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Clinical case

Hypersensitivity pneumonitis induced by the yeasts Trichosporon asahii and Candida parapsilosis associated with humidifier fever

Pneumopathie d'hypersensibilité induite par les levures Trichosporon asahii et Candida parapsilosis associée à la fièvre des humidificateurs

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Abstract

Here, we present a case of hypersensitivity pneumonitis to Yeasts (Trichosporon asahii and Candida parapsilosis) and associated with humidifier fever linked to exposure to gram negative bacteria and endotoxins. The association of HP and humidifier fever is rarely reported.

Key clinical message: Anamnesis should explore the use of a humidifier in the case of fever or any HP with an undetermined cause and look for germs in the humidifier.

Keywords: Hypersensitivity pneumonitis; Humidifier fever; Candida; Trichosporon asahii.

Résumé

Nous présentons ici un cas de pneumopathie d'hypersensibilité aux levures (Trichosporon asahii et Candida parapsilosis) associée à une fièvre des humidificateurs liée à une exposition à des bactéries gram négatives et à des endotoxines. L'association pneumopathie d'hypersensibilité et fièvre des humidificateurs est rarement rapportée.

Message clinique clé : L'anamnèse doit explorer l'utilisation d'un humidificateur en cas de fièvre ou de toute pneumopathie d'hypersensibilité de cause indéterminée et rechercher des germes dans l'humidificateur.

Mots-clés : Pneumopathie d'hypersensibilité ; Fièvre ; humidificateur ; Trichosporon asahii.

Introduction

Hypersensitivity Pneumonitis (HP) is a lung disease caused by large and recurrent inhalation of antigens. Diagnostic criteria are based on antigen exposure, clinical, lowered diffusing capacity for carbon monoxide (DLCO) imaging (ground glass, centrilobular nodules, air trapping on expiratory high resolution computer tomography), compatible bronchoalveolar lavage (lymphocytosis and mastocytosis), whether or not associated with the presence of immunoglobulin G (IgG) precipitins [1, 2]. Its annual incidence is estimated to be about 0.9 to 2 cases per 100,000 population [3-5]. The main etiologies are farmer's lung, bird breeder's lung, and domestic HP [6].

In contrast, respiratory pathologies associated with

humidifier use (humidifier-HP and humidifier fever) are rare [7. The first cases of humidifier-HP involved warm-water humidifiers, and were associated with thermophilic actinomycetes; subsequent cases involving ultrasonic cold-water humidifiers revealed different pathogens, such as molds or bacteria [8]. Humidifier fever is rarely reported in the literature [9-11] and represents a diagnostic challenge for the physician. Repeated febrile episodes, associated with hyperleucocytosis and increased C-reactive protein (CRP), should lead to the suspicion of exposure to endotoxins, classically reported in farmers, particularly in the form of organic dust toxic syndrome [12], or experimentally after inhalation of endotoxins in humans [13]. Gram negative bacteria containing endotoxins have been detected in humidifier fever (HF) in Japan [9] and in Germany [10, 11]. The association between HP and humidifier fever is exceptionally reported [14].

We present here the first case of HP associated to yeasts, Trichosporon asahii and Candida parapsilosis, with humidifier fever and exposition to Gram negative bacteria and endotoxins.

Clinical case

A retired 63-year-old woman was admitted to the pulmonary department on January 2020 for progressive dyspnea on exertion over the previous 15 days. She had a history of allergic asthma (dust mites, cat, pollens) since childhood, treated with inhaled long-acting beta2-agonists and corticosteroids. She was a former smoker (20 pack-year) who had ceased 15 years prior to presentation. There was no birds, mould or humidity in the home. Intermittent febrile episodes at 38-38.5°C had occurred over the previous 9 months. Eight months before admission, a blood count recorded hyperleukocytosis at 10,200/ mm3, neutrophilia at 7,049/mm3, CRP at 20.8 mg/l. Two weeks prior to admission, the leukocytosis was at 10,550/ mm3 with neutrophilia at 7,611/mm3, and CRP at 73.1 mg/L. Twenty-four hours before hospitalization, leukocytosis was 13,100/mm3, neutrophilia 10,860/mm3 and CRP at 25.2 mg/l. Multiple lines of antibiotics including amoxicillin and ceftriaxone had not resulted in any improvement in febrile episodes.

Clinical examination showed a dyspneic patient with preserved general condition. The temperature was 37°C, and peak expiratory flow 320 L/min (normal value 420). Physical examination revealed some fine crackles at the bases.

An arterial blood gas test performed on admission recorded hypoxia at 56 mm Hg. The chest X-ray was normal. Inspiratory injected high resolution computed tomography was normal, without any pulmonary embolism. However, mild traping was present on expiratory images (fig. 1). Laboratory studies revealed leukocytosis at 10,800/mm3 with CRP at 10 mg/l; D-dimers and procalcitonin were normal. Antinuclear antibodies, connective tissue antibodies, anti-neutrophil cytoplasm antibodies, brucellosis, typhoid fever, Coxiella serology, and sputum smear tests were all negative, while cardiac ultrasound ruled out endocarditis. Pulmonary function tests performed two days after admission revealed lowered TLCO was (72% of predicted), small bronchial obstruction (FEF 25-75 28% of predicted), without decrease in lung volumes (total lung capacity (TLC) at 111%, FVC at 106%). Broncho-alveolar lavage performed after bronchodilator aerosol 6 days after hospitalization revealed hyper-cellularity, at 467,000 cells/ml (standard between 100,000 and 150,000 cells/ml in a non-smoker), with hyper-lymphocytosis at 32%, neutrophilia at 10% and mast cells at 1%. The tests for viruses, bacteria and mycobacteria were negative. Aspergillus. fumigatus, Micropolyspora faeni and pigeon breeder's serologies were negative.

