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Diagnostic challenges of hypersensitivity pneumonitis with autoimmune features: Dealing with more than a coincidence?

To the Editor,

Besides the well-known relationship between connective tissue diseases (CTDs) and several forms of interstitial lung disease (ILD), the recognition of autoimmune features in idiopathic interstitial pneumonias led to the establishment of the IPAF (interstitial pneumonia with autoimmune features) denomination and classification criteria in 2015.[1]

Hypersensitivity pneumonitis (HP) and several CTDs share T cell dysregulation, suggesting a greater likelihood of autoimmune disease in HP patients. A previous study of a cohort of chronic, fibrotic HP patients found that fifteen percent of these patients revealed either the presence of a defined CTD or some autoimmune features suggestive of CTD. These patients were identified as having ''HP with autoimmune features'' (HPAF) and seemed to have a worse survival rate than non-HPAF HP patients.[2]

We report a case of a 72-year old man who is followed as a Pulmonology outpatient due to obstructive sleep apnea syndrome, under home continuous positive airway pressure (CPAP) therapy, chronic obstructive pulmonary disease with mild centrilobular emphysema and mediastinal lymph node enlargement. Inhalation exposure is relevant due to former smoking habits (thirty pack-years), close contact with birds in the backyard, occasional use of sauna and Turkish Baths. As for past medical history, the patient also has arterial hypertension, dyslipidemia, unknown chronic liver disease and a previous rheumatological diagnosis of psoriatic arthritis, currently without directed therapy; a previous hospital admission happened due to community-acquired pneumonia. Chronic medications are an association of two anti-hypertensive drugs and atorvastatin.

Follow-up chest high-resolution CT scans showed progressive, unspecific, peripheral lower lung lobes intralobular reticulation (Fig. 1), as well as lymph node enlargement (14 mm) in the left paratracheal station (4L). Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) was performed; the 4L station was identified and sampled and its cytological analysis was unremarkable.

Meanwhile, the patient reported worsening exertional dyspnea. Body plethysmography identified a mild obstructive ventilatory defect: FEV1/VC ratio equal to 64.2% and FEV1 equal to 2.41 L (86% of the predicted value). There was no lung diffusion impairment. Fibreoptic bronchoscopy with bronchoalveolar lavage (BAL) in the middle

