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Case Report

Primitive Epithelioid Hemangioendothelioma (EHE) of the Pleura. A Case Report and Literature Review

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Abstract

Epithelioid vascular tumors present a challenging diagnostic problem, especially if they originate in unusual locations, such as the pleural serosa. For these reasons, a case of a Primitive Pleural Epithelioid hemangioendothelioma observed by us deserves to be reported.

Keywords: Epithelioid Hemangioendothelioma (EHE); Pleura; Woman

Introduction

Case

Woman 60 years old, has for some time been experiencing respiratory difficulties. A TC scan found that there was an almost complete opacification of the right lung area occupied by abundant and extensive pleural effusion (more evident in the mid-basal area), with associated homolateral pulmonary atelectasis and consolidation phenomena of right lung parenchymal, misdirection of the mediastinal structures is documented. Some enlarged lymph nodes in the ilo-mediastinal area are documented. Deviated aerial tracheal tape (Figure 1). At thoracoscopy multinodular thickness of the right parietal pleura, of pearl in appearance with lung adhesions. Some small bioptic fragments were taken from the nodular neoformations (Figure 2).

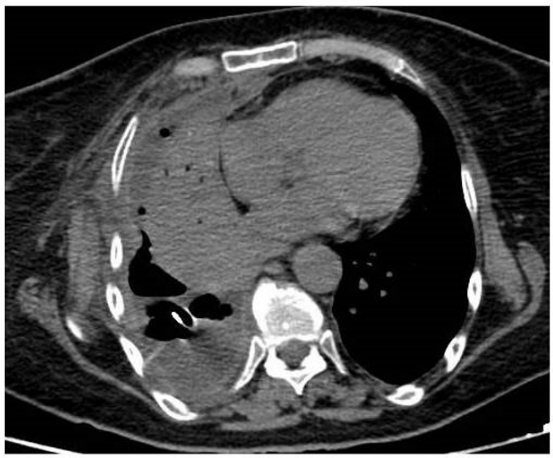

Figure 1: CT Scan Thorax - The right pleural cavity is occupied by a profuse effusion that collapses the lung.

Materials and Methods

The material was fixed in buffered formalin and embedded in paraffin. Some sections were stained with Hematoxylin Eosin, others were subjected to an immunohistochemical investigation with a large panel of antibodies reported in table 1.

Figure 2: Thoracoscopy. Two nodular thickenings can be seen on the parietal pleural serosa.

Histology

In a myxoyaline context, there is a lively cell proliferation consisting mainly of spindle-shaped elements, sometimes very thin, sometimes with more abundant, amphophilic cytoplasm (Figure 3). Mixed with these elements, there are clusters and cords of various shapes and sizes made up of cells of epithelioid appearance and aggregation (Figure 4). The nuclei are often bulky and hyperchromatic, with moderate atypia. Intracytoplasmic lumens are found in both spindle and epithelioid elements with moderate frequency (Figure 5). There is no frequent or atypical mitotic activity.

VIM	K AE1-AE3	K MNF116	K7	K 5/6	K 8/18	EMA	CD34	Cd31	CD99	D2-40 (Podoplan)	CD68	TTF1	S1oo	Smact	Desm-	E Cader.	ER	Cal	HBM E	CD45	KI67

Table 1

Immunohistochemistry

The results of the immunohistochemical investigation are described in the following table 2.

VIM	KAE1-AE3	KMN F116	K7	K 5/6	K 8/18	EMA	CD34	Cd31	CD99	D2-40 (Podoplan)	CD68	TTF1	S1oo	Smact	Desm-	E Cader.	ER	CaL	HBM E	CD45	KI67
+	+	0	0	0	+	0	-+	+	+	+	0	0	0	0	0	0	0	0	0	0	<10%

Table 2

Discussion

This oncological entity was for the first time from Weiss and Enzinger in 1982 who summarized it as follows: "Epithelioid hemangioendothelioma is a unique tumor of adult life which is characterized by an" epithelioid "or" histiocytoid "endothelial cell. Forty-one cases of this rare tumor have been recognized at the Armed Forces Institute of Pathology. They may occur in either superficial or deep soft tissue, and in 26 cases appeared to arise from a vessel, usually a medium-sized or large vein. They are composed of rounded or slightly spindled eosinophilic endothelial cells with rounded nuclei and prominent cytoplasmic vacuolization. The latter feature probably represents primitive lumen formation by a single cell. The cells grow in small nests or cords and only focally line well-formed vascular channels. The pattern of solid growth and the epithelioid appearance of the endothelium frequently leads to the mistaken diagnosis of metastatic carcinoma" [1]. The authors specify that the adoption of the term Hemangioendothelioma indicates a lesion with borderline behavior and the epithelioid component is not exclusive to a defined clinical-pathological entity, as it is present in lesions with benign and malignant behavior.

Over the years, with the acquisition of more data on the natural history of this neoplasm, the opinion has been forming that it is a tumor with malignant potential. Indeed, the World Health Organization (WHO 2002) classification describes EHE as lesions that fall into the category of locally aggressive tumors with metastatic potential [2].

Other authors believe that EHE of soft tissue is better regarded as a fully malignant, rather than borderline, vascular neoplasm, albeit the prognosis is better than in conventional angiosarcoma [3,4].

Tumors with identical characters, as well as in soft tissues have been reported in different sites, including the lung [5], liver [6], bone [7], pleura and peritoneum [8], skin [9], lymph node [10], stomach [11] and brain [12]. The real incidence of the pleural localization of the tumor is not easy to define. An extensive review of EHE does not report pleural localization (possibly included in pulmonary that represents 12% of all EHE [13].

