

ORIGINAL PAPER

Histopathological diagnosis of cutaneous vascular sarcomas

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Abstract

Cutaneous sarcomas represent a heterogeneous group of mesenchymal lesions. This study investigates the histopathological and immunohistochemical features in different cases of angiosarcoma and Kaposi's sarcoma (cutaneous vascular sarcomas), which are representative for medical practice. The clinical-histopathological-immunohistochemical correlations render possible the differential diagnosis and a proper treatment can be applied to obtain a favorable prognosis.

Keywords: angiosarcoma, Kaposi's sarcoma, immunohistochemistry, vascular sarcomas.

□ Introduction

Skin cancers account for 15–20% of all malignant tumors.

Cutaneous sarcomas are relatively rare malignant connective tissue tumors – almost 5% of all cutaneous malignant tumors.

Cutaneous sarcomas represent a heterogeneous group of mesenchymal neoplasms including fibrohistiocytic tumors (atypical fibroxantoma, dermatofibrosarcoma protuberans), fibroblast tumors (fibrosarcoma, myxofibrosarcoma), smooth muscle tumors (leiomyosarcoma), skeletal muscle tumors (rhabdomyosarcoma), peripheral nerve sheath tumors (malignant perineural sheath tumor, MPNST), lipomatous tumors (liposarcoma), and vascular tumors (angiosarcoma, Kaposi's sarcoma) [1–7].

Frequently, sarcomas are found in older adults. Sarcomas are usually manifested by deep lesions and they may also affect the subcutaneous tissue. The preferential sites are the extremities, especially the thigh, then trunk, head and neck and retroperitoneum.

Most sarcomas appear spontaneously and do not have a known etiology.

Cutaneous lesions present as plaques or nodules. Their main characteristics are cellular and nuclear atypia, rapid, invasive and destructive growth, metastases and a high tendency to local recurrences [1, 3, 8–12].

The general information about the patient (age, sex, pathological history) together with the specific data about the tumor (size, location, growth pattern, atypia, mitotic rate, presence of necrosis, ulceration and hemorrhage areas) are important features for a correct diagnosis and prognosis evaluation [13–18].

The treatment of cutaneous sarcomas consists of surgical excision, radiotherapy and chemotherapy [1, 3, 4, 14].

These article reviews cutaneous vascular sarcomas with particular emphasis on the histopathologic and immunohistochemical features for diagnostic, treatment and prognostic purpose.

□ Material and Methods

The research group comprises 27 cases of cutaneous vascular sarcomas (seven cases of angiosarcoma and 20 cases of Kaposi's sarcoma from all histological stages (patch, plaque and nodular). The surgical excision samples were fixed in 10% buffered formalin, paraffin embedded and stained with Hematoxylin–Eosin for histopathological examination. Immunohistochemical staining was performed using the following antibodies: CD34, CD31, actin, myoglobin, desmin, cytokeratin and vimentin (Table 1).

Table 1 – Antibodies used for immunohistochemical staining

Antibody	Specificity / Reactivity	Company	Dilution	Clone
CD34	Endothelial antigen; Hematopoietic precursor	Immunotek	1:100	Qbend 10
CD31	Endothelial antigen	Neomarkers	1:30	JC/70A
Actin	The actin from the smooth muscle tissue	SIGMA, St. Louis, Mo, USA	1:1500	PC10
Cytokeratin	Cytokeratin marker	Immunotek	1:200	KL1
Vimentin	Mesenchymal marker	DAKO, Glostrup, Denmark	1:50	V9

■ Results

The **angiosarcoma** is one of the rare sarcomas, which occur on the head and neck, especially on the scalp and face of elderly men. Histopathologically, the angiosarcoma is characterized by multiple vascular channels of different sizes lined by endothelial, atypical cells, disposed on one or more layers. The atypical endothelial cells are more protuberant than normal cells, pleomorphic, with pale, light eosinophilic cytoplasm and voluminous and hyperchromatic nuclei. Lymphocytic infiltrate is present (Figures 1 and 2). Tumoral cells show an alveolar (Figure 3) or fasciculate pattern.

Immunohistochemical staining reveals that angiosarcomas express vimentin, CD34 and actin and show a diffuse positivity for myoglobin (Table 2) (Figure 4).

