CASE STUDY

Aggressive form of pleural epithelioid haemangioendothelioma: complete response after chemotherapy

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ABSTRACT: Epithelioid haemangioendothelomas are rare tumours of endothelial origin. They can develop in any tissue but occur principally in the lung and liver. Their usual course is a slow progression, so that they can be treated by surgery. In aggressive forms, no treatment has proved efficient to date. This study, describes a case of bilateral pleural epithelioid haemangioendothelioma that extended to the peritoneum. The histological diagnosis was confirmed by both conventional examination and immunohistochemistry. After six courses of carboplatine plus etoposide, a complete response was obtained. The complete remission is still lasting at 18 months after the diagnosis and the patient is healthy.

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Epithelioid haemangioendothelioma (EHE) is a rare form of cancer initially described by DAIL and LIEBOW [1] in 1975. This tumour can be found in any organ but is most often found in the liver and lung. Usually, its evolution is slow, but aggressive forms have been described. This study presents a case of a pleural EHE with peritoneal extension characterized firstly by a rapid and aggressive progression and secondly by a high chemosensitivity with complete response to chemotherapy.

Case report

A 50-yr-old female was admitted for a spontaneous right pleural effusion revealed by a routine chest radiograph. The only associated disease was a maturity onset diabetes treated by oral sulphamide. Extrapulmonary physical examination was normal and she had not lost weight recently. The thoracocentesis revealed a serosanguineous exudative effusion. Cytological examination of the pleural fluid showed a high cellularity with many malignant cells. A cerebral and thoracoabdominal computed tomography (CT) scan was performed together with a bone scintigraphy to evaluate the disease extension. In addition to the right pleuritis, a minimal contralateral pleural effusion and a peritoneal effusion were found. A right thoracoscopy for pleural biopsies and pleurodesis was performed.

Histological examination of the pleural biopsy showed some lesions [3]. Positive stainings with an anti-vimentin antibody and anti-factor VIII polyclonal antibodies (Dako, Copenhagen, Denmark) (fig. 2) and for BNH9 monoclonal antibody (Dako) (fig. 3). Staining with the anti-cytokeratin antibodies were negative, which excludes the diagnosis of a metastatic carcinoma or malignant mesothelioma. Hormonal receptors for oestrogen (30% of cells) and progesterone (40% of cells) were present. The diagnosis of EHE was made. Within a few weeks a neoplastic chylous ascite developed, the pleural effusion relapsed and extended to the contralateral side, the patient’s clinical condition deteriorated and the disease rapidly progressed. Chemotherapy with carboplatine and etoposide was started. A dramatic improvement occurred early after the first course of treatment, with a decrease of the pleural and peritoneal effusions. After the sixth course, thoracoabdominal CT scan confirmed a complete remission. Only a minimal bilateral pleural thickening was observed. The complete remission is still lasting 18 months after the diagnosis and the patient is healthy.

Discussion

EHE is a rare form of cancer which tends to follow an intermediate course between haemangioma and conventional angiosarcoma [1]. This tumour is characterized by an epithelioid or histiocytoid endothelial cell proliferation. EHE mainly affects females during the sixth decade. It can be found in any tissue, and various forms have been described in many organs and soft tissues. There is no specific clinical or biological marker for EHE. The two main locations of EHE are the liver [2] and lung [3–5]. EHE was first described in its pulmonary form by DAIL and LIEBOW [1] under the denomination of intravascular bronchioloalveolar tumour.

Recently, KITAISHI et al. [5] reported 21 pulmonary cases. In the typical pulmonary forms, EHE presents as bilateral nodules which are slow growing. Chest pain, cough and sputum are common nonspecific symptoms. The disease can result in a restrictive respiratory failure and death after several years [5]. A pleuritis secondary to the pulmonary lesion can occur [5, 6]. Although previously described as an isolated pleural form [7, 8], EHE confined to the serous are extremely rare. The diagnosis is suspected on histological features and confirmed by immunohistochemistry [3, 8]. EHE is characterized by the presence of numerous well-formed vessels and multiple intracellular vacuoles. Mitotic figures do not always occur, but, their presence is indicative of a poor prognosis. An inflammatory reaction can accompany the malignant lesions [3]. Positive stainings with an anti-vimentin antibody and anti-factor VIII, BNH9 or anti-CD31 antibodies...
confirm the diagnosis [9]. The anti-vimentin antibody is instrumental in proving the conjunctival origin of tissues, whereas anti-factor VIII and BNH9 prove its endothelial origin. Anti-factor VIII and BNH9 stain highly differentiated and undifferentiated endothelial cells, respectively. Negative stainings contribute to the diagnosis. Notably, the negativity of anti-cytokeratin staining excludes tumours of an epithelial origin. This is most important in pleural primitive tumours in order to exclude mesothelioma or carcinoma [8]. The presence of hormonal receptors, which have previously been reported in pulmonary EHE [10], indicates that hormonotherapy could be discussed as a treatment in cases with a relapse.

Prognosis and treatment of EHE depend on their localization. In limited pulmonary or hepatic forms, which usually progress slowly, surgical excision of the nodules seems appropriate (wedge resection or lobectomy have been described), although no therapy in asymptomatic patients can be considered [5, 11, 12]. Occasional spontaneous remissions have been published [5]. In the series of Kitachi et al. [5], five patients have received chemotherapy (mitomycin C, 5-fluorouracil, cyclosphosphamide, vincristin, tegafur or cisplatin) with no beneficial effect, confirming its classic chemoresistance. Aggressive forms have been described. The pleural forms of EHE were, to date, always uniformly aggressive [7, 8, 12]. In this way, Lin et al. [8] have described six pleural EHE with a rapid and fatal evolution in all cases. These aggressive forms are often disseminated with the involvement of serous, bone, lung and liver. Recently, one case of EHE in-