Variable Response to Long-term Corticosteroid Therapy in Chronic Beryllium Disease*

Akshay Sood, MD, MPH, FCCP; William S. Beckett, MD, MPH, FCCP; and Mark R. Cullen, MD

**Objectives:** Chronic beryllium disease (CBD) shares many of its characteristics with sarcoidosis and is often treated with corticosteroids. There is limited available literature regarding the effect of long-term corticosteroid therapy on the natural history of CBD.

**Methods and materials:** We conducted an observational retrospective study of six patients with CBD who received prolonged corticosteroid treatment with a mean pulmonary function test follow-up period of 10.1 years. Five of the six patients were exposed to beryllium at the same workplace. The diagnosis in four of the six cases was confirmed by a positive beryllium lymphocyte proliferation test result on blood or BAL fluid. Periodic pulmonary function tests were analyzed in relation to removal from beryllium exposure and treatment with corticosteroids.

**Measurements and results:** Two broad patterns of response were noted in these patients. The first pattern seen in two patients showed no improvement in FVC or diffusion capacity of the lung for carbon monoxide (DLCO) with corticosteroids. However, a significant improvement in these parameters was noted on cessation of beryllium exposure in one of the two patients. The second pattern showed an initial improvement in FVC and DLCO with corticosteroids, which was not sustained. An improvement was noted on stopping beryllium exposure.

**Conclusions:** The response to long-term corticosteroids in CBD, quite like that in sarcoidosis, is variable. Significant lung function improvement may be seen following cessation of beryllium exposure.

(CHEST 2004; 126:2000–2007)

**Key words:** beryllium; chronic beryllium disease; corticosteroids; sarcoidosis

**Abbreviations:** BLPT = beryllium lymphocyte proliferation test; CBD = chronic beryllium disease; DLCO = diffusion capacity of the lung for carbon monoxide; TLC = total lung capacity

Beryllium is a lightweight metal with high tensile strength and high heat-absorptive properties that make it very attractive for use as an alloy in many applications, including electronics, aerospace, automotive, communications, nuclear weapons, and household appliances. The use of beryllium alloys continues to grow, and it is estimated that as many as 800,000 workers in the United States are exposed currently. Exposure to beryllium can result in beryllium sensitization, subclinical, acute, or chronic beryllium disease (CBD).

CBD is a chronic hypersensitivity granulomatous disease that resembles sarcoidosis and principally affects the skin, lungs, and lymphatic system. Common presenting symptoms include exertional dyspnea, nonproductive cough, fatigue, and weight loss. Radiographic abnormalities include hilar and mediastinal lymphadenopathy and lung infiltrates (Fig 1). The typical pulmonary function abnormalities include a restrictive pattern with a reduction in diffusion capacity of the lung for carbon monoxide (DLCO). The classic pathologic change in CBD is the well-developed noncaseating granuloma that is indistinguishable from sarcoidosis (Fig 2). Many individuals with CBD, therefore, receive an incorrect diagnosis of sarcoidosis if the occupational history is omitted or ignored. The combination of an appropriate beryllium exposure history, evidence of beryllium sensitization as suggested by positive blood or BAL beryllium lymphocyte proliferation test (BLPT) or positive beryllium skin patch results, and histopathologic features of noncaseating granulomas distinguishes CBD from sarcoidosis. The greatest morbidity in CBD is caused by lung involvement that is associated with a progressive decline in lung volumes and diffusing capacity, eventually resulting in respiratory failure and cor pulmonale. Published mortality rates for CBD vary widely for unclear reasons, from 5.8 to 38%.

In contrast to CBD, acute beryllium disease presents
like chemical pneumonitis either during or shortly after high levels of exposure with resolution following cessation of exposure. While acute beryllium disease has become increasingly rare among the modern workforce, medical surveillance is increasingly able to identify a new category of patients with subclinical beryllium disease. These patients are usually asymptomatic and have normal chest radiograph and pulmonary function test results, but have granulomata on transbronchial lung biopsy and positive blood and/or BAL cell BLPT results.

A key element in the management of all forms of beryllium disease is removal from workplace exposure. In addition, CBD is often treated with corticosteroids. The use of corticosteroids is based on the hypothesis that suppression of the hypersensitivity reaction (i.e., granulomatous process) will prevent the development of fibrosis. However, there is little available literature regarding the effect of corticosteroids on the natural history of CBD. This study analyzes the long-term pulmonary function response to stopping beryllium exposure and to corticosteroid treatment in individuals with CBD.

