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CASE REPORT

Spindle cell angiosarcoma as primary cutaneous tumor - Case report and brief literature review

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Angiosarcoma is a rare, aggressive malignant tumor of vascular origin, often characterized by rapid growth and infiltrative behavior. While it commonly occurs in the skin, particularly on the scalp of elderly patients, it can also affect other regions. We present a case of a 76-year-old male with a rapidly growing, well-demarcated nodule on the dorsum of the hand, which was excised for pathological examination. Histopathological analysis revealed spindle-shaped tumoral cells with a storiform pattern, poor vascularization, and immunohistochemistry positivity for CD31 and CD34. The case underscores the importance of distinguishing angiosarcoma from other spindle-cell tumors, such as leiomyosarcoma and atypical fibroxanthoma, and highlights the essential role of immunohistochemistry in achieving an accurate diagnosis. Early detection and appropriate surgical management are crucial for optimal outcomes in patients with this aggressive malignancy.

Keywords: angiosarcoma, rare, immunohistochemistry

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Introduction

Angiosarcoma is a rare and aggressive malignant tumor of vascular origin that can affect the skin, bone, soft tissue or various viscera. The most common locations involved are the limbs, but the entity can also occur in the retroperitoneum, head and neck region or trunk, involving the subcutaneous tissue or the muscles. The tumor is highly infiltrative and often presents with rapid growth accompanied by various symptoms, such as pain, swelling or bleeding. Due to the tumor's abundant vascularization and high risk of blood vessel rupture, patients sometimes present with recurrent or persistent hematoma and even anemia [1,2].

In elderly patients, who are most commonly affected, angiosarcomas often arise in the head and neck region, especially on the scalp. In younger populations and particularly in children, the tumor is more frequently encountered in deeper tissues and the mediastinum [1,3].

Cutaneous angiosarcomas appear de novo or can be associated with various conditions, such as von Recklinghausen disease, various neurofibromatosis or hereditary disorders which predispose patients to malignant proliferations. Other factors, such as radiation exposure, foreign materials or previous trauma, have also been associated with the development of soft tissue or cutaneous angiosarcoma. Radiation exposure is particularly associated with breast angiosarcoma, which carries a high risk of metastasizing to the contralateral breast and viscera [4,5].

From a pathogenesis point of perspective, angiosarcomas are heterogenous tumors which [that]present a variety of features, with minimal changes observed in the *TP53* or PIK3CA/AKT/mTOR pathways [1,6].

Macroscopically, angiosarcomas exhibit various sizes, can appear solid, multinodular and hemorrhagic, with well-defined or irregular in shape. Depending on the grade of differentiation, the tumor may present a spongy appearance (indicating better differentiation) or predominantly solid, fleshy areas (indicating poor differentiation). The tumors are usually violaceous, nodular or resembling ecchymosis [1,7].

Cytologically, angiosarcoma can display various features, as cells adopting epithelioid or spindle morphologies, sometimes exhibiting a mixture of both. Epithelioid angiosarcomas typically show predominantly solid areas and diffuse proliferation of polygonal cells with marked pleomorphism and poor vascularization. Other subtypes may feature anastomosing blood vessels, extensive hemorrhage and sheets of spindle or epithelioid cells with abundant cytoplasm and pleomorphic nuclei with prominent nucleoli. Immunohistochemistry plays a crucial role in diagnosing these tumors, as they are positive for markers such as CD31, CD34 and ERG, which are particularly important in differentiating angiosarcomas from other entities with similar features [1, 8-10].

Angiosarcomas exhibit very rapid growth and dissemination to adjacent or distant organs, most commonly affecting the lungs, making a proper and accurate diagnosis critical for patient outcomes.

Methods

We describe the case of 76-year-old male patient with no significant medical history who presented to the Plastic Surgery Department with a rapidly growing nodule (over a few months) on the left hand, corresponding to the 5th metacarpal region and without notable symptoms. The tumor was excised, and the specimen was sent for further

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examination to the Pathology Department of the Clinical County Hospital Mureș.

