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Sclerosing Mediastinitis of Pulmonary Hilar Type Report of a Case

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ABSTRACT. A case of sclerosing mediastinitis of pulmonary hilar type is presented. Sclerosing mediastinitis is an unusual postinflammatory sclerotic reaction of the mediastinum which presents challenging diagnostic and therapeutic problems when it involves the major bronchi. The clinical, pathological and etiological aspects of this disease entity are summarized.

Key words : sclerosing mediastinitis — lung

Sclerosing mediastinitis, also known as mediastinal fibrosis, fibrosing mediastinitis or mediastinal collagenosis, is an unusual postinflammatory sclerotic reaction of the mediastinum. This disease process may predominate in the paratracheal region or in the pulmonary hilar or subcarinal regions.[1] Thereby, it may be designated and subclassified with such an affix. In addition, it may involve adjacent veins, arteries, nerves, the esophagus, the tracheobronchial tree or the lung parenchyma, and may cause a variety of symptomatology depending upon the structures involved and the degree to which they are functionally compromised. Histologically, the lesion is characterized by acellular eosinophilic hyalinized materials and collagenous tissue in serpiginous bands or in broad amorphous masses. The etiology and pathogenesis of sclerosing mediastinitis still remains to be elucidated, although many investigators in western countries have suggested that histoplasmosis may be a causative agent, and that the caseating granulomas in mediastinal lymph nodes evoke the fibrosing process.[1–4] Since the All Japan Statistical Survey collected twelve Japanese cases in 1971,[5] it has received much attention and an increasing number of case reports have appeared in this country as well.[6–9]

Herein, we present our case of sclerosing mediastinitis, and summarize this disease entity briefly.

CASE REPORT

A 52-year-old man had been in good health until early in 1982, at which time he started to experience coughing and serous sputum expectoration. On April 13, he suddenly expectorated blood-tinged sputum and then 200 - 300 ml of blood. He was admitted to another hospital where medication and rest

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alleviated the symptom. Chest x-ray and bronchographic examinations revealed a tumor in the left upper lobe. There was no history of tuberculosis or travel to a foreign country. He was a smoker of 30 - 40 cigarettes per day and a moderate drinker. He was transferred to the Kawasaki Medical School Hospital on May 25, 1982. Physical examination on admission showed a slight funnel chest with diminished respiratory sound in both upper lung fields and low pitched rhonchi in the left lower lung field. No rales were audible. Routine hematological and blood chemical studies were negative. Blood gas showed pH 7.4, pO_2 83.1 mmHg, pCO_2 40.3 mmHg and BE +0.1. C-reactive protein was 3.6 mg/dl, the erythrocyte sedimentation rate was 88/1 hr and the antistreptolysin-O titer was 60 U. A cold agglutinine test was positive at 1:128 dilution. A tuberculin skin test was strongly positive with induration, but a sputum culture yielded no growth. Protein paper electrophoresis disclosed a slight increase of α_2 globulin (12.8%). Carcinoembryonic antigen was less than 1.9 ng/ml and α-fetoprotein was less than 5 ng/ml. The results of a routine chest x-ray (Fig. 1), tomography, bronchography and computed tomographic (Fig. 2) studies indicated that a tumor shadow, 3.5 cm diameter, was located in the hilar portion of the left lung, encased segmental bronchi B_4 and B_5, and in part compressed the left main bronchus with severe stenosis. The left lower lobe was atelectatic.

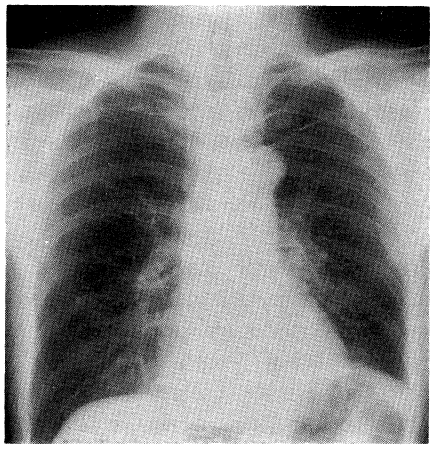

Fig. 1. Chest x-ray film taken on admission. Note the widening of the mediastinum on the left side.

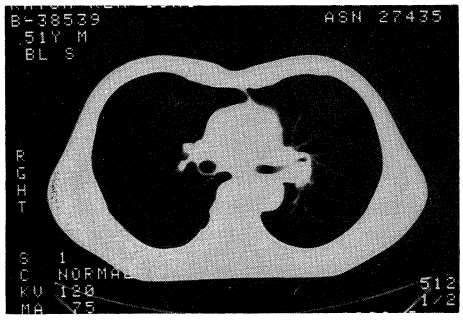

Fig. 2. CT scan showing a compression of the bronchus.

