

Hypersensitivity pneumonitis with normal high resolution computed tomography scans

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A case of symptomatic hypersensitivity pneumonitis with normal high resolution computed tomography (CT) scans is presented. The patient, a 32-year-old man with systemic lupus erythematosus, had a chronic, progressive history of respiratory symptoms, abnormal findings on examination and abnormal pulmonary function tests but normal high resolution CT scans of the chest. Diagnosis was made through open lung biopsy. Clinical improvement was seen on removal of the offending antigen. The literature on the utility of high resolution CT scans in hypersensitivity pneumonitis is reviewed.

Key Words: *Extrinsic allergic alveolitis; High resolution computed tomography; Hypersensitivity pneumonitis*

Hypersensitivity pneumonitis, also known as extrinsic allergic alveolitis, refers to a spectrum of lung diseases resulting from an immunologically mediated reaction to a variety of inhaled antigens found in organic dusts. Establishing a correct diagnosis often requires a high degree of clinical suspicion. A history of antigen exposure with subsequent respiratory symptoms and appropriate changes in pulmonary function tests are suggestive of hypersensitivity pneumonitis. While plain chest radiography does little to support or refute the diagnosis, high resolution computed tomography (CT) scans have begun to play a significant role. However, open lung biopsy, especially in subacute or

Pneumopathie d'hypersensibilité associée à des scintigraphies à haute résolution normales

RÉSUMÉ : On présente ici un cas de pneumopathie d'hypersensibilité symptomatique accompagnée de résultats normaux à la scintigraphie à haute résolution. Le patient, un homme de 32 ans, atteint de lupus érythémateux disséminé, présentait des symptômes respiratoires chroniques et progressifs, d'anomalies à l'examen et d'anomalies aux tests de fonction pulmonaire, alors que le résultat des scintigraphies pulmonaires était normal. C'est la biopsie pulmonaire qui a permis de poser le diagnostic. L'amélioration clinique a été observée lors de l'élimination de l'antigène nocif. On passe ici en revue la littérature sur l'utilité des scintigraphies à haute résolution dans la pneumopathie d'hypersensibilité.

chronic disease, remains the gold standard. This report describes a patient with chronic, progressive respiratory symptoms and normal high resolution CT scans. The diagnosis of hypersensitivity pneumonitis was made through open lung biopsy.

CASE PRESENTATION

A 35-year-old man was referred to the Mount Sinai Hospital Respiratory Clinic in May 1996 for evaluation of dyspnea and weight loss. He had a nine-year history of systemic lupus erythematosus that had been complicated by pleural and pericardial effusions as well as pneumonitis. He had not

TABLE 1
Serial pulmonary function test results of a 35-year-old man with hypersensitivity pneumonitis

| | September 1993 | | | June 1996 | | May 1997 | |
|---|----------------|----------|-------------|-----------|-------------|----------|-------------|
| | Predicted | Observed | % predicted | Observed | % predicted | Observed | % predicted |
| TLC (L) | 9.9 | 5.7 | 57 | 7.7 | 78 | 7.2 | 73 |
| Functional residual capacity (L) | 6.3 | 3.8 | 59 | 6.5 | 102 | 5.0 | 79 |
| VC (L) | 6.9 | 3.2 | 46 | 2.0 | 29 | 3.5 | 51 |
| Residual volume (L) | 3.0 | 2.5 | 84 | 5.7 | 192 | 3.7 | 124 |
| Residual capacity/TLC | 30.1 | 43.5 | 148 | 74.0 | 246 | 51.4 | 170 |
| FVC (L) | 6.9 | 3.1 | 44 | 2.0 | 29 | 3.5 | 51 |
| FEV ₁ (L) | 5.3 | 2.0 | 37 | 0.9 | 17 | 1.7 | 32 |
| FEV ₁ /FVC | 76.8 | 64.5 | 83 | 45.0 | 59 | 48.6 | 62 |
| Mean expiratory flow at 50% VC (L/s) | 6.9 | 1.3 | 19 | 0.4 | 6 | 0.8 | 12 |
| Mean expiratory flow at 25% VC (L/s) | 3.4 | 0.6 | 17 | 0.2 | 6 | 0.4 | 12 |
| Airway resistance (cm H ₂ O/L/s) | 0.7 | 2.4 | 227 | 2.9 | 448 | 2.0 | 238 |
| Dlco (mL/min/mmHg) | 28.8 | 18.3 | 56 | 12.2 | 42 | 17.7 | 54 |
| TLC (helium dilution) (L) | 9.9 | 5.7 | 58 | 4.6 | 47 | 5.9 | 60 |

Pulmonary function test results showing a mild to moderate combined obstructive-restrictive pattern with significant reduction in diffusing capacity and progressively worse air trapping from 1993 to 1996. The results from 1997 are after the termination of antigen exposure. Dlco Diffusion capacity of the lung for carbon monoxide; FEV₁ Forced expiratory volume in 1 s; FVC Forced vital capacity; TLC Total lung capacity; VC Vital capacity

been hospitalized for his disease for the previous five years and was maintained on prednisone 10 mg daily. He had been evaluated at another clinic three years earlier for similar complaints. His pulmonary function test results from that evaluation, which revealed a mixed obstructive and restrictive ventilatory defect, are shown in Table 1.

