Bronchial Stenosis in Chronic Sarcoidosis*

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Two patients with chronic sarcoidosis developed marked stenosis and obstruction of the segmental bronchial orifices. Bronchoscopy and radiographic studies suggested that the bronchi were involved by extensive peribronchial fibrosis in the central portions of the lungs. In one patient, the bronchial narrowing showed no change over a seven-year period, despite improvement of the pulmonary involvement following corticosteroid and chlorambucil therapy. The bronchial narrowing is probably due to granulomatous involvement of the bronchial walls with subsequent scarring and stenosis.

Sarcoidosis may affect the lungs in a variety of ways. In the acute and subacute stages, sarcoi
d granulomas are found in the alveolar septa, the subpleural fibrous tissue, and the peribronchial and perivascular connective tissues. In patients who develop chronic pulmonary disease, alternating areas of fibrosis, emphysema, and bronchietasis are the rule.

The characteristic pulmonary function derangement is a restriction pattern, although many of these patients also have diffusion abnormalities. Obstruction has been reported in some cases, but is much less common. Obstruction in the active stages is usually due to the presence of endobronchial sarcoid granuloma formation or to bronchial compression from enlarged lymph nodes. In chronic sarcoidosis, obstruction due to fibrosis and bronchiolar narrowing may occur.

The purpose of this report is to present two patients with chronic sarcoidosis who had severe respiratory obstruction due to fixed narrowing of the orifices of the major bronchi. The radiographic and bronchoscopic findings suggested that the narrowing was caused by bronchial encasement by extensive surrounding peribronchial fibrosis.

CASE REPORTS

Case 1

Case 1 was a 52-year-old white woman who had spent her entire life in Utah until she and her husband moved to England in February, 1969. She soon developed gradually increasing dyspnea on exertion, fatigue, nervousness, weight loss, and partial loss of scalp hair. She sought medical help, but no diagnosis was made until 15 months later in May, 1970, following a transfer to Germany. A chest x-ray film at that time revealed upper lobe infiltrates, scarring, and right pleural thickening. Results of skin tests for tuberculosis, histoplasmosis, and coccidioidomycosis were all negative. A liver biopsy showed "non caseating granuloma consistent with sarcoidosis."

Five months later, in October, 1970, and while still in Germany, she developed progressive shortness of breath and wheezing. Her chest x-ray film was reported as showing no change. She was treated with prednisone, 30 mg per day, and her condition seemed improved. An additional episode of acute dyspnea associated with a thrush infection of the mouth and throat was treated with nystatin (Mycostatin), and her dyspnea improved. Her prednisone dosage was gradually decreased to 5 mg per day.

In November, 1971, she returned to the United States and was seen at the University of Utah Medical Center. She still had dyspnea on slight exertion and an occasional sense of fullness in the throat. The only abnormality on physical examination was the presence of bronchial breath sounds over the lower one-half of the right lung. Chest x-ray films (Fig 1A) were unchanged from those taken in Germany 18 months earlier. Data from pulmonary function studies are shown in Table 1.

The prednisone therapy was discontinued, and two months later, in January, 1972, she developed cough and increasing shortness of breath. Physical examination was unchanged except for the presence of rather marked stridorous-type breathing and the presence of bronchial breath sounds bilaterally. The tuberculin skin test (standard purified protein derivative [PPD-S, second strength]) was still negative. Results of laryngoscopy were normal, but bronchoscopy revealed angulation, distortion, rigidity, and stenosis of the bronchi on the right. The stenosis was estimated to be at least 60 percent in the right upper and lower lobes and at least 50 percent in the right middle lobe. Laminagrams and bronchograms confirmed the presence of diffuse stenosis of the

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Table 1—Results of Pulmonary Function Studies in Case One