Results

Clinically, the nodule appeared well-defined shape, with a slightly reddish coloration, discreet white scaling on the surface and margined by firm areas resembling hyperkeratosis. (Figure 1)

On gross examination, we analyzed a cutaneous sample measuring 35 x 20 mm, which featured a nodule with total dimensions of 13 x12 x7 mm, located 6 mm from the closest surgical resection margin. On the surface, the nodule presented a white-violaceous color with the surrounding area slightly elevated. On cut section, the tumor showed a heterogenous appearance, with alternating white and brown areas.

Microscopic examination using the standard hematoxylin-eosin stain revealed a tumor proliferation partially delineated by a poorly defined epithelial collarette. The tumor was located in the reticular dermis and exhibited a solid architecture. The tumor cells were elongated and spindle-shaped, arranged in intersecting fascicles with focal storiform pattern. These cells demonstrated pleomorphism, eosinophilic cytoplasm and elongated, hyperchromatic and enlarged nuclei with prominent nucleoli. We identified a total of 15 mitoses per mm^2. Among the tumor cells, we observed poorly defined vascular structures of irregular shape containing red blood cells, along with extravasated red blood cells scattered throughout the tumor stroma and subtle cleft-like spaces. Necrosis was absent. Resection margins were negative. (Figure 2, Figure 3, Figure 4)

Immunohistochemistry profile of the proliferation presented positive reaction for CD34 and CD31 immunostains, with proliferation index Ki67 expressed in 50%. Immunoreactions for markers CD99, CD68, SMA, SOX10, CD10 and S100 were negative. (Figure 5, Figure 6, Figure 7, Figure 8)

Five months follow up: the patient does not present recurrence or distant dissemination.

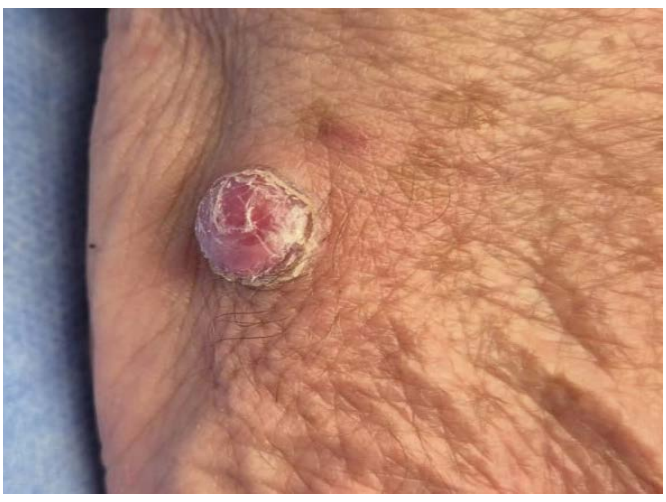

Fig. 1. Clinical aspect of the tumour.

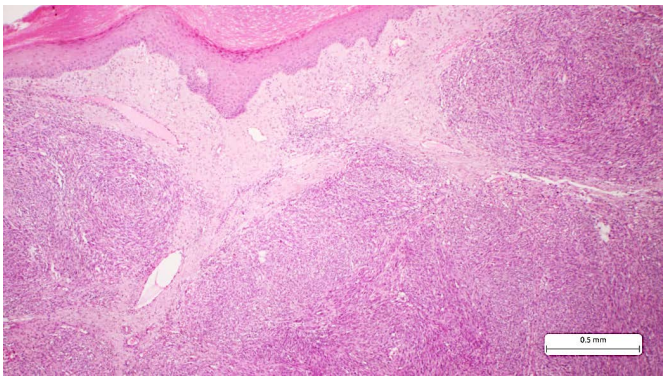

Fig. 2. The tumor exhibits a solid architectural pattern, with no involvement of the overlying epidermis.

