Familial Cryptogenic Fibrosing Pleuritis With Fanconi’s Syndrome (Renal Tubular Acidosis)*

A New Syndrome

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We describe two siblings with a progressive unrelenting and unique syndrome of bilateral fibrosing pleuritis of unknown cause occurring in association with Fanconi’s syndrome (renal tubular acidosis). The parents of the siblings were second cousins. Both siblings had identical pleural histologic characteristics and identical urinary metabolic defects. This condition resulted in the development of severe respiratory failure in both patients and ultimately the death of the older sibling at the age of 21 years.  

(Chest 1995; 107:576-78)

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Key words: fibrosis; pleura; renal tubular acidosis

Bilateral pleural disease may be associated with a number of disorders. In most cases, the cause is clear and rarely progressive. We describe a brother and sister, the parents of whom were second cousins, who developed bilateral fibrosing pleuritis in conjunction with the renal tubular defect, Fanconi’s syndrome. Despite a number of therapeutic interventions, this resulted in the slow but unrelenting development of chronic respiratory failure and the death of the older patient. A third male sibling has Fanconi’s syndrome but no pleural disease and a fourth male sibling has neither disorder. An association between this congenital renal condition and pleural disease has not been previously described. However, in common with the only previous report of cryptogenic fibrosing pleuritis, the histocompatibility antigen HLA B44 was found in both siblings.

CASE REPORTS

CASE 1

In 1980, an 18-year-old man was noted to have proteinuria and glycosuria on routine urinalysis and was referred to this hospital. There was no previous relevant medical history. Clinical examination disclosed no abnormalities at this time, but the patient was below the third percentile for height and weight. On further assessment, he was found to have glycosuria with a normal glucose tolerance test, proteinuria, and aminoaciduria, hypercalciuria, and hypophosphatemia. The serum alkaline phosphatase level was elevated. Skeletal bone survey showed that bone age was retarded by 2 years and a bone biopsy confirmed the presence of osteomalacia. Hypouricemia was also noted, but there was no hypokalemia, and urinary acidification was normal. In 1985, he presented with symptoms of malaise and fatigue. A chest x-ray film revealed right pleural shadowing. Pleural aspirate confirmed an exudative effusion but was otherwise noncontributory. Pulmonary function tests showed a restrictive pattern of disease but with an above normal coefficient of gas transfer: percent predicted FEV1, 19; forced vital capacity (FVC), 21; diffusing capacity for carbon monoxide (single-breath), 25; coefficient of

FIGURE 1. Computed tomographic scan of thorax showing extensive bilateral pleural thickening in patient 1 preponderantly affecting the right lung.

CT=computed tomography; FEV1=forced expiratory volume in 1 second; FVC=forced vital capacity; KCO=coefficient of gas transfer
gas transfer (KCO) 124. There was no pathologic evidence of focal bacterial, fungal or tuberculous infection, asbestos-related disease, thromboembolic disease, autoimmune disorder, or malignancy. He had smoked 20 cigarettes a day for 5 years. Prescriptions for medications known to be associated with fibrosing syndromes had never been given to the patient. Bronchoalveolar lavage differential cell counts were normal. The computed tomography (CT) scan of the thorax revealed right-sided pleural thickening. He underwent a right-sided pleural decortication which did not significantly improve his pulmonary function. Pleural histologic findings revealed marked pleural fibrosis with organizing fibrin on the surface with focal lymphocytic collections at the fibrofatty junctions. No asbestos bodies were noted. Subsequently, he developed a pleural rub on the left side of his chest and a CT scan of the thorax showed the emergence of extensive bilateral pleural thickening (Fig 1). He was given therapeutic trials of a number of anti-inflammatory agents including orally administered corticosteroids, penicillamine, and colchicine. However, his condition deteriorated and he died 5 years after presentation owing to respiratory failure secondary to progressive bilateral pleural thickening.

CASE 2

The 23-year-old sister of the previously reported patient presented with a history of dyspnea and vague chest pain in 1986. A chest x-ray film showed bilateral pleural thickening which was confirmed by a CT scan of the thorax (Fig 2). Pulmonary function tests confirmed a restrictive defect with an above normal coefficient of gas transfer: percent predicted FEV₁, 32; FVC, 36; diffusing capacity for carbon monoxide (single-breath), 29; KCO, 118. Bronchoalveolar lavage differential cell count was normal. There was no evidence of any associated pathologic condition. An open pleural biopsy was performed which showed an identical histologic pattern to that of her brother. Again, no asbestos bodies were found. Urinary biochemistry revealed glycosuria, proteinuria, aminoaciduria, hypercalcuiuria, and normal urinary acidification. Hypophosphatemia and hypouricemia but no hypokalemia also were noted. The skeletal bone survey was normal. These serum and urinary biochemical abnormalities were identical to that of her brother. This patient was treated with oral corticosteroids, but over a 6-year period she has demonstrated a slow decline in vital capacity. Similarly, repeated CT scans of the thorax show increasing pleural fibrosis. The HLA typing was carried out and revealed identical haplotypes in both siblings (Table 1).

COMMENT

There are two other male siblings in the family. Although one of these siblings has been found to have classic Fanconi's syndrome, neither has any evidence of pleural disease after 8 years of follow up. The unaffected sibling carries HLA B44, but the sibling with Fanconi's syndrome does not.

