Short report

Primary angiosarcoma of the vulva: report of a case misdiagnosed as a benign tumor

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Primary vulvar angiosarcomas have a propensity for varied macroscopic and histologic appearance that initially may not suggest a vascular malignant neoplasm. Therefore, the rarity of the lesion and it's morphologic diversity may contribute to the high rate of misdiagnosis. We present the case of a 43-year old patient with a primary vulvar lesion, initially misdiagnosed as an angiofibroma. Microscopic examination of the recurrence together with immunohistochemical profile were in favor on a poorly differentiated angiosarcoma. Early diagnoses can improve prognoses in angiosarcomas and, in the case of recurrences, as in the present case, may lead to changes in therapy.

Key words: primary angiosarcoma, vulva, morphology, immunohistochemistry, management.

Dear Editor,

A 43-year old pacient with no relevant clinical history was admitted to the Gynecology Department in another hospital, for a well-demarcated vulvar mass involving left major labia in 2018. The lesion was surgically removed in fragments. Macroscopic examination revealed multiple fragments with variable diameter of 15-42mm, soft consistency and white to red color. Microscopic examination identified hypocellular areas with prominent stromal hyalinization admixed with more hypercellular areas represented by a proliferation of spindle cells with scattered mitoses, surrounding numerous closely packed, interanastomosing vascular channels. Multiple areas of hemorrhage as well as numerous macrophages and multinucleated giant cells were identified throughout the tumor (Fig. 1A-E). The lesion was diagnosed as an angiofibroma and no additional treatment was recommended. Three years later the pacient presented to her gynecologist with complains of vulvar pain and she was reffered to our hospital. At clinical examination, 2 additional vulvar lesions were identified, both involving left major labia, one superficially located, of 60 mm diameter and the second one with deeper location, of 32 mm diameter. Both lesions were solid, had a soft consistency and grey color, with hemorrhagic areas on the cut surface, mimicking a benign lesion, of fibroma or leiomyoma-like (Figure 1F). On microscopic examination however, the two nodules had same morphology, with a proliferation of spindle tumor cells, arranged in fascicles arround small or larger blood vessels, lined by atypical endothelial cells and containing eritrocytes. The spindle tumor cells presented moderate to marked nuclear pleomorphism and scattered mitotic figures (Fig. 1G-O). Immunohistochemically, the tumor

