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Case reports

# An unexpected effect of teleworking: acute clinical manifestations of a hypersensitivity pneumonitis to home parrots

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## Abstract

Hypersensitivity pneumonitis (HP) is a complex inflammatory and/or fibrotic immune-mediated disease that involves lung parenchyma and small airways caused by an inhaled antigen in susceptible individuals. It is currently the third most frequent interstitial lung disease (ILD) after idiopathic pulmonary fibrosis (IPF) and connective tissue disease with ILD. Diagnosis of HP is often challenging as identifying a causative agent is one of the main arguments in diagnosis along with specific serum IgG testing, suggestive HRCT and/or BAL, and in some cases histopathological findings. However, in up to 60 % of cases, exposure is not identified despite a thorough exposure history. HP is more frequent associated with occupational exposures, up to 20%, but non-occupational environmental exposure remains an important cause. We present a case of bird fancier's lung that illustrates the challenges and the importance of identifying the culprit antigen as the elimination of exposure in combination with corticosteroids can lead to improvement in lung function, symptoms and leads to a better prognosis and may stop of evolving in sever fibrotic forms of HP.

**Keywords**: *hypersensitivity pneumonitis, interstitial lung disease, occupational lung disease*

## Introduction

Hypersensitivity pneumonitis (HP), previously known as extrinsic allergic alveolitis is an inflammatory and/or fibrotic disease affecting the lung parenchyma and small airways caused by a complex immune-mediated reaction induced by an inhaled antigen in susceptible individuals [1, 2]. Currently new guidelines switch from the classic clinical classification of HP in acute, subacute, and chronic form to non-fibrotic or fibrotic HP, considering that histopathological and imaging signs of fibrosis are the primary determinant of prognosis [1, 3, 4, 5]. Diagnosis of HP can be challenging and requires a thorough occupational and environmental exposure history, multidisciplinary discussion of clinical and radiologic data, assessment of bronchoalveolar lavage lymphocytosis and in some cases histopathologic findings [1, 3]. Although identifying a culprit exposure is one of the pillars in diagnosis of HP, cryptogenic cases are frequently reported, missing or incomplete exposure histories leading to misclassification.

## Case report

A 41-year-old non-smoking female presented in our clinic in March 2020, complaining of progressively worsening dyspnea, easy fatigability for small exertion, non-productive cough for the last 4 weeks. She mentioned that she had been having flu-like symptoms with fever, cough and runny nose for 2 days in the beginning.

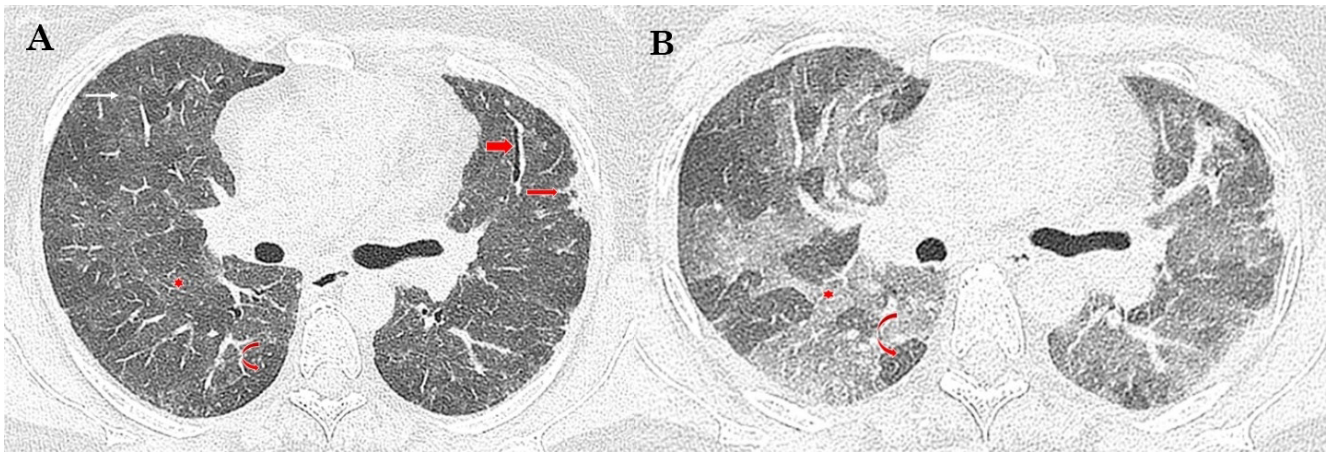
She had no family history, no relevant illnesses and no known allergies. She was not on medication.

