Ayurvedic Medicine and the Lung

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**Established Facts**

- Hypersensitivity pneumonitis (HP) is characterized by non-IgE-mediated immunologic reaction to inhaled allergen within the lung parenchyma, and the antigens responsible are bacteria, molds, yeasts or fowl. Uncommonly HP can be caused by drugs where radiological and histopathologic features are indistinguishable from immunologic reaction to inhaled organic antigens.

**Novel Insights**

- This is the first report of HP as a result of a consumed ayurvedic compound. Ayurveda is alternative medicine that is readily available and whose focus is on building a healthy metabolic system through herbal drug concoctions.

**Key Words**

Ayurvedic medicine · Hypersensitivity pneumonitis · Dyspnea · Cough

**Abstract**

A middle-aged Indian woman with knee pain had consumed ayurvedic medicine (Ostolief and Arthrella tablets) daily for 6 months. She presented to the respiratory clinic with worsening dyspnea, cough and weight loss of 2 months’ duration. She was a homemaker, never-smoker and did not keep birds. Physical examination detected fine end-inspiratory crackles. There was no clubbing of the fingers, joint deformity or swelling, skin lesion or enlarged cervical lymphadenopathy. High-resolution computed tomography showed diffuse centrilobular nodules with ground-glass attenuation. Restrictive ventilatory defect (FVC 44% predicted, FEV\textsubscript{1}/FVC ratio 93%) was observed on spirometry, and the autoimmune screen was negative. Bronchoalveolar lavage fluid revealed lymphocytosis with an increased CD4/CD8 (T helper:T suppressor) ratio. Cultures for bacteria, mycobacteria, fungi, viruses and *Pneumocystis carinii* were negative. Alveolitis with infiltration of interstitium by lymphocytes and peribronchiolar noncaseating granulomas were observed on bronchoscopic lung biopsy. A diagnosis of hypersensitivity pneumonitis as a result of ayurvedic medicine was made. She was advised to stop the offending medicine; high-dose steroids and bactrim prophylaxis were commenced and tapered over 3 months with good response and radiological resolution. She was followed for 1 year without relapse.

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A 52-year-old Indian woman was referred to the respiratory clinic for exertional dyspnea, productive cough and weight loss of 3 kg over 2 months. She had no fever but right knee pain for which she had been taking the ayurvedic compounds Ostolief and Arthrella for 4 months with some relief. She was a homemaker, a lifelong non-smoker with no recent overseas travel, she did not keep pets or birds at home, and she denied exposure to organic chemicals and hot water aerosols. She was afebrile, and there were finger clubbing and bilateral fine inspiratory crackles. No cervical lymphadenopathy or joint deformity was detected. The leukocyte count was raised to 12 × 10^9/l without eosinophilia; the erythrocyte sedimentation rate was elevated at 62 mm/h, and the rheumatoid factor was 10.4 U/ml (<10.3). The chest X-ray showed bilateral poorly defined nodular opacities, a restrictive ventilatory pattern on spirometry FEV₁ 1.11 liter (54% predicted), FVC 1.19 liter (44% predicted), FEV₁/FVC ratio (93% predicted), and diffuse centrifibular nodules on high-resolution computed tomography (HRCT) (fig. 1a–d). Bronchoalveolar lavage (BAL) revealed an inverse CD4/CD8 ratio of 0.4 (0.7–2.5), negative cultures for bacteria, mycobacteria, fungi, viruses and Pneumocystis carinii. Bronchoscopic lung biopsy confirmed alveolitis with lymphocytic infiltration of the interstitium and peribronchiolar noncaseating granulomas suggestive of hypersensitivity pneumonitis (HP). A diagnosis of ayurvedic-induced HP was made.

HP is a complex syndrome of varying intensity, clinical presentation and natural history. It is characterized by a non-IgE-mediated immunologic reaction to inhaled allergens within the lung parenchyma [1]. The antigens responsible are bacteria, molds, yeasts or fowl. Indirect exposure through a partner has also been shown to cause HP which can complicate the identification of the offending antigen. Uncommonly HP can be caused by drugs such as methotrexate, cyclophosphamide, mesalamine, fluoxetine, amitriptyline and paclitaxel where radiologic features of HP resulting from chronic antigen exposure without acute episodes or progressive disease may lead to chronic HP resulting from chronic antigen exposure without acute episodes [7]. A cluster analysis of a large group of HP patients has recently failed to identify acute, subacute and chronic categories of HP and has proposed only acute and chronic categories [8]. The main differential diagnosis of acute HP is lung infection. Differential diagnoses for chronic HP include idiopathic interstitial pneumonia and sarcoidosis. HP presents with inspiratory crackles more often than sarcoidosis (87% vs. 15%), while hilar and/or mediastinal lymphadenopathy is observed in sarcoidosis (46 vs. 2%). Granulomas are seen along the airways of HP in a perilymphangitic pattern in sarcoidosis. Laboratory tests are usually not useful for diagnosis as it is unclear whether false negatives result from inappropriate antigens tested or whether HP can occur in the absence...
ELISA is the preferred method for the determination of precipitins or total IgG antibodies. Inhalation challenge tests lack protocol standardization and are not recommended. Typical spirometry abnormality is a restrictive ventilatory pattern with low diffusing lung capacity for carbon monoxide. A mixed obstructive/restrictive pattern may be observed in patients with farmer’s lung due to emphysema [4].

HRCT may show diffuse airspace opacification or bilateral ground-glass attenuation in acute HP; it may show centrilobular nodules, lobular areas of decreased attenuation and vascularity on inspiratory images and air trapping on expiratory images in subacute HP, and interstitial fibrosis and honeycombing in chronic HP. However, lobular areas with decreased attenuation, centrilobular nodules and the absence of lower zone predominance differentiate chronic HP from idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia [9].

BAL lymphocytosis is mandatory but not specific. The CD4/CD8 ratio is usually reduced but can be increased to levels observed in sarcoidosis. Acute HP is characterized by bronchiolocentric lymphoplasmacytic infiltrate, fibrin deposition and neutrophilic infiltrates; subacute HP is...
characterized by bronchiolocentric pneumonitis with interstitial lymphoplasmacytic infiltrates, cellular bronchiolitis and small, loosely arranged granulomas, and chronic HP by fibrosis with honeycombing that is similar to usual interstitial pneumonia. A recent report suggests cathepsin K as a sensitive immunohistochemical marker for microgranulomas in HP [4, 8–10].

The cornerstone of therapy is antigen avoidance, and corticosteroids are recommended in severe cases or when the offending antigen cannot be completely removed. Inhaled steroids and pentoxifylline have been used in some studies and in lung transplantation for chronic fibrotic HP [4, 8]. The outcome of HP is highly variable but with appropriate management most cases of acute and subacute HP show an improvement or normalization of lung function. Our patient was advised to stop the ayurvedic medication. Daily oral prednisolone 60 mg (1 mg/kg/day) with co-trimoxazole prophylaxis against Pneumocystis jirovecii was commenced, and tapered over 3 months with a good response and complete radiological resolution. She was followed for 1 year without relapse (fig. 2). This is the first report of HP due to ayurvedic medication. Clinicians should maintain a high index of suspicion in patients with clinical and radiological features of interstitial lung disease, and a history of antigen exposure should be carefully elicited.

References