METHODS AND MATERIALS

The investigators conducted an observational retrospective cohort study of six subjects with CBD who were enrolled in the Beryllium Case Registry and seen at Yale University School of Medicine Occupational and Environmental Medicine program. The subjects received prolonged follow-up and treatment with corticosteroids during the period 1971 to 1996.

The diagnosis of CBD was established on the basis of their occupational history of documented beryllium exposure; supportive clinical, radiologic and pulmonary function presentation; and histopathologic evidence of noncaseating granulomas on biopsy. The chest radiographs of all patients were noted to have bilateral interstitial infiltrates and hilar adenopathy at the time of diagnosis. All subjects had restrictive physiology on their pulmonary function tests. The diagnosis was confirmed immunologically by a positive BLPT result on either blood or BAL fluid on four of the six cases; one patient (patient 6; Table 1) had elevated beryllium levels in the lung and cervical lymph node tissue, and another patient (patient 4; Table 1) met the published clinical criteria for CBD.

Figure 1. Posteroanterior radiographic view of the chest of patient 1 showing bilateral hilar adenopathy and diffuse symmetric interstitial infiltrate. Reproduced with permission from Cullen et al.

Figure 2. Open-lung biopsy of patient 1. Top: Granulomatosis was diagnosed on lung tissue after biopsy. Multiple epithelioid granulomas that are becoming hyalinized are surrounded by dense fibrosis and sparse population of lymphocytes. Lesions are present similar to that seen in aging lesions of idiopathic sarcoidosis (hematoxylin-eosin, original $\times 100$). Bottom: The lung architecture is obscured by epithelioid granulomatosis without necrosis. Lung interstitial space and alveoli are filled with a lymphohistiocytic infiltrate (hematoxylin-eosin, original $\times 100$). Reproduced with permission from Cullen et al.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Pattern of Response</th>
<th>Employment History</th>
<th>Years of Exposure</th>
<th>Age of Onset of Respiratory Complaints, yr</th>
<th>Comorbidities*</th>
<th>Interval Between Respiratory Complaints and Biopsy Diagnosis, yr</th>
<th>Test Sample for Immunologic Confirmation</th>
<th>Doses of Oral Prednisone*</th>
<th>Follow-up Period, yr*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pattern 1</td>
<td>Melter for first 2 yr, refiner for next 6 yr, and subsequently moved to the finishing department out of refinery</td>
<td>8</td>
<td>25</td>
<td>Asthma diagnosed at 2 yr, bilateral pneumonia at 6 yr</td>
<td>10 for sarcoidosis (open-lung biopsy), 15 for CBD</td>
<td>BLPT positive for BAL and blood</td>
<td>Initial dose, 40 mg/d at 11 yr, tapered between 11 yr and 15 yr to off</td>
<td>Follow-up period between 8 yr and 30 yr</td>
</tr>
<tr>
<td>2</td>
<td>Pattern 1</td>
<td>Melter for 5.3 yr</td>
<td>&lt;10</td>
<td>26</td>
<td>Peptic ulcer, alcoholic pancreatitis</td>
<td>4 for sarcoidosis (liver biopsy), 8 for CBD</td>
<td>BLPT positive for both BAL and blood</td>
<td>Initial dose 40 mg daily at 13.75 years and tapered between 13.75-19.2 years to off</td>
<td>Follow-up period between 10 yr and 15.5 yr, lost to follow-up between years 5 to 10</td>
</tr>
<tr>
<td>3</td>
<td>Pattern 2</td>
<td>Melter for 5.25 yr</td>
<td>5.25</td>
<td>28</td>
<td>Sinusitis</td>
<td>5 for sarcoidosis (transbronchial biopsy), 12 for CBD</td>
<td>BLPT positive for both BAL and blood</td>
<td>Initial dose, 60 mg oral every other day started at 13.75 yr and tapered between 10.25 to 12 yr to off</td>
<td>Follow-up period between 10 yr and 15.5 yr, lost to follow-up between years 5 to 10</td>
</tr>
<tr>
<td>4</td>
<td>Pattern 2</td>
<td>Melter for 4.5 yr</td>
<td>&lt;10</td>
<td>33</td>
<td>Schistosoma mansoni hepatitis at 4.7 yr</td>
<td>0.5 for presumptive CBD (open-lung biopsy)</td>
<td>BLPT negative for blood, BAL improperly processed</td>
<td>Initial dose 40 mg started at 4.75 yr tapered between 4.75 yr and 5.5 yr to 15 mg, and then continued till 15.5 yr</td>
<td>Follow-up period between 4.75 yr and 15.5 yr, started at 15.5 yr and tapered between 12 yr to off, due to relocation to Puerto Rico</td>
</tr>
<tr>
<td>5</td>
<td>Pattern 2</td>
<td>Crusher/separator for first 11 yr, and subsequently mixer/sampler for 5 yr</td>
<td>16</td>
<td>38</td>
<td>None</td>
<td>1 for CBD (transbronchial biopsy)</td>
<td>BLPT negative for blood, positive for BAL</td>
<td>Initial dose of 60 mg/d started at 16.4 yr, tapered to off between 16.4 yr and 17.4 yr, resumed at 17.8 yr at 30 mg alternating with 5 mg every other day, dose increased to 60 mg/d at 18.5 yr and tapered again between 18.5 yr and 26.75 yr</td>
<td>Follow-up period between 16.3 yr and 26.9 yr</td>
</tr>
<tr>
<td>6</td>
<td>Pattern 2</td>
<td>Machinist (grinding and polishing metal) for 6 yr</td>
<td>6</td>
<td>44</td>
<td>Peptic ulcer, Mycobacterium gordonae cervical lymphadenitis at 7 yr and Mycobacterium xenopi chest wall abscess at 11 yr</td>
<td>6 for presumptive CBD</td>
<td>Lang and lymph node beryllium levels elevated</td>
<td>Initial dose of 20 mg oral started at 6.4 yr and increased to 60 mg at 9.25 yr, and subsequently tapered to off at year 11.3</td>
<td>Follow-up period from 6.25 yr and 15.0 yr</td>
</tr>
</tbody>
</table>

