoma. *Pathol Res Pract.* 2008, 204, 837-843.
14. Wechter ME, Wu JM, Marzano D, Haefner H. Management of Bartholin duct cysts and abscesses: a systematic review. *Obstet Gynecol Surv.* 2009, 64, 395-404.
15. Hisaoka M, Kouho H, Aoki T, [et al.]. Angiomyofibroblastoma of the vulva: a clinicopathologic study of seven cases. *Pathol Int.* 1995, 45, 487-492.
16. Horiguchi H, Matsui-Horiguchi M, Fujiwara M, [et al.]. Angiomyofibroblastoma of the vulva: report of a case with immunohistochemical and molecular analysis. *Int J Gynecol Pathol.* 2003, 22, 277-284.
17. McCluggage WG, Patterson A, Maxwell P. Aggressive angiomyxoma of pelvic parts exhibits oestrogen and progesterone receptor positivity. *J Clin Pathol.* 2000, 53, 603-605.
18. Bigotti G, Coli A, Gasbarri A, [et al.]. Angiomyofibroblastoma and aggressive angiomyxoma: two benign mesenchymal neoplasms of the female genital tract. An immunohistochemical study. *Pathol Res Pract.* 1999, 195, 39-44.
19. Ustun C, Malazgirt Z, Kandemir B, [et al.]. Angiomyofibroblastoma of the vulva: case report. *Pathol Int.* 1998, 48, 964-966.
20. Laskin WB, Fetsch JF, Tavassoli FA. Angiomyofibroblastoma of the female genital tract: analysis of 17 cases including a lipomatous variant. *Hum Pathol.* 1997, 28, 1046-1055.

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