ful. The children may be of low birth weight, usually due to premature delivery, but are apparently without other ill effects. The underlying condition affecting the mother generally worsened as the pregnancy continued. Successful management included supplemental oxygen and other types of therapy as needed. Most infants were delivered vaginally.

These limited studies, as well as our patient, demonstrate that despite the increased respiratory and cardiac demands of pregnancy, women with severe pulmonary fibrosis can have a manageable pregnancy with a normal outcome.

REFERENCES


Epithelioid Hemangiendothelioma*

A Rare Tumor with Variable Prognosis Presenting as a Pleural Effusion

Frederick A. Bevelacqua, M.D., F.C.C.P.;† Quentin Valensi, M.D.;‡ and Donald Hulnick, M.D.§

The chest x-ray film a 22-year-old man showed a large right-sided pleural effusion that was grossly hemorrhagic when aspirated. A computerized tomographic scan showed a complex mass with cystic components contiguous with the diaphragm. On thoracotomy the mass was found to be arising from the diaphragm and had the consistency of an organizing hematoma. Pathologic studies showed the mass to be an epithelioid hemangiendothelioma. This rare tumor has never been reported previously as arising from the diaphragm. It has a variable prognosis, but surgery remains the treatment of choice. In this report, we review the clinical and pathologic characteristics of this unusual tumor, as well as the distinctive roentgenographic findings with which it presented.

Epithelioid hemangiendothelioma is a rare tumor which is characterized by an "epithelioid" endothelial cell that demonstrates many of the features of normal endothelium, including the presence of factor VIII-associated protein. This tumor tends to have an angiocentric location and may occur in either superficial or deep soft tissue. It has occasionally been reported as arising in liver, lung, and mediastinum; however, to our knowledge, this tumor has never previously been reported as arising from the diaphragm. The findings from the computerized tomographic scan in this case were quite unusual and showed a large cystic mass contiguous with the diaphragm. This tumor is generally thought to follow a clinical course intermediate between that of a hemangima and angiosarcoma. Although there are certain histologic characteristics that may suggest a more malignant potential, the clinical course in most instances remains unpredictable.

CASE REPORT

A 22-year-old man was admitted to another hospital because of low-grade fever of several days' duration and a right-sided pleural effusion. His past medical history was otherwise unremarkable. A thoracocentesis revealed a serosanguineous exudative effusion. Cyto logical findings were negative for malignancy. The level of glucose and pH were normal. Gram stain, acid-fast stain, and cultures were negative. Testing with purified protein derivative of tuberculin (PPD) was unreactive. The patient then underwent a pleural biopsy, which showed only acute and chronic inflammation. Because of his persistent pleural effusion, he underwent a repeat thoracocentesis.

---

*From the Departments of Medicine, Pathology, and Radiology, New York University Medical Center, New York.
†Clinical Assistant Professor of Medicine.
‡Associate Professor of Pathology.
§Assistant Professor of Radiology.

Reprint requests: Dr Bevelacqua, 650 First Avenue, New York City 10016

Figure 1. Computerized tomographic scan of chest shows well-defined but slightly irregular multicystic mass (M) inseparable from liver (L) or diaphragm. Note soft-tissue components in wall of lesion and separating low-density regions. H, Heart.
and pleural biopsy, which were again nondiagnostic.

On subsequent referral to New York University Hospital, the patient's chest x-ray film showed what appeared to be a soft-tissue density abutting the right hemidiaphragm and a small amount of freely layering fluid. Thoracic ultrasound demonstrated a cystic mass with thick internal septations consistent with a loculated effusion or cystic tumor. Another thoracocentesis done under ultrasonic guidance yielded about 600 ml of grossly bloody fluid. The fluid was exudative, with a normal level of glucose and pH. Stains, cultures, cytologic studies, and cell block were all unremarkable, as on the previous occasions. A computerized tomographic scan of the chest was done, which showed a small amount of free pleural fluid and a cystic mass with internal septations of soft-tissue density (Fig 1). The liver was normal, but it could not be determined whether the mass arose from the lung, pleura, or diaphragm. The patient finally underwent an exploratory thoracotomy, where a lobulated hemorrhagic mass with the appearance of an organizing hematoma was found originating from the diaphragm. The mass, along with about one third of the diaphragm, a portion of the right lower lobe, and associated parietal pleura, was excised. A Marlex patch was used to reconstruct the diaphragm.