^{67}Ga-scintigraphy showed an accumulation in the left hilar region. One of repeated cytologic examinations was reported as class IV, but no apparent malignant cells were seen. On June 15, 1982, under a tentative diagnosis of squamous cell carcinoma of the lung, a left thoracotomy with a left pneumonectomy was performed. Originally, a pathological diagnosis of postinflammatory pseudotumor was made but after the review, sclerosing mediastinitis of pulmonary hilar type was considered a better description of this lesion. Postoperatively, the patient was troubled by low grade fever, mild liver dysfunction, stress ulcer, and atrial fibrillation. A chest x-ray showed compensatory over-inflation of the right lung and mild pulmonary hypertension. He was discharged on Aug. 31, 1982 and was followed up at our outpatient clinic. On July 3, 1985, he was readmitted through the emergency department for acute pancreatitis. His serum amylase was 584, elastase 598 and urinary amylase 759. His white cell count was 13,900. A week later, symptoms disappeared and laboratory data returned to normal. Examination of the lung disclosed no recurrence of the disease. No evidence of retroperitoneal fibrosis was obtained. The patient was discharged on July 10, 1985.

PATHOLOGICAL FINDINGS

The resected left lung contained a mass lesion in segments 4 and 5. The lesion was mainly confined to the hilar and peribronchial tissue, but also involved in part pulmonary parenchyma as well as the left atrium and adventitia of the pulmonary vein (Fig. 3). The bronchi were embedded within the mass and

Fig. 3. All the features of sclerosing mediastinitis are seen in this pulmonary hilar section. The fibrous lesion is peribronchial and the fibrosis is more prominent in the central portion than the periphery where cellular infiltration is still present. Note that a pulmonary vein is obliterated. (H-E. ×5)

narrowed. In toto, it was fairly well-defined and measured $3.5 \times 3.5 \times 3.5$ cm in size. The left main bronchus, resected at 2.3 cm proximal to the origin of the left upper lobe bronchus, was also surrounded by a thin rim of grey tan tissue which was apparently an extension of the main mass. The bronchial mucosa was unremarkable. The histological appearance was variegated. The central portion of the lesion tended to be fibrotic and sclerotic (Fig. 4). Hyalinized eosinophilic bands ran haphazardly and in serpiginous form (Fig. 5),

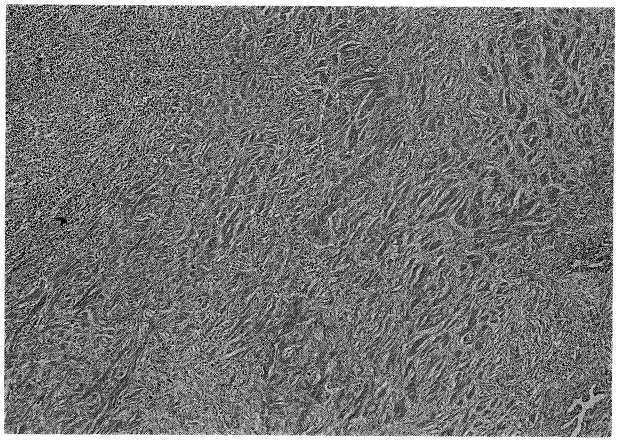

Fig. 4. A fibrotic area with eosinophilic bands. (H-E, ×25)

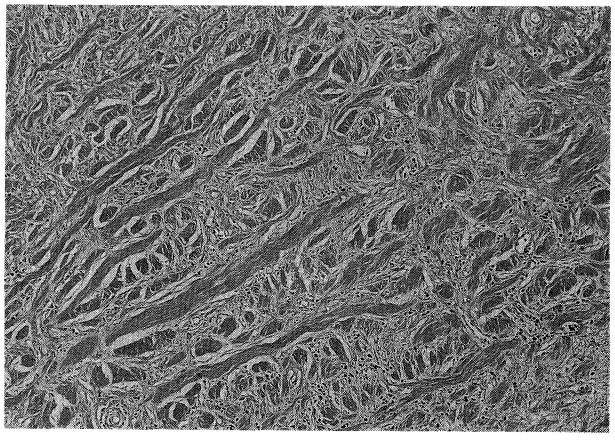

Fig. 5. Higher magnification of Fig. 4. Eosinophilic fibrous bundles impart some resemblance to keloidal tissue. (H-E, ×60)