The occupational history was unremarkable for antigen exposure. She had been working in an office as an economist for the last 17 years. Her office is located in a building apparently with proper maintenance and she did not report any symptoms at work or after the working hours. Even more, at the moment the symptoms began she was working from home since the first lock-down due to the COVID pandemic. During the pandemic and teleworking she started to make bread in her leisure time using flour 2-3 times a week in the last 3 months. She constantly had a pair of parrots since childhood, but no other relevant environmental or occupational exposures.

On physical examination the patient was alert, temporo-spatially oriented, with a BMI of 33.1 kg/m2, afebrile, a respiratory rate of 18 cpm, blood pressure of 150/80 mm Hg, heart rate of 120 bpm and pulse oximetry 94% on room air. The pulmonary auscultation revealed a slight overall decrease of vesicular murmur and bilateral basilar crackles. The cardiac auscultation and abdominal examination showed no pathological changes. She had no palpable lymphadenopathy or peripheral edema, and the remaining physical examination was normal.

The chest high resolution computed tomography (HRCT) revealed diffuse mosaic attenuation of the lung parenchyma, with better delineation of the low-density areas in the expiratory phase suggestive of air-trapping. Some areas showed patchy ground-glass opacities alternating with normal lung and air-trapping, findings consistent with "three-density pattern" (or "headcheese" sign). Also, there are pleural thickening, interstitial reticulation, septal thickening with consecutive mild traction bronchiectasis in the subpleural regions (Figure 1). Other findings were enlarged mediastinal lymph nodes and a small hiatal gastric hernia.

**Figure 1.** Three-density pattern. HRCT (A) inspiratory and (B) expiratory images showing the three different densities: high attenuation/ground glass opacity (red star), lucent lung (areas of decreased attenuation) (curved red arrow) and normal lung (white arrow), demarcated from each other. Interstitial reticulation (thin red arrow). Traction bronchiectasis in (A) (thick red arrow).




A proper 6-minute walk test (6MWT) could not be performed as the patient oxygenation level dropped from 94% in ambient air to 84% after a 50 m walk.

Pulmonary-function tests (PFT) indicated severe restriction with vital capacity (VC) 39% of predicted values and low-value total lung capacity (TLC). Technical considerations impeded measurement of diffusing capacity of carbon monoxide (DLCO) (Table 1).

Blood tests revealed moderate inflammatory syndrome with ESR 70 mm/h, Fibrinogen 586 mg/dL, thrombocytosis 454* 103/μL. Also, urinalysis, antinuclear (ANA), anti-Sm, anti-Ro52, anti-SCL 70, anti-Jo1, anti-dsDNA antibodies, cANCA, pANCA, C3, C4 were within normal range. Serum angiotensin-converting enzyme (ACS) was normal, 19.7 u/L. Bronchoscopy revealed diffuse bilateral bronchitic pattern.

**Table 1.** Dynamics of pulmonary function tests over time

| Date | TLC (L) | % of predicted | RV (L) | % of predicted | FVC (L) | % of predicted | FEV1 (L) | % of predicted | FEV1/FVC % | DLCO (ml/min/kPa ) | % of predicted |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Diagnosis** | 2,94 | 59 | 1,64 | 102,1 | 1,16 | 25,6 | 1,05 | 37,2 | 89,96 | - | - |
| **3 months** | 3,62 | 72,8 | 1,38 | 85,8 | 2,2 | 67,4 | 1,87 | 66,5 | 85 | - | - |
| **1 year and 3 months** | 3,68 | 74 | 1,42 | 87 | 2,18 | 65 | 1,89 | 67 | 83 | 4,59 | 53 |

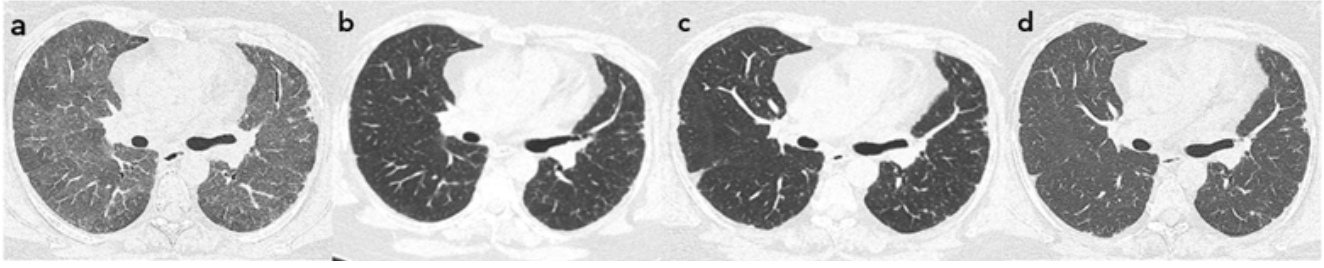
The bronchioloalveolar lavage (BAL) performed in the left lower lobe showed 74.2% lymphocytes with sub unitary CD4+/CD8+ lymphocyte ratio (0.82), 17.8% macrophages, 7% granulocytes of which 2.6% neutrophils, 4.4% eosinophils, 1% mastocytes. No tumoral cells were present. Microscopic exam and cultures were negative for TB and other pathogens.

