

Uncommon pattern in soft tissues epithelioid sarcoma

CARMEN ARDELEANU^{1, 2)}, MARIA COMĂNESCU³⁾,
VIOLETA COMĂNESCU⁴⁾, F. ANDREI¹⁾

¹⁾Immunohistochemistry Department,

„Victor Babeș” National Institute of Pathology, Bucharest

²⁾“Carol Davila” University of Medicine and Pharmacy, Bucharest

³⁾University Hospital, Bucharest

⁴⁾Emergency County Hospital, Craiova

Abstract

Epithelioid sarcoma (ES) is a rare tumor, but extremely versatile, simulating easily both clinically and morphologically multiple benign lesions as granulomas and malignant tumors as achromic melanomas or carcinomas. Especially the histological aspects are suggesting for an epithelial tumor. The atypical biological behavior of tumor is conferred by: a propensity for lymph nodes metastases, large dimensions of tumor, unusual localizations. *Aim:* to report some peculiar histological and immunophenotypic aspects in soft parts epithelioid sarcoma. *Materials and methods.* We analyzed retrospectively three cases of epithelioid sarcomas with unusual clinico-morphological (large dimensions), histopathological (absence of necrosis) and immunohistochemical (IHC) patterns selected from 200 consecutive soft parts malignant tumors of “Victor Babeș” National Institute Bucharest files. For the immunohistochemical (IHC) staining, the following antibodies were used: vimentin, EMA, cytokeratins (KL1, CK19), S-100 protein, CD68, p53 protein, vascular markers (CD31, CD34, FVIII-related antigen), HMB45, MELAN A. *Results.* The tumors had unusually large dimensions, the absence of necrosis, a vaguely alveolar pattern; the IHC staining showed a strong positivity of S-100 protein, a variable expression of cytokeratins KL1 and CK19, in association to a scarce positivity for EMA, zonal positivity for CD34 and diffuse reaction for vimentin. *Conclusion.* The immunophenotype of ES may have a large variability and the correlation to clinico-morphological aspects is necessary for a good diagnostic assessment.

Keywords: soft tissues, epithelioid sarcoma.

Introduction

The epithelioid sarcoma (ES) was described by Enzinger [1] as a rare tumor simulating granuloma or carcinoma. Its histogenesis is unknown and the tumor is appearing in young patients, mainly in limbs.

The microscopic nodular infiltrative aspects presenting or not central necrosis are suggestive for an inflammatory granuloma, an epithelial tumor, an achromic melanoma, or for other soft parts tumor, like epithelioid sclerosing fibrosarcoma [2] or epithelioid sarcoma-like hemangioendothelioma [3].

The tumor cells are large, polygonal or rounded, with abundant eosinophilic cytoplasm, sometimes with rhabdoid aspect, vesiculous nuclei and prominent nucleoli. Cytoplasmic vacuoles and pseudo-vascular spaces are suggestive for a vascular origin and this is the reason for denomination of such ES, as „angiomatoid ES” [4].

The atypical biological behavior of epithelioid sarcoma is conferred by: a propensity for lymph nodes metastases, large dimensions of tumor, unusual locations.

The clinically apparent benign aspects and the relative long period free of metastases may arise diagnostic confusion with benign tumors [5], especially in incipient disease [6].

The outcome of tumor is dependent on tumor size (tumors more than 5 cm are aggressive), location (a deeply localized tumor in limb is more aggressive), number of local recurrences and metastases [7].

The IHC of tumor is characterized by a coexpression of two intermediate filaments, vimentin and cytokeratin, low or high molecular weight; other useful markers are CD34 and EMA. S-100 protein is usually negative.

CD31 (PECAM – platelet endothelial cell adhesion molecule) was considered one of the most specific vascular antigens useful in the differential diagnosis of vascular malignant tumors.

ES was considered devoid of this antigen, but recently, it was observed in some ES and described as a membranous staining [8].