and imparted some resemblance to keloidal tissue. There were some areas of broader eosinophilic amorphous materials. In routine sections with polarized light, hyaline material showed a fine fibrillar birefringence. Congo red staining with polarization was negative for amyloid. There were a few scattered lymphocytes and plasma cells, but no fibroblastic cells were present in this area. The outskirts of the lesion in addition to some areas within the central hyalinized tissue showed intense plasmacytic and lymphocytic infiltration (Fig. 6). Scattered

plasma cells with Russell bodies and lymph follicles with rare germinal centers were seen. Granulation tissue formation with fibroblastic and angioblastic elements was mild. There were also scattered neutrophils with occasional accumulation. The fibrotic process with or without the lymphoplasmacytic infiltration extended into the lamina propria of the bronchi and bronchial glands. Bronchial cartilage was intact except for several areas where the outer border of the cartilage was permeated with lymphoplasmacytic and neutrophilic infiltrates

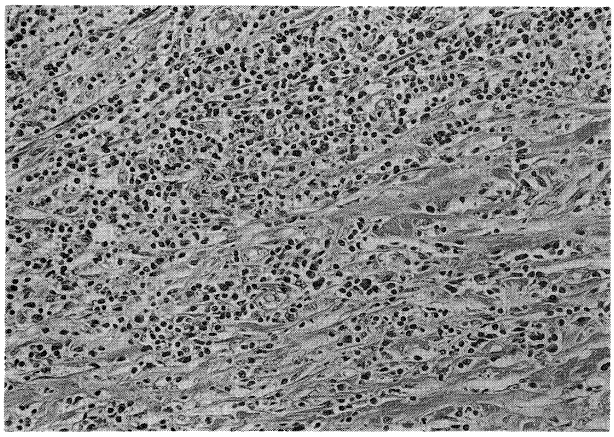

Fig. 6. A peripheral portion of the lesion showing lymphocytic and plasmacytic infiltration. (H-E, ×120)

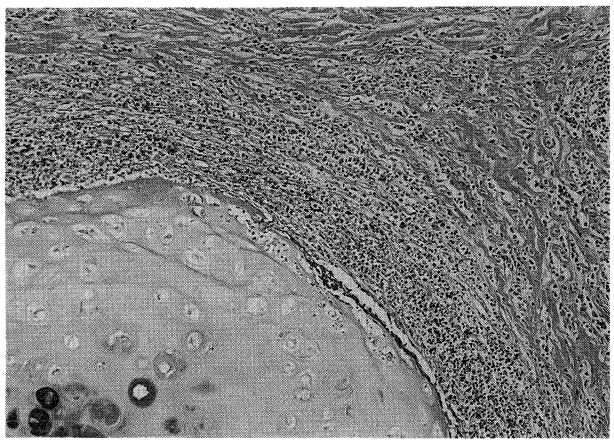

Fig. 7. Bronchial cartilage, the outer border of which is permeated by cellular infiltrates. (H-E, ×60)

(Fig. 7). The walls of two branches of the pulmonary vein in the vicinity of the bronchi were almost entirely replaced by fibrous tissue. Lumina were narrowed but not thrombosed. No cellular infiltration or fibrinous exudate was present. Hyalinized connective tissue surrounded small arteries but their walls were intact with focal muscular hyperplasia and mild intimal fibrosis. Similarly, hyaline material encased nerve bundles. No caseous area, calcification, or ossification was identified anywhere in the submitted specimen. Efforts to identify micro-

organisms with hematoxylin-eosin, Brown-Brenn, PAS, Grocott, and Ziehl-Neelsen staining were all fruitless. The lung parenchyma surrounding the lesion showed mild thickening of the alveolar walls with mild fibrosis and lymphocytic infiltration. Adjacent lymph nodes showed massive deposits of carbon and silica pigments. No similar or other granulomatous lesions were present.

