Chronic Fibrous Mediastinitis and Superior Vena Caval Obstruction Due to Histoplasmosis

Denver, Colorado

Superior vena caval obstruction has been alleged to be caused by a wide variety of pathological conditions, some rather common and specific while others are relatively rare and indeterminate as to etiology. This troublesome syndrome was first described clinically by William Hunter 200 years ago according to McCord et al. In their excellent review, McIntire and Sykes cite that Fischer’s series of 252 cases, reported prior to 1904, was comparable as to symptomatology and prognosis to the 250 cases appearing in the literature from 1904-1946.

Superior vena caval obstruction related to chronic fibrous mediastinitis was uniformly felt to be due to tuberculosis or syphilis until about 35 years ago. Surgical or autopsy verified cases of idiopathic fibrous mediastinitis have been reported with increasing frequency since that time. Improvement in diagnostic technic of syphilis and tuberculosis were felt responsible for this change. The possibility of considerable diagnostic error was noted, particularly in earlier cases.

In the verified cases of chronic fibrous mediastinitis reported, a granulomatous lymph node has frequently been associated with the process and occasionally has contained calcium. Other clinical cases have also shown this relationship. A diagnosis of tuberculosis has occasionally been made on the basis of these findings, however, when a specific statement has been made about microscopic findings of caseous granulomas, acid fast bacilli have not been demonstrated. The unreliability of tissue etiologic diagnosis without demonstration of organisms has been well documented by Puckett.

In 1925 Knox noted that other agents which produce granulomata, such as the mycoses, might be the cause of fibrous mediastinitis. As late as 1956 Gillespie suggested that upper an lower respiratory infections, bronchopneumonia, influenza, tularemia, trauma, rheumatic fever, and a tendency to form keloids might be implicated in chronic fibrous mediastinitis.

Gillespie reported the case of a seven-year-old girl from a rural community of southern Illinois who developed superior vena caval obstruction in 1954, three and one half years after “virus-pneumonia.” Chest roentgenogram showed multiple areas of fibrosis and calcification in both lung fields, rather marked infiltration or fibrosis in the upper two thirds of the right lung and pleural thickening along the right upper mediastinum. Blood serum complement fixation for histoplasmosis was 1:64 (yeast phase antigen). The histoplasmin skin test was strongly positive, but the old

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From Fitzsimons Army Hospital and U.S. Army Medical Research and Nutrition Laboratory.
tuberculin 1:1000 was negative. A clinical diagnosis of pulmonary and mediastinal histoplasmosis was made. The child was referred to Vanderbilt University Hospital where right thoracotomy revealed massive leathery fibrosis of the mediastinum and thrombosis of the superior vena cava andazygos vein. Unroofing and partial phlebolysis of the incompletely occluded vena cava provided symptomatic relief from superior caval obstruction. Histoplasma capsulatum could not be demonstrated in the fibrous tissue submitted for histologic study. We are in complete concurrence, however, with the clinical diagnosis of mediastinal histoplasmosis.

During the past two years we have observed four similar cases at Fitzsimons Army Hospital which are felt to be secondary to histoplasmosis. These cases are the basis for this report as it is felt that histoplasmosis has an important place in the etiology of "idiopathic" chronic fibrous mediastinitis, and may be responsible for many such cases previously considered to be of tuberculous etiology.

**Case 1**: This 27 year old Negro was in good health until 1952 when he had a sore throat and coughed up bright red blood. He was then asymptomatic until May, 1956 when a similar episode occurred followed by blood-streaked sputum for about 18 hours.

On May 16, 1956 he was admitted to Fitzsimons Army Hospital. Physical examination was normal. Chest roentgenogram showed a homogenous spherical density four centimeters in diameter which involved the anterior segment of the left upper lobe. In 10 days there was complete resolution of this process. The white blood cell count and sedimentation rate were normal. Skin tests revealed PPD No. 2 positive, coccidioidin 1:100 negative and histoplasmin 1:100 positive. Three gastric cultures for *M. tuberculosis* were negative. Bronchoscopy was normal. Esophagoscopy revealed extensive vascularity of the esophagus but no other abnormality. He was returned to duty July 6, 1956.