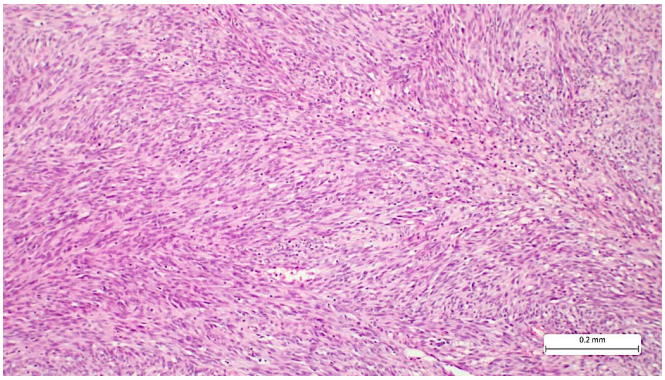

Fig. 3. Fasciculate aspect of the tumour along with focal storiform areas consisting of spindle cells. Red blood cells can be observed in the lumen of blood vessels and in between the tumour cells.

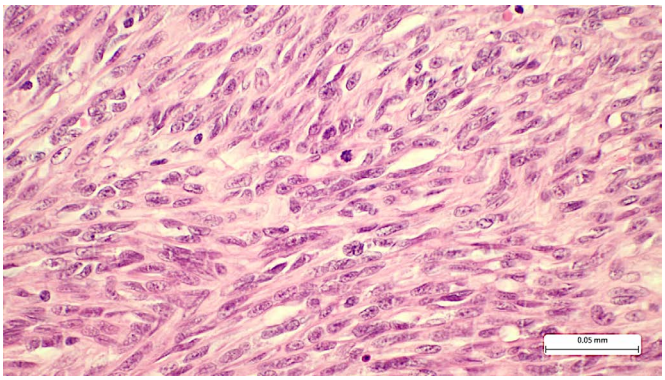

Fig 4. Spindle cell tumor proliferation with significant cytological atypia and mitoses.

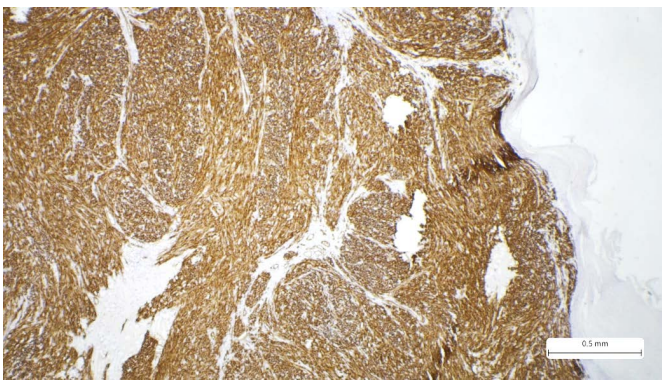

Fig. 5. Immunohistochemistry reaction revealing diffuse and strong positivity for marker CD31.

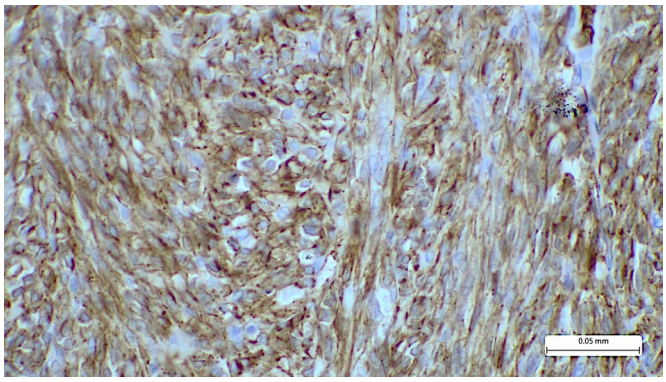

Fig. 6. Immunohistochemistry reaction revealing diffuse and strong positivity for marker CD31.