<table>
<thead>
<tr>
<th>Test</th>
<th>Measured</th>
<th>% of Predicted</th>
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<tr>
<td>Forced expiratory vital capacity</td>
<td>2,326 ml</td>
<td>77</td>
</tr>
<tr>
<td>Forced expiratory volume (1 sec)</td>
<td>1,414 ml</td>
<td>55</td>
</tr>
<tr>
<td>Maximal midexpiration flow</td>
<td>51 L/min</td>
<td>48</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>3,633 ml</td>
<td>76</td>
</tr>
<tr>
<td>Residual volume</td>
<td>1,493 ml</td>
<td>89</td>
</tr>
<tr>
<td>Diffusing capacity (16.7 ml per min per mm Hg) (normal 19.9)</td>
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origins of the segmental bronchi (Fig 1B and 1C), and the stenosis actually appeared to be greater than the estimate at bronchoscopy. Chlorambucil therapy was begun, but it was poorly tolerated and was discontinued. She was discharged on symptomatic therapy, with no further change in symptoms.

Case 2

Case 2 was a 71-year-old white woman who was admitted to the University of Utah Medical Center on July 8, 1970, with hoarseness and increasing shortness of breath over a six-week period. She had had a respiratory illness in 1963 which was treated with antibiotics, but it had never completely cleared. Her x-ray film at that time was negative.

In 1965, she developed a second episode of "pneumonia," and the chest x-ray film showed marked abnormalities (Fig 2A). A scalene node biopsy at that time revealed noncaseating granuloma consistent with sarcoidosis. A bronchial biopsy obtained from the right intermediate bronchus during bronchoscopy showed the same changes. The three lobar bronchi on the right were estimated to be 80 percent narrowed. The left main bronchus "felt as if it were surrounded by cement" and was completely immobile. The bronchoscope could not be passed for any appreciable distance into the left bronchus, and the left upper and lower lobe orifices were not seen.

Corticosteroid therapy was started (dosage unknown), with marked improvement in her dyspnea, and some clearing in her x-ray film. However, she developed Cushingoid changes and weakness. The steroids were discontinued, and bronchodilators and chloroquine therapy were tried without demonstrable improvement.

She continued to have exertional dyspnea and intermittent respiratory infections until June, 1970, when she developed increasing dyspnea, wheezing, cough and hoarseness. Her

Figure 1A (upper left). Chest roentgenogram in January, 1972, reveals bilateral hilar masses, scars extending to periphery of lungs, and emphysematous appearing areas in periphery of lungs, especially on right. Figure 1B (center) Right bronchogram (only one side was done because of patient's poor pulmonary function). There is marked stenosis of orifices of all segmental bronchi. Lower lobe bronchi filled and were of more normal caliber distally. Upper lobe bronchi never filled beyond stenotic origins. Figure 1C (bottom) Tracheobronchial laminagram. There is stenosis of segmental bronchial orifices bilaterally. Branches to right upper lobe and superior segment of right lower lobe are severely narrowed and appear to be almost totally obstructed. (Patient 1)
chest x-ray film showed progressive involvement of the lungs (Fig 2B).

On physical examination, she appeared healthy except for slightly labored respirations at rest. There were bronchial breath sounds throughout the lungs, and harsh breath sounds were heard over the main stem bronchi. P2 was louder than A2. The physical examination was otherwise not remarkable. Laboratory studies revealed a hematocrit of 42.3 percent and a leukocyte count of 9,400/cu mm. Results of skin tests for tuberculosis, histoplasmosis, coccidioidomycosis, blastomycosis, and mumps were all negative. Pulmonary function studies over the period of observation are detailed in Table 2. A combination of severe restriction and obstruction is revealed. Chest laminagrams showed marked stenosis of the orifices of the major bronchi. She was treated with bronchodilators, intermittent positive pressure breathing (IPPB), oxygen, expectorants, and 60 mg of prednisone per day and was "covered" by isoniazid and pyridoxine. She was symptomatically improved, and her pulmonary function also improved, but she developed marked Cushingoid changes and marked fluid retention. She was started on chlorambucil therapy (6 mg/day) with symptomatic improvement. She became less dyspneic and there was an improvement in the chronic cough which had been a major complaint throughout her illness. Her x-ray films showed improvement (Fig 2D). The parenchymal infiltrates decreased, although the major bronchial obstruction did not show any change on repeat lung laminagrams.