DISCUSSION

Mediastinal fibrosis was probably first described by Hallet in 1948.[10] The disease had been attributed to syphilis or tuberculosis by the 1940s, when its etiology began to be questioned, and the term "idiopathic mediastinal fibrosis" was increasingly used. In 1956, Gillespie[11] reported the first case of mediastinal fibrosis attributed to histoplasmosis on the basis of serologic findings. Similar case reports followed and organisms were demonstrated in the tissue by periodic acid Schiff and methenamine silver staining, although *Histoplasma* have never been successfully cultured from this disease. In 1967, Schowengerdt *et al.*[2] reviewed 103 reported cases of granulomatous mediastinitis and 77 cases of mediastinal fibrosis and concluded that they were the same disease differing only in the relative amount of granulomatous inflammation and fibrosis. In a review of his own 14 cases of sclerosing mediastinitis, Eggleston[1] emphasized the presence of caseous necrosis both in the mediastinal lesion and in nearby lymph nodes. Caseous necrosis was identified in all of his five autopsied and two lobectomy specimens. In five of these seven specimens, organisms morphologically *typical of Histoplasma capsulatum* were identified with methenamine silver stains. Caseation was seen even in 2 of 12 biopsied materials. In our case, in contrast, caseating granuloma was not present in either the hilar lesion itself or in neighboring lymph nodes. Neither was *Histoplasma* identified. Therefore, it seems to be preferable not to confine this disease entity to those caused by *Histoplasma* only. It rather constitutes a disease complex with similar morphological characteristics and is merely a rather non-specific tissue reaction caused by a variety of etiologies. In fact, cases of mediastinal fibrosis without association with histoplasmosis, or caseating granuloma, and particularly ones in Japan,[7,9] where histoplasmosis is quite rare,[12] have been reported. In addition, occasional cases have been reported in association with retroperitoneal fibrosis.[13,14] Many similarities between sclerosing mediastinitis and retroperitoneal fibrosis, Riedel's struma, and orbital pseudotumor have been noted.[15] Histoplasmosis has never been reported as a cause in these diseases.

The mechanism of the response is not known. The appearance of the sclerotic reaction is histologically different from that seen in most conditions associated with fibrosis, such as seen in the repair of infectious or traumatic insults. In the latter cases, finely fibrillar or amorphous hyaline materials associated with dispersed lymphoplasmacytic infiltration of sclerosing mediastinitis are not usually seen. The sclerosis in sclerosing mediastinitis, therefore, may be the result of an exceptional host response as Goodwin *et al.*[3] stated. A variety of infectious agents, toxic substances, lymphostasis, and a host dysimmune status may play an important role in this process.[16] A positive tuberculin skin test in our case may be noteworthy. Although there was no histological evidence of tuberculosis in the resected lung, tuberculous infection must have been present

and it cannot be excluded that it was somehow responsible for the mediastinal sclerosis.

Sclerosing mediastinitis is regarded as a self-limiting but long-lasting disease. In its early stages (Osmond's stage I & II[17]), clinical signs and symptoms may be minimal. By the time the diagnosis is made, it has usually progressed to a complete sclerosis (Osmond's stage III). Then, it may give the impression of neoplastic disease to the clinician.[18,19] In our patient, loss of lung volume and a mass shadow in the mediastinum were adequate to clinically suspect a neoplastic process. Surgical exploration would have been the logical approach to establish the diagnosis and to eliminate the problem. In general, it is said that once sclerosis is completed, the treatment of choice should be the alleviation of the symptom by surgery. When obstructive pneumonitis or occlusion of a pulmonary vein is extensive, pneumonectomy may be necessary.

In our case, the inflammatory and fibrosing or sclerosing process was localized mainly in the left perihilar tissue. Although the extent of mediastinal involvement was not evaluated appropriately, the nature of the lesion was compatible with sclerosing mediastinitis in a descriptive sense. The superior vena cava syndrome is frequently reported as a common symptom in sclerosing mediastinitis. The absence of this symptom in our case is most likely due to its presence in the left lung and the localization in the pulmonary hilar portion. Eggleston[1] subclassified cases of this disease clinically; (1) those that predominantly involved the paratracheal region and (2) those with pulmonary hilar or subcarinal involvement. The former is frequently associated with the superior vena cava syndrome while the latter is characterized by cough, hemoptysis, dyspnea, or symptoms of congestive heart failure. Hemoptysis like that seen in our patient is usually considered to be secondary to pulmonary vein obstruction. Our case should therefore be considered to be of the pulmonary hilar type.

Lastly, the difference between sclerosing mediastinitis and pulmonary hyalinizing granuloma (PHG) should be mentioned. PHG was described by Engleman *et al.* in 1977.[20] It is characterized by multiple bilateral pulmonary nodules consisting of extracellular, eosinophilic hyaline lamellae which resemble those of sclerosing mediastinitis. The hyaline materials of PHG usually show the histochemical characteristics of amyloid,[21] which is absent in sclerosing mediastinitis. Some investigators, however, have regarded this as a disease related to sclerosing mediastinitis. A minority of patients with multiple hyalinizing granuloma have later developed fibrosing mediastinitis[20] or retroperitoneal fibrosis.[20,22] They, therefore, may be essentially similar in pathogenesis. The critical difference between these two diseases is the location of the lesions, namely intrapulmonary in PHG and extrapulmonary in sclerosing mediastinitis, and the multicentricity of PHG.

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