

# Angiofibroma-like perineurioma. Report of a case

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## SUMMARY

We report an unusual perineurioma with numerous vessels, showing a strong similarity with angiofibroma. A 2,5 x 2 x 2 cm subcutaneous/dermal tumor occurred in 58-ys-old male in the left brachial region. Histologically, it was composed of haphazardly arranged bland spindle cells and it contained prominent vasculature. In rare foci, the tumor cells showed thin bipolar processes and an onion-like perivascular whorling pattern. Immunohistochemically, expression of perineural cell markers EMA, claudin-1 and CD34 was limited to perivascular foci and to rare cells among the vessels. In addition, the tumor expressed CD10 diffusely. Our finding indicates that diagnosis of perineurioma should be considered also by tumors with an "angiofibromatous" morphology. Especially soft tissue angiofibroma, which often express EMA (perineural cell marker), shows a strong resemblance to angiofibroma-like perineurioma.

**Keywords:** perineurioma – angiofibroma – soft tissue – EMA – claudin-1

## Perineurióm podobný angiofibrómu. Kazuistika

### SÚHRN

Prezentujeme prípad perineuriómu s neobvykle bohatou vaskularizáciou, ktorá spôsobila podobnosť s angiofibrómom. Šlo o dermálny/subkutánný tumor ľavého ramena u 58-ročného muža. Tumor mal rozmery 2,5 x 2 x 2 cm. Histologicky bol tvorený blandnými fibroblastoidnými bunkami usporiadanými zväčša nepravidelne, len s ojedinelým špirálovitým radením okolo ciev. Malé množstvo buniek malo bipolárne tenké výbežky. Cievky predstavovali druhú prominentnú zložku lézie. Imunohistochemicky bola zistená expresia perineurálnych markerov (EMA, kladín-1 a CD34) v perivaskulárnych bunkách a v malej časti buniek vzdialených od ciev. Tumor bol ďalej difúzne pozitívny na CD10. Náš nález ukazuje, že diagnózu perineuriómu je potrebné zvažovať aj pri bohato vaskularizovaných léziách s „angiofibroma-like“ morfológiou. Demonštrovaný prípad perineuriómu sa veľmi podobal na recentne popísaný angiofibróm mäkkých tkanív (u ktorého bola často pozorovaná aj expresia EMA).

**Kľúčové slová:** perineurióm – angiofibróm – mäkké tkanivá – EMA – kladín-1

Cesk Patol 2013; 49(2): 86–88

Soft tissue perineurioma is a benign tumor composed of perineural fibroblasts (1). It occurs most often in adult patients, in superficial soft tissue of extremities and trunk. The cells of perineurioma are arranged in a storiform, whorled or short fascicular pattern (1–3). Prominent vascularization does not belong to previously described morphology of perineurioma. Recently, we have seen a case of perineurioma which contained numerous vessels, and which therefore showed a strong similarity to angiofibroma.

## MATERIAL AND METHODS

The tumor tissue was fixed in Bouin solution, subsequently in 10% formalin, and then it was processed routinely. The sections were stained with hematoxylin and eosin. For immunohistochemistry, the following primary antibodies were used: S100 (polyclonal, 1:400), alpha-smooth muscle actin (clone 1A4, 1:1000), desmin (clone D33, 1:3000), GLUT-1 (polyclonal, 1:200), EMA (clone E29,

1:700), CD35 (Ber-MAC-DRC, 1:50) (all from DAKO, Glostrup, Denmark), claudin-1 (polyclonal, 1:50, Zymed, San Francisco, USA), CD34 (clone Qbend/10, 1:800), CD10(clone 56C6, 1:50) (both from Novocastra Lab., Newcastle upon Tyne, UK), pancytokeratin (AE1/AE3/PCK26, prediluted), vimentin (V9, prediluted), CD99 (O13, prediluted), CD21 (2G9, prediluted) (all four from 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 claudin-1 and CD10. Appropriate positive and negative controls were applied.

