Epitheloid Hemangioendothelioma

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Vascular tumours are quite rare and span a broad range. A special entity is characterized by epithelioid or histiocytoid endothelial cells, earlier included in a group of neoplasms designated as 'histiocytoid hemangioma' (1). Owing to the different clinicopathological features of a subgroup, the term 'epithelioid hemangioendothelioma' (EHE) was applied by Weiss & Enzinger in 1982 (2). Vascular tumours composed mainly of these cells are further divided into epithelioid hemangioma, epithelioid hemangioendothelioma and epithelioid angiosarcoma (3). However, owing to the overlapping histologic features they are also considered as a continuous spectrum of lesions, where EHE represents a borderline or low-grade malignant variant (4).

CASE REPORT

A 56-year old male had suffered for about 10 years from a non-specific pain with paraesthesia in his left arm and left side of the thorax. Three years earlier he had been in a traffic accident and suffered a minor whiplash injury to the cervical spinal cord. For at least one year the patient had noticed a single tender nodule in the left axilla, about 1 cm in diameter. It was palpable in close connection with the vessels. An ultrasonography verified a tumour mass with indistinct limits located close to the arteria axillaris. The neurological deficits were mainly associated with the nervus ulnaris.

The patient was operated on and an almost 2 cm large, rather dense tumour was exposed, which was found to be adherent to the arteria axillaris as well as the vena axillaris and nervus radialis. Finally, it was possible to cut the tumour free from these anatomical structures, macroscopically probably without any remaining tumour.

A microscopic examination showed a vascular tumour with a small occluded central vessel and spreading centrifugally, with a myxohyaline stroma and striking intracytoplasmic lumina (Fig. 1). Only a few mitoses could be seen and mild nuclear atypia. Further immunohistochemical staining confirmed the reticulin pattern as well as a strong positivity for CD31 (Fig. 2), an endothelial cell marker (5). The final diagnosis was epithelioid hemangioendothelioma, where it was doubtful from a microscopic view whether the excision was radical.

The patient has now been followed for 4 years with clinical examination, ultrasonography of the left axilla and the liver and pulmonary x-ray at regular intervals without any sign of recurrence or metastatic spread. Initially, the unspecific pain and paraesthesia of the left arm diminished but later on became aggravated, indicating sequelae after the whiplash injury.

DISCUSSION

Vascular tumours are infrequent and show a wide clinicopathologic variation ranging from benign via semimalignant to fully malignant. In The Swedish Cancer Registry 278 cases of hemangioendothelioma, malignant angiomatous tumours and hemangiosarcomas were found during the period 1958 to 1995 (these three tumour types are grouped together). A re-evaluation of the histopathology of these cases would surely result in a redefinition, but the number still gives an estimation of the frequency. The sex distribution was almost equal, with 56% female patients, and with a vast majority of older patients, median age 67 years and a range from 1 month to 91 years of age.

The morphologic spectrum of EHE is shifting, but some characteristic patterns have been documented: plump cells with eosinophilic hyaline cytoplasm, cytoplasmic vacuoles representing primitive vascular lumina, cells arranged in cords, a chondromyxoid matrix and papillary tufts of plump cells within lymphovascular spaces (4). Confirmatory evidence is described as erythrocytes within cytoplasmic vacuoles or primitive tumour-cell lined channels,

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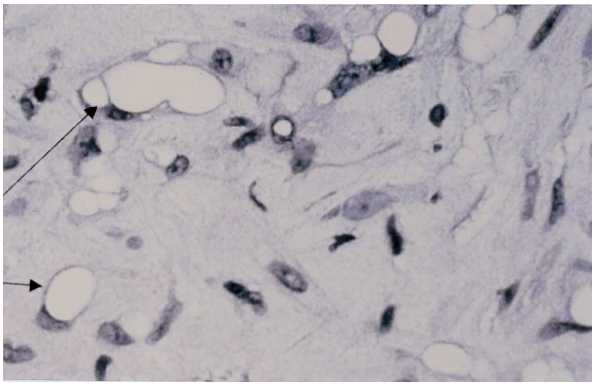

Fig. 1. Arrows indicating intracytoplasmic vacuoles, representing primitive vascular lumina (H & E × 300)

immunohistochemical evidence of vascular differentiation; e.g. factor VIII-related antigen, and ultrastructural evidence of endothelial differentiation. A special diagnostic problem could be the unclear demarcation against epithelioid angiosarcoma (4). From a differential diagnostic perspective, it should be pointed out that EHE might occur in a wide variety of anatomic locations, such as soft tissues, liver, lung and bone, where it may suggest metastatic carcinoma as well as myxoid chondrosarcoma (4, 6, 7). Furthermore, multiple-site involvement has also been described (6–8).

In two series of well-defined patient populations suffering from EHE in different locations, the most common clinical finding was a mass of shifting diameter, often painful (2, 3). The tumours were predominantly located in the extremities, trunk and head and neck region. They could be situated in different anatomic layers, such as deep, soft tissues, subcutaneously, dermal or perifascial.

The treatment in all cases was surgical excision, with different margins. In a few cases adjuvant treatment with radiotherapy and, in a couple of patients, also chemotherapy was given (2, 3). No clear-cut prognostic factors could be found, but in one of the studies bivariate (but not multivariate) analysis showed that the rate of mitoses and nuclear atypia correlated with a poor outcome (3). Furthermore, the other referred investigation advocated that mitoses > 1/10 HPF (high power fields), significant cellular atypia, focal spindling of tumour cells and necrosis were associated with a more malignant behaviour and a poorer prognosis (2). No relationships were seen between grade or the diameter of the tumour and the time to recurrence, metastatic spread or death.

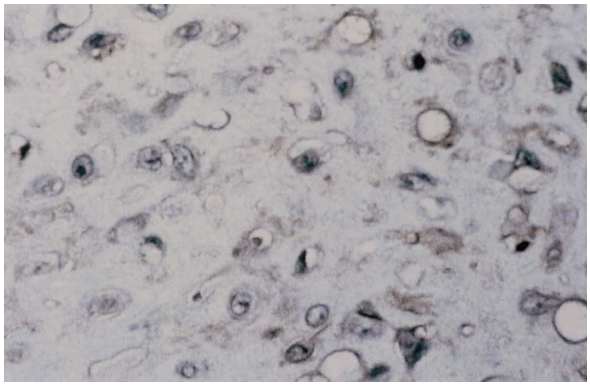

Fig. 2. Immunohistochemical staining with the endothelial marker CD 31.

The malignant potential of EHE is well illustrated by the follow-up results in the two studies; 24/30 patients in the first series were on average followed for 39 months and showed 3 cases with local recurrence, 5 with systemic metastases and 4 patients who died of EHE (3). In the other patient material, follow-up comprised 31 out of 41 cases, with a median follow-up time of 18 months, where 20 patients showed no signs of tumour, 6 had developed distant metastases and 3 patients had experienced local recurrence (2). A more malignant course was seen for EHE in the liver, with 5-year survival in 9/32 patients (28%) and in the lungs in 7/17 patients (41%) (6, 7).

Based on these results, the classification of EHE as a low-grade or borderline malignant tumour, as in the WHO classification of soft-tissue tumours under the heading 'intermediate endothelial tumours', could be debated (9). It therefore seems advisable to carry out a thorough clinical investigation to search for metastases at the initial diagnosis, as well as recurrent disease during follow-up, especially since no reliable prognostic factors have been established. Moreover, owing to the rareness and shifting histologic appearance of vascular neoplasms, examination by more than one pathologist should be advocated.

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