Pneumonia

Hypersensitivity pneumonitis in a teenager

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Abstract

English:

Hypersensitivity pneumonitis (HP) is an interstitial lung disease (ILD), consequence of an alveolar allergic reaction against various inhaled allergens occurring in susceptible individuals, manifesting as an acute or chronic granulomatous alveolar allergic process against inflammation of the lung parenchyma. The clinical presentation can mimic acute respiratory infections (in acute form) or an idiopathic ILD (in chronic form); the diagnosis of HP is difficult if the exposure to allergen is not suspected.

We present the case of a male teenager, pigeon breeder, presenting with recurrent episodes of dyspnoea and fever, initially considered and treated as pneumonia. The diagnosis of HP was based on suggestive imaging changes, lymphocytic alveolitis at bronchoalveolar lavage with a low CD4/CD8 ratio and a thorough anamnesis for exposure and positive IgG serum precipitins against pigeon debris. The patient improved over a few months only by avoiding exposure to the incriminated allergen. ILDs in children and adolescents are considered rare diseases, with HP being one of the possible causes in older children and adolescents.

Keywords

hypersensitivity pneumonitis • pigeon breeder’s disease • interstitial lung diseases in children

Pneumonită de hipersensibilitate la un adolescent

Rezumat

Romanian:

Pneumonita de hipersensibilitate (PH) este o pneumopatie interstițială difuză, consecință a unei reacții alergice alveolare față de diferiți alergeni inhalați, ce apare la indivizii susceptibili și se manifestă ca o inflamație granulomatoasă acută sau cronică a parenchimului pulmonar. Manifestarea clinică poate模拟 infecția respiratorii (în forma acută) sau o pneumopatie interstițială difuză idiopatică (în forma cronică), diagnosticul de PH fiind dificil dacă nu se suspectează o expunere la pneumalergeni.

Prezentăm cazul unui adolescent, crescător de porumbei, care s-a prezentat pentru episoade recurente de dispnee și febră, considerate și tratate inițial ca pneumonie. Diagnosticul de PH s-a bazat pe modificările imagistice sugestive, alveolita limfocitară la lavajul bronhoalveolar cu raport CD4/CD8 scăzut, o anamneză de expunere amănunțită și serologia pozitivă pentru precipitine IgG împotriva dejectelor de porumbei. Starea pacientului s-a ameliorat în câteva luni prin simplu întrerupere a expunerii la alergenii incriminați. Pneumopatiile interstițiale difuze la copii sunt considerate câteva boli rare, PH fiind una dintre etiologiele posibile la copii mari și adolescenți.

Cuvinte-cheie

pneumonită de hipersensibilitate • boala crescătorilor de păsări • pneumopatii interstițiale difuze la copii

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Introduction

Interstitial lung diseases (ILDs) are a group of more than 200 diseases with various etiologies, which share the diffuse involvement of the lung parenchyma but have different evolutions according to their aetiology: fibrotic or remissive. ILDs are rare diseases in adults and extremely rare diseases in children, where the aetiology varies depending on age. For the children younger than 2 years of age, the manifestations of genetic mutations, especially the ones that alter the genes for the surfactant proteins, are more frequent. In contrast, in the children older than two years of age, hypersensitivity pneumonitis (HP) and other exposures are the most prevalent causes.

HP, also known as extrinsic allergic alveolitis, represents a lung inflammatory syndrome (1) caused by an allergic reaction triggered by repeated exposure to a great variety of aerosoles and small organic particles (<5 µm) capable to reach the alveoli (2,3).

From the diagnostic point of view, HP represents a challenge because it needs a high clinical suspicion, the identification of exposure to an inhaled allergen and the integration of imaging, bronchoalveolar lavage findings, identification of serum precipitins and, sometimes, lung biopsy (2). Because of the evolution to irreversible lung involvement (3), the treatment principles include the cessation of the antigen exposure and, in severe cases, association of pharmacological treatment (4).