On March 1, 1957 he had hemoptysis lasting about 24 hours and was rehospitalized for further evaluation.

**Residence History**: He was born in Missouri and had been stationed during military service in Kansas, Kentucky, California, Japan, Nebraska, Ohio, Wyoming, Massachusetts and Colorado.

Physical examination on re-admission was normal. White blood cell count and differential were normal. Chest roentgenogram March 5, 1957 revealed a five centimeter, soft, spherical infiltration in the anterior segment of the left upper lobe with an increase in the markings in the lingula (Figs. 1A and 1B). Within 10 days the pulmonary infiltration cleared. Bronchoscopy showed only hemorrhagic mucosa of the left upper

![FIGURE 1A](image1a.png)  ![FIGURE 1B](image1b.png)

**Figure 1** (Case 1): (A) PA and (B) left lateral chest roentgenogram showing spherical infiltration in the anterior segment of the left upper lobe.
lve bronchus. A left scalene lymph node revealed reactive hyperplasia. Serologic studies for fungi revealed:

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On review of the serial roentgenograms slight enlargement of the left superior mediastinum was noted. Exploratory thoracotomy was recommended because of recurrent hemoptysis and pulmonary infiltration which was thought to be secondary to a lesion in the segmental bronchus, possibly a bronchial adenoma.

On April 5, 1957, left thoracotomy was performed. Thick adhesions from the inferior edge of the upper lobe to the chest wall and pericardium were found. Upon freeing these adhesions and opening the fissure, the bronchus to the lingula appeared to be involved in a hard mass, however, the lung was normal to palpation. A similar thick fibrous mass surrounded the pulmonary artery to such an extent that it could not be exposed. Further exploration revealed complete involvement of the great vessels arising from the arch of the aorta in a similar block of almost stony hard material that extended down into the aortic window. Biopsy material was obtained by excising this fibrous tissue overlying the aortic arch and from the area between the aortic arch and the pulmonary artery, and a subcarinal lymph node.

**Pathology:** One specimen consisted of a plaque of extremely firm, fibrous, connective tissue measuring 5.5 x 2.5 x 0.6 centimeters in greatest dimensions. One surface was soft and congested, while the other surface was yellowish-gray and nodular. The cut surface presented a homogeneous pink fibrous appearance. Submitted separately was an irregular fragment of anthracotic lymphoid tissue, measuring 1.3 centimeters in diameter occupied centrally by a 4.0 mm. nodule of partially calcified caseous material. Sections revealed remarkably dense swollen avascular collagenous tissue infiltrated by moderate numbers of plasma cells and occasional lymphocytes. Sections of the partially calcified, necrotic material revealed organisms strongly suggestive of histoplasma capsulatum. The periphery of the nodule showed only hyalinized fibrous connective tissue without any recognizable cellular activity.

**Course Since Surgery:** He has been asymptomatic since thoracotomy seven months ago.

**Case 2:** This 25 year old white man was well until December 1, 1956, when he dates the onset of weakness, lethargy, and increasing pressure sensations in his head. About January 28, 1957, he developed swelling of his neck. He was hospitalized February 7, 1957, after several episodes of syncope and it was noted that he had lost 10 pounds in weight. Physical examination revealed swelling of the face, neck and upper extremities, marked conjunctival and oropharyngeal suffusion, papilledema and marked venous engorgement of the upper extremities, anterior and posterior chest wall and neck (Fig. 2A). Moderate lymphadenopathy of the anterior and posterior cervical chain and axilla lymph nodes were noted. Because of the superior vena caval obstruction he was transferred to Fitzsimons Army Hospital.

His past history was non-contributory.

**Residency History:** He was born and reared in Minnesota. He received basic training at Fort Leonard Wood, Missouri, in 1954 and had been serving Alaska until his present illness.

Chest roentgenograms on admission (Fig. 2B) revealed a right superior mediastinal mass 3 centimeters in diameter projecting anteriorly as seen in the left anterior oblique projection, but not visualized as a tumor on lateral view.