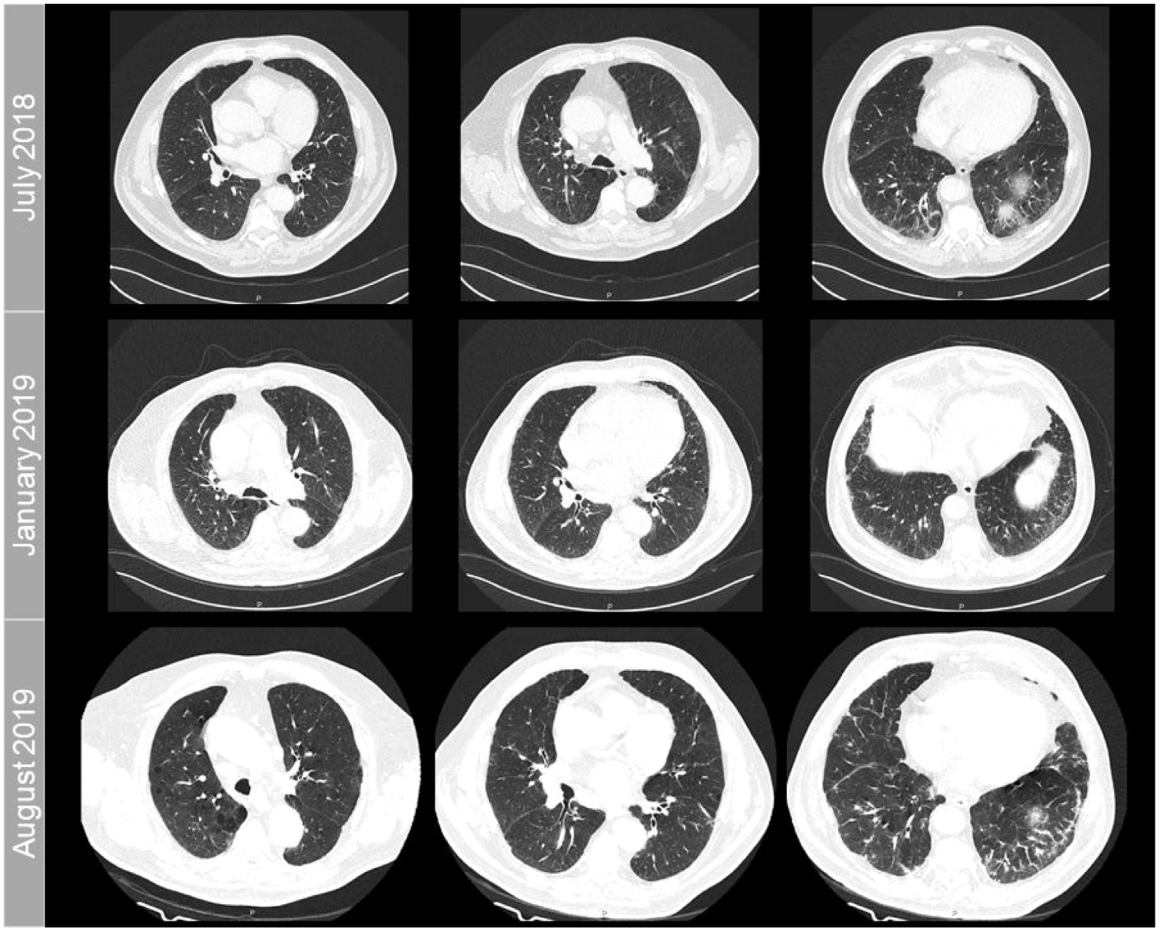

Figure 1 Follow-up chest CT scan axial images showing progressive, unspecific peripheral intralobular reticulation in the lower lung lobes. The time when the scans were performed is indicated on the left of each row of images. For comparative purposes, the images in each column correspond to identical axial planes.

lobe was performed. BAL fluid cellular analysis showed a normal total cell count, an intense lymphocytic alveolitis (55.6%) and a CD4/CD8 ratio of 1.87; bronchial wash and BAL were negative for malignant cells or microbiological agents. Serum immunological study was positive for anti-nuclear antibodies (1/1000 titer, speckled pattern).

The decision to perform transbronchial lung cryobiopsy (TBLC) was made in ILD interdisciplinary meeting for diagnostic clarification. Histological analysis of three samples from the right lower lobe showed features suggestive of both HP and autoimmunity (Fig. 2).

A working diagnosis of HPAF was established in an ILD multidisciplinary meeting.

This case report shows the diagnostic challenges of HPAF. It is still unclear whether autoimmune features in HP are a distinct HP clinical phenotype or an unrelated finding. However, we think that both HPAF and non-HPAF HP patients deserve further study in future prospective studies, specifically regarding immunosuppressive therapy outcomes.