Case presentation

A 16-year-old male patient, recreational breeder of 70 pigeons, presented moderate exercise dyspnoea, productive cough with mucous-purulent sputum and episodes of acute dyspnoea, symptoms that started two and a half months before. Previously, he was admitted twice in a county hospital from his residence area with the suspicion of bacterial pneumonia. In both cases, he received antibiotic treatment, with short-term improvement of symptoms, only during the hospitalization period. Because of the persistence of the symptoms, he presented in our clinic, where several additional investigations were performed, to assess the aetiology: chest radiography, CT scan, lung function tests and bronchoscopy with bronchoalveolar lavage (BAL).

a) Chest radiography showed discrete bilateral interstitial reticular and nodular changes (Figure 1).

b) CT scan identified diffuse, bilateral, ground-glass opacification, with poorly delimited nodules (ground-glass nodules) – distributed and diffused craniocaudally and predominant in the central-lung zones, more suggestive for an inflammatory cause rather than a fibrotic one (Figures 2–6). The CT scan was performed in an outpatient clinic before the patient’s presentation, with 5 mm slices, and it was not repeated with thin slices (HRCT) to avoid an undue high radiation exposure in a young patient.

c) The results of the lung function tests showed:

• an insignificant decline in the oxygen saturation from 97% to 96%, but patient could walk for only 450 m (57% of the predicted value) (six-minute walk test);

• mild restriction (vital capacity of 2.94 l – 74% of the predicted value, forced expiratory volume in one second of 2.21 l – 68% of the predicted value, with an FEV1/FVC ratio of 91.89%) and a normal total lung capacity (spirometry) and

• moderate decreased alveolar–capillary diffusion (4.79 l – 56.2% of the predicted value).

d) Moreover, sputum bacteriologic examination was negative for tuberculosis.

e) BAL from the medium lobe bronchus recovered 100 ml from 120 ml instilated and showed a significant hypercellularity: 57.4 × 10⁶ cells (normally, for non-smokers, less than 13 × 10⁶ cells). The differential cytology identified a lymphocytic alveolitis: macrophages 15.0% (normally >84%), lymphocytes 74.2% (normally <13%), granulocytes

Figure 1. Chest X-ray at presentation.
Figure 2–6. CT scan images showing ground-glass opacities with craniocaudal distribution and fine micronodules ("ground-glass" nodules).
10.4% (normally <3%), neutrophils 9.8% (normally <3%),
ev eosinophils 0.6% (normally <0.5%) and mastocytes 0.4% (normally <0.5%). It should be mentioned that the increased
neutrophils percent is eclipsed by the overwhelming
lymphocytosis of 74.2%, which is also associated with
the presence of mastocytes and plasmocytes in the BAL
fluid. The analysis of the immunological cellular markers
evidentiated a CD4/CD8 ratio of 0.5 (normally 1.1–3.5),
significantly decreased (less than 1). Moreover, cytology
did not show any cancer cells, and Ziehl–Neelsen staining
was negative for acid-fast bacilli. The BAL result is
suggestive of HP.

From the medical history and investigations, the suspected
diagnosis was HP. In order to confirm it, serum tests for IgG
antibodies were performed, which returned positive against
pigeon allergens.
The patient was discharged with the recommendation to
cease the exposure to pigeons, with no medical treatment,
considering the moderate symptoms and alteration of lung
function tests.
At one month follow-up, the evolution was spontaneously
favourable, with resolution of exercise dyspnoea and
normalisation of chest radiography and lung function tests.