Laboratory studies revealed normal complete blood count, urinalysis, and liver function studies. He did not react to No. 2 PPD or coccidioidin but was 2+ to 1:100

**Figure 2:** (A) Infrared photograph before surgery showing engorgement of collateral veins of neck, thorax and arms. (B) Chest roentgenogram showing the right peritracheal mediastinal lesion. (C) Superior vena cava in situ with transection of the azygos vein and complete occlusion of the lumen. (D) Homologous aortic graft in situ at completion of anastomosis of the right innominate vein to the ariule. (E) Hemisection of the superior vena cava and azygos vein showing fibrous occlusion of the lumen. The upper fragment is the superior vena cava at the junction with the left innominate vein showing marked mural thickening. (F) Characteristic keloidal fibrous tissue with pulmonary, pleural and neural involvement. (G) Wall of the caseating granuloma in the peritracheal lymph node imbedded in fibrous tissue. (H) Characteristic organisms of *H. capsulatum* demonstrated in caseous material by Gomori silver methenamine stain.
FIGURE 3B

(Case 3) (A) Chest roentgenograms showing the right hilar mass with linear and nodular infiltration of the right upper lobe. (B) Branch of the pulmonary artery showing marked disruption of the wall by collagenous fibrous tissue and mature thrombus formation.
chronic fibrous mediastinitis. The venous pressure in both arms was 44 centimeters of saline. Serological studies for fungi revealed:

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He was presented to the Tumor Board, where it was felt that this was probably a lymphoma and exploratory thoracotomy recommended. On March 25, 1957 right thoracotomy revealed extensive venous collaterals in the thoracic wall. On opening the chest, the lung appeared and felt normal. In the superior aspect of the right hilar region, there was a fixed, hard mass about 7.5 centimeters in diameter. Striking the mediastinum, the azygous vein, superior vena cava, the left innominate vein, the trachea and right bronchus. A biopsy was taken from the angle between the superior vena cava and azygous vein. Below a 6 to 8 mm. fibrous capsule was a conglomerate, caseating mass which had an appearance of granuloma (Fig. 2C). There was no evidence of neoplasm. As the great vessels were dissected it was apparent that the azygous vein was completely fibrotic and thrombosed and that this mass involved the wall of the superior vena cava, causing complete obliteration at the level of an azygous vein. The process extended from the pericardium to the right innominate vein. The phrenic nerve was bound down in the fibrous mass. The azygous vein and superior vena cava were excised and the vena cava replaced from the right innominate vein to the auricle by an aortic homograft (Fig. 2D).

Pathology: The surgical specimen was received in two portions (Fig. 2E); the largest consisted of the inferior portion of the superior vena cava and the azygous vein. The internal diameter of the superior vena cava visualized inferiorly was 1.0 centimeter but was funnel-shaped and occluded by firm fibrotic thrombus. The superior aspect of this specimen presented an irregular lumen 6.0 mm. in diameter. Longitudinal hemisection revealed that the lumen of the terminal segment of the azygous vein was completely obliterated by a firm thrombus. This thrombus was firmly attached to the indurated wall and extended irregularly into the superior vena cava, merging with the previously described lesion. The upper fragment of the superior vena cava revealed similar mural thickening composed of avascular fibrous connective tissue upon the inner aspect of which there was a similar thrombus. Microscopic sections of all tissue presented a homogeneous, sclerotic, collagenous tissue extending irregularly around and through all structures observed (Fig. 2F). There was a moderately-heavy chronic inflammatory cell infiltrate consisting primarily of plasma cells with minimal numbers of lymphocytes and occasional eosinophiles. Multiple sections failed to reveal any evidence of a specific granulomatous process.

The lymph node removed from the tracheal chain showed an inappased caseous granuloma surrounded by keloidal fibrous tissue (Fig. 2G). Gomori silver methenamine stains of the caseous material revealed morphologically typical organisms of histoplasma capsulatum (Fig. 2H). Acid-fast stains were negative.