Faced with these repeated febrile and respiratory episodes suggestive of acute hypersensitivity pneumonitis and the association with hyperleukocytosis and increased CRP, the consequent search for an environmental origin revealed the daily use of an ultrasonic humidifier in the home for about 2 years (Fig.2). Over time, the patient had refilled the water when needed, but without cleaning the

water reservoir. Bacteriological and mycological analysis of the humidifier water tank found colonies of T. asahii and C. parapsilosis and the presence of Enterobacter cloacae and Acinetobacter sp. Precipitins (electrosyneresis) were positive with 2 arcs for T asahii and C. parapsilosis. Endotoxins in the humidifier water were at 3900 Endotoxin Units (EU)/ml (quantitative limulus assay).

The patient received an oral corticotherapy (60 mg prednisone/24H [1mg/kg]), from the day of admission because she had difficult breathing (especially at night). This resulted in a rapid improvement in her respiratory condition. She returned home after one week's hospitalization with decreasing corticosteroid doses and removal of the humidifier from the house. The patient rapidly recovered from the clinical symptoms, with the disappearance of dyspnea and no recurrence of febrile episodes. One month later, recovery of pulmonary function was observed with TLC at 129% of predicted, FVC at 120%, FEV1 at 100%, and post-BD FEV1/FVC at 70%, but with a continuing mild diffusion disorder (DLCO 79% of predicted).

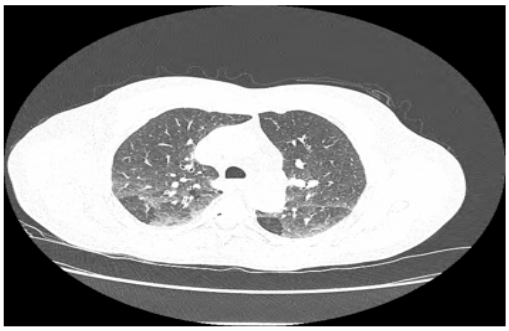

Figure 1: Injected chest CT scan: Mosaic attenuation with significant trapping was shown on the expiration CT, suggestive of HP

Figure 2: Bottom of the humidifier water tank

Discussion

Given the risk of a severe attack (hypoxic patient on arrival at the hospital), and due to the lack of standardization (mixture of non-specific antigens and non specifc irritants), a provocation test was not performed in this patient. The diagnosis of humidifier-HP nevertheless be considered certain because of the diagnostic criteria all present in this patient (an isolated air trapping on the HRCT is a pattern that may be seen with HP) [1]. This case of humidifier-HP was due to yeasts (Trichosporon. asahii and Candida. parapsilosis colonies in the humidifier water tank and positive yeast IgG precipitins by electrosyneresis). Evidence for HF were also found; intermittent febrile episodes, with hyperleukocytosis and neutrophilia, increased CRP, and evidence of gram-negative bacteria in the water tank, along with endotoxins. The diagnosis was confirmed by the patient's clinical improvement after she stopped using the humidifier at home. The recovery of DLCO was slower (79% of predicted) than of FVC, in accordance with what is observed in the follow-up study of pulmonary function in farmer's lung [15]. Post-bronchodilator FEV1/FVC being at 70%, the final diagnosis of obstructive lung disease in this patient was asthma and not asthma-COPD-overlap (ACO) [16].

No hypersensitivity pneumonitis with the detection of T asahii in the humidifier has been described to our knowledge. This yeast is classically found in acute [17] or chronic [18] summer type HP, the most frequent HP in Japan; it occurs classically during the hot and humid summer period after exposure to mould in wooden houses. It is due to exposure to T. asahii or T. mucoides, originally named T. cutaneum [19]. Three cases of humidifier-related HP have been described after contamination with Candida albicans [20, 21] or Candida guilliermondii [22] but none associated with Candida. paraspsilosis.

Humidifier fever is associated with gram-negative bacteria, which contain endotoxins. Bacteria found in our observation (Enterobacter cloacae, Acinetobacter sp.) were also reported in publications in Japan

[9], Germany [14] and USA [23]. The high level of endotoxins found in the humidifier (the typical level in tap water is 25 EU/ml [24]) may have exacerbated the hypersensitivity allergic reaction as shown in animal [25] and clinical studies [26].

Conclusion

We report a case of humidifier-HP associated to yeasts, Trichosporon asahii and Candida parapsilosis. The association of humidifier-HP and humidifier fever is exceptionally reported. Anamnesis should explore the use of a humidifier in the case of any HP or fever with an undetermined cause.

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