**COMMENT**

Both of these patients had the expected marked restrictive lung changes characteristic of sarcoidosis, but in addition they also had marked obstruction. Although there was marked bronchial stenosis in both cases, it was surprising that the bronchial mucosa appeared normal in Case 1 and showed only one small area of abnormality in Case 2. The bronchi were completely immobile and rigid, and radiographic studies demonstrated that the narrowed bronchi were surrounded by dense perihilar masses. Prior x-ray films were available in Case 2, and although there was considerable change in the parenchymal infiltration, the narrowed bronchi showed no change from 1965 to 1972. These findings strongly suggest that the bronchi were surrounded by extensive permanent dense perihilar fibrosis.

**DISCUSSION**

Permanent stenosis of the major bronchi in chronic sarcoidosis has been reported infrequently.

**Figure 2A** (left). Chest roentgenogram in 1965 three years after onset of illness. There are linear and nodular densities in both lungs and perihilar infiltration of lung on left side.

**Figure 2B** (center). Chest roentgenogram in March, 1970. There has been progression of nodular and linear densities in lungs, and perihilar infiltration is now bilateral and more extensive than in 1965. **Figure 2C** (right). Chest roentgenogram in March, 1971, after treatment with prednisone, then chlorambucil. There has been marked regression of pulmonary and perihilar infiltration, but there is evidence of extensive fibrosis, with upward retraction of hilum, and numerous scars are seen radiating outward to lung periphery.

**Figure 2D.** Tracing of laminagram of tracheobronchial tree reveals narrowing of segmental bronchi bilaterally. (Original did not reproduce satisfactorily). Tr—trachea, RUL—right upper lobe, BI—bronchus intermedius, LUL—left upper lobe, RUL—right upper lobe.

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Table 2—Pulmonary Function Studies During Period of Observation of Patient Two

<table>
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<tr>
<th></th>
<th>Predicted Value</th>
<th>7/6/70*</th>
<th>9/14/70</th>
<th>10/19/70**</th>
<th>3/29/71</th>
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<tbody>
<tr>
<td>FEV₁†</td>
<td>2,425 ml</td>
<td>1,063</td>
<td>1,468</td>
<td>1,259</td>
<td>1,871</td>
</tr>
<tr>
<td>FEV₂†</td>
<td>2,000 ml</td>
<td>536</td>
<td>888</td>
<td>777</td>
<td>982</td>
</tr>
<tr>
<td>MMEF*</td>
<td>107 L/min</td>
<td>13</td>
<td>24</td>
<td>23</td>
<td>29</td>
</tr>
<tr>
<td>MBC†</td>
<td>63 L/min</td>
<td>20</td>
<td>43</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>O₂ sat</td>
<td>92-95%</td>
<td>91</td>
<td>93</td>
<td>88.5</td>
<td>91.5</td>
</tr>
</tbody>
</table>

*Started on prednisone 60 mg/day
**Started on chlorambucil 6 mg/day;
  prednisone dosage decreased to 10 mgm/day
†Forced expiratory volume (1 sec)
‡Maximal mid-expiratory flow
§Maximal breathing capacity

In two large series describing the roentgenographic changes in sarcoidosis,²,¹⁶ this complication was not described. However, occasional patients with sarcoid bronchostenosis have been reported previously. Citron and Scadding⁷ reported three similar patients with dyspnea, stridor, cough, and multiple bronchial strictures, and Honey et al⁸ also reported two cases of bronchostenosis in the late stages of sarcoidosis and stated that this complication was probably very rare. Longcope and Freiman¹⁵ described patients with sarcoidosis who developed large tumor-like masses which compressed and distorted the bronchi, but it was not specifically stated whether these bronchial abnormalities were central or peripheral in the lung nor how much obstruction was present. Mallory⁹ described the pathologic changes in six patients with chronic pulmonary sarcoidosis and stated that conglomerate granulomatous formation and fibrosis may occur in addition to the scarring and fibrosis seen subpleurally, in the alveolar septa, and along the perivascular connective tissues.