Course Since Surgery: Immediately following surgery relief of the superior vena cava obstruction was evident with complete disappearance of the edema of the upper extremities, head, and neck and a fall in the venous pressure in the upper extremities. Five months later, however, swelling of the head, neck, and arms reappeared but has not progressed to the extent seen prior to thoracotomy.

Angiography now reveals complete obstruction of the right innominate vein and reconstructed superior vena cava. At present, eight months, after thoracotomy, it is quite obvious that more extensive venous collaterals are present over the lateral and anterior aspects over the superior and inferior epigastric regions. Elevation of the head of his bed is not required, and he is relatively asymptomatic except with vigorous physical activities. Additional reconstructive vascular surgery does not appear warranted or feasible.

Case 2: This 30 year old white man was well until May, 1955 when he began losing weight without apparent cause. About three weeks later, while flying at 30,000 feet, he experienced sudden shortness of breath, slight substernal chest pain, and non-productive cough attributed to decompression. However, the symptoms continued and on June 14, 1955 he was hospitalized at Barksdale Air Force Base because of a chest roentgenogram showing right hilar enlargement. Histoplasmin, PPD Nos. 1 and 2 skin tests were negative but O.T. was questionably positive. Sputum examinations were negative. He was returned to duty June 27, 1955. On July 8, 1955 he first noted hemoptysis with continued blood streaking for five days. A chest roentgenogram revealed an increase in the right hilar mass and resulted in his evacuation to Fitzsimons Army Hospital for further observation.

His past history was non-contributory.
FIGURE 4B

Figure 4 (Case 4): (A) Chest roentgenogram, July 18, 1955, showing right pleural thickening, enlargement of a lymph node about the bronchus intermedius and collapse of the right middle lobe. (B) Ossous metaplasia of mediastinal fibrous tissue obtained at second thoracotomy.
Residence History: He was born in Michigan, travelled through the United States, and had lived several years in northwestern Louisiana preceding his illness.

Physical examination revealed a well-nourished, well-developed man who appeared in good health. Mild generalized non-tender lymphadenopathy was present. A few fine rales were heard in the right midlung field posteriorly. A grade-II, apical systolic cardiac murmur was heard.

Admission chest roentgenogram (Fig. 3A) revealed soft nodular and linear infiltrations of the right upper lobe and marked prominence of the right hilar and peritracheal area.

Laboratory studies showed a normal complete blood count, urinalysis and cardiolipin. Numerous sputum cultures were negative for M. tuberculosis and pathogenic fungi. Skin tests: Histoplasmin 1:1000 2+ (conversion), PPD Nos. 1 and 2, coccidioidin negative. Serological studies for fungi revealed:

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Course in Hospital: Bronchoscopy was normal and bronchial washings negative for fungi, M. tuberculosis and tumor cells. Scalene node biopsy showed reactive hyperplasia. Exploratory thoracotomy October 26, 1956 revealed marked vascular adhesions over the posterior segment of the right upper lobe, necessitating retropleural dissection. A large tumor-like mass was found in the hilum, involving all structures, predominately around the upper lobe. A further tumor-like mass found in the anterior segment measured 2.5 x 4 centimeters. The mediastinal mass extended to include the superior vena cava from the pericardium approximately eight centimeters superiorly. The main stem pulmonary artery, bronchus, the lower trachea, and the superior pulmonary vein were included in the mass. Biopsy of the posterior mediastinum revealed fibrous tissue with acute and chronic inflammatory reaction. Further dissection showed occlusion of the pulmonary artery branch to the posterior segment of the right upper lobe by the tumor-like mass. A biopsy was removed as a biopsy specimen. The axygos vein was similarly completely occluded and excised without bleeding. The fibrotic process also involved the contiguous pericardium and the superior and lateral wall of the right atrium. Venous pressure in the superior vena cava above the obstruction was 26.5 centimeters of saline. An enlarged hilar node was removed and the procedure terminated since individual dissection and ligation of structures preparatory for right upper lobectomy were impossible.

