ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Hypersensitivity pneumonitis in childhood

Pneumonite de hipersensibilidade na infância

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ABSTRACT

We report the clinical, epidemiological, and radiological features of hypersensitivity pneumonitis, a rare cause of respiratory failure in pediatrics. An 8-year-old male patient, from a rural area, was admitted to a tertiary care facility for fever, vomiting, dry cough, progressive dyspnea, anorexia, and weight loss for 15 days, associated with tachypnea, respiratory effort, hypoxia, and fine rales at the right base. Chest computed tomography showed ground-glass opacities, diffuse involvement, and predominantly centrilobular and acinar distribution, characteristic of hypersensitivity pneumonitis. In the review of living conditions and habits, the patient's guardian reported the presence of an aviary and interaction with birds of various species in the residence, supporting the presumptive diagnosis of hypersensitivity pneumonitis, after ruling out other causes of respiratory failure. Corticosteroid therapy was started with methylprednisolone 1 mg/kg/day for 7 days, followed by tapering over subsequent weeks. The patient's condition improved, and he was discharged home after receiving guidance on environmental control and the importance of removing the triggering antigens. Hypersensitivity pneumonitis is an uncommon syndrome in the pediatric population. It can lead to respiratory failure and pulmonary fibrosis and should therefore be considered in patients with a positive epidemiological history. Due to its rarity and similarity to other respiratory diseases, collecting data on patients' lifestyle habits is highlighted as an important diagnostic tool.

Keywords: Lung diseases, interstitial, child, respiratory insufficiency.

RESUMO

Neste relato descrevemos as características clínicas, epidemiológicas e radiológicas da pneumonite de hipersensibilidade, uma causa rara de insuficiência respiratória em pediatria. Paciente masculino, com 8 anos de idade, proveniente da zona rural, admitido em serviço terciário por quadro de febre, vômitos, tosse seca, dispneia progressiva, anorexia e perda de peso há 15 dias, associado a taquipneia, esforço respiratório, hipóxia e estertores finos em base direita. Tomografia computadoriza de tórax demonstrou opacidades com atenuações em vidro fosco, com comprometimento difuso e distribuição predominantemente centrolobular e acinar, característicos de pneumonite por hipersensibilidade. Na revisão das condições e hábitos de vida, foi relatado pela responsável do paciente a presença de um aviário e convívio com aves de várias espécies na residência, reforçando a hipótese diagnóstica, após descartadas outras causas de insuficiência respiratória. Iniciado corticoterapia com metilprednisolona 1 mg/kg/dia por 7 dias, seguido de redução progressiva nas semanas posteriores. Paciente evoluiu com melhora do quadro e alta hospitalar, após orientações sobre controle ambiental e importância do afastamento dos antígenos desencadeantes. A pneumonite por hipersensibilidade é uma síndrome incomum na população pediátrica, que pode levar à insuficiência respiratória e fibrose pulmonar, devendo ser considerada nos pacientes com epidemiologia positiva. Pela sua raridade e semelhança com outras infecções respiratórias, ressalta-se ainda a importância da coleta de dados sobre os hábitos de vida dos pacientes, destacando sua importância para a elucidação diagnóstica.

Descritores: Doenças pulmonares intersticiais, criança, insuficiência respiratória.

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Submitted: 06/18/2022, accepted: 07/10/2022.

Arq Asma Alerg Imunol. 2022;6(3):413-7.

http://dx.doi.org/10.5935/2526-5393.20220048

Introduction

Hypersensitivity pneumonitis (HP), also referred to as extrinsic allergic alveolitis, is a complex syndrome involving a number of lung diseases, predominantly in the small airways.[1] It results from an immune reaction to an inhaled agent, particularly an organic or mineral antigen, such as fungi, thermophilic bacteria, mold, animal proteins (found in bird feathers and droppings), and low molecular weight chemicals (isocyanates).[1]

The incidence of HP varies according to the location studied and geographical and environmental characteristics. The analysis of a large United States healthcare claims database (150 million unique enrollees) showed that the 1-year prevalence rates for HP ranged from 1.67 to 2.71 per 100,000 persons and increased with age to 11.2 per 100,000 in people aged 65 years and older.[2] In Brazil, the occurrence of HP is estimated at 3% to 13% among interstitial lung diseases.[3] To date, few cases have been reported in the pediatric population.

HP has a diverse clinical presentation, including cough, fever, weight loss, dyspnea, respiratory failure, and in more severe cases, pulmonary fibrosis. Several classification schemes have been proposed due to this great variability. One of them classifies the disease into acute (symptoms within hours of exposure), subacute (symptoms within weeks of exposure), and chronic (continued antigen exposure, with no defined frequency).[3]

Corticosteroid therapy for 7 to 14 days with dose tapering may be a useful treatment option. However, the main pillars of HP treatment are environmental control and avoidance of exposure.[4]

Case description

An otherwise healthy 8-year-old boy from a rural area was admitted to a tertiary care hospital with fever, vomiting, dry cough, progressive dyspnea, anorexia, and weight loss for 15 days, with no improvement after two antimicrobial regimens. Physical examination showed tachypnea, moderate respiratory effort, hypoxemia, and crackles at the right base. He was admitted to a pediatric ward for diagnostic workup.