*Years are since date of employment.
†Duration of time, in years, between beryllium exposure and onset of respiratory symptoms.
conducted at various pulmonary function test laboratories associated with Yale University hospitals in southern Connecticut using the American Thoracic Society guidelines. These tests included measurement of FVC, total lung capacity (TLC), and single-breath DLCO by nitrogen-washout technique. Based on the American Thoracic Society guidelines for spirometry and single-breath DLCO, a minimum change of 15% in FVC and 9% in DLCO over time was considered clinically important. If both tests did not show a similar change in value, a greater reliance was placed on FVC for examining changes over time.

**RESULTS**

The six subjects with CBD in this retrospective study had a mean pulmonary function test follow-up period of 10.1 years (median, 9.7 years) [Table 1]. All six subjects were men: four Hispanics (patients 1 through 4) and two African Americans (patients 5 and 6). Prior to the establishment of a definite diagnosis of CBD, all the six cases were initially diagnosed as “sarcoidosis.” Interestingly, all subjects were either nonsmokers or light smokers with a < 10 pack-year smoking history who quit after the sarcoidosis diagnosis was established. The median age of onset of respiratory complaints was 30.5 years. The median latency period between the beginning of occupational exposure and the onset of respiratory complaints was approximately 4 years. The median duration of beryllium exposure was approximately 5.6 years, and exposure had ceased prior to the time of report of this article in all cases. The median duration between the onset of respiratory complaints and the diagnosis of sarcoidosis was 3 years. The median duration between the diagnosis of sarcoidosis and that of CBD was 2.5 years. This duration may not reflect current medical practice that may have changed due to increased physician awareness of the health effects of beryllium and availability of the BLPT.