Pathology: The specimen consisted of tissue removed from the right lung, the pleura, the mediastinum and the azygos vein. Sections revealed a marked fibrous connective tissue process of a predominately mature pattern with foci of fibroblastic activity (Fig. 3B). This was infiltrated by moderate to marked numbers of plasma cells and occasional lymphocytes and eosinophiles without respect to anatomic boundaries such as pleura, fascia or vein. No granulomatous disease was observed. The mediastinal lymph node showed only reactive hyperplasia.

Course Since Surgery: He was returned to limited duty January 10, 1956 but failed to regain weight, tired easily, had recurrent anterior chest pain, productive cough, and hemoptysis. He was rehospitalized March 17, 1956 when examination revealed generalized mild lymphadenopathy, decrease in breath sounds over the upper chest bilaterally, and occasional wheezing over the left upper lobe area. A pericardial friction rub was noted for two weeks. Multiple lymph node biopsies showed reactive hyperplasia.

He was temporarily retired with a diagnosis of "Fibrosis, proliferation of lung, mediastinum, superior vena cava, azygos vein, pericardium and right auricle of heart, chronic, progressive, of unknown cause."

Since April 1956 although he has remained active he has had recurrent anterior chest pain and pulmonary hemorrhage about every two to three weeks requiring hospitalization on three occasions. In September, 1957 he was permanently retired.

Case 4: This 30 year old white woman was admitted to Fitzsimons Army Hospital March 11, 1955 having first been hospitalized November 22, 1954 at the United States Army Hospital, Regensburg, Germany.

Her illness began November 18, 1954 with chills, fever, and hacking non-productive cough. Two days later she began having right pleuritic chest pain and was hospitalized. Chest roentgenogram showed right pleural effusion. White blood cell count was 10,150 with normal differential distribution. Thoracentesis November 26, 1954 yielded about 500 cc. straw-colored fluid with specific gravity of 1.017 and cell count of 1,700 WBC, 61 per cent lymphocytes and 39 per cent neutrophils. The pleural fluid was reported as showing an occasional acid-fast bacillus however culture was negative for M. tuberculosis. Skin tests: PPD No. 2 and coccidioidin were negative but histoplasmin was 3+. She was transferred to Fitzsimons Army Hospital March 11, 1955.
with a diagnosis of tuberculosis pleurisy with effusion. Her past history was non-contributory.

Residence History: She was born in Mississippi and subsequently lived in Tennessee and Kentucky. Her only overseas station was in Germany from mid-1952 until returning to the States in March 1955.

Physical examination on admission was within normal limits except for slight decrease in vocal fremitus in the right base posteriorly and a few fine post-tussic rales in the same area.

Laboratory studies showed a normal complete blood count, urinalysis, and cardiopulmonary function tests. Numerous gastric cultures were negative for M. tuberculosis and pathogenic fungi. Repeated skin tests confirmed the negative tuberculin and coccidioidin, but the histoplasmin was strongly positive. Chest x-ray film revealed persistent right hilar thickening and a mass in the right hilum associated with collapse of the right middle lobe (Fig. 4A).

Course vs. Treatment: Between February 1, 1955 and March 28, 1955 she had three episodes of hemoptysis. On the latter occasion she was bronchoscopied and blood was seen coming from the right lower lobe area. She was rebronchoscopied April 26, 1955 and severe stenosis of the bronchus intermedius was noted. The mucous was granular, friable, shaggy-appearing and bled easily. The right middle lobe orifice could not be visualized. The secretions obtained by bronchoscopy were negative on culture for M. tuberculosis and on Papanicolaou's smear for malignancy.