Taking into account clinical presentation, non-specific inflammatory syndrome, HRCT findings and BAL lymphocytosis with sub unitary CD4+/CD8+ ratio and the fact that an infectious disease, sarcoidosis, and an interstitial lung disease associated connective tissue disease (CTD-ILD) was excluded the diagnosis of hypersensitivity pneumonitis was made. The culprit exposure was yet to be determined between the parrots and the flour. As HRCT was typical for fibrotic HP (mixed inflammatory plus fibrotic) it was reasonable to consider exposure to parrots, but at the same time acute onset of symptomatology and recent exposure to flour, although less frequent that bird fancier's lung (BFL), was also a possible cause. We recommended an extensive serum IgG testing against: Aspergillus, fungi mixture (Gmx6), wheat flour (G f4), Micropolysora faeni (Gm51) and protein serum, droppings, serum, and feathers of parrots (Ge92).

Corticosteroid (CS) treatment was initiated starting with 32 mg per day of methylprednisolone for one month with subsequent decrease to 24 mg/day for another month, then 16 mg until re-evaluation, treatment with pomp inhibitors and Ca+ d3 was also added. We also advised her to avoid exposure to flour and parrots.

Upon 3 months, at reevaluation, she stopped using flour, and was clinically much better under treatment, with dyspnea for moderate exertion, 98% oxygenation in ambient air and decrease to 81% after moderate effort, without crackles at auscultation. PFT revealed moderate restriction with vital capacity (VC) 67.4% of predicted but with improvement by over 800ml in FEV1 and 1L in FVC (Table 1). HRCT showed marked improvement with small areas of "ground glass" remaining and persistent subpleural interstitial thickenings (Figure 2). She did not make specific IgG testing recommended and she still has the pair of parrots. We continued (CS) treatment with constant dose reduction.

**Figure 2.** HRCT in time: at diagnosis (a), after 3 (b) and 6 months (c) of corticosteroid treatment, at 1 year and 3 months (d)



At reevaluation at 6 months from diagnosis patient is asymptomatic, desaturates from 98% in ambient air to 86% after 4 floors, has normal clinical exam, HRCT unchanged compared to previous examination (Figure 2) and she is still on 8 mg per day of methylprednisolone that "helped" her gain 20 kg since she started CS treatment. We decided to lower the dose at 4 mg per day and revise her evolution after 3 months. That never happened as the patient showed after 9 months (at 1 year and 3 months since he was diagnosed) with the reappearance of symptoms: dyspnea for moderate exertion, dry cough, without crackles, recurrence of inflammatory syndrome (ESR 70 mm/h), leukocytosis (13.76 * 103/μL) and thrombocytosis (448* 103/μL). PFT were comparable with previous testing and DLCO was 53% of predicted (Table 1). At 6MWT covered 400 m with significant desaturation from 99% ambient air at rest to 87% with dyspnea on the Borg scale from 0 initial to 3 final and HRCT with minimal areas of "ground glass" basal bilateral, micronodular infiltrations and diffuse pulmonary subpleural reticulation (Figure 2). The relapsing presentation suggested that the etiologic agent might be the exposure to parrots or another unidentified antigen.

She finally managed to dose IgG recommended with positive result only for protein serum, droppings, serum, and feathers of parrots (62.6 mg/l). Also, she remembered that similar symptomatology occurred 10 years ago when she received corticosteroid therapy with remission of symptoms. This might exclude the contribution of the flour antigens to the exacerbation of a chronic fibrotic form due to exposure to parrot allergens. However, as the exposure to flour was interrupted several months before, we cannot completely exclude this possibility, as the titer of antibodies drops after exposure cessation. Another perspective of the exacerbation is the teleworking effect, which have for sure contributed to a higher duration of exposure to the allergens she was already sensitized. We reintroduced low dose of CS (8 mg of methylprednisolone) for 3 months with good clinical evolution with remission of symptoms. She renounced at parrots and it is currently without treatment and symptoms free.

## Discussion

HP is currently the third most frequent ILD after idiopathic pulmonary fibrosis (IPF) and connective tissue disease-related interstitial lung disease (CTD-ILD) (2). Due to the nonspecific findings on presentation and the overlap of these findings with other interstitial lung diseases (ILDs), exposure history remains an important element for HP diagnosis. We present this case in an occupational medicine journal because both suspected antigens (avian and flour) to which this patient was exposed are frequent in HP. Therefore, the occupational anamnesis should always include the environmental exposure for a proper diagnosis. Sometimes, as in our case, the past exposure is more relevant than the current exposure.