All patients except patients 1 and 2 received corticosteroids shortly after the start of respiratory complaints. Patient 1 acquired chronic progressive respiratory symptoms starting insidiously as early as 1 year following the start of beryllium exposure. However, this was initially diagnosed as asthma, and efforts were made to curtail his exposure to metal fumes. Despite these measures, his clinical symptoms worsened. A diagnosis of sarcoidosis was finally established at 11 years, at which time he was placed on corticosteroids. Immunologic confirmation of CBD was obtained at 16 years. Patient 2 was unavailable for follow-up shortly after a diagnosis of sarcoidosis was made by a percutaneous liver biopsy at 5.3 years following the start of beryllium exposure. At that time, he was noted to have mild respiratory and constitutional symptoms and hilar adenopathy with mild reticulonodular infiltrates. Beryllium exposure was stopped, but no corticosteroid therapy was begun at that time due to “relative paucity” of symptoms. He subsequently returned to follow-up at 10 years without any progression in his clinical or radiologic picture. Following immunologic confirmation, a diagnosis of CBD was definitively established at 12 years. His clinical deterioration, however, began at 13.75 years (8.5 years following cessation of beryllium exposure), following which corticosteroids were started. While the median duration from onset of respiratory complaints to start of corticosteroids for patients 1 and 2 was 9.9 years, the corresponding time interval for patients 3 through 6 was 1.1 years. These subjects showed two broad patterns of response to removal from beryllium exposure and long-term treatment with corticosteroids. The first pattern (seen with patients 1 and 2) [Fig 3, Table 2] showed no significant improvement in FVC or DLCO with corticosteroids. However, a significant improvement in these parameters was noted on stopping beryllium exposure in patient 2.

The second pattern (seen in patients 3 through 6) [Fig 4, Table 2] showed an initial improvement in FVC and DLCO with corticosteroids that was not sustained. An improvement in these parameters was also noted on stopping beryllium exposure. This was the most common pattern, and was seen in four of the six patients. In addition, one of the four patients (patient 3) showed a spontaneous improvement in FVC and TLC several years after corticosteroids had been discontinued. Two of the four patients (patients 3 and 5) received a second course of corticosteroid therapy in a lower dose. The pulmonary function response to the second course was markedly less than the first course.

These results show a variable long-term response to long-term corticosteroid therapy in CBD, a response reminiscent of pulmonary sarcoidosis, a closely similar...
Table 2—Percentage Change in Pulmonary Functions Following Corticosteroid Therapy*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Change in FVC, %</th>
<th>Change in DLCO, %</th>
<th>Pattern of Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+9</td>
<td>-15</td>
<td>Pattern 1</td>
</tr>
<tr>
<td>2</td>
<td>+7</td>
<td>-25</td>
<td>Pattern 1</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Percentage change in pulmonary function is obtained by comparing the precorticosteroid pulmonary function value with the highest value obtained during corticosteroid therapy.

**DISCUSSION**

CBD is a hypersensitivity granulomatous disease that continues to occur in 2 to 5% of beryllium-exposed workers, despite efforts to reduce workplace exposures. Both beryllium exposure and a beryllium-specific cell-mediated immune response are required for the development of CBD. The disease/exposure relationship between beryllium and CBD is not linear. CBD has been diagnosed in individuals with very low level or casual exposures, such as secretaries, security guards, and spouses of exposed workers. The exposure threshold below which no cases of CBD occur remains unknown. The immune response to beryllium appears to depend on an individual's genetic susceptibility. Allelic differences have been shown in the major histocompatibility complex class II molecules human leukocyte antigen-DR and human leukocyte antigen-DP in patients with CBD as compared with nondiseased beryllium-exposed individuals. However, it is likely that genetic susceptibility to CBD is multifactorial and that other genes are also involved in regulating the immune response in pathogenesis of this disease.

Although stopping beryllium exposure in patients with CBD is usually recommended, most previous studies indicate that disease progression is the general rule even after cessation of exposure. However, Hardy in 1955 suggested that the natural history of CBD is quite variable, and suggested that some patients with abnormal radiographic findings could remain free of “disability.” In 1978, Sprince and colleagues also reported that chest radiographic and gas exchange abnormalities disappeared in a “great” proportion of untreated patients within 3 years of reduced exposure. Unfortunately, these cases had only limited assessments; only four had biopsy confirmation of disease and no case had immunologic confirmation. In a brief report by Nishikawa et al in 1990, two of eight cases of CBD that were confirmed by lung biopsy and BLPT showed radiographic clearing within 1 year of removal from exposure.