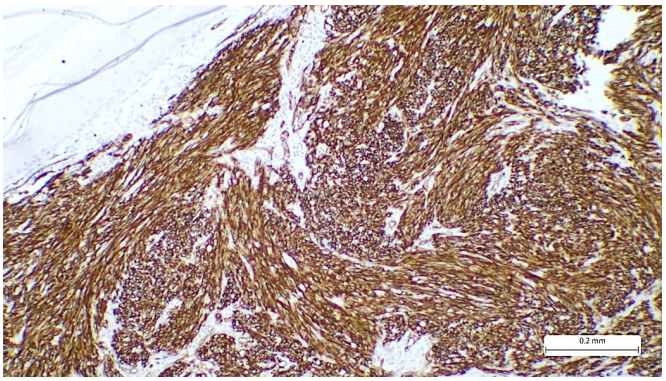

Fig. 7. Immunohistochemistry reaction revealing diffuse and strong positivity for marker CD34.

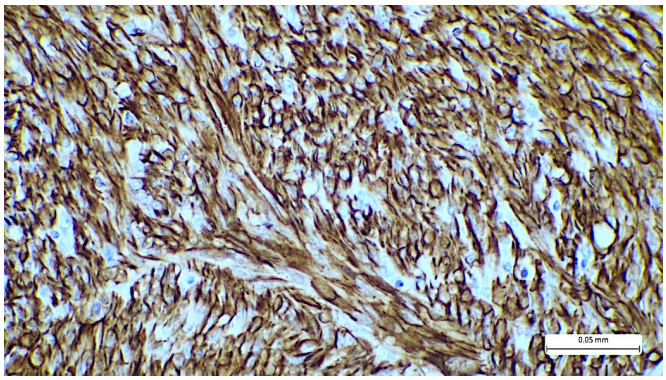

Fig. 8. Immunohistochemistry reaction revealing diffuse and strong positivity for marker CD34

Discussions

Cutaneous angiosarcomas are tumors originating in the dermis, derived from endothelial cells of blood or lymphatic vessels. The tumor can be encountered in older individuals, especially in the cephalic extremity, head and neck regions, with the scalp being a frequent site due to UV exposure, a significant risk factor. Other regions that may be involved in this age group could be the trunk and the limbs. Conditions associated with the development of angiosarcoma include pre-existent lymphedema and prior radiation therapy. Our patient did not present any of these conditions but exhibited a tumor proliferation on the dorsum of the hand.

Clinically, angiosarcomas may appear as violaceous papules, plaques, or nodules of varying sizes, sometimes accompanied by bleeding or ulceration. In our patient the tumor was a rapidly growing nodular lesion, brown and violaceous on the cut section, relatively well-demarcated and without ulceration [11-14].

Histologically, angiosarcomas exhibit with high variability. They are commonly poorly defined, with an infiltrative pattern and dermal localization. The tumor architecture may include variably formed vessels, ranging from anastomosing to poorly developed structures. In rare cases, a predominantly solid pattern is observed, making differential diagnosis essential. Solid areas can appear as sheets of tumoral cells, without clear evidence of vascular differentiation or with poorly defined cleft-like spaces [1,2]. The most common solid variant is epithelioid angiosarcoma, although spindle-cells-rich areas may be also identified. Usually, spindle cells are often arranged in fascicles. Cytologically, tumoral cells typically have abundant eosinophilic or even amphophilic cytoplasm, enlarged nuclei, prominent nucleoli and a high mitotic count.

In our patient, the tumor proliferation was bordered by a poorly defined epithelial collarette and located in the reticular the dermis, sparing the epidermis. The tumor was relatively well-defined and composed of spindle cells arranged in fascicles, with focal areas exhibiting a storiform pattern. The cells displayed significant pleomorphism, nuclear enlargement and prominent nucleoli. Discrete vascular formation was noted along with slit-like spaces and red blood cell extravasation [15-17].

