ATYPICAL MULTICENTRIC “SCLEROSING HEMANGIOMA OF THE LUNG” A BENIGN MESENCHYMAL TUMOR OF THE PULMONARY INTERSTITIUM?

By T.H. Abdullas, M.D., Review Fellow and Resident, Department of Pathology, University of South Alabama Medical Center, Mobile, Alabama

W.J. Pollock, M.D., Assistant Professor of Pathology, University of South Alabama Medical Center, Mobile, Alabama

E.A. Dowling, M.D., Chief, Laboratory of Surgical Pathology and Professor of Pathology, University of South Alabama Medical Center, Mobile, Alabama

Abstract

A case of multicentric sclerosing hemangiomas of the lung with recurrent hemoptysis and previously unreported pneumothorax is presented. The variable histology of the tumor nodules presented the opportunity to make observations pertinent to the histogenesis of this tumor which has been a subject of debate in surgical pathology for approximately 25 years. Our observations suggest that sclerosing hemangiomas of the lung arises from pluripotential mesenchymal cells in the pulmonary interstitium. Focal differentiation of these interstitial cells, as noted in this case, into fibroconnective tissue, osteoid, fat, angiomatous tissue and bone may help explain the variable histology observed in case reports. This variable differentiation supports a mesenchymal histogenesis. Ultrastructural studies demonstrated that many of the interstitial cells had features of fibroblasts and myofibroblasts.

Key Words

1. Histogenesis
2. Multicentric
3. Sclerosing
4. Hemangioma
5. Fibroblasts/Myofibroblasts
6. Differentiation
7. Mesenchyme or Mesenchymal

Introduction

In 1956 Liebow and Hubbell coined the name "sclerosing hemangioma of the lung" for a benign tumor of the lung that was composed largely of vascular tissue, fibrous connective tissue and stromal lipid. Since the original description of this lesion, many cases have been reported in the literature and there has been much discussion regarding the histogenesis of this tumor. This case report deals with a patient having several multiple tumor nodules in various stages of development, and afforded us the opportunity to study the evolution of these lesions. Evidence noted in this case strongly suggests a mesenchymal histogenesis.

Address correspondence and reprint request to:
Dr. T. Abdullas
Dept. of Pathology and Laboratory Medicine
Akbar Clinic
4000 East 3rd Street
Panama City, Florida 32401

Case Report

A 27 year old Iranian-American male was admitted to the University of South Alabama Medical Center on 6/16/82 and 7/23/82 for evaluation of recurrent hemoptysis and spontaneous pneumothorax of the right lung. The patient gave a history of chest pain, dyspnea, and recurrent hemoptysis of three years' duration. Eighteen months prior to his first admission he was evaluated at the Mobile County Health Department (Alabama) and was found to have a positive skin test for tuberculosis. INH therapy was discontinued after one month by him, because of gastrointestinal disturbances.

Significant physical findings on these admissions were signs secondary to pneumothorax. Routine hemograms and biochemical investigations were within normal limits. Sputum studies did not reveal bacteria, fungi, or malignant cells. Chest x-rays showed nodules in the right middle and right lower lobes with an associated right pneumothorax (See Fig. 1). A transbronchial biopsy on the first admission revealed only moderate interstitial fibrosis. During the second admission the patient had a thoracotomy with biopsies of the right middle and right lower lobes. Microscopic examination of the nodules demonstrated multiple sclerosing hemangiomas of the lung. Post-thoracotomy x-rays suggested that all nodules were removed with the biopsy resection.

Recovery was uneventful and the patient remained asymptomatic for nine months. In May of 1983 the patient again had an episode of hemoptysis and chest pain but without recurrent pneumothorax. Radiographic studies of the chest were negative and the patient was discharged to be followed in the outpatient clinics.

Pathology

Gross Findings: Biopsies of the right middle and right lower lobes were received in Carsons's formalin and measured 5 x 2.5 x 1 cms and 4 x 3 x 1.5 cms, respectively. The tissue was pinkish-brown and contained numerous subpleural and intraparenchymal nodular foci of grayish tissue. The surrounding parenchyma was congested and had decreased crepitance. A bony spicule was encountered in the subpleura of the right middle lobe biopsy.