Discussion

HP, despite its name, is not an atopic condition, because it
does not associate eosinophilia or increase in the IgE level.
HP is determined by repeated exposure to a multitude of
inhaled particles in the domiciliary, professional or ambient
environment – the majority are organic particles, but there
is cited HP after exposure to a great variety of professional
dusts, including metallic particle exposure (5).
The most frequent incriminated pneumo-allergens are the
aviary proteins (a mixture of debris of feathers and droppings),
fungi and thermophilic actinomycetes (such as the ones
found in the hay for animals or in the air conditioner devices
and also in bathrooms, sauna or swimming pools) (5).
Repetitive exposure in susceptible individuals can generate
an IgG-mediated allergic reaction, which can determine
immunopathological response in the lung parenchyma (2).
Classically, an acute, a subacute and a chronic form are
described (5), which, usually, overlap, because it is not
certain yet if they represent different stages of the disease
(2) or if they are outdated criteria (6). The acute form appears
in episodes, connected with a peak of exposure to inhaled
allergens – because it is reported that it is much more probable
that the sensitization would be produced by a mixture rather
than by a single agent (6), with clinical manifestations similar
to an acute respiratory infection (fever, cough, dyspnoea and
radiologic changes, which can be easily confounded with
an infectious pneumonia). Frequently, the patients receive
antibiotic therapy, with improvement, especially because of
the temporary cessation of the exposure, as in the case of
our patient. The recurrence of the episodes should elicit the
suspicion of another aetiology.

Chronic HP has a clinic, functional and imagistic aspect that is
much more similar to chronic interstitial pneumonias, especially
with idiopathic pulmonary fibrosis (6,7). The evolution
of chronic HP may be progressive, with development of
pulmonary fibrosis and complications (hypoxemic respiratory
failure, cor pulmonale) and premature death. The prognosis
of chronic HP is much worse if the incriminated allergen is not
identified (5).

Typically, the HP diagnosis workup starts with the diagnosis
of ILD and the HP suspicion is raised after a detailed
anamnesis, intending to identify a possible exposure to
inhaled allergens (6).
The diagnosis is confirmed by compatible HRCT changes
(ground-glass areas alternating in mosaic with normal
ventilated areas, with cranio-caudal distribution and ground-
glass nodules (6)); in chronic HP, changes may also appear that
are determined by fibrosis (traction bronchiectasis and even
honeycombing) and through BAL changes with lymphocytic
alveolitis (8). Decreased CD4/CD8 ratio is a particular
characteristic for acute HP. In chronic forms, there can be
a normal CD4/CD8 ratio and an increase in the neutrophil
percentage in the BAL fluid. Our patient, with a short-term
evolution and HRCT aspect of acute HP, presented a very
high proportion of lymphocytes in BAL, with a decreased CD4/
CD8 ratio, suggestive of acute HP. Anyway, in children, the
ratio can be normally low, due to an increase in CD8, making
this diagnostic tool less powerful than in adults (9).

Pulmonary biopsy is not typically considered necessary
for the diagnosis of HP, especially if the HRCT aspect is a
characteristic for HP. BAL has high counts of lymphocytes,
and the history of exposure is doubled by serum identification
of specific IgG precipitins. A biopsy may be needed for
differentiation from an idiopathic interstitial pneumopathy,
especially idiopathic pulmonary fibrosis, in chronic HP with
progressive evolution and without an identified inhaled
allergen (chronic occult HP). The characteristic histologic
aspect consists of inflammatory granulomas, but there could
be also associated fibrotic lesions with architectural distortion
in the chronic subtype (2).
It is considered that in the adult population, HP has a
prevalence of 0.3–0.9 in 100,000 inhabitants (6,10), lower
as compared to idiopathic pulmonary fibrosis, but the
epidemiologic data may be highly underestimated. A different
perspective comes from the evaluation of cohorts of patients
investigated for an ILD, where chronic HP is one of the
possible diagnoses. This can lead to 18–30% of chronic HP
among the ILDs, with some registries showing a proportion of up to 47% of HP (11). In children and teenagers, the ILDs have a very low prevalence, being considered orphan diseases; a Danish report identified an incidence of two cases per year with a prevalence of 0.4/100,000 children (2). In young ages, less than two years, the majority are connected to genetic alteration of the surfactant proteins with familial aggregation.