Attempts to clear the severe endobronchial disease with antibiotics was unsuccessful until thoracotomy was performed to facilitate drainage from the right main stem bronchus. At thoracotomy, July 21, 1955, the entire right lung was densely adherent to the chest wall by multiple vascular adhesions. A hard, tumor-like mass was found involving the hilum, extending into the mediastinum and left hemithorax. As the posterior aspect of the hilum was freed the mass was found to "encase in a cement-like" both main stem bronchi, carina and about two centimeters of the lower trachea. Part of the "tumor" extended anteriorly and involved the lateral portion of the superior vena cava from the level of the azygos vein to its entrance into the right atrium juxtapositionally. The lower lobe felt as if there was extension into the lung parenchyma itself. The mass was adherent to the esophagus; the right pulmonary artery and vein were also grossly involved. Multiple biopsies of tissue removed from the right main stem bronchus, the wall of the superior vena cava and the lymph nodes from the superior mediastinum and near the carina were obtained.

Gross examination of the lymph nodes revealed complete loss of normal lymphoid architecture due to fibrosis. Examination of fragments of bronchus and superior vena cava showed dense homogeneous fibrous connective tissue without evidence of granulation tissue or caseation. Microscopic examination confirmed the gross impression of a mature dense fibrosing process involving the bronchial wall and the tissues about the superior vena cava. Sections of the lymph node showed fibrosis without evidence of specific granulomatous inflammation.

Following surgery repeated bronchoscopy was done in an attempt to dilate the bronchus intermedius. Due to failure of obtaining diagnostic tissue thoracotomy was
repeated September 19, 1955. The right middle and lower lobes were markedly fibrotic and expanded poorly after decortication. Extensive further calcification of the mediastinal and hilar mass had occurred precluding definitive surgery. Generous biopsies were removed from the mediastinal pleura, the lung and right main stem bronchus. Grossly these were fragments of dense fibrous connective tissue showing on cut surface foci of dense calcification. Microscopic examination disclosed mature fibrous connective tissue with foci of marked fibroblastic activity accompanied by large numbers of lymphocytes, plasma cells and occasional eosinophils. No granulomatous inflammatory process was observed, and considerable osseous metaplasia was present (Fig. 4B).

The tracheostomy was repaired October 10, 1955 after repeat bronchosopic dilatation of the bronchus intermedius relieved stenosis to about 20 per cent. She was discharged home October 15, 1955. On November 11, 1955 she was readmitted for treatment of mild serum hepatitis (19 pints of whole blood were given during previous surgery July and September, 1955), and discharged home December 17, 1955. In March, 1956 she began having cough productive of one-fourth cupful yellowish sputum daily. Bronchoscopy revealed moderately opaque mucosa of the right main stem bronchus which bled easily. Mild stenosis of the right upper, middle and lower lobe orifice was noted but little changed from six months before. She has been well, doing full time work as a teacher since April, 1956. The most recent chest roentgenograms, February, 1957, reveal minimal fibrothorax and linear fibrosis of the right lower chest, and questionable increase in calcification of the hilar and mediastinal mass (Figs. 4C and 4D).

Discussion

It is doubtful that the incidence of the superior vena caval syndrome is decreasing because there is rather conclusive evidence that primary tumors of the lung are on the increase, and there are trends which cause us to believe that mediastinal tumors may likewise be increasing. Jaffe,21 in a study of 100 necropsies with carcinoma of the lung, found that seven of the tumors had invaded and obliterated the superior vena cavae—all of these had developed extensive venous collaterals in the chest wall. There has been a remarkable decrease in the incidence of residuals of syphilis during the past 15 to 20 years; we must surmise, therefore, that syphilitic mediastinitis and aortitis which formerly gave clinical or pathologic evidence of superior vena caval obstruction is seldom seen.

It is our impression that the incidence of mediastinitis of most types is declining. The possible exception to this clinical impression is the extensive fibrosering mediastinitis now thought to be rather characteristic of histoplasmosis. There is indirect but presumptive evidence that pyogenic infections, in this antibiotic era, seldom result in symptomatic chronic mediastinitis.

Of 250 cases of superior vena caval obstruction reported between 1904 and 1946,22 62 (24.8 per cent) were due to chronic fibrous mediastinitis. Of these 62, 16 were considered to be idiopathic, 27 luetic and 19 tuberculous. During this period the number of cases reported as idiopathic chronic fibrous mediastinitis changed from none (1904-1921), to 5 per cent (1922-1938), to 11.7 per cent (1934-1946). Although this change may be related to efficacy of treatment of syphilis it seems probable that the change was due to a greater tendency of pathologists to report cases as idiopathic when proof of etiology was lacking.