The use of corticosteroids in CBD is based on the hypothesis that suppression of the hypersensitivity reaction (i.e., granulomatous process) will prevent the development of fibrosis. However, there is little available literature regarding the effect of corticosteroids on the natural history of CBD. In 1969, Stockelke et al described a case of complete remission of CBD but only after treatment with adrenocorticotropic hormone. Ferris studied long-term pulmonary function data on three patients with CBD and one patient with acute beryllium pneumonitis and found a variable and short-lived response to corticosteroids. Ferris also suggested that corticosteroids might initially reduce inflammation and transiently improve pulmonary functions, only to deteriorate again as irreversible fibrosis sets in. Gaensler et al noted two types of pulmonary function response curves in a 3-year follow-up of 11 patients receiving corticosteroids: one that showed an improvement, albeit short lived, and another that showed no improvement or a slight decline in pulmonary functions. In the seven patients who had serial alveolar-arterial oxygen gradient measurements, no long-term improvement in the gradients was noted. In addition, a number of patients without corticosteroids showed no significant functional deterioration. Gaensler et al in 1958 commented that “the similarity in performance between the CBD group and sarcoidosis is striking.” Stoeckle et al also observed that corticosteroids improve the condition of a variety of, but not all of the cases. He also noticed that a dose of 15 to 30 mg of prednisone is more effective than 60 to 80 mg of prednisone.

When Seeler attempted an analysis of the effect of corticosteroids on 382 cases from the Beryllium Case Registry, he found a favorable effect on mortality among 126 treated patients. In these patients, the mortality was 16% compared to 39% among the 256 untreated patients. No pulmonary function test data were available in this study. Seeler stated: “However, the interpretation of this data are uncertain in that many of the survivors who have not been treated have lived an appreciably longer time with their disease than those living on steroid therapy.” From the study of DeNardi, a similar analysis on mortality was made on his 70 patients. The mortality of the treated patients was 10%, whereas that of the untreated patients was 31%. Seeler rightly commented that these studies could not separate apparent therapeutic improvement from patient selection.

Still another factor in evaluation of corticosteroid response may be the timing of the treatment. Many patients are not administered corticosteroids until the disease is well established. Among 29 of the 44 treated patients (66%) in one review, 2 years had elapsed between the onset of their illness and corticosteroid therapy, a period during which significant fibrosis can occur.
Previous studies on the natural history of clinically apparent CBD suffer from an inadequate disease definition and the lack of biopsy and immunologic confirmation of disease. In addition, several studies on CBD have included acute beryllium lung disease. The latter has a very different natural history from CBD; it is more likely to respond to corticosteroids and may also spontaneously remit. The natural history of CBD has changed over the decades because of better disease definition and earlier detection due to widespread screening and improvement in workplace exposure conditions. The disease is now being discovered in its earlier or subclinical stage, and acute beryllium pneumonitis associated with heavy exposures is now distinctly rare. Despite these drawbacks, several important conclusions can be drawn from the studies on the natural history of CBD. First, the disease varies in its clinical presentation. Second, the disease varies in its rate of progression. Third, while removal from exposure and/or corticosteroids may be medically prudent, it is not clear to what extent such measures will change the natural history of CBD.

The results of the current study show a variable long-term response to long-term corticosteroid therapy in CBD, a response reminiscent of pulmonary sarcoidosis. The most common pattern of response in CBD is a short-lived improvement in pulmonary functions associated with corticosteroid therapy. Further, stopping beryllium exposure itself is associated with an improvement in pulmonary functions in a majority of patients.

Even though there are insufficient data to make an evidence-based therapy recommendation, an early trial of corticosteroid therapy may be initially recommended in the treatment of this disease, in addition to cessation of beryllium exposure. However, the investigators recommend that corticosteroid therapy should be guided by changes in serial pulmonary function measurements. Rarely, the disease may remit spontaneously in the long term for unclear reasons. Similar disease remissions have been described in pulmonary sarcoidosis.

There are several strengths of the current study. All cases were established on the basis of relevant exposure history, appropriate clinical physiologic and radiographic presentation, and pathologic evidence of granulomatous disease. Four of the six cases had positive BLPT results.
blood or BAL fluid, one case had elevated beryllium levels in two different biopsy specimens (lung and cervical lymph node tissue), and one case met the published clinical criteria for CBD, but had negative peripheral blood immunologic test findings, and an improperly processed BAL fluid that yielded nonviable lymphocytes that could not be tested for proliferation with beryllium salts. This “gold standard” case definition in the majority of cases lends the greatest specificity to the clinical diagnosis. All cases originated in the same time frame and from the same geographic area; five were from the same workplace and the sixth was from a manufacturing plant nearby. The longitudinal follow-up and exposure tracking of the five patients from the refinery are also strengths of this study.