ILDs in children older than 2 years can be determined by identifiable causes, can be associated with systemic diseases or may be idiopathic (Table 1) (12). HP may appear in older

Table 1. Interstitial lung diseases in children older than 2 years and teenagers

| Disorders with known causes | Disorders with unknown causes |
|-----------------------------|-----------------------------|
| Infection (8–10%) | Viral infection (eg. cytomegalovirus infection, infection with Epstein–Barr virus) |
| | Bacterial infection (eg. *Pertussis, Legionella, Mycoplasma, Chlamydia, or Mycobacterium* species) |
| | Fungal infection (eg. infection due to *Histoplasma, Aspergillus or Pneumocystis* species) |
| Environmental conditions (13%) | Exposure to organic dusts (hypersensitivity pneumonitis [7–12%]) |
| | Exposure to inorganic particulates (eg. silica, asbestos, talc, zinc) |
| | Exposure to chemical fumes, gases |
| Drugs | Antineoplastic agents |
| | Other drugs or elements (eg. penicillamine, nitrofurantoin, gold) |
| Previous lung injuries | Chronic aspiration pneumonitis (4%–5%) |
| | Resolving acute respiratory distress syndrome |
| | Bronchopulmonary dysplasia |
| | Lymphoproliferative disorders (10%) |
| | Metabolic disorders |
| | Lysosomal storage disorders (eg. Gaucher disease, Niemann–Pick disease) |
| | Degenerative disorders (eg. pulmonary microlithiasis [1%]) |
| | Immunodeficiency-associated ILD |
| Disorders with unknown causes | Undetermined (19–27%) |
| | Pulmonary haemorrhage syndromes |
| | Desquamative interstitial pneumonia (4–8%) |
| | Lymphocytic interstitial pneumonitis (6%) |
| | Lymphangiomatosis (4%) |
| | Nonadenoviral bronchiolitis obliterans (4%) |
| | Sarcoidosis (2%) |
| | Pulmonary alveolar proteinosis (2%) |
| | Eosinophilic syndromes (2%) |
| | Idiopathic bronchiolitis obliterans organizing pneumonia (BOOP) |
| | Bronchocentric granulomatosis (1%) |
| | Nonspecific interstitial pneumonia (correlates with ABCA3 deficiency) |
| | Acute interstitial pneumonitis |
| ILDs associated with systemic diseases | Connective tissue diseases (2–4%) (juvenile rheumatoid arthritis, dermatomyositis/polymyositis, systemic sclerosis, systemic lupus erythematosus, ankylosing spondylitis, Sjögren syndrome, Behçet syndrome, mixed connective tissue disease) |
| | Autoimmune diseases (anti-glomerular basement membrane antibody disease) |
| | Pulmonary vasculitis |
| | Liver disease (chronic active hepatitis, primary biliary cirrhosis) |
| | Bowel disease (2%) (eg. ulcerative colitis, Crohn’s disease) |
| | Amyloidosis |
| | Neurocutaneous disorders (tuberous sclerosis, neurofibromatosis, ataxia–telangiectasia) |
| | Bronchiolitis obliterans |
children and teenagers with intrinsic predisposition and repetitive exposure to inhaled allergens. The most frequent exposure in children is birds, HP being described especially in households where a bird cage is the usual pet. It was also anecdotally described in children with exposure to pheasant farm, turkey breeders, parental pigeon breeding or wild city pigeons nesting just outside home (13–19).

Our patient presented constant recreational exposure to pigeons, with the development of a subacute form of HP. The condition was spontaneously remissive after the cessation of the exposure, with imaging, functional and clinical complete remission after three months. The systemic corticosteroid treatment may be recommended in severe forms, which associate respiratory failure or severe functional alteration, for a period of 3–6 months, but there is a lack in evidence about its efficacy (2,3). The failure to identify and remove the incriminated allergen is an unfavourable prognosis factor, being associated with a higher mortality rate in adults (3,20). In children, mortality due to HP is not cited.

Several differential diagnoses were considered. Tuberculosis, another lung granulomatosis, was excluded by the absence of acid-fast bacilli in the BAL fluid. Sarcoidosis was excluded by the very low CD4/CD8 ratio in the BAL fluid. The patient received repeated courses of antibiotics for a presumed pneumonia, but the favourable evolution is considered to be not due to the antibiotics but due to the eviction of allergen exposure on the duration of hospital admission.

Conclusions

We present a rare case of HP to pigeons in a teenager, with complete resolution after cessation of exposure to the identified avian allergen, with no need for corticosteroid treatment.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Consent was obtained from the patient for publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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