Histologic Findings: Sections of the biopsy specimen were prepared for light microscopy in the usual man-
A. X-ray of chest in 1979 showing no abnormalities.

B. X-ray of chest in April 1982 showing nodular densities in right middle and lower lobes.

C. X-ray of lung in June of 1982 showing right pneumothorax.
Four major histological patterns of so-called "sclerosing hemangioendothelioma" of the lung: A. Sclerotic; B. Papillary; C. Solid or Cellular; D. Hemorrhagic (Hematoxylin-Eosin X43)

Figure III.
Red blood cell extravasation was prominent in some foci of sclerotic tissue (Hematoxylin-Eosin X666)

Figure IV.
A sclerosing interstitial blood lake was seen dissecting into the alveolar and pleural space. This finding could explain mechanism of hemoptysis and spontaneous pneumothorax (Hematoxylin-Eosin X170)
Figure V.
Young tumor nodules showed a whorling pattern of spindle-shaped cells. (Hematoxylin-Eosin. X170)

Figure VI.
Tumor nodules showing mesenchymal differentiation into A. Osteoid (1) and B. Angiomatosus tissue (2) bone (3) and fat (4) were observed. (Hematoxylin-Eosin. X170)
ner and were stained with hemotoxylin, eosin, Masson’s trichrome, reticulin, acid fast, Comori’s methenamine silver, Giemsa, iron, alcian blue/PAS and Verhoeff-van Gieson stains. Light microscopic examination revealed variably sized nodules compressing the surrounding parenchyma in a pushing manner. The largest nodules in the right middle and right lower lobes measured 1 and 1.3 cm, respectively, in diameter. These nodular lesions showed the classical sclerotic, cellular (solid), hemorrhagic and papillary histologic patterns as described by Katzenstein, et al in 19804 (See Fig. II). The sclerotic pattern which accounted for over 75% of the mass of these larger nodules was represented by proliferating fibroblastic cells with a whorled arrangement. Foci of red blood cell extravasation were noted in this sclerosis (See Fig. III). Varying amounts of ages of collagen were noted. Trapped alveoli and engorged blood vessels were present within the fibrous connective tissue. The main tumor nodule in the right middle lobe biopsy showed a large organizing interstitial lake of blood communicating with the alveolar and pleural spaces (See Fig. IV). The larger nodules contained papillary foci in areas of alveolar entrapment and on the periphery of the nodules. The alveolar pneumocytes lining the papillary projections and entrapped alveoli showed mild hyperplasia. The hemorrhagic components of these larger nodules were characterized by blood in entrapped and adjacent alveolar spaces. The solid or cellular pattern was represented by syncytia of collapsed and/or compressed clusters of alveoli. Other associated features involved scattered foci of hemosiderin-laden macrophages, lymphocytes, cholesterol clefts, adipose tissue and mast cells.

The smaller tumor nodules showed predominantly a proliferation of spindle-shaped cells arranged in a whorling pattern (See Fig. V). These smaller nodules ranged in size from 0.3 to 0.8 cm in diameter and had a sclerotic histologic pattern composed of young collagen. Rarely, some of these nodules showed foci of differentiation into osteoid, angiomatous tissue, adipose tissue and bone (See Fig. VI). The pleura and subpleura of the right lower lobe biopsy showed organizing hemorrhage, fibrosis and small cystic spaces, probably lined by mesothelial cells. The histologic feature common to all nodules was the proliferation of spindle-shaped fibroblastic cells.

Electron Microscopy: The tissue submitted for electron microscopy was fixed in 10% Carson’s formalin, post-fixed in osmium tetroxide, dehydrated in graded alcohols, embedded in open and sectioned with an LKB ultratome. Ultra thin sections were stained with uranyl acetate and lead citrate and examined in a Zeiss 109 electron microscope. Ultrastructural examination of the pulmonary nodules revealed that the spindle cell component was composed largely of fibroblasts and myofibroblasts (See Fig. VII). The entrapped alveolar pneumocytes were separated from the spindle cell component by a well formed basement membrane and numerous red cells could be identified within the alveolar spaces.