In some cases aberrant immunophenotypical features need to be interpreted in histopathological and clinical context, as reported by Arber [5] who found cases negative for Vimentin.

It is to retain also a more aggressive biological behavior for “proximal” type of ES occurring in deep soft tissue of the limb girdles [4].

Material and methods

We analyzed retrospectively three cases of epithelioid sarcomas with unusual clinico-morphological, histopathological and immunohistochemical (IHC) patterns, selected from 200 consecutive soft parts malignant tumors of „Victor Babeș” National Institute Bucharest files.

The tumor samples were fixed in buffered 10% formalin, paraffin embedded and sectioned at 4 µm, then stained routinely by Hematoxylin-Eosin; a Gömöri argentic impregnation was performed.

For the immunohistochemical (IHC) staining, the following antibodies were used:

- Vimentin (DAKO, Glostrup, Denmark, 1:50);
- EMA (DAKO, 1:100);
- Cytokeratin KL1 (Immunotech, Marseille, 1:100);
- CK19 (Novocastra, Newcastle upon Tyne, UK, 1:50);
- S-100 protein (DAKO, 1:500);
- CD68 (DAKO, 1:100);
- p53 protein (DAKO, 1:50).

As vascular markers CD31 (DAKO, 1:40), CD34 (Immunotech, 1:50), and F VIII-related antigen (DAKO, 1:100) were used. An indirect triserial Avidin-Biotin-Complex method was performed, as following: deparaffinization in xylene and alcohol series, rehydration, washing in phosphate saline buffer (PBS), incubation with normal serum, for 20 minutes, incubation with primary antibody overnight, LSAB kit (DAKO), washing in carbonate buffer and development in 3,3'-DAB hydrochloride / H₂O₂; nuclear counterstain with Mayer's Hematoxylin.

☞ Results

The three selected cases were male patients and they were 9, 43 and 57 years of age at the time of initial diagnosis. The tumors were situated in axilla, respectively, arm and thigh and all were more than 8 cm in the largest diameter.

Histological appearance showed an invasive nodular pattern; the tumoral cells were large, polygonal or rounded, disposed in discohesive or compact lobules (Figure 1), sometimes vaguely alveolar; the tumor cells had eosinophilic cytoplasm (Figure 2), a large vesicular nucleus and prominent nucleolus (Figure 3); numerous atypical mitoses and moderate peritumoral cellular inflammatory infiltrate were observed.

In two cases, the compact pattern of proliferation and the polygonal shape of large cells caused difficulties in distinguishing ES and poor differentiated carcinoma.

The third case had a nodular pattern and areas of pseudoangiomatous hyperplasia as showed by Gömöri argentic impregnation (Figure 4).

Immunohistochemical staining showed a diffuse positivity for vimentin in all three cases (Figure 5); EMA had a zonal membranous positivity in all cases (Figure 6); KL1 was positive in two cases and CK19 was expressed zonally in one case.

CD34 had a focal positivity in two cases especially around pseudovascular structures (Figure 7).

S-100 protein showed an unusually strong diffuse positivity in one case and only scarce expression in the remaining two cases (Figure 8).

CD68 was positive in rare macrophages in a case with a rich inflammatory infiltrate; p53 protein expression was increased in one case (~40% of tumor cells positive).

Vascular markers as CD31 and FVIIIvW were negative in all cases as well as HMB45 and MELAN A.

☞ Discussions

ES is a malignant tumor with confusing clinical and morphological features. It mimics benign inflammatory

lesions and malignant tumors as squamous cell carcinoma, malignant melanoma, synovial sarcoma etc.

An increased precision of ES IHC profile is necessary for ruling out these types of lesions in the differential diagnosis.

In this study the cytokeratins used showed a variable expression. KL1 as pancytokeratin, CK19 and CK7 were positive each in a different case. Cytokeratins expression in the ES is useful for differentiate it from a synovial sarcoma; the last is expressing usually CK19 and CK7, only rarely observed in ES [9, 10].