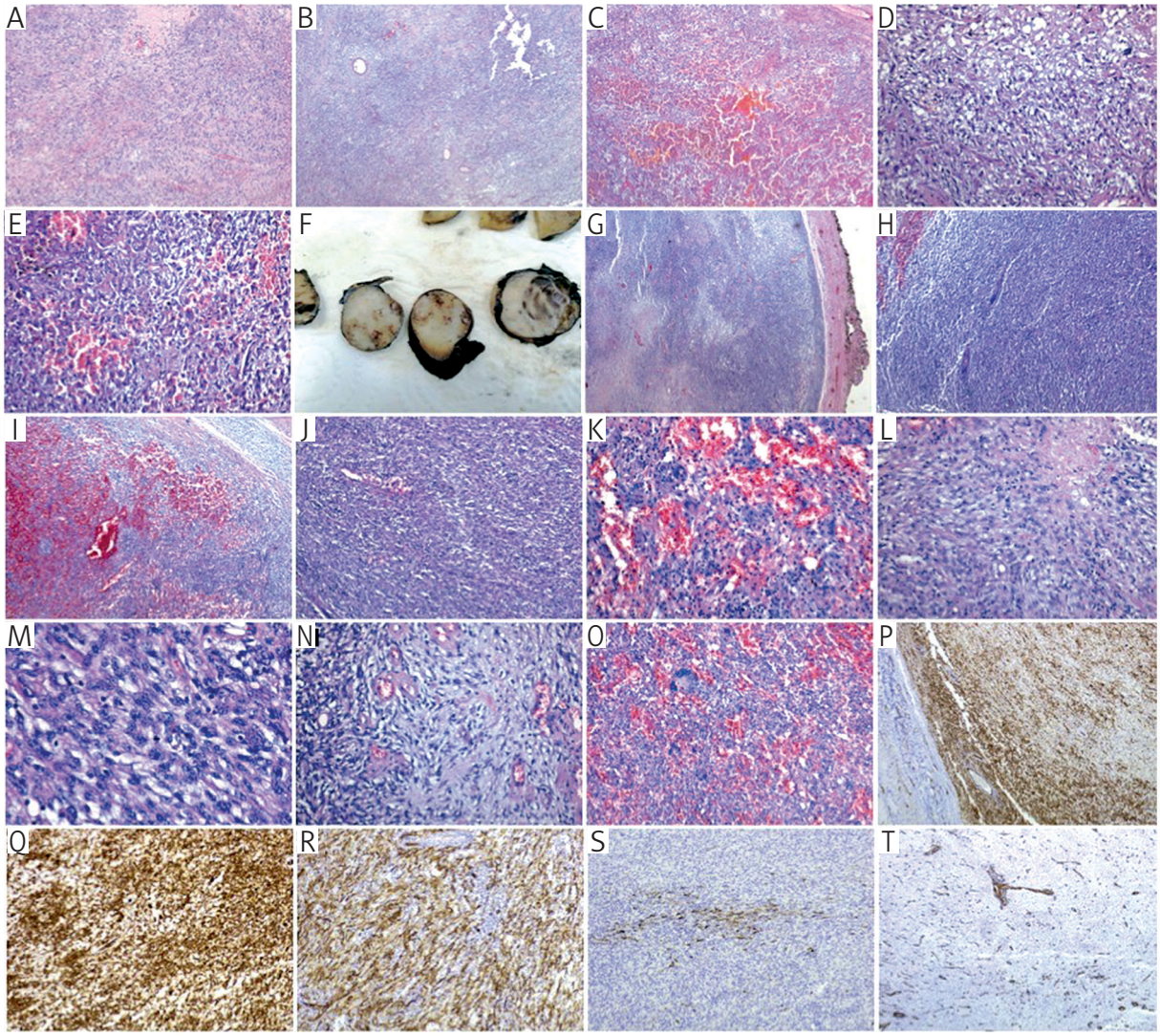

Fig. 1. Microscopic examination of the first lesion (diagnosed as an angiofibroma in 2018) identified mostly hypocellular areas with prominent stromal hyalinization (A) admixed with more hypercellular areas (B) represented by a proliferation of atypical spindle cells with scattered mitoses, surrounding numerous closely packed, interanastomosing vascular channels (C, D); multiple areas of hemorrhage as well as multinucleated giant cells were identified throughout the tumor (E); 2 additional solid vulvar lesions were surgically removed in 2021, both of soft consistency and grey color, with perypheral hemorrhagic areas on the cut surface, mimicking a benign lesion, of fibroma or leiomyoma-like (F); microscopic examination of both nodules revealed well-demarcated lesions at the periphery (G) with a proliferation of spindle tumor cells, arranged in fascicles (H) arround large or small blood vessels (I, J), lined by atypical endothelial cells and containing eritrocytes (K); areas of necrosis (L), scattered atypical mitotic figures (M), hypocellular areas (N), multinucleated giant cells (O) were identified; the tumor cells were diffuselly positive for CD31 (P, R) and CD34 (S) while only focally for panCK (T) and negative for smooth muscle actin (U)

cells were diffusely positive for CD31, CD34, focally positive for panCK and negative for SMA, Desmin, H-Caldesmon, D2-40, c-kit, DOG1, CK7, HMB45, MelanA (Fig. 1 P-U). The morphology and immunohistochemical profile were compatible for poorly differentiated vulvar angiosarcoma. Pathology slides from 2018 were reviewed, and were found to have similar morphology in the hypercellular areas, being reinterpreted as primary angiosarcoma of the vulva with local recurrence and the patient was reffered to the Oncologic Department.

Angiosarcomas are aggresive malignant mesenchymal neoplasms of endothelial origin, mostly developing in the skin of head and neck of erderely white males [1]. Although they can arise anywhere in the body, angiosarcomas rarely occur in the female genital tract. Most reported cases of gynecologic angiosarcomas have developed in the uterus and ovaries while vulvar angiosarcomas are extremely rare, with only 7 cases documented so far in English literature to the best of our knowledge [2, 3, 4, 5, 6, 7, 8]. Vulvar angiosarcoma develops rarely spontaneously,

as a primary lesion, without recognized associated risk factors, mostly being diagnosed as secondary angiosarcoma, for which chronic lymph edema, local radiotherapy for various malignant tumors (such as vulvar squamous cell carcinoma), foreign bodies, certain chemical exposures and familial syndromes (including BRCA mutations, Maffucci Syndrome, and Klippel-Trenaunay syndrome) were previously incriminated [1, 9].

Angiosarcomas have a propensity for a varied macroscopic and histologic appearance that initially May not suggest a vascular malignant neoplasm. In secondary angiosarcomas, the clinical history is very helpful in establishing the diagnosis of such a rare tumor. In the present case, however clinical history described a benign vulvar tumor, diagnosed as an angiofibroma and no further therapy was recommended. Vulvar angiosarcomas are often mistaken for benign lesions upon clinical and macroscopic presentation, leading to diagnosis and treatment delays. This is due to the fact that the lesion usually presents as large and friable, hemorrhagic mass, with poorly defined margins and ulceration but cases presenting as small white papules or as painless well-demarcated grey to white nodule, mimicking a fibroma or leiomyoma with hemorrhagic areas such in the present case have been also described.

Microscopically, angiosarcomas can have a wide range of appearance, from closely packed, interanastomosing vascular channels lined by atypical endothelial cells and surrounded by prominent stromal hyalinization (suggestive for a benign tumor) alternating with a reticular, fascicular, or solid growth in poorly differentiated areas, with hemorrhage and necrosis. Some variants have a spindled or epithelioid morphology, making them hard to recognize as a vascular tumor (being compatible with high-grade sarcomas, malignant mixed mullerian tumors, poorly differentiated or sarcomatoid carcinomas or malignant melanomas) [10]. Immunohistochemical examination however is very helpful especially in primary angiosarcomas mimicking a benign tumor, the tumor cells staining for CD31, CD34, and/or factor VIII. Immunoreactivity for cytokeratins may be strong but only focal, more often in the epithelioid variant. Results for the immunohistochemical staining of S100, HMB45, CD99, desmin, h-caldesmon, EMA, and ER and PR are usually negative. Early diagnoses can improve prognoses in angiosarcomas and, in the case of recurrences, as in the present case, may lead to changes in therapy.

The authors declare no conflict of interest.

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