Discussion

The term “sclerosing hemangioma of the lung” was coined by Liebow and Hubbell in 1956. It described a group of benign tumors characterized by sclerosing vasoformative tissue, old hemorrhage and stromal adipose tissue (lipid). They identified two patterns, a “blue” pattern and a “red” pattern. The histological similarity to sclerosing hemangiomas in the skin undoubtedly influenced the name chosen for these lesions. Angiomatous tissue was observed to be the major component and an endothelial cell origin was proposed. Clinically, sclerosing hemangiomas of the lung usually present as an asymptomatic solitary lesion on routine chest x-ray. Radiographically, these tumors are usually well circumscribed without involvement of the surrounding parenchyma. Some may show an air meniscus sign. Some authors have reported that most lesions are seen in the right lung fields, while others have reported no predilection for either lung. Sclerosing hemangiomas of the lung are more common in the periphery and subpleura. Bronchial involvement has not been reported. Scant hemoptysis is the most common symptom and may be accompanied by coughing, chest pain, dyspnea and respiratory infections. Our patient was unusual in that he had multiple lesions and several episodes of spontaneous pneumothorax. This tumor predominates in women. In contrast, our case was of a male. We can find no previous report of spontaneous pneumothorax associated with sclerosing hemangioma of the lung.

Katzenstein, et al in 1980 reviewed 51 cases of this tumor and described sclerotic, hemorrhagic, cellular and papillary patterns. Chan, et al in 1982 observed these major histologic patterns in their series of 14 cases from Hong Kong. The variable histologic appearance of sclerosing hemangioma of the lung probably reflects a combination of mesenchymal histogenesis, differentiation and reaction. Proposed cells of origin include the endothelial cell, mesenchymal cells, and undifferentiated alveolar lining mesenchymal cell. Pneumocytes, mesothelial, and mesenchymal elements, including osteoid, bone, adipose tissue and vascular tissue.
Figure VII.
Electron microscopic studies confirmed that the predominant cell of benign proliferation is the fibroblast-myofibroblast. (X3000)
FIGURE VIII: Some Cells and Tissue Derived from Mesenchyme

*Serous Linings (Mesothelium)

*Pneumocytes

Notochord

*Smooth and Striated Muscle (Myocytes)

Fat

Peripheral Nerve Sheath

*Cartilage (Chondrocytes)

MeSENCHYME

*Osteoid (Osteocytes)

Microglia

*Myxomatous

*Blood and Lymph Vessels (Endothelial cells)

*Fibrous Connective Tissue (Fibroblasts)

*Fibrous Connective Tissue normally found in the pulmonary interstitium and associated parenchyma. Striated muscles are not found.
These observations suggest that sclerosing hemangiomas of the lung arise from undifferentiated pluripotent mesenchymal cells of the pulmonary interstitium. It is our belief that the epithelial components as represented by the type II pneumocytes are entrapped by the proliferating fibrous connective tissue. This entrapping fibrous connective tissue is also responsible for the alveolar clustering producing the papillary component of some lesions. A mesenchymal concept of histogenesis readily explains the variable histologic patterns that have been described in sclerosing hemangiomas (See Fig. VII).

It is paradoxical that what were once classified as sclerosing hemangiomas of the skin are now fibrous histiocytomas. The varied mesenchymal differentiation potential noted in sclerosing hemangioma of the lung could be encompassed by calling it a benign mixed mesenchymal tumor of the pulmonary interstitium. Although the term sclerosing hemangioma is perhaps a misnomer, it may be desirable to retain this terminology, because of the unique clinical, historical and morphological characteristics of this lesion. A mesenchymal histogenesis can best explain the common and varied histology of this lesion. Inevitably, we feel that sclerosing hemangioma of the lung will be classified with fibrohistiocytic lesions as are "sclerosing hemangiomas" of the skin.

Acknowledgements

We are grateful for the critical comments of Dr. William Gardner, Chairman of the Department of Pathology, the technical assistance of Mr. Reece Nelson Coxley and the varied support of all at the University of South Alabama Medical Center who contributed to the realization of this paper.

References