Table 2 – Angiosarcoma: IHC results

Case no.	Actin	CD34	CD31	Cytokeratin	Vimentin
1.	+	+	-	-	+
2.	+	+	-	-	+
3.	+	+	-	-	+
4.	+	+	-	-	+
5.	+	+	-	-	+
6.	+	+	-	-	+
7.	+	+	-	-	+

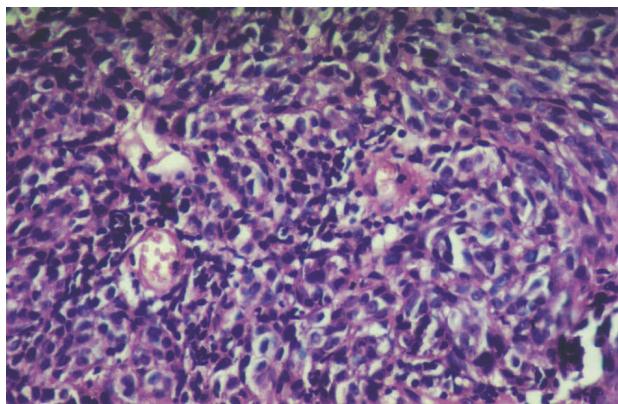


Figure 1 – Angiosarcoma. Vascular channels with different sizes lined by endothelial, pleomorphic, atypical cells with voluminous and hyperchromatic nuclei (HE stain, ob. 40×).

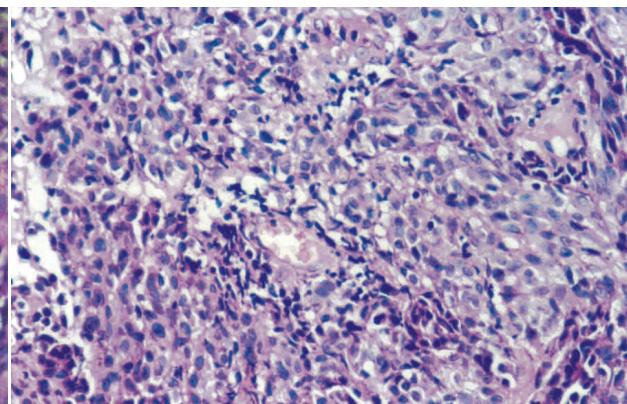


Figure 2 – Angiosarcoma of the scalp and face of elderly men. Tumoral cells with atypical, vesicular, tachychromatic nuclei (HE, ob. 40×).

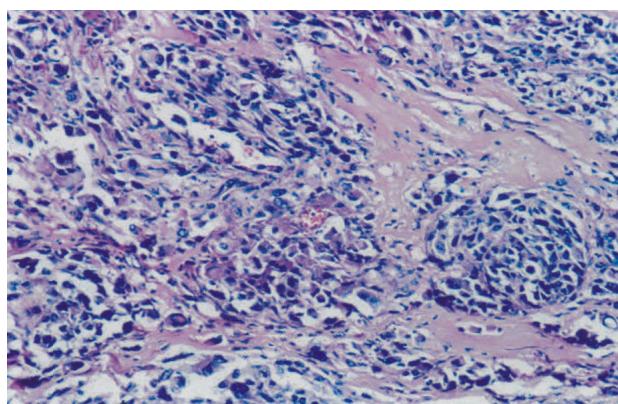


Figure 3 – Angiosarcoma, alveolar pattern (HE stain, ob. 40×).

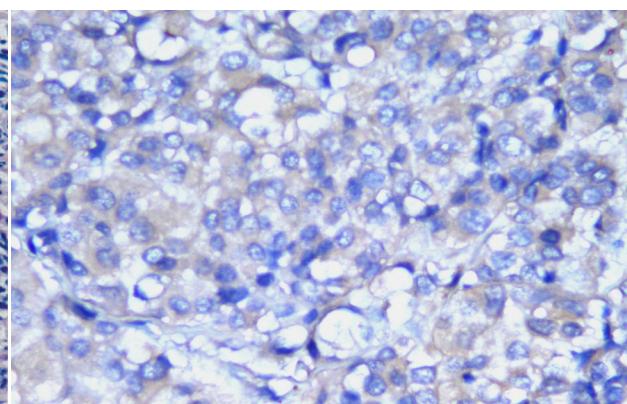


Figure 4 – Angiosarcoma. IHC staining for myoglobin; diffuse positive (ob. 20×).

Kaposi's sarcoma (KS) is a mesenchymal tumor characterized by the proliferation of spindle-shape cells, usually in a directional streaming pattern, neoangiogenesis, inflammation with fibrosis and hyperemia (extravasated erythrocytes and hemosiderin storage). It represents the most common tumor associated with HIV-infection.

HHV-8 (also known as KS-associated Herpes virus, KSHV) is considered the etiologic agent in KS.