Over the six weeks preceding his initial visit to the clinic, his dyspnea had worsened and his weight loss progressed. His deterioration started after an upper respiratory tract infection. He had a dry cough, but denied any hemoptysis, anorexia, worsening arthralgias or new skin rashes. He had been treated with a 10-day course of clarithromycin with no change in his symptoms. He smoked a package of cigarettes daily, a habit that had continued for 19 years. His wife was also a smoker. He had two cats, a dog and a cockatiel, which he kept in his bedroom. Current medications were prednisone 10 mg daily, salbutamol and ipratropium bromide (one to two puffs of each as needed). His physical examination revealed a respiratory rate of 24 breaths/min, decreased breath sounds bilaterally, a prolonged forced expiratory time and diffuse wheezes. Late inspiratory crackles were audible over the anterior lung fields. A chest roentgenogram was unchanged compared with a film done three years previously, showing hyperinflation and left pleural thickening. His spirometry had deteriorated significantly, revealing a forced expiratory volume in 1 s of only 1.53 L (27% predicted).

His prednisone was increased to 30 mg daily, but he had trouble tolerating the higher dose and was intermittently non-compliant. Full pulmonary function testing performed six weeks after his initial visit revealed significant worsening of his airflow obstruction compared with three years previously (Table 1). There was associated gas trapping and a further reduction in his diffusion capacity. His condition deteriorated, and he was admitted to hospital one week later in respiratory distress requiring admission into intensive care. He

responded to 24 h of bilevel positive airway pressure therapy combined with parenteral steroids, antibiotics and nebulized bronchodilators. A ventilation-perfusion scan was indeterminate and Doppler studies of the legs were negative. All cultures were negative. A two-dimensional echocardiogram was suggestive of pulmonary hypertension with a right ventricular systolic pressure of 55 mmHg (assuming a right atrial pressure of 10 mmHg). Contiguous 8×11 mm contrast enhanced axial images of the chest and high resolution CT images of the lungs were obtained. The lung parenchyma was normal. There was no evidence of interstitial disease, pleural disease, or abnormalities of the trachea or major bronchi. Three days later, a second CT of the chest using inspiratory and expiratory cuts showed air trapping diffusely throughout the middle and lower lungs.

A definitive diagnosis had still not been established. There was no evidence of lung destruction consistent with emphysema. There was no interstitial or pleural disease, and no lymphadenopathy. Significant gas trapping was present, but not in a pattern consistent with bronchiolitis obliterans. Pulmonary hypertension was suggested by the echocardiogram. However, investigations were not consistent with recurrent pulmonary emboli. Given the patient's symptoms, as well as the evidence of significant air trapping with increasing total lung capacity and low diffusion capacity, the clinical suspicion of hypersensitivity pneumonitis was high, despite normal high resolution CT scans.

An open lung biopsy was performed in November 1996. Two specimens of the right lower lobe were submitted to pathology for assessment. A few hemorrhagic adhesions were seen on the pleural surface. Microscopically, the sections revealed patchy, predominantly chronic, interstitial inflammatory infiltrate with peribronchiolar accentuation (Figure 1). The majority of the inflammatory cells were lymphocytes, with occasional plasma cells and histiocytes. Rare, non-

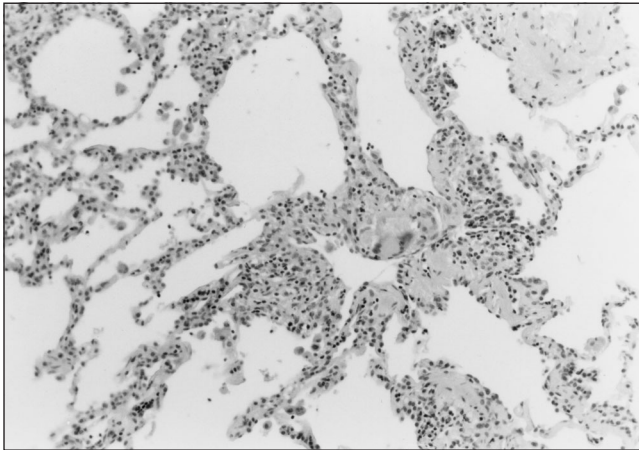


Figure 1) Open lung biopsy showing an interstitial, chronic inflammatory infiltrate with a loose, non-necrotizing granuloma in the wall of a small airway. (Hematoxylin and eosin stain, original magnification $\times 400$)

necrotizing granulomas were present, some of which were seen in small airway walls. These granulomas were composed of epithelioid histiocytes and multinucleated giant cells. There was minimal fibrosis and no evidence of vasculitis. The presence of cellular, chronic interstitial pneumonia with temporally uniform lymphocytic infiltrate, peribronchiolar accentuation, multiple non-necrotizing granulomas and minimal fibrosis was consistent with a diagnosis of hypersensitivity pneumonitis.