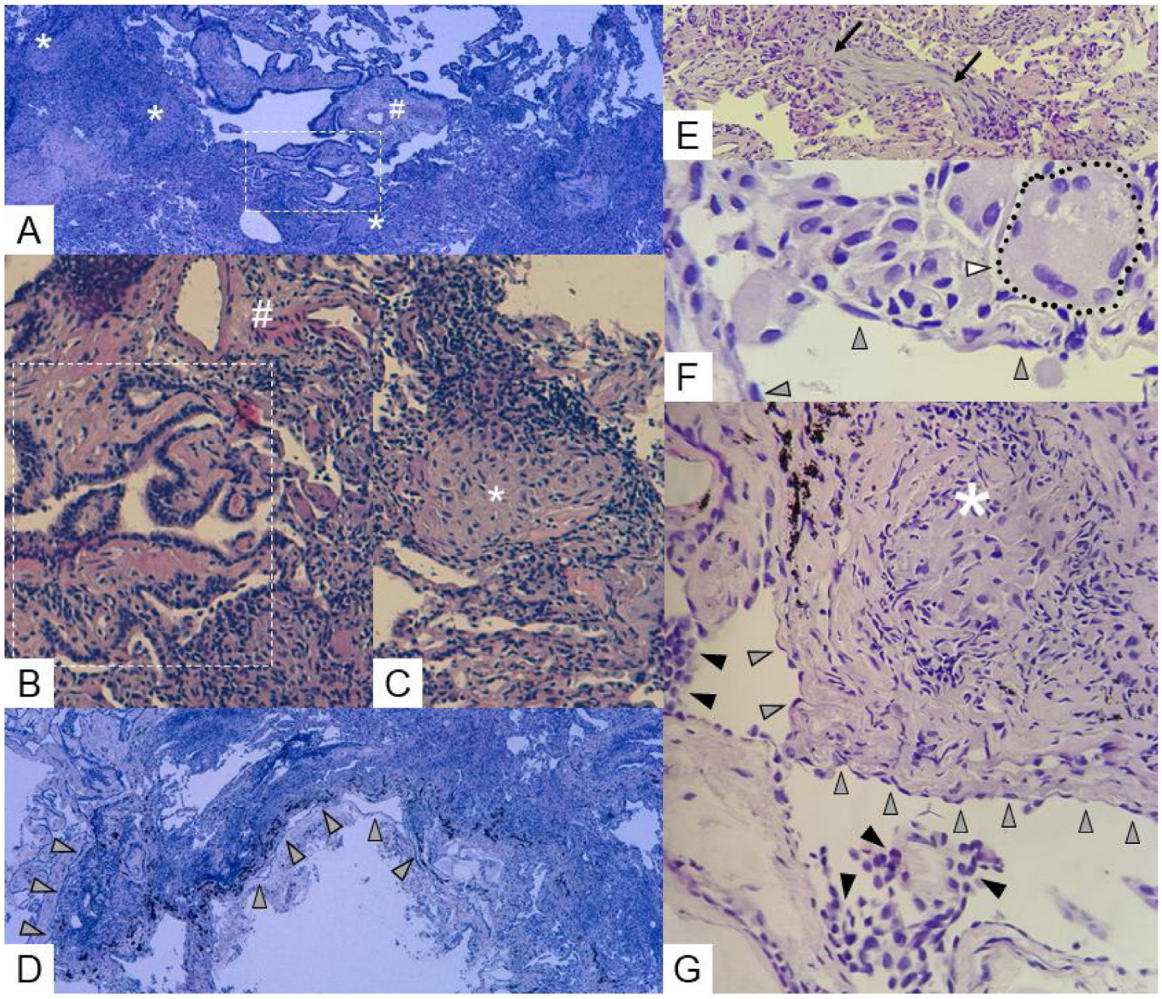

Figure 2 TBLC histopathology findings in HPAF. There are expressive peribronchiolar and subpleural changes, typical of HP and CTDs, respectively.
(A) A prominent, dense interstitial chronic inflammatory infiltrate without lymphoid follicles with a predominantly bronchiolocentric distribution is seen. There are extensive lesions of peribronchiolar metaplasia (white - - - - -) and loose aggregates of epithelioid histiocytes – epithelioid granulomas (white *). A centrilobular region is marked with white # – hematoxylin and eosin (H&E) staining, 40× magnification.
(B) Detail of a lesion of peribronchiolar metaplasia (white - - - - -), adjacent to the centrilobular region (white #) – H&E staining, 200× magnification.
(C) Detail of an epithelioid granuloma (white *) – H&E staining, 200× magnification.
(D) A moderate cellular chronic inflammatory infiltrate, extensively involving subpleural areas (▶), as well as alveolar septa, is also seen – H&E staining, 40× magnification.
(E) Detail of organizing pneumonia lesion (→) – H&E staining, 200× magnification.
(F) Detail of a multinucleated giant cell (▷and ●●●●●●●) adjacent to the visceral pleura (▶) – H&E staining, 400× magnification.
(G) Detail of a pleura-centered epithelioid granuloma (white *) and focal mesothelial reactivity (▶) interspersed with normal pleural mesothelium (▶) – H&E staining, 200× magnification.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Juvenile dermatomyositis and pneumomediastinum: a case of a very rare complication