A review on malignant vascular tumors of the pleura underlines the difficulty of distinguishing EHE from true angiosarcoma and concludes in the following way: "The histological distinction between pleural EHE and epithelioid angiosarcoma is still not clear because of the lack of convincing evidence of the existence of histological low-grade pleural EHE with comparable biological behavior. Diffused epithelioid pleural vascular tumors, even those with EHE features, should be considered as highly malignant lesions because of their invariably fatal outcome" [14]. In this publication, there are 26 cases of tumors retrieved from the literature of which 7 were diagnosed as EHE.

By inserting the Pleural epithelioid Hemangioendothelioma request in Pubmed, 24 items are obtained between 1997 and 2021 in which 32 cases are reported. In the series, there are 19 males and 13 females. The average age is around 55 years with a range between 30 and 85 years [15-39].

The lesion presents clinically with chest pain and pleural effusion. The radiological and thoracoscopic picture can simulate mesothelioma [40].

The microscopic picture over the years has been enriched with some details, but fundamentally, it reflects Weiss and Enzinger's original description. It is a proliferation of elements of a spindle-shaped form in a myxoyalin matrix among which are found cords, strands and nests of epithelioid cells with glassy eosinophilic cytoplasm. The nuclei are vesicular, variously hyperchromatic. A characteristic of this lesion is the intracytoplasmic lumens that are present both in the spindle cells and in the epithelioid elements; these elements have been defined as "blister cells" and are considered to be the initial phase in the formation of the vascular structures. The immunohistochemical investigation confirmed what the morphology had indicated. EHE expresses at least one of the endothelial markers (CD31, CD34, ERG). Usually, CD 31 and ERG are expressed more frequently; CD 34 less frequently. Cytokeratin is expressed in 25% of cases. Biomolecular investigations have been conducted on these lesions, but they are not the subject of our discussion [41].

The case observed by us has all the characteristics of the EHE. On clinical, instrumental as well as pathological levels. Clinically, it began with respiratory distress. The radiological investigation showed an abundant liquid effusion in the right pleural cavity (Figure 1). The thoracoscopic investigation highlights a thickening and nodularity of the right parietal pleura (Figure 2). The morphological pattern of the lesion fulfills all the criteria indicated for its diagnosis. The basic stroma is myxoyaline (Figure 3a), the spindle cell component is made up of mainly thin elements (Figure 3b), the epithelioid component is organized in nests cords and strands (Figure 3 c, d; 4 a, b, c, d). The characteristic intracytoplasmic lumens (blister cells) are present (Figure 5 a, b, c, d). Moderate nuclear atypia is present.

Figure 3: a- Cellular component embedded in a myxoyaline Stroma (HE 125X), b- Cellular component, consisting of thin spindle cells (HE125X), c-d Cords and nests of epithelioid cells.

Figure 4: a-b-c-d- Nests of epithelioid cells (HE 125X, 200X).

Figure 5: a-b-c-d- Cells with intracytoplasmic lumen (blister cells) HE 200X).

The immunophenotypic profile shows clear expressiveness for Vimentin (Figure 6 a, b), Cd 31 (Figure 6 c, d), K AE1-AE3 (Figure 7 c, d), K 8/18 (Figure 8 a, b), C-40 (podoplanin) (Figure 9 a, b), Cd99 (Figure 9 c, d) and the usually negative CD 34 (Figure 7 a, b).

Figure 6: a-b Vimentin positive in spindle an epithelioid cells (!25X), c-d CD 31 positive in spindle and epithelioid cells (!25 X).

Figure 7: a-b- CD 34 Spindle and epithelioid cells completely negative (125, 250X), c-d- K AE1-AE3 positive in spindle and epithelioid Cells (125, 200X).

Figure 8: a-b- K 8/18 Positive in spindle and epithelioid cells (125, 200X), c-d- Ki 67 rare positivity in spindle and epithelioid cells (125, 200X).

Figure 9: a-b- Podoplanin Intense positivity in spindle and epithelioid cells (175. 200X), CD 99, c-d- Intense positivity in spindle and epithelioid cells (125, 200X).

C-40 (Podoplanin) is an antibody that is not usually present in the immunohistochemical panel for the diagnosis of these tumors, but there are recent reports in the literature that indicate its constant, intense expression in vascular neoplasms including EHE. This expressivity is considered useful in the differential diagnosis with other epithelioid neoplasms, especially if one takes into account the inconstant expressiveness, in this lesion, of the specific vascular markers. Whether this positivity is to be considered an aberrant phenomenon, or if, on the other hand, it has a meaning in tumorigenesis, it is not clear. In this second hypothesis, we could also hypothesize a lymphatic histogenesis for these lesions [42]. The mesothelial markers, Calretinin and HBME, were completely negative.

The expressivity of CD 99 in vascular tumors is not reported in the literature in either a positive or a negative sense. In Pathology Outlines, under CD 99, vascular tumors do not appear among the lesions that express it, nor among the negative ones. We limit ourselves to signaling a phenomenon that could only be aberrant or expressing some characteristic not hitherto unidentified.

Regarding the prognosis of this tumor, the unanimous opinion is that it is a neoplasm with a very severe prognosis, even in morphologically less aggressive forms. In our case, the proliferation index was less than 10% (Figure 8 c, d).

Conclusions

The pleural localization of EHE is an event that, albeit rare, must be kept in mind in the differential diagnosis with the more common mesothelioma and the not rare metastases of carcinoma. In particular, it should be kept in mind when the diagnostic markers for mesothelioma or carcinoma are not sufficiently significant.

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