Immunohistochemistry is particularly important in identifying the endothelial origin of solid tumor. Angiosarcomas typically express endothelial markers such as CD31, CD34, D2-40 and ERG. [15] In our case, the tumor showed diffuse and strong positivity for CD31 and CD34. The proliferation index Ki67 was approximately 50%.

To establish the final diagnosis and rule out other conditions with other pathologies with similar features, immunohistochemistry for SMA, S100, CD10, SOX10, CD99 and CD68 was also performed.

Given the fasciculate pattern and spindle-cells morphology, cutaneous leiomyosarcoma was considered as a differential diagnosis. This tumor originates in smooth muscle and typically grows in the dermis and subcutis. In well-differentiated cases, the tumor cells are, spindle-shaped, with bland, hyperchromatic nuclei, prominent nucleoli. The cytoplasm is eosinophilic, fibrillar. Storiform areas, pleomorphism and high mitotic activity are common. In poorly differentiated cases, diagnosis is challenging and requires at least three positive immunohistochemical markers: SMA, desmin and caldesmon. At least one marker must be positive, and more than 70% of the cases exhibit two positive markers. However, none of these markers are specific for leiomyosarcoma, and therefore it is recommended that at least two should be positive for the diagnosis. There are cases however (dedifferentiated or pleomorphic leiomyo-

sarcoma) in which demonstrating the muscle differentiation of the tumor is very difficult, and the diagnosis is made if the patient's pathological history supports it or in the presence of classic features of conventional leiomyosarcoma. The most common marker that exhibits positivity is SMA, which in our case was negative [1,18-20].

Another important differential diagnosis was atypical fibroxanthoma (AFX). This tumor occurs mostly in the head and neck region and is rare in the extremities. It typically presents as a rapidly growing, well-circumscribed dermal lesion, often polypoid and ulcerated. AFX is characterized by fascicles and sheets of polygonal, epithelioid, and histiocytoid cells, often with multinucleated tumor cells and significant pleomorphism. AFX presents various variants, including spindle cell variants, clear cell variant or pigmented variant. The differential diagnosis with other entities is made with the help of immunohistochemistry. Even though a specific marker for atypical fibroxanthoma does not exist, the tumor presents often positivity for markers vimentin, SMA, CD10 while focal expression for CD 99, CD31 and CD68 is also commonly seen. In our case, CD31 immunostaining was intense and diffuse, and all the other mentioned markers were negative. Atypical fibroxanthoma is negative to CD34, marker that was positive in our case. Therefore, we can conclude the most important tool in achieving the final diagnosis was the immunohistochemistry profile [21-23].

Other vascular tumors including Kaposi sarcoma and Kaposiform hemangioendothelioma, were excluded based on the histological features and the patient's clinical history. Spindle cell melanoma was also considered, but excluded based on the IHC profile, as this tumor presents positivity for S100 and SOX10, markers that were negative in our case [24].

The primary treatment for angiosarcoma is surgical excision, followed by radiation therapy and chemotherapy. Additional treatment options, including immunotherapy, are under development and show promising potential for the future.

Conclusion

This case highlights the rarity and complexity of angiosarcomas, particularly when occuring in atypical locations. The tumor's relatively well-demarcated growth, spindle-cell morphology and storiform pattern are notable features that differ from the typical presentation of this malignancy. Immunohistochemistry positivity for for CD31 and CD34 was essential for confirming the diagnosis and excluding other spindle-cell neoplasms. Through this case, we contribute to the understanding and diagnostic approach of cutaneous angiosarcoma and aim to enhace future management strategies for this challenging malignancy.

Authors' contribution

ACT: (Conceptualization; Funding acquisition; Investigation; Writing – original draft; Writing – review & editing)
ABL: (Formal analysis; Methodology; Supervision; Visualization; Writing – review & editing)
CF: (Methodology; Supervision; Validation)
OSC: (Supervision; Investigation; Visualization)

Conflict of interest

None to declare.

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