## CASE REPORT

In 58-year-old patient, the subcutaneous/dermal tumor grew slowly for 5 years. Recently, a small superficial ulceration developed on the surface. The tumor was excised and submitted for examination. **Grossly**, the 2,5 x 2 x 2 cm dermal/subcutaneous nodule was unencapsulated, and of rubbery consistency. Its cut surface was of a homogeneous glistening appearance. **Histologically**, the tumor contained bland appearing spindle cells in fibromyxoid stroma and prominent vasculature. The spindle cells were usually arranged haphazardly or in ill-defined fascicles (Fig. 1A). In rare perivascular areas, they created vague perivascular whorls (Fig. 1B). In these foci, the cells showed thin bipolar processes, whereas in

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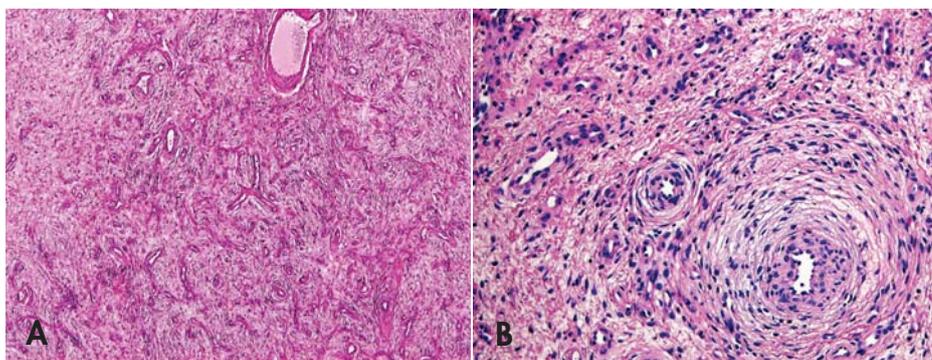
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**Fig. 1.** Angiofibroma-like perineurioma. Microscopic features. **A:** At low-power, an angiofibroma-like morphology is apparent, with rare and subtle concentric perivascular arrangement of the cells. **B:** Onion-like perivascular arrangement of the cells (hematoxylin and eosin, magnifications x40, x100, respectively).

the areas among the vessels, the majority of the spindle cells were ovoid or tadpole-shaped. The vessels were usually small and thin-walled, with frequent branching (Fig. 1A). The minority of the vessels were medium-sized, with a clearly-visible pericytic or muscular coat. Prominent vasculature was absent in only rare areas of the tumor. In the lateral excision margin, the lesion was well-circumscribed. The tumor extended to the lower resection margin, and therefore the evaluation of the tumor margin was not possible.

**Immunohistochemically**, the tumor was strongly and diffusely positive for vimentin. EMA, claudin-1, and CD34 were positive in some perivascular areas with a whorled arrangement of the cells and in rare cells of the major cell population among the vessels (Figs. 2A–B). Alpha-smooth muscle actin was limited to pericytes and to muscle cells of the vessels (Fig. 2C). CD10 stained almost all tumor cells (Fig. 2D). CD34 and actin highlighted also the prominent vasculature of the lesion. S100 protein, desmin, pancytokeratin, GLUT-1, CD99, CD21 and CD 35 were all negative.

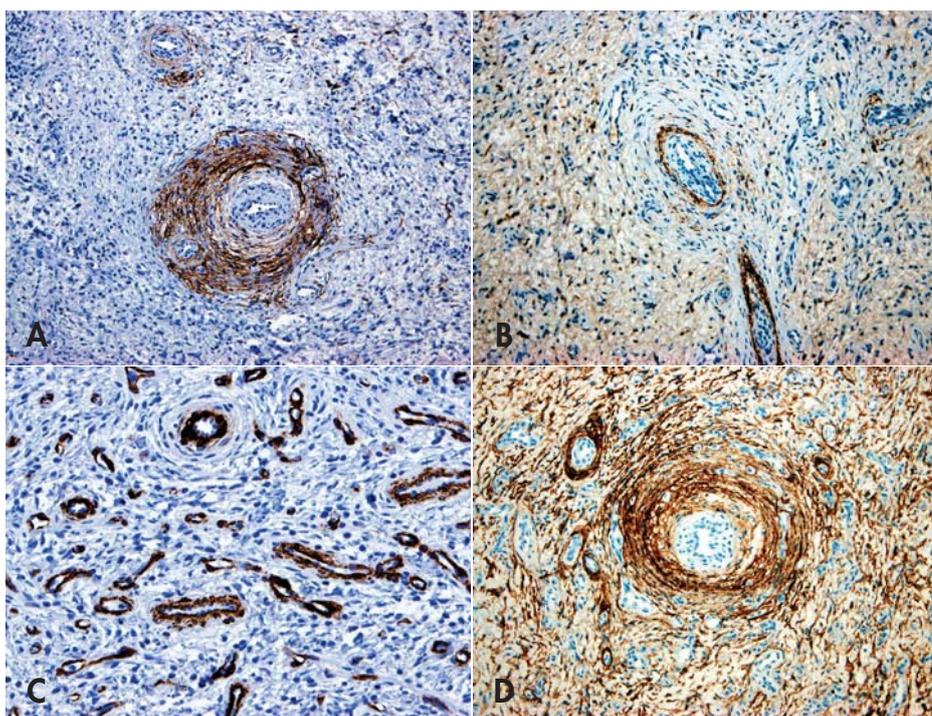
## DISCUSSION

Known morphology of perineurioma is characterized by spindle cells arranged in a storiform, whorled or fascicular pattern, with various grades of collagenization and without prominent vascularization (1–3). In our case, the dominant pattern of the lesion was “an-

