When considering the tissue diagnosis of a malignant pleural mesothelioma, the possibility of a metastatic adenocarcinoma must be excluded, for a minute biopsy of a malignant mesothelioma may be mistaken for adenocarcinoma. Routinely, a tissue stain for tumor mucin secretion should be performed because while approximately 50 percent of metastatic adenocarcinomas secrete mucin, malignant mesotheliomas never do. In this case, tumor stains for mucin were negative, and, furthermore, the necropsy failed to reveal an adenocarcinoma elsewhere.

Over the past 15 years, an increasing incidence of asbestos-related diseases has resulted in new information concerning the biological behavior of malignant mesotheliomas. As in this case, more than half develop metastases to the hilar and the mediastinal lymph nodes, as well as to the liver and other abdominal viscera. The malignant pleural mesothelioma does not invade the lungs. It grows round the lungs' surfaces, encasing them, the heart, and great vessels and leads to death usually within one to two years of diagnosis. The usual clinical signs and symptoms are unilateral pleural pain, weight loss, and bloody pleural effusion.

The hepatic calcifications in the present case formed in foci of metastatic mesothelioma within ischemic tumor necrosis and hemorrhage. Such dystrophic calcification is a "gravestone" to dead tissue.

Only one other case of malignant pleural mesothelioma associated with massive hepatic calcifications has been reported, and it, like the present case, initially presented with roentgenographic findings of massive hepatic calcifications. Also, in both cases, the malignant pleural mesotheliomas were initially occult. Since malignant pleural mesotheliomas are occurring more often, massive calcifications within their liver metastases may become a more frequent roentgenographic finding.

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Figure 2. Photomicrographs of both (a) carcinomatous and (b) sarcomatous components from this mixed malignant mesothelioma (hematoxylin-eosin, original magnifications x 225).

REFERENCES


Subglottic Stenosis in Wegener's Granulomatosis

James H. Lampman, M.D.; Renato Querubin, M.D.; and Prasadarcio Kondapalli, M.D., F.C.C.P.

A patient with treated Wegener's granulomatosis had an inflammatory subglottic laryngotracheitis during remission from systemic features of the disease. The lesion enlarged insidiously until a critical point of stenosis occurred in the subglottic region, leading to stridor. Subglottic stenosis, another of the protean findings in Wegener's granulomatosis, may be seen more frequently in the future as patients survive longer in immunosuppressant-induced remissions.

*From the Departments of Medicine and Otolaryngology, Case Western Reserve University School of Medicine at Cleveland Metropolitan General Hospital, Cleveland.
Therapy in Wegener's granulomatosis is assessed by monitoring characteristic lesions in target organs and by following acute phase reactants. The need for awareness of unusual sites of disease in this entity is demonstrated by the following case in which an inflammatory subglottic stenosis developed insidiously during apparent remission and ultimately led to stridor.

CASE REPORT

In January 1973 a 21-year-old man had sterile mastoiditis, polyarthritis, rash, tongue ulcer, and a transient pulmonary infiltrate. Treatment with prednisone led to remission of symptoms. In March 1974, he had hemoptysis, and chest roentgenogram showed a cavity in the anterior segment of the right upper lobe. Bronchoscopy and bronchial biopsy failed to establish a diagnosis. Subsequently, the patient noted recurrent hemoptysis, rash, and polyarthritis. Erythrocyte sedimentation rate (ESR) was 52 mm/hr, and renal function was normal. On July 5, 1974, the right upper lobe cavity was resected. Histologic study of the cavitated lung showed a necrotizing granulomatous reaction involving the parenchyma, bronchioles, and arteries, compatible with Wegener's granulomatosis. A diagnosis of "limited" Wegener's granulomatosis was made. The patient responded rapidly and completely to azathioprine, 100 mg/day, which he continued receiving for 15 months.

Twelve months after discontinuation of azathioprine therapy (October 1976), he was admitted because of severe headache and nasal obstruction. His ESR was 42 mm/hr. A biopsy specimen of nasal mucosa showed vasculitis. On direct laryngoscopy, the subglottic larynx was noted to be erythematous, but its lumen fully patent. Azathioprine therapy was re instituted but was discontinued three months later by the patient because he felt well. The ESR remained at 7 mm/hr or less after this hospitalization.

Two years later, in September 1978, the patient experienced stridor during a viral upper respiratory tract infection. The ESR was 4 mm/hr. A flow-volume loop suggested significant extrathoracic fixed airway obstruction. Neck laminagrams and laryngogram showed a subglottic mass narrowing the airway lumen circumferentially, thickest on the posterior wall (schematically shown in Fig 1). Bronchoscopy showed an erymhematosus mass located primarily on the posterior wall, partially obstructing the airway, starting 0.3 cm below the true cords and extending 2 cm downward. Biopsy showed acute and chronic inflammatory infiltrate and multinucleated giant cells (Fig 2 and 3). Necrotizing vasculitis was not seen.