The limitations of this study include the following: use of retrospective data obtained from abstracting medical records, which may introduce information bias; use of different pulmonary function laboratories, which may result in increased variability of data; a small number of patients; use of variable doses, duration, and tapering schedules of oral corticosteroids at the discretion of treating physicians; and inadequate exposure data of the sixth patient. The observations of this study are not relevant to a newly recognized category of patients with “subclinical” beryllium disease with normal chest radiographic and pulmonary function test results, but with granulomata on transbronchial lung biopsy and positive BLPT results by blood and/or BAL cells.

CONCLUSION

In summary, the response to long-term corticosteroid therapy in CBD is quite variable. Significant lung function improvement may also be seen following cessation of beryllium exposure. An early trial of corticosteroids may be prudent in the management of this disease, in addition to cessation of beryllium exposure. However, corticosteroid therapy should be guided by changes in serial pulmonary function measurements. This study, therefore, provides important information about long-term pulmonary function response to corticosteroids in CBD and supports the observation made by Gaensler et al in 1958 that “the similarity in performance between chronic beryllium disease and sarcoidosis is striking.”

REFERENCES

4. Aronchick JM, Rossman MD, Miller WT. Chronic beryllium disease: diagnosis, radiographic findings, and correlation with pulmonary function tests. Radiology 1987; 163:677–682
20. Rossman MD. Chronic beryllium disease: diagnosis and management. Environ Health Perspect 1996; 104S:945–947
27. Newman LS, Kreiss K. Nonoccupational beryllium disease masquerading as sarcoidosis: identification by blood lympho-
Idiopathic Pleuroparenchymal Fibroelastosis*

Description of a Novel Clinicopathologic Entity

Stephen K. Frankel, MD, FCCP; Carlyne D. Cool, MD; David A. Lynch, MD; and Kevin K. Brown, MD, FCCP

*From the Interstitial Lung Disease Program, National Jewish Medical and Research Center, Denver, CO.

Materials and Methods

The clinical database of the Interstitial Lung Disease Program at National Jewish Medical and Research Center was reviewed for cases of combined pleural and lung parenchymal fibrosis for visit dates between 1996 and 2001. All living study subjects had been prospectively enrolled in our specialized center of research longitudinal study of interstitial lung disease that was approved by our institutional review board and supported by the National Institutes of Health. Case records were abstracted for all clinical data. Radiographic studies were reviewed by an expert thoracic radiologist (D.A.L.). Surgical lung biopsy specimens were reviewed by an expert pulmonary pathologist (C.D.C.).

Between 1996 and 2001, we identified five cases of a unique idiopathic pleuroparenchymal lung disease characterized by a clinical presentation suggestive of a chronic idiopathic interstitial pneumonia, marked pleural and parenchymal radiographic involvement with an upper lobe predominance, and surgical lung biopsy findings that did not fit with any of the currently defined interstitial pneumonias. The pathologic findings included the following: (1) intense fibrosis of the visceral pleural; (2) prominent, homogenous, subpleural fibroelastosis; (3) sparing of the parenchyma distant from the pleura; (4) mild, patchy lymphoplasmacytic infiltrates; and (5) small numbers of fibroblastic foci present at the leading edge of the fibrosis. In this report, we characterize the clinical, radiographic, physiologic, and pathologic findings of this entity, which we term idiopathic pleuroparenchymal fibroelastosis.

(CHEST 2004; 126:2007–2013)

Key words: idiopathic; interstitial lung disease; pathology; pleural fibrosis; pulmonary fibrosis

Abbreviations: CMF = cyclophosphamide, methotrexate, and fluorouracil; HLA = human leukocyte antigen; HRCT = high-resolution CT; IIP = idiopathic interstitial pneumonia; UIP = usual interstitial pneumonitis

Between 1996 and 2001, we identified five patients with a cryptogenic syndrome of clinically significant chest symptoms, radiographic pleuroparenchymal abnormalities, and fibroelastotic changes seen on surgical lung biopsy specimens. Moreover, the pathologic findings in these five cases were distinctive and could not be classified within any of the currently defined idiopathic interstitial pneumonias (IIPs). None of the patients had evidence of a characterized connective tissue disease, sarcoidosis, human leukocyte antigen (HLA)-B27–related disease, hypersensitivity pneumonitis, infection, asbestosis, or other pneumoconiosis. Thus, we report five cases of an idiopathic pleuroparenchymal fibroelastotic syndrome with unique pathology.