A large variety of antigens, more than 300 that span over a wide range of occupations, had been incriminated as cause for HP [6]. Inciting antigens can be broadly classified into bacteria, fungi, animal proteins, plant proteins, low molecular weight chemicals, and metals [1, 3, 6,]. Although is estimated that 12–28% of HP cases are directly attributable to workplace exposures, of which the most common is farming, exposure can be household related or recreational [2]. Reportedly in up to 60% of cases, a trigger is not identified [6]. The most commonly implicated exposures are birds (up to 30% of HP cohorts) from feather dust (bloom), droppings and serum, most commonly derived from pigeons, budgerigars (parakeets), cockatiels, parrots, canaries, and duck and goose down products [2], followed by specific exposures in the farm environment, home or domestic fungal or bacterial contamination, occupational metalwork fluid exposure and mushroom spores, respectively [2, 7].

Only in a small proportion of people who are exposed to these antigens develop HP due to genetic susceptibility determined by polymorphisms of the major histocompatibility complex (MHC) Class II molecules [1, 6]. Although the relationship between the clinical course and factors related to exposure such as concentration of the agent, duration and frequency of exposure, particle conformation is observed, it is far from being elucidated [1].

HP typically presents with cough, dyspnea. Constitutional symptoms, such as fever, chills, weight loss, and malaise may be present. The presentation symptoms may be acute (days to weeks), insidious (months to years), or recurrent [8]. While an acute presentation with or without constitutional symptoms seems more consistent with nonfibrotic HP and the insidious presentation seems more consistent with fibrotic HP, the pattern of symptom onset has not been rigorously evaluated with respect to fibrosis status [8] Furthermore, some patients with chronic HP may develop acute worsening of their respiratory condition as seen in our case.

A positive IgG antibody against specific antigens only

indicates that the patient has likely been exposed to a potential cause of HP at some point in his or her life and does not confirm diagnosis [2, 6]. Furthermore, these tests have very high false-negative rates and the specific antigen may not be represented in the testing panel. It may be desirable to consider exploring the source of the potential causative agent in the patient's domestic, social, and/or work environment before assignment of a diagnosis of HP, particularly when other diagnostic findings of HP are less certain (e.g., no BAL lymphocytosis, probable or indeterminate CT or biopsy patterns) [1].

The presence and the extent of fibrotic changes are of major importance, as the extent of pulmonary fibrosis has been shown to positively correlate with increased mortality in patients with HP. Therefore, HRCT examination in both inspiratory and expiratory phase is important in subsequent classification in fibrotic HP (i.e., mixed inflammatory plus fibrotic or purely fibrotic) or nonfibrotic HP (i.e., purely inflammatory) [1, 9]. "Head cheese" sign or "three-density pattern" is considered to be highly specific reflecting both the infiltrative (ground glass opacities) and obstructive (air trapping) elements of HP, being an useful tool in diagnostic process [1, 9].

Bronchoalveolar lavage (BAL) is the most sensitive test in identifying the alveolitis in patients suspected of having HP. In ATS/JRS/ALAT HP guidelines, an expert panel agreed that 30% BAL fluid lymphocytosis was a reasonable threshold for distinguishing between HP and IPF or sarcoidosis [1].

The evolution of lung damage and irreversible disease process in HP is characterized by chronic and persistent antigen exposure. The length and degree of antigenic exposure is directly related to disease progression. Continuous antigen exposure increases the risk for fibrotic development [10]. Bird Fancier's lung has been found to progress more often to severe chronic forms than other forms of HP, such as farmer's lung, which can improve spontaneously [8].

Wherever possible, the inciting antigen should be avoided. Patients with HP should be regularly monitored to assess for progression as the progressive forms of HP may benefit from recently approved antifibrotic drug. Immunosuppression is commonly used in the treatment of HP being useful in nonfibrotic forms of HP, but has not been shown to slow the progression of fibrotic disease [11]. Early recognition and control of the culprit agent is the only effective intervention that can stop this chronic evolution. Thus, a comprehensive patient history to identify potential exposures associated with HP is an essential part of the clinical assessment.

## Conclusion

The diagnostic of HP can be challenging as is the result of a combination of antigen finding with or without serum precipitins (IgG antibodies), suggestive HRCT, laboratory findings (non specific inflammatory syndrome), compatible LBA, and clinical presentation. Classical occupational antigens for occupational HP could be encountered in the home environment and teleworking could exacerbate the clinical evolution.

Clinical course is highly variable and prompt diagnosis and antigen avoidance is key to management together with CS treatment that hasten recovery.

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