A corollary, in this respect, seems to apply to tuberculous involvement of mediastinal nodes and structures. The clinical impression that tuberculosis rarely results in chronic fibrous mediastinitis and superior vena caval obstruction is based upon the following facts and assumptions: 1) earlier diagnoses and institution of highly effective antituberculosis therapy during the past decade; 2) tuberculosis control in dairy herds and almost universal pasteurization of dairy products in this country—a lim-
ited experience in the resection of pulmonary tuberculosis in foreign born women dependents of service men has often revealed a calcific hilar adenitis and angitis more extensive than that seen in American patients but in no instance was there evidence of extensive mediastinal fibrosis; 3) over 1200 patients have undergone pulmonary resections for proved tuberculous lesions at this hospital during the past 10 years without the surgeons finding any evidence of significant mediastinitis as portrayed by the four cases reported; neither have resected mediastinal lesions, solitary or multiple, which proved to be chronic tuberculous lymphadenitis been associated with massive mediastinal fibrosis or vena caval obstruction; 4) Auerbach states that he has never demonstrated tuberculous mediastinitis producing superior vena caval obstruction.

The salient pathologic features of this disease appear to be a progressive evolution of remarkably dense sclerotic fibrous tissue characterized by swollen angular clumps of collagen alternating with fibrocytes. This description parallels the microscopic appearance of a cutaneous keloid, as noted by Knox. The process displays a remarkable tendency to invade all structures with which it comes in contact without respect to anatomic boundaries. This "keloidal fibrous tissue" is accompanied by moderate numbers of plasma cells and lesser numbers of lymphocytes and occasional eosinophils. Osseous metaplasia is occasionally observed.

Proliferative collagenous replacement of lymph nodes renders histologic and cultural confirmation of histoplasma capsulatum difficult unless lymphoid tissue is obtained at thoracotomy prior to complete replacement of the granulomatous process with dense fibrous tissue. Buried within such lesions there may be found caseating granulomata which contain organisms typical of histoplasma capsulatum.

Clinicians, surgeons, and pathologists who have reviewed the literature and their clinical experiences with chronic fibrosing mediastinitis or superior vena caval obstruction since the turn of the century report that from 15 to 50 per cent of such lesions were secondary to chronic inflammatory diseases. Of the specific varieties, tuberculosis and syphilis always have been included or implicated; however, such diagnoses were often presumptive as unequivocal laboratory proof has only seldom been evident, excluding aortic aneurysms. In view of our present concepts of fibrosing mediastinitis, we propose that a significant percentage of such lesions considered in the past to be tuberculous, syphilitic, thrombotic, traumatic, rheumatic, cicatricial (keloid), or idiopathic in nature were actually due to the rather uniform response of the mediastinal lymph nodes and related anatomical structures to histoplasma capsulatum infection.

SUMMARY

Four patients, age 25 to 30 years, with bronchial or mediastinal venous obstruction due to chronic fibrous mediastinitis are reported.

Fibrous mediastinal lesions with various degrees of calcification were so extensive, obliterating anatomical planes, that pulmonary resections were technically impossible or considered unwise.

Clinical and laboratory findings with uniform gross and microscopic appearance of these intrathoracic lesions, in our opinion, has given us a sufficient basis to make a diagnosis of chronic fibrous mediastinitis due
to histoplasmosis. Morphologically typical organisms of histoplasma capsules were demonstrated in the caseous material from a granulomatous lymph node in one patient and organisms highly suggestive of such a fungus disease were found in another.

Multiple mediastinal biopsies from the other two patients were not conclusively diagnostic in that no lymph node demonstrating such early collagenous replacement of necrotic foci was encountered although the typical hyalinized fibrous and calcific tissue was in abundance.

Discussion points are presented dispelling the past opinions that severe chronic mediastinitis and associated superior vena caval obstruction may be the result of a tuberculous process.