Dear Editor,

Juvenile Dermatomyositis (JDM) is a systemic autoimmune myopathy that affects mostly the muscles and skin. It usually manifests with nonspecific systemic signs preceding typical symptoms of the disease mainly symmetrical proximal muscular weakness and pathognomonic skin lesions, i.e. heliotrope and Gottron papules. Idiopathic inflammatory myopathies are rare in the pediatric group of which the most prevalent is JDM.[1] Spontaneous pneumomediastinum (PNM) associated with Dermatomyositis (DM) is even rarer, with 81 cases reported overall,[2] 2 of those in children.[3,4]

We report the case of a 10 year-old caucasian boy, who presented to the emergency room with an eight-month history of fever, photosensitivity, cutaneous lesions on hands and face, arthralgia, proximal muscular weakness, significant weight loss (10 kg), dyspnea on minimal exertion and dysphonia. The patient was previously healthy, with no personal history of pulmonary disease or tuberculosis. Initial physical examination showed tachycardia, tachypnea, decreased breath sounds at pulmonary bases and diffuse crepitations. He also had heliotrope and Gottron's papules (on the hands, elbows and knees), malar rash, Raynaud's phenomenon, and arthritis in the 3rd right proximal interphalangeal joint (Fig. 1). The Childhood Myositis Assessment Scale(CMAS) score (which assesses the patient's overall muscular strength, with a maximum score of 52) was 15. Laboratory work-up showed elevated muscle enzymes (creatine phosphokinase and aspartate aminotransferase), negative anti-nuclear antibody, negative antibodies to extractable nuclear antigens (ENA), negative double-stranded native DNA and negative anti-neutrophil cytoplasm antibody (ANCA). Specific myositis antibodies were unavailable for testing. Based on the presumed diagnosis of JDM, he received intravenous pulse of methylprednisolone and subcutaneous methotrexate. On the first day of hospitalization, the patient suddenly developed cough, worsened respiratory distress and palpable cervical emphysema. An urgent computed tomography scan showed bilateral mild pneumothorax, extensive PNM with subcutaneous emphysema and bilateral pulmonary consolidations, more prominent in bases, associated with ground-glass attenuation areas (Fig. 2). Treatment was with conservative, as well as broad spectrum antibiotics due to impossibility of exclude infection, but respiratory distress worsened at day fifteen. Intravenous immunoglobulin was administered, with no response, and he also started sulfamethoxazole + trimethoprim due to leukopenia. The patient was submitted to orotracheal intubation and drainage of PNM, with no significant improvement. By this time, pneumothorax had improved just with conservative measures. However, despite mechanical ventilation support and management of shock the refractory hypoxemia continued and he died after 23 days of hospitalization.

Although JDM affects primarily the muscles and skin, it can involve many tissues and organs, including the lungs.[2,5–7] Lung disease can present as aspiration pneumonia, interstitial lung disease (ILD) or respiratory muscle weakness.[5] There are limited data regarding the occurrence of PNM in JDM due to its rarity; its frequency in adults with inflammatory myopathies varies in the literature, but the largest cohort reported a prevalence of 2.2 %.[5] Risk factors for the occurrence of PNM in DM are: history of ILD, early age of onset (below twenty years old), cutaneous vasculopathy, normal or slightly increased levels of muscle enzymes (amyopathic dermatomyositis), previous use of glucocorticoids and the presence of anti-MDA5[2]. There is no data for risk factors in JDM. The findings on his CT-scan were also suggestive of ILD, although infection was an important differential diagnosis. The main risk factor for DM-associated PNM is the presence of ILD, with a prevalence of 10–43 %