From a clinical point of view, Kaposi's sarcoma can be classified in four groups: classical Kaposi's sarcoma, Kaposi's sarcoma in Africa, AIDS-associated Kaposi's sarcoma and Kaposi's sarcoma and iatrogenic immunosuppression.

From a histological point of view, three stages were

described in KS evolution: patch (Figure 5), plaque (Figure 6) and nodular (Figure 7).

The patch stage is characterized by multiple neof ormation vessels of irregular shape in the upper reticular dermis. The vascular spaces are lined by flattened or more oval endothelial cells, with little atypia. The anastomosis between pre-existing blood vessels and new vessels was observed. Extravasated erythrocytes and deposits of hemosiderin surround the vascular structures. Sparse lymphocytes and plasma cells are also seen. In some cases, spindle endothelial cells proliferate around blood vessels in the dermis.

The plaque stage shows the same characteristics as the patch stage, but in an exaggerated form. An increased number of vascular channels (more

extensive angioproliferation), a denser inflammatory infiltrate, and numerous extravasated erythrocytes and siderophages can be observed.

In nodular and tumoral stages of Kaposi's sarcoma (Figures 8 and 9), nuclear atypia with atypical mitoses,

irregular vessels surrounded by tumor cells, erythrocyte extravasation and the presence of siderophages (Figure 10) may be encountered. The tendency of cell deposition in a directional streaming pattern can be usually mentioned.

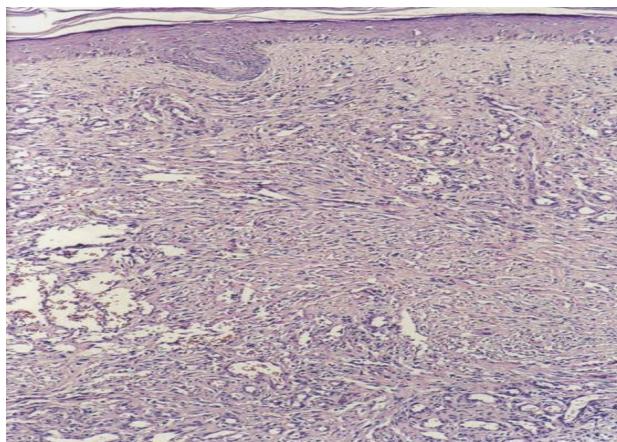


Figure 5 – Kaposi's sarcoma, incipient stage (HE stain, ob. 10×).

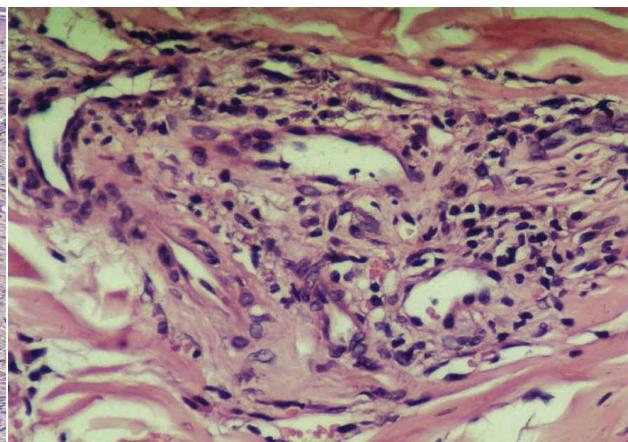


Figure 6 – Kaposi's sarcoma: plaque stage. Blood vessels surrounded by endothelial cells and spindle-shaped cells with atypical nuclei; inflammatory infiltrate (HE stain, ob. 40×).

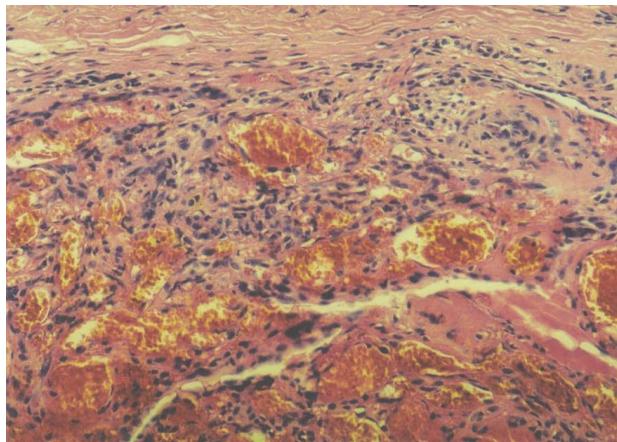


Figure 7 – Kaposi's sarcoma: tumoral/nodular. Numerous blood vessels surrounded by spindle-shape cells with elongated nuclei and acidophilic cytoplasm (HE stain, ob. 20×).