The antigen causing this condition was unclear. The patient did have a cockatiel at home, but it was uncertain whether this bird could produce enough antigen exposure to cause this reaction. Serum precipitins to cockatiel were positive. The patient subsequently removed the bird from his bedroom for a trial period. He experienced marked improvement in his sense of well-being and was able to climb stairs without limitation despite being on only 5 mg of prednisone daily. He later gave the bird away. After being free of this antigen exposure for one year, pulmonary function tests were repeated. They continued to show a combined restrictive and obstructive pattern with increased airway resistance but were significantly improved (Table 1); they have remained stable over the past 18 months. The patient is maintained on salmeterol 50 μg bid, fluticasone 250 μg bid and prednisone 1.25 mg daily. He has continued to abstain from smoking and convinced his wife to quit also. He no longer keeps a bird.

DISCUSSION

A symptomatic patient with two normal high resolution CT scans diagnosed with hypersensitivity pneumonitis on open lung biopsy is presented. Hypersensitivity pneumonitis refers to a spectrum of disease with three commonly recognized syndromes – acute, subacute and chronic. The diagnosis is suspected in a patient with respiratory symptoms and possible antigen exposure. Pulmonary function tests often reveal a restrictive or obstructive pattern with reduced diffu-

sion capacity. Serum precipitins are of minimal help to the diagnosis because they reflect exposure to a specific antigen, which may not be clinically relevant. Chest radiography is notoriously insensitive for the detection of hypersensitivity pneumonitis. Epler et al (1) found that 38% of patients with hypersensitivity pneumonitis had normal chest radiographs. This was supported by Remy-Jardin et al (2), who documented normal chest x-rays in seven of 21 patients with subacute disease and in one of 24 patients with chronic disease.

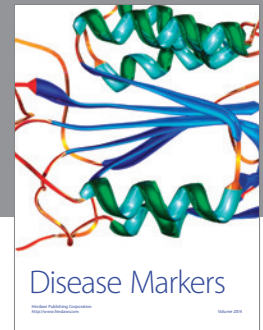
CT, especially high resolution CT scanning, is now playing a major role in diagnosing hypersensitivity pneumonitis. Many studies have examined the correlation between CT scan abnormalities and clinical disease, but such studies are limited by small numbers, a retrospective design, and the frequent absence of definitive diagnoses through transbronchial or open lung biopsy. The most common findings are ground glass attenuation – often bilateral and symmetrical – and nodules (2-6). A retrospective study by Hansell et al (7) of 22 patients with hypersensitivity pneumonitis (based on history, examination, chest x-ray, and positive serum precipitins or lung biopsy with consistent pathological features) supported the high frequency of such patterns, but interobserver agreement was poor. Decreased attenuation and mosaic perfusion was the most common finding in this study, with acceptable interobserver agreement (7). This serves to remind the clinician that subtle radiographic findings are subject to varied interpretation.

High resolution CT scans have been shown to be more sensitive than conventional CT scans. A study of diffuse infiltrative lung disease by Remy-Jardin et al (8) showed that 15% of micronodules were missed on conventional CT scans, and high resolution CT scanning was the only technique that allowed assessment of areas of ground glass attenuation. Only one study was found in which patients with hypersensitivity pneumonitis had normal CT scans (6). Hansell and Moskovic (6) examined the CT scans of 21 patients with hypersensitivity pneumonitis. Three patients had normal CT scans; however, these patients did not have any evidence of reduced gas transfer or a restrictive pattern on pulmonary function tests, and had only minimal symptoms (6). This is in contrast to our patient, who was symptomatic and had progressively worsening pulmonary function tests. Over time, his total lung capacity increased while his diffusion capacity decreased. When the high resolution CT scans of the chest were shown to be normal with no evidence of the anticipated emphysematous changes, clinical suspicion remained high. Open lung biopsy was pursued to reach the definitive diagnosis of hypersensitivity pneumonitis. Despite our patient's history of systemic lupus erythematosus, interstitial pneumonia with granulomatous features is not recognized as a pulmonary manifestation of this disease.

Undoubtedly, high resolution CT has a promising role in the diagnosis of hypersensitivity pneumonitis. However, as this report demonstrates, the technique is not infallible. When a high index of clinical suspicion is present in the face of normal scans, further investigation and biopsy are warranted to establish a correct diagnosis.

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