DISCUSSION

We describe two siblings, a brother and sister, who developed progressive fibrosing pleuritis of unknown origin in conjunction with Fanconi's syndrome (renal tubular acidosis). Pleural fibrosis may commonly occur with a number of clinical conditions including bacterial, fungal, or tuberculous infection, thromboembolic disease, malignancy, autoimmune disorders, asbestos-related disease and some medications. Often the diagnosis is obvious and the pleural fibrosis is not progressive. Additionally, the syndrome of cryptogenic fibrosing pleuritis has been described in four unrelated patients. Although the histologic appearances are similar in our two patients, they differ in that our two patients did not respond to oral corticosteroids. Fanconi's syndrome may be a primary inherited condition or associated with a number of systemic or renal disorders. Despite extensive assessment over an 8-year period, we have found no evidence of any associated conditions in any of the affected siblings. Characteristics of our patients differ slightly from the usual biochemical abnormalities associated with this condition in that urinary acidification is normal. The fact that our patients have an identical biochemical abnormality is consistent with an inherited defect. The coexistence of Fanconi's syndrome and progressive fibrosing pleuritis has not been previously described. It is difficult to explain what relationship, if any, there may be between these two conditions in our patients. Although a common environmental factor cannot be fully excluded, it is possible that both conditions are genetically linked disorders. It is interesting to note that our patients with pleural fibrosis both have HLA B44 in common with the four patients previously described, and one sibling found to have Fanconi's syndrome but not to have pleural fibrosis does not express HLA B44. Although this is a common histocompatibility antigen (25% of the Irish population), its association with our two cases suggests a possible association between this antigen and pleural fibrosis.

REFERENCES


Table 1—HLA Typing in Patients and Parents

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FIGURE 2. Computed tomographic scan of thorax showing bilateral pleural thickening in patient 2 preponderantly affecting the left lung.
The Churg-Strauss Syndrome*

A Case Report With Angiographically Documented Coronary Involvement and a Review of the Literature

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The Churg-Strauss syndrome (CSS) is an unusual disease that presents as a systemic vasculitis and peripheral eosinophilia in a patient with chronic atopic disease. Although often not prominent on initial presentation, cardiac involvement is a major cause of morbidity and mortality in patients with CSS. We report a case of a young woman with CSS who had a myocardial infarction. Coronary arteriography was performed for recurrent chest pain and demonstrated diffuse vasculopathy consistent with vasculitis in CSS. We have also included a review of the literature on cardiac involvement in CSS. (Chest 1995; 107:575-580)

CSS=Churg-Strauss syndrome

Key words: allergic granulomatous angiitis; Churg-Strauss syndrome; coronary vasculitis

The Churg-Strauss syndrome (CSS), also known as allergic granulomatous angiitis, is a multisystem disease of unknown etiology. The 1990 American College of Rheumatology Criteria for CSS require that four of the following six criteria be met: (1) asthma; (2) eosinophilia (>10% of leukocytes by differential cell count); (3) mononeuropathy or polyneuropathy; (4) migratory or transient pulmonary infiltrates; (5) paranasal sinus abnormality; and (6) extravascular eosinophils.1 While it is believed to be a rare disorder, recent reports of "limited forms" of the disorder2,3 and the general difficulties in the diagnosis and classification of the vasculitides suggest that this entity may be underdiagnosed.

Recognition of this syndrome is important because it responds well to proper therapy while the outcome is poor in untreated patients.4-7 Also, involvement of one organ system may dominate the initial presentation, thus obscuring the diagnosis.

Cardiovascular and pulmonary physicians in particular need to be aware of this entity because a large number of deaths in this disease are related to cardiac causes (vida infra). We report the case of a young woman with CSS who had a myocardial infarction. Coronary angiography was performed for recurrent chest pain and supported the diagnosis of coronary vasculitis.

CASE REPORT

The patient is a 32-year-old woman who was previously healthy except for a 2-year history of asthma. The patient developed radiographically documented sinusitis 3 months before admission to our hospital. She was treated with antibiotics, during which time she developed bloody diarrhea. A colonic biopsy specimen showed a nonspecific vasculitis. The patient then developed weakness of all four extremities and became bedridden over a period of 3 to 4 weeks. Electromyography and nerve conduction studies showed sensorimotor axonal polyneuropathy. Laboratory studies were notable for a mild leukocytosis with 57% eosinophils. There was no history of tryptophan ingestion.

After a 3-week stay at a rehabilitation center during which time she had no improvement in her neuromuscular status, she was transferred to our hospital for further evaluation. The patient developed chest pain and ST-segment elevation in leads V4-V5 on her electrocardiogram. She was transferred to the cardiac care unit where creatine kinase values were elevated with elevation of the MB fraction. She developed postinfarction angina and was taken to the catheterization laboratory. Results of hemodynamic studies were unremarkable. Left coronary angiography (Fig 1) revealed abrupt cutoffs of both divisions of a large obtuse marginal branch and other smaller branches. Right coronary arteriography (Fig 2) revealed marked changes in caliber of several small branches. There was also a paucity of septal branches off the posterior descending artery.

DISCUSSION

Although involvement of all organ systems has been described, the vasculitis of CSS seems to involve the lungs, skin, heart, and peripheral nerves with the greatest frequency.4,5,7 The original report by Churg and Strauss7

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FIGURE 1. Arteriogram of the left coronary artery in the left anterior oblique projection shows abrupt termination of both divisions of the large obtuse marginal branch (arrows). Irregularity of the larger arteries and truncation of smaller branches are also seen.