Chest radiograph showed bilateral diffuse micronodular interstitial infiltrate. Computed tomography (CT) of the chest (Figures 1 and 2) showed ground-glass opacities, diffuse involvement, and predominantly centrilobular and acinar distribution, in addition to areas of air trapping at the lung bases, suggestive of HP. Bacterial, viral, and fungal pneumonia, atypical tuberculosis, and bronchiolitis from other causes were ruled out.

In the review of living conditions and habits, the patient's guardian reported the presence of an aviary with about 20 birds in the residence, with which the patient had direct contact by assisting in their care, cleaning, and feeding. Given the epidemiology and imaging suggestive of subacute HP, treatment with methylprednisolone 1 mg/kg/day was initiated and maintained for 7 days.

As a complementary investigation, spirometry for pulmonary function evaluation and bronchoalveolar lavage cellularity analysis were ordered. However, the tests were not performed due to patient limitations.

After corticosteroid therapy and removal of the child from home, he showed complete resolution of symptoms and no longer required oxygen therapy. He was discharged from the hospital with prednisolone 1 mg/kg/day, for later withdrawal. The patient and family members were informed of the importance of avoiding re-exposure to the causative agent to prevent further outbreaks and irreversible lung damage.

Discussion

HP is a diffuse interstitial lung disease of immunoallergic origin caused by repeated exposure to organic or mineral antigens, such as fungi (*Aspergillus*, *Penicillium*, *Micropolyspora faeni*), thermophilic bacteria, mold, animal proteins (present in bird feathers and droppings), and low molecular weight chemicals (isocyanates).[1]

Although the pathogenesis of HP is poorly understood, in genetically predisposed individuals, exposure to these agents is believed to cause sensitization and disease, leading to the production of specific IgG antibodies, with participation of cytokines and interleukins, episodic lung inflammation, formation of immune complexes, and influx of mononuclear cells into the lung parenchyma. This mechanism is also described for delayed hypersensitivity, especially in the subacute form, mediated by CD4 T and T helper lymphocytes.[5]

HP is described mainly in adults because it is often associated with occupational exposure. Although HP can affect people of all ages, it is rare in the pediatric population and probably underdiagnosed, as it is often initially confused with other respiratory tract infections.[6]

There are few data on the prevalence and incidence of HP in children. Studies have estimated the incidence of diffuse interstitial pneumonia in children to be 1.3 to 3.6 cases per million. Among these cases, HP accounts for 2% to 25% of the occurrences.[6,7]

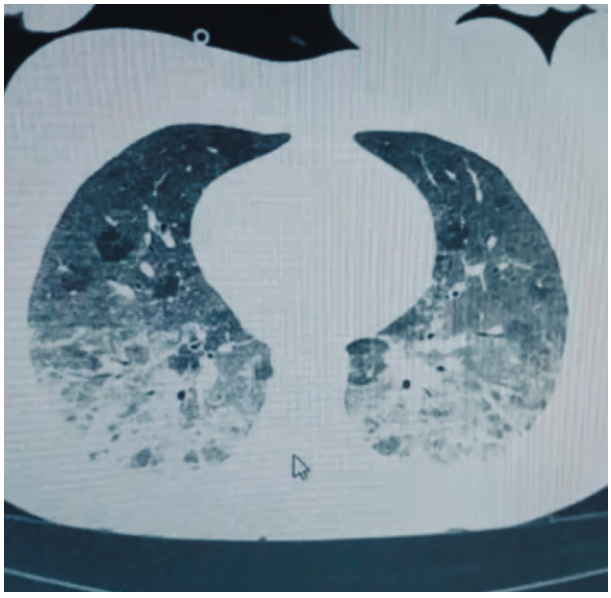

Figure 1
Chest CT scan showing areas of diffuse ground-glass pattern, with small bilateral areas of opacity

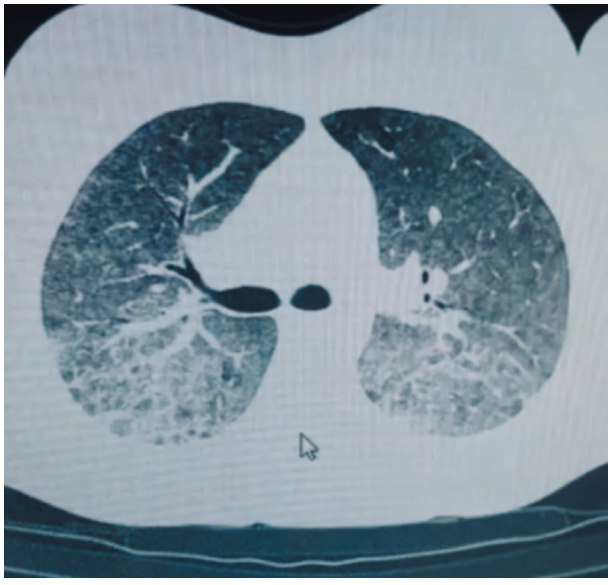

Figure 2
Chest CT scan showing areas of ground-glass pattern and interlobular septal thickening