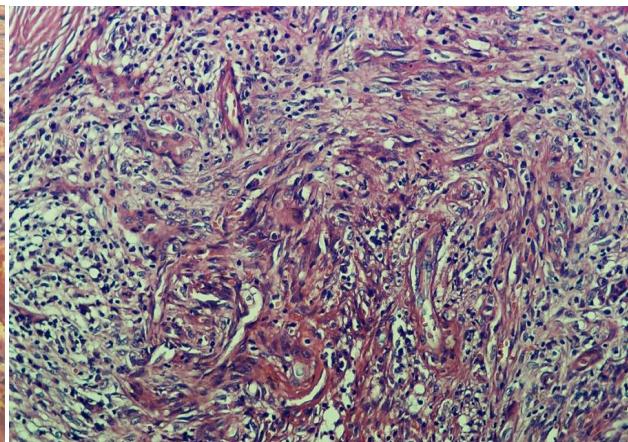


Figure 8 – Kaposi's sarcoma: tumoral stage. Blood vessels surrounded by fascicle of spindle-shaped cells; atypical mitoses (HE stain, ob. 20×).

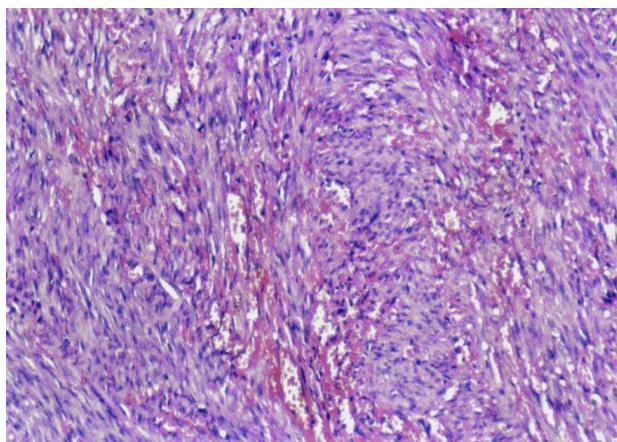


Figure 9 – Kaposi's sarcoma: tumoral stage. Bland spindle cells forming slit-like spaces occupied by red blood cells (HE stain, ob. 10×).

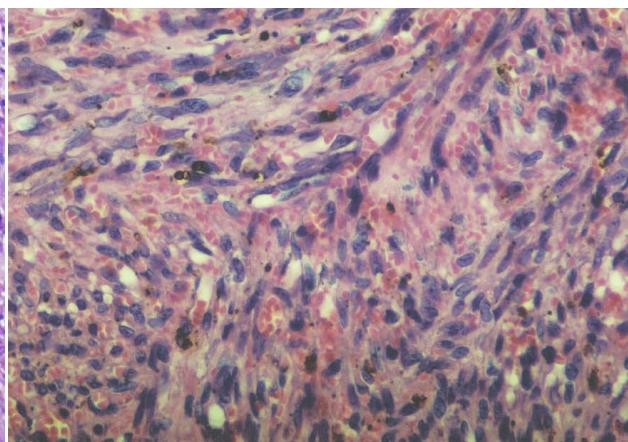


Figure 10 – Group DM+P – Another early sign of DR – Adventitial cell loss; the cells are responsible for vessel shape preservation (VG-stained retina specimen, ob. 40×).

In Kaposi's sarcoma, immunohistochemical staining showed a diffuse vimentin-positivity; CD34 (Figure 11) and CD31 (Figure 12) were positive in vascular structures and cytokeratin was negative (Table 3).

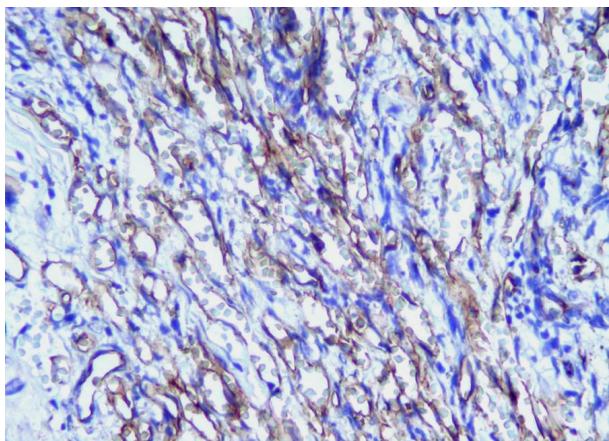


Figure 11 – Kaposi's sarcoma (IHC staining for CD34; positive; ob. 20×).