On light-microscopic examination the mass was composed of cords or small nests of round to slightly spindle-shaped epithelioid cells with prominent cytoplasmic vacuolization, round nuclei, and eosinophilic cytoplasm. The cytoplasmic vacuolization probably represents primitive lumen formation by single cells which, in turn, communicate with large capillaries. A myxohyaline matrix which resembled cartilaginous tissue occupied the bulk of the neoplasm. Occasionally, fragments of erythrocytes were seen in some of the cytoplasmic vacuoles. Well-formed vascular channels lined by many cells were essentially absent. Instead, the vascular channels were small and recapitulated the appearance of vascular channels during angiogenesis. A stain for factor VIII-associated protein was also positive. Central to all cases of epithelioid hemangioendothelioma is the epithelioid quality of the endothelial cells, with the properties described previously. In this case, frequent mitotic figures were seen, suggested a malignant potential. Figure 2 is an electron photomicrograph of an epithelioid hemangioendothelioma cell with scattered Weibel-Palade bodies (fine grid-like structures of under-mined significance), which are very characteristic of epithelioid hemangioendothelioma and confirm the diagnosis of this very uncommon soft-tissue neoplasm.

DISCUSSION

Epithelioid hemangioendothelioma is a rare neoplasm that tends to follow a clinical course intermediate between hemangioma and conventional angiosarcoma. This tumor is characterized by an epithelioid or histiocytoid endothelial cell. Weiss and Enzinger, who contributed to the elucidation of this rare neoplasm, proposed the name, "epithelioid hemangioendothelioma." They reviewed 41 cases at the Armed Forces Institute of Pathology and found that the most common location of the tumor was the extremities; however, other sites have been reported, including four cases arising in the liver and three arising in the lung.

In the latter, epithelioid hemangioendothelioma was initially given the title, "intravascular bronchioloalveolar tumor (IVBAT)" until its true endothelial origin was recognized.

Histologically and clinically, this neoplasm can be distinguished from hemangioma and conventional sarcomas. Unlike ordinary hemangioma, epithelioid hemangioendothelioma tends to develop during adult life. Generally, epithelioid hemangioendothelioma does not demonstrate a predilection for skin or superficial soft tissues and usually lacks large well-formed vascular channels. The majority of angiosarcomas are fatal, whereas epithelioid hemangioendothelioma appears to have a recurrence rate of 10 percent and a metastatic rate of 20 percent. Therefore, it has been suggested that the term, "epithelioid hemangioendothelioma," be modified with the qualification "benign" or "malignant," depending on the clinical course. Unfortunately, recurrences have been known to occur up to 12 years after the original excision. The histologic features which appear to be useful in predicting the metastatic potential of this neoplasm are the prevalence of mitotic figures and the degree of cellular pleomorphism. One of the histologically more interesting aspects of this tumor is the "epithelioid" endothelial cell which demonstrates many of the immunohistochemical characteristics of normal endothelium, including factor VIII-associated protein, junctional attachments, pinocytic vessels, and Weibel-Palade bodies.

In many of the cases previously reported, the tumor arose from a vessel; however, frequently the nature of the vessel could not be discerned, and at surgery the lesion looked grossly like an organizing thrombus or hematoma, as was the case here. The unusual roentgenographic features of this case, together with the consistently negative pleural fluid cytologic findings and pleural biopsies, presented a diagnostic dilemma that was resolved only with open thoracotomy. Thus far, the treatment of choice for epithelioid hemangioendothelioma is complete surgical excision. There has been little experience with irradiation or chemotherapy, and the long-term prognosis remains unclear.

ACKNOWLEDGMENTS: We thank Ms. Rosemary Gandolfo and Ms. Rebecca Copeland for superb secretarial assistance and to Ms. Virginia Meyer for expert technical assistance.

REFERENCES