giofibromatous”, because of a rich vasculature and haphazardly arranged bland spindle cells. Therefore, we initially considered the tumor to be a soft tissue angiofibroma (4,5). The lesion lacked typical “textbook features” of perineurioma, such as storiformity or a prominent whorled pattern. The perineuriomatous nature was indicated only by subtle features, such as rare perivascular whorls and focally visible cells with thin bipolar processes. Immunohistochemically, the lesion showed expressions of perineural cell markers EMA and claudin-1 (6,7). However these expressions were strong only focally, being usually limited to perivascular areas where the spindle cells were arranged in concentric perivascular whorls. It seems to us that the tumor is composed of fibroblasts which acquire fully-developed perineural phenotype only in some areas, like it was suggested for perineuriomas/fibroblastic polyps of the colon (8,9). Such a phenotypical change of the fibroblast toward perineural cells was demonstrated already by an in vitro study of Bunge et al. (10).

In addition to perineural cell markers, we observed an expression of CD10. The significance of this finding is unclear, as CD10 does not appear to be lineage-specific. It was described in various soft tissue lesions, including various nerve sheath tumors (11,12).

As mentioned above, the morphology of the present tumor is very similar to the so-called soft tissue angiofibroma (4,5). It differs only in a subtle and focal whorled pattern. Soft tissue angiofibroma was described quite recently (in 2012 April issue of *Am J Surg Pathol*) (4). It shows an angiofibromatous morphology cha-



**Fig. 2.** Angiofibroma-like perineurioma. Immunohistochemical findings. **A:** EMA-positivity in perivascular cells and in rare cells of the stroma. Quite similar was expression of CD34. **B:** positivity for claudin-1. **C:** actin expression is limited to the pericytes. **D:** diffuse CD10 expression (SABC technique, magnifications x100).

characterized by prominent vasculature and spindle-shaped fibroblast-like cells. Moreover, it is often positive for EMA. Marino-Enriques and Fletcher comment that EMA positivity in angiofibroma probably does not indicate perineural cell differentiation, because the histological features of the lesion are different from the known pattern of perineurioma (4). However, immunostains for other perineural cell markers, such as claudin-1 and GLUT-1, were not performed in their study. Thus, the line of cell differentiation in soft tissue angiofibroma remains unclear. In our opinion, EMA reactivity and morphologic overlap with such vascular-rich perineurioma as seen in our case indicate that perineural differentiation in soft tissue angiofibroma cannot be entirely ruled out for the present time, and that additional studies are needed.

Besides soft tissue angiofibroma, the differential diagnosis in our case included vascular-rich lesions such as cellular angiofibroma (13,14), angiomyo-fibroblastoma (15) and superficial angiomyxoma (16). Cellular angiofibroma and angiomyo-fibroblastoma are in principle lesions of the genital region, and their occurrence in ex-

tragenital locations is extremely rare (17,18). In addition, cellular angiofibroma (13,14) lacks the whorled pattern of perineurioma, its vessels are usually hyalinized, and it may contain adipocytes (resembling a spindle cell lipoma). It should be negative for perineural cell markers, with the exception of CD34. A subset of cellular angiofibromas is positive for myoid markers, such as actin and desmin. Angiomyo-fibroblastoma (15) clearly shows a myoid phenotype with expression of actin and/or desmin. Superficial angiomyxoma (16) is more myxoid in comparison with perineurioma, and it is negative for perineural cell markers.

In conclusion, we demonstrated an unusual case of angiofibroma-like perineurioma. The tumor contained prominent vasculature and spindle cell proliferation, with subtle patterns indicating perineural cell differentiation of the lesion. Immunohistochemical expressions of perineural cell markers EMA, claudin-1 and CD34 were helpful for correct diagnosis. Our case shows that angiofibroma-like perineurioma should be included in differential diagnosis of highly vascularized spindle cell lesions.

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