EMA was present in all cases, but with a focal staining. Weiss [11], Hasegawa [12] and Dabbs [13] found expression for EMA and cytokeratins in all cases investigated.

Unluckily this is completely helpless for distinguish among epithelioid sarcoma [13] and carcinomatous metastasis, the single clue comes from morphology. Useful appears to investigate several epithelial markers, more than a few cytokeratins subtypes.

In a case there was a strong expression for S-100 protein, but only very few cells were reactive in the other two cases; completely lack of expression for neural markers (NFT, NSE) ruled out an epithelioid schwannoma.

Only one of our cases had a significant positivity for p53 (30 to 50% of tumoral cells) comparing to Hasegawa who found more than 80% of cases expressing it.

Infectious necrotizing granuloma should be disregarded also helped by IHC, knowing this entity lacks EMA and CK.

Challenging is to differentiate epithelioid sarcoma of epithelioid variety of hemangioendothelioma.

Billings [3] has investigated seven cases of epithelioid sarcoma with angiomatoid features and found in all cases cytokeratin and vimentin positive with no expression for CD34, contradictory to Arber [5] which found some cases vimentin negative and CD34 positive.

Anyway, epithelioid sarcoma is rarely reactive for CD34 apart from epithelioid vascular tumors that show always reaction for vascular markers as CD31, FVIIIvW and Fli-1 [8] and weak expression for cytokeratins.

☞ Conclusions

In conclusion, the results showed an unusually strong staining for S-100 protein in a case, a variable expression of cytokeratins and EMA, a zonal positivity for CD34 and a diffuse reaction for Vimentin.

The immunophenotyping of such a tumor is important because in correlation to the anatomo-clinical features permits a good differential diagnosis and rules out a large number of pseudotumoral or tumoral lesions with a completely different specific treatment.

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Figure 1 – Epithelioid sarcoma. Proliferation of large, mostly polygonal cells with a compact pattern (HE staining, ob. ×10)

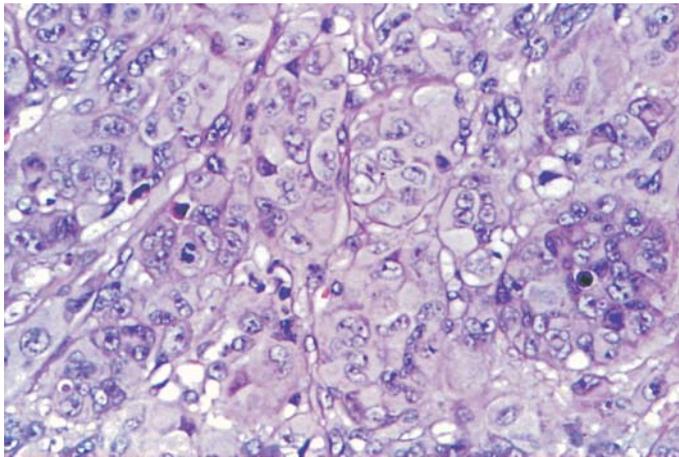
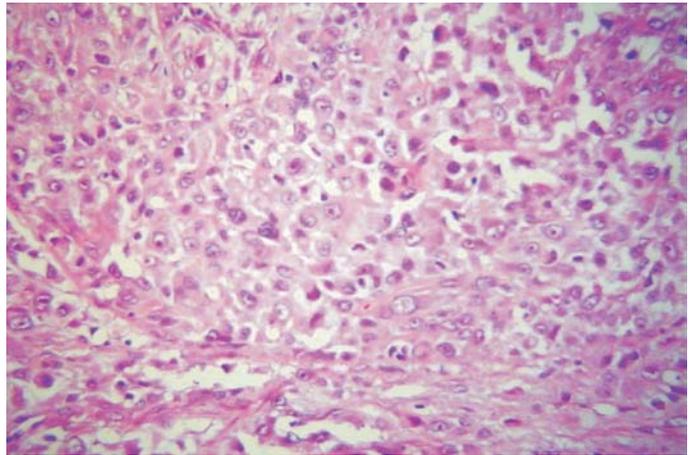