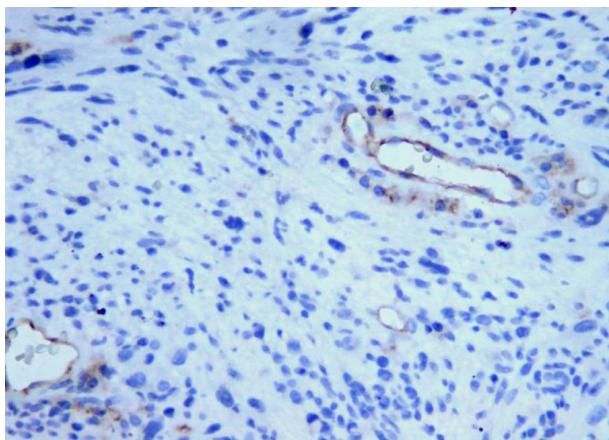


Figure 12 – Kaposi's sarcoma (IHC staining for CD31; positive; ob. 20×).

Table 3 – Kaposi's sarcoma: IHC results

Case no.	Actin	CD34	CD31	Cytokeratin	Vimentin
1.	+	+	IR	-	+
2.	+	+	+	-	+
3.	+	+	+	-	+
4.	+	+	+	-	+
5.	+	+	+	-	+
6.	+	+	+	-	+
7.	+	+	+	-	+
8.	+	+	+	-	+
9.	+	+	IR	-	+
10.	+	+	+	-	+
11.	+	+	+	-	+
12.	+	+	+	-	+
13.	+	+	+	-	+
14.	+	+	+	-	+
15.	+	+	+	-	+
16.	+	+	+	-	+
17.	+	+	+	-	+
18.	+	+	+	-	+
19.	+	+	+	-	+
20.	+	+	+	-	+

Discussion

The histopathological examination and immunohistochemical tests are still the most useful tools for pathologists in cancer studies. These data are correlated with the clinical observations and give an almost complete picture used in differential diagnosis and prognosis of a cancer type. Also, it can have an important value in establishing the correct treatment.

The aims of this study were the histopathological examination of 27 cases of cutaneous vascular sarcomas (seven cases of angiosarcoma and 20 cases of Kaposi's sarcoma) and the immunohistochemical analysis of these cases using monoclonal antibodies for detection of tumor proliferation origin. These research studies help us to construct a pattern for a protocol of histopathological study on the selected cases.

We concluded that cutaneous sarcomas form a heterogeneous group of neoplasms with a varied panel of microscopic appearances, the positive and differential diagnosis being necessary. These neoplasms are relatively rare.

Usually, cutaneous sarcomas can occur at any age, but these neoplasms are rare in children. Both genders are affected, with predominance in men. Most sarcomas appear solitary and have a profound invasion; the usual sites are the extremities (Kaposi's sarcoma). Angiosarcomas occur usually in head and neck area at elderly men.

The etiologies of cutaneous sarcomas are unknown for most of the cases, except Kaposi's sarcoma (HHV-8 – also known as KSHV), and some smooth muscle tumors (EBV). In angiosarcomas, especially after radical mastectomy (Steward-Treves syndrome) some complications may appear usually due to local immunosuppression.

As an essential and distinct feature of these tumors is the increased tendency to recurrences.

Clinically, the lesions present as plaques or nodules that can ulcerate in last stages. Also, areas of necrosis can be observed.

Histopathologically, cutaneous sarcomas are characterized by invasiveness, not being encapsulated and imprecise delimitation by the neighboring tissues. The cellular and nuclear atypical size, form and color, as well as atypical mitoses are frequently present. The tumors prove to be highly cellular showing a characteristic storiform pattern.

Cutaneous vascular sarcomas are malignant neoplasms of endothelial cells. Their histopathological appearance consists of multiple irregular vascular spaces lined by atypical endothelial cells with large, pleomorphic, tachychromatic nuclei.

In Kaposi's sarcoma, the vascular component is related to the cellular, sarcomatous component. The last one consists of fascicles of spindle-shaped cells, orientated in different directions, in a storiform pattern.

Angiosarcoma, as well as Kaposi's sarcoma, expressed CD34 (endothelial marker), actin and vimentin, but did not express cytokeratin.

We did not observe CD31-expression in the angiosarcoma cases included in our study.

The immunohistochemical techniques related to morphology help us identify and classify these tumors.

Conclusions

The diagnosis of such tumors can be confirmed by immunohistochemical staining. In correlation with anatomo-clinical findings, this method allows a good differential diagnosis and rules out a large number of lesions with a completely different specific treatment.

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