RESUMEN

Se hace mención de cuatro enfermos de 25 a 30 años de edad con obstrucción venosa bronquial o bilateral debida a mediastinitis fibrosa crónica.

Las lesiones fibrosas mediastinales con varios grados de calcificación eran tan extensas y abliteraban planes anatómicos, que la resección pulmonar fue técnicamente imposible o considerada imprudente.

Los hallazgos clínicos y de laboratorio con apariencia macro y microscópica de estas lesiones intratorácicas, de acuerdo con nuestra opinión, nos dan base suficiente para hacer el diagnóstico de mediastinitis fibrosa crónica debida a histoplasmosis. Histoplasma capsulátum típico se encontró en el material caseoso de un ganglio granulomatoso en un enfermo, en otro se encontraron organismos que sugerían fuertemente una micosis.

Las biopsias múltiples de los otros dos enfermos no condujeron a diagnóstico concluyente, pues no se encontró ganglio alguno demostrando tan temprana substitución por colágena de los focos necróticos, aunque había tejido en abundancia hialinizado típico fibroso y tejidos calcificados.

Se discute y se descarta la opinión del pasado de que la mediastinitis severa crónica y la obstrucción de cava resultante puedan ser resultados de una afección tuberculosa.

RESUME

Les auteurs rapportent les observations de quatre malades, âgés de 25 à 30 ans, atteints d'obstruction veineuse médiastinale ou bronchique, imputable à une médiastinite fibreuse chronique.

Les lésions fibreuses médiastinales, présentant différents degrés de calcification, furent si extensives, obliterant les plans anatomiques, que les résections pulmonaires furent techniquement impossibles, ou considérées comme inopportunes.

Les constatations cliniques et bactériologiques, montrant aussi bien macroscopiquement que microscopiquement l'existence des lésions intrathoraciques, ont donné aux auteurs des éléments suffisants pour faire le diagnostic de médiastinite fibreuse chronique, due à l'histoplasmosis. Des germes morphologiquement typiques d'histoplasma capsulatum furent mis en évidence dans le caséum obtenu à partir d'un nodule granulomateux chez un malade, et des germes hautement évocateurs de cette mycose furent découverts chez un autre.

Des biopsies médiastinales multiples chez les deux autres malades ne
purent permettre de conclusion car on ne put découvrir aucun ganglion avec la refonte collagène précoce des foyers nécrotiques bien qu'il y eut en abondance les aspects caractéristiques de tissu fibreux hyalin et de calcifications.

Les auteurs présentent les arguments qui détruisent l'opinion qu'on avait naguère selon laquelle la médiastinite chronique grave associée à l'obstruction de la veine cave supérieure pouvait être le résultat d'un processus tuberculeux.

**ZUSAMMENFASSUNG**


Befunde aus Klinik und Laboratorium mit einheitlichem makroskopischem und mikroskopischem Aussehen dieser intrathorakalen Veränderung haben uns unserer Auffassung nach eine genügende Grundlage geliefert, um die Diagnose einer chronischen fibrösen Mediastinitis infolge Histoplasmose zu stellen. Morphologisch typische Organismen von histoplasmocapsulatum liessen sich in dem käsigen Material aus granulomatösen Lymphknoten bei einem Patienten nachweisen, und bei einem anderen Patienten wurden Organismen gefunden, die in hohem Grade für eine solche Pilzkrankheit verdächtig waren.

Multiple mediastinale Biopsien von den zwei anderen Patienten waren diagnostisch nicht überzeugend insofern, als keine Lymphknoten zu finden waren, die einen so frühen kollagenen Ersatz von nekrotischen Herden aufwiesen, obgleich das typische hyalinisierte fibröse und verkalkte Gewebe in grosser Menge vorhanden war.

Hauptpunkte einer Diskussion werden dargestellt, die anstelle der früheren Auffassung treten, wonach eine schwere chronische Mediastinitis und damit verknüpft ein Verschluss der oberen Hohlvene die Folge eines tuberkulösen Prozesses sei.

**REFERENCES**

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