The patient breathed more comfortably after dilation of the airway with a 7-mm bronchoscope. A regimen was instituted consisting of oral cyclophosphamide, 100 mg daily, and prednisone, 30 mg daily. Two weeks later, bronchoscopy showed some regression of the subglottic stenosis, and an 8-mm instrument was easily admitted. Flow-volume loop had improved. One week later, further regression of the lesion had taken place.

In January 1979, an upper respiratory tract infection led to subglottic edema and stridor again. Intravenous steroid, misted air, and rest led to a return to baseline within 12 hours. By July 6, 1979, studies showed a diminution of the inflammatory subglottic mass and improvement in the size of the airway. Despite occasional brief episodes of dyspnea associated with viral upper respiratory tract infections, symptoms improved. On Dec 17, 1979, cyclophosphamide therapy was discontinued.

Figure 1. Schematic diagram of subglottic mass.

Figure 2. Photomicrograph of tissue from subglottic mass. Multinucleated giant cells and plasma cell infiltrate (hematoxylin and eosin, × 400).

Figure 3. Photomicrograph of tissue from subglottic mass. Inflammatory infiltrate, focal necrosis, and granulation tissue (hematoxylin and eosin, × 50).
DISCUSSION

This case illustrates that an inflammatory laryngotracheostenosis may develop insidiously during a phase of apparent remission of Wegener's granulomatosis. The vocal chords and distal trachea were relatively spared, while the subglottic larynx and uppermost trachea were constricted by fibrosis, edema, and inflammatory mononuclear cell infiltrate. Owing to the slowly progressive nature of the constricting lesion, the patient was able to adjust his breathing pattern gradually without complaint, until a critical point of stenosis was reached.

The subglottic site was noted to be a target for Wegener's granulomatosis in 1954 by Godman and Churg, who showed that in two of their seven cases, "striking lesions of the larynx and trachea" were present consisting of "edema, congestion, and extensive ulceration of the mucosa, particularly in the subglottic area." In one of their cases, stridor occurred paroxysmally. The histologic picture typically lacks the necrotizing granulomas or vasculitis seen in other organs. The ulcerative lesions of the trachea and larynx seen in up to 30 percent of untreated cases seem to be infrequent in the era of immunosuppressant treatment. Rarely, in a case of active disease, the larynx, trachea, and bronchi may be diffusely affected with ulcers, infiltration, and cicatricial stenotic lesions. Hypothetically, the granulomatous stenosis seen in our patient may represent smoldering disease activity, which in the untreated state would have resulted in a florid ulcerative lesion.

It is unlikely that the subglottic lesion results from any cause other than Wegener's granulomatosis itself. Histologic and bacteriologic studies have failed to identify likely infectious agents. Relapsing polychondritis, amyloidosis or sarcoid, conditions linked rarely to laryngostenosis, were not in the clinical picture. Posttraumatic stenosis caused by cicatrizied granulomas induced by endotracheal intubation is unlikely, since this typically occurs within three weeks of extubation, and in most cases the intubation has lasted longer than 24 hours. However, in a few cases in which steroids or immunosuppressants were administered (not for Wegener's granulomatosis), there developed a delayed fibrous stenosis of the larynx as late as five months after extubation. Several cases of subglottic stenosis have occurred in Wegener's granulomatosis in the absence of a history of intubation, occasionally as a presenting finding.

This type of subglottic lesion may be seen more frequently in the future as patients with Wegener's granulomatosis live longer in immunosuppressant-induced remissions. The case reported illustrates the need for vigilance in discovering and monitoring target sites during and after treatment of this disease.

REFERENCES


Myocarditis in Legionnaires' Disease*

David Gross, M.D.; Howard Willens, M.D.; and Steven M. Zeldis, M.D., F.C.C.P.

A case of Legionnaires' disease is described in which the characteristic features of multifocal pneumonia, rhabdomyolysis, renal failure, hepatic and CNS involvement are accompanied by the previously undescribed complication of myocarditis. Clinical and laboratory findings of myocardial involvement included overt heart failure, a new gallop, an abnormal ECG, elevated myocardial specific enzymes and an abnormal thallium scan. All of these abnormalities resolved completely after recovery.

Legionnaires' disease is usually associated with multi-organ involvement, including pneumonia and renal and hepatic abnormalities. We present a case that included myocarditis, a complication not previously described to our knowledge.

CASE REPORT

A 51-year-old woman factory worker was hospitalized in May 1979 with complaints of fever, multiple rashes, myalgias, weakness, nausea and nonproductive cough. She had been in

*From the Department of Medicine, Queens Hospital Center Affiliation of the Long Island Jewish-Hillside Medical Center, Jamaica, NY, and the School of Medicine, Health Sciences Center, State University of New York at Stony Brook, Stony Brook, NY.

Reprint requests: Dr. Zeldis, Division of Cardiology, Heart Institute, Long Island Jewish Medical Center, New Hyde Park, NY 11042