In view of the extensive hilar and perihilar fibrosis seen in many cases of chronic sarcoidosis,²,¹⁶ it is surprising that marked bronchostenosis does not occur more frequently than it does. It is probable that some degree of stenosis is often present but is not detected either because it is not suspected or because it is not severe, or because it is masked by the marked restriction and diffusion abnormalities which are so often present.

The exact cause and sequence of changes leading to bronchostenosis in these patients is uncertain. One possible explanation is that the stenoses are the result of healed endobronchial sarcoid lesions. Bronchial granulomata in the acute phase of the disease have been reported frequently,⁸,¹¹-¹⁴,¹⁷-¹⁹ and the granulomata are sometimes large enough to cause narrowing and atelectasis.²,⁵,¹⁰,¹⁶,¹⁸,¹⁹ Bronchial biopsy was positive in the two cases of bronchostenosis reported by Honey et al,⁸ in two of three cases reported by Citron and Scadding,⁷ and in one of the cases reported above. However, it should be noted that endobronchial sarcoid alone does not invariably, nor even usually, lead to bronchial stenosis. The latter complication is rare, and recent studies indicate that bronchial involvement is common in sarcoidosis even when the bronchi appear normal at bronchoscopy.⁸,¹³,¹⁷-¹⁹ Citron and Scadding⁷ believed that the stenotic bronchi resulted from either direct invasion of the bronchial wall by the sarcoid process or from pressure from adjacent lymph nodes. Although hilar adenopathy may cause bronchial narrowing and obstruction in the acute stages of sarcoidosis,¹⁴,¹⁵ it is unlikely that it would cause symmetrical encasement of the bronchi. There was no radiographic evidence of hilar adenopathy in either of our cases. It is possible, however, that fibrosis and contraction of enlarged matted lymph nodes could result in multiple permanent bronchial stenoses.

It should be emphasized that the clinical course of the patients with chronic bronchostenosis is quite different from the usual patient with chronic pulmonary disease due to sarcoidosis. They have frequent episodes of bronchitis and pneumonia and may develop stridor during these acute episodes. The stridor is occasionally severe and may even mimic upper airway obstruction. Pulmonary function studies show moderate to marked obstruction in addition to the more common abnormalities of pulmonary restriction and diminished diffusing capacity. Although there was no radiographic evidence of change in the severity of bronchostenosis, Patient 2 did show considerable subjective improvement, a decrease in her peripheral pulmonary infiltrates on x-ray film, and improvement in pulmonary function studies when she was treated with corticosteroids and chlorambucil.

REFERENCES

1 Nickerson DA: Boeck's sarcoid. Report of six cases in which autopsies were made. Arch Pathol 24:19-29, 1937
2 Freundlich IM, Libshitz HI, Glassman LM, et al: Sarcoidosis, typical and atypical thoracic manifestations and
STAINED GLASS WINDOWS BY CHAGALL

In June 1959, Dr. Miriam Freund, the National President of Hadassah, and Joseph Neufeld, the architect who designed the Hadassah-Hebrew University Medical Center, stopped in Paris on their return from Jerusalem and went to see Marc Chagall. At this meeting it was decided that Chagall would design the stained-glass windows for the synagogue that was to be part of the Medical Center. Chagall devoted the next two years to this task. When at last he achieved results that satisfied him completely, this prodigious work was exhibited in Paris in June 1961 and the following winter at the Museum of Modern Arts in New York. In February 1962, the stained-glass windows were finally permanently installed in the synagogue. Today their luminous images glow from dawn to dusk beneath the sky of the Holy Land. The windows are approximately eleven feet high and eight feet wide. The essence of the Jerusalem

Windows lies in color, in Chagall's magical ability to animate material and transform it into light. Words do not have the power to describe Chagall's color, its spirituality, its singing quality, its dazzling luminosity, and its sensitivity to the inflections of the soul and the transports of the imagination. It is simultaneously jewel-hard and foamy, reverberating and penetrating, radiating light from an unknown interior. Chagall's palette is inexhaustible, quick in sharp or subtle contrasts and, as in the latest paintings, it can enliven with infinite nuances a vast expanse dominated by a single color. Thus, the transparency and flashing brilliance of his color enabled it to be sublimated into a medium which was eminently suited to a religious subject.