The clinical presentation of HP in children is similar to that in adults, with dyspnea on exertion and cough as the most common symptoms in children. Weight loss and fever are also frequently found. Physical examination reveals crackles in almost two-thirds of cases.[6]

Several classifications have been proposed because of the variable presentation of HP. Currently, the most widely used one classifies the disease into acute, subacute, and chronic. The acute form presents as a flu-like feverish syndrome, with dry cough and dyspnea, beginning at 4-8 hours after exposure to the antigen. It accounts for approximately 25% of cases and is often confused with viral or bacterial infections,[6] and the symptoms usually improve within a few days. Chest radiograph may reveal a fleeting micronodular pattern in the lower- and mid-lung zones, but patients usually have normal chest radiographs.[8]

The subacute form, as in the present case report, is characterized by gradual development of a productive cough, dyspnea, fatigue, anorexia, and weight loss. Physical examination usually reveals tachypnea and diffuse crackles, and chest radiograph may be normal or show micronodular or reticular opacities that are usually more apparent in the upper- and mid-lung zones.[6,7] In the chronic form, the onset of symptoms is insidious. Digital clubbing may be observed in advanced disease and may help predict clinical deterioration. Disabling and irreversible respiratory findings due to pulmonary fibrosis are characteristic and associated with increased mortality. At this stage, removal of exposure usually results in only partial improvement.[7]

In addition to this classification, a recent clinical practice guideline on the diagnosis of HP in adults recommends the categorization of HP into fibrotic and nonfibrotic according to the presence of radiographic or histological fibrosis. According to the guideline, this classification would better define the clinical course and prognosis of the disease.[9] Although intended for adults, this guideline is the first to provide well-defined criteria for the diagnosis of HP. First, detecting the causative antigen is essential for consideration of HP, workup, and treatment. Serum IgG testing against potential antigens provides no causal relationship and there is no standard hypersensitivity panel; therefore, it has limited applicability. The bronchoalveolar lavage is typically inflammatory, with a predominance of lymphocytes.[9]

As for complementary tests, high-resolution CT of the chest is essential for diagnosis and indicative

of HP when showing at least one of the following findings: ill-defined centrilobular nodules, mosaic attenuation, air trapping, or a three-density pattern (the latter is indicated as highly specific). In their absence, high-resolution CT is indeterminate for HP. Regarding the distribution of lung injury on CT scans, HP is considered typical when it affects the mid-lung zone.[10]

Lung biopsy is not mandatory to establish the diagnosis and may be helpful in doubtful cases. In acute HP, histopathology shows peribronchovascular fibrin deposition and interstitial accumulation of neutrophils, lymphocytes, and macrophages.[11] In subacute HP, there is a classic histological triad of cellular bronchiolitis, predominantly lymphocytic interstitial infiltrate, and interstitial noncaseating granulomas or isolated giant cells. In chronic HP, histopathology shows chronic bronchiolitis, with varying degrees of fibrosis, and peribronchiolar fibroblastic foci.[11,12]

The clinical practice guideline also classifies patients as having definite, high- confidence, moderate-confidence, low-confidence, and not-excluded diagnoses based on information on exposure, CT scans, and bronchoalveolar lavage.[9] Our patient, with a history of exposure to birds, characteristic CT findings, and no bronchoalveolar lavage, had a moderate-confidence diagnosis of HP. In all cases, lung biopsy ensures a definite diagnosis.

Most children are treated with steroids, like our patient. Corticosteroids are widely used for their rapid therapeutic response. However, the identification and removal of the causative agent is paramount for a good response to treatment. Lack of antigen avoidance may lead to disabling and irreversible lung damage in chronic HP.[13]

Corticosteroid therapy approaches include the use of oral steroids and intravenous pulse steroids.[14] There is no consensus on the dosage and duration of treatment, but it should aim at the lowest possible dose and shortest duration. Despite the lack of randomized clinical trials on the topic, the use of immunosuppressive and antifibrotic agents may be considered in adults.[15]

Long-term prognosis depends on factors related to the causative antigen and the patient. Exposure to bird antigens for more than 6 months is associated with residual pulmonary abnormalities. Younger patients are more likely to have a full recovery. Overall, individuals with acute HP show the most marked improvement, with almost complete recovery of lung function. Conversely, those with pulmonary fibrosis have a worse outcome and may progress to respiratory failure, sometimes fatal.[16]

In this context, guidelines on the most appropriate treatment for HP are imperative, especially in the pediatric population for which data are scarce. Moreover, because HP is an uncommon syndrome with a challenging diagnosis, it should always be considered in patients with a positive epidemiological history in order to avoid complications and unfavorable patient outcomes.

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No conflicts of interest declared concerning the publication of this article.

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