Figure 2 – Epithelioid sarcoma with a vaguely alveolar pattern. Eosinophilic cytoplasm of tumor cells (HE staining, ob. ×20)

Figure 3 – Cellular details: large vesiculous nuclei, prominent nucleoli (HE staining, ob. ×40)

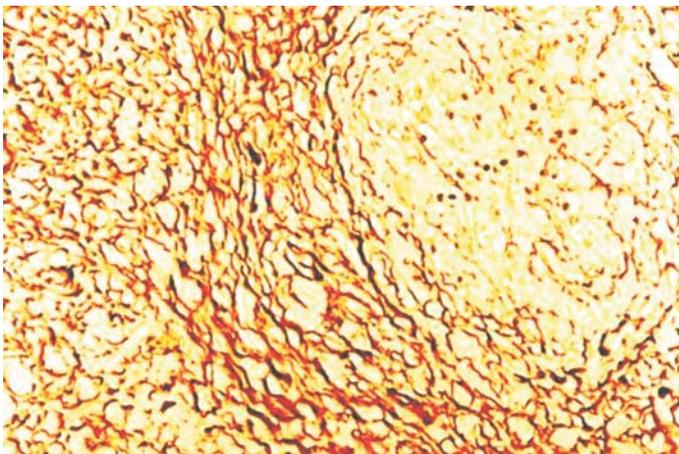
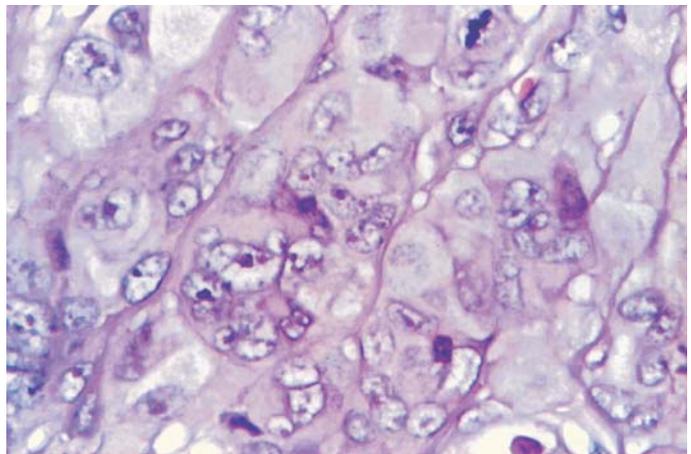


Figure 4 – Hyperplastic vascular structures (Gömöri's argentic impregnation, ob. ×10)

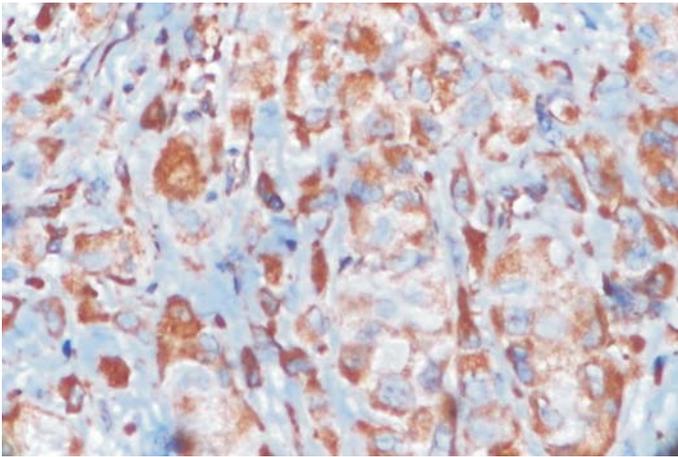


Figure 5 – Epithelioid sarcoma. Diffuse positive reaction for vimentin (IHC staining for vimentin, ob. ×20)

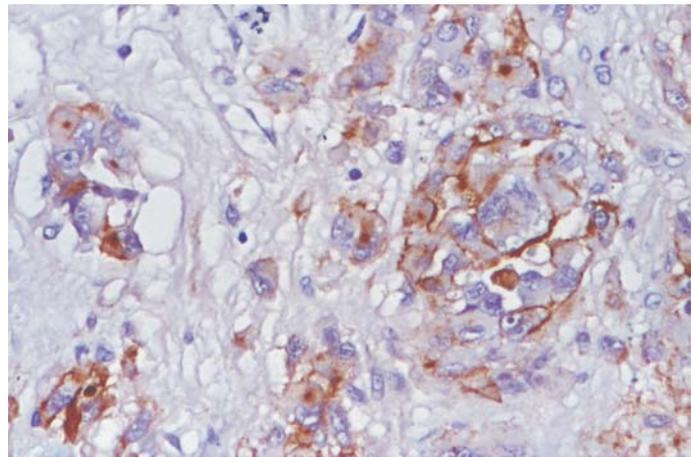


Figure 6 – Zonal expression of EMA in epithelioid sarcoma (IHC staining for EMA, ob. ×20)

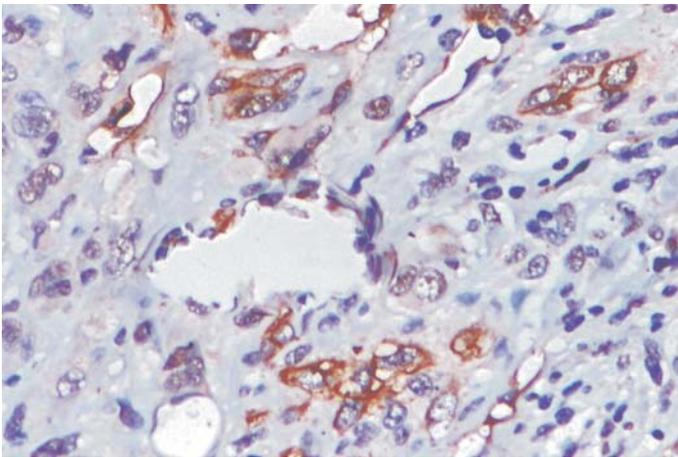


Figure 7 – CD34 positive cells predominantly perivascular (IHC staining for CD34, ob. ×20)

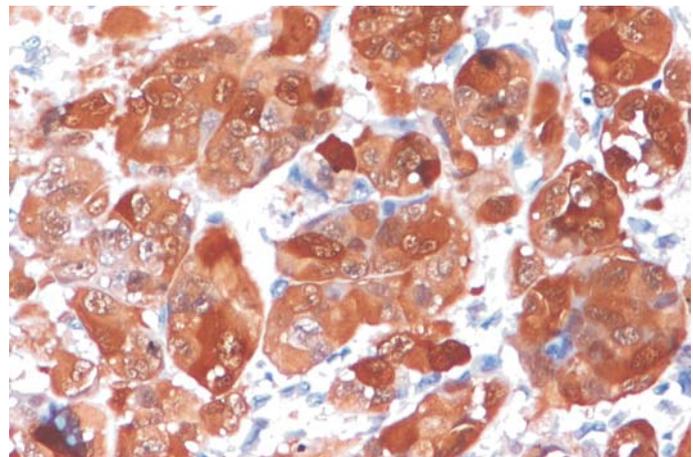


Figure 8 – Strong and diffuse expression of S-100 protein (IHC staining for S-100 protein, ob. ×20)

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Mailing address

Carmen Ardeleanu, Associate Professor, M. D., Ph. D., Immunohistochemistry Department, “Victor Babeş” National Institute of Pathology, Avenue Independenței no. 99–101, sector 5, 050 096 Bucharest, Romania; Phone +4021–319 27 34, E-mail: carmena@vbabes.ro

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