Biopsy-proven recurrent, acute, familial hypersensitivity pneumonitis: A case report and literature review

Tiffany Winstone\textsuperscript{a,b,\ast}, Cameron J. Hague\textsuperscript{c}, Andrew Churg\textsuperscript{d}, Joanne L. Wright\textsuperscript{d}, Robert Schellenberg\textsuperscript{a,b}, Chris Ryerson\textsuperscript{a,b}

\textsuperscript{a} Department of Medicine, University of British Columbia, Vancouver, Canada
\textsuperscript{b} Centre for Heart Lung Innovation, University of British Columbia, Vancouver, Canada
\textsuperscript{c} Department of Radiology, University of British Columbia, Vancouver, Canada
\textsuperscript{d} Department of Pathology, University of British Columbia, Vancouver, Canada

ARTICLE INFO

Keywords:
Hypersensitivity pneumonitis
Familial hypersensitivity pneumonitis
Organic antigen
Interstitial lung disease

ABSTRACT

Hypersensitivity pneumonitis (HP) is characterized by inflammation of the lung parenchyma that is induced by exposure to an inhaled organic antigen. We present a case of recurrent, acute HP caused by repeated transient exposure to a down sleeping bag in a patient with a family history of chronic bird-associated hypersensitivity pneumonitis. The patient’s recurrent symptoms, changes in physiology, and radiographic findings coincided with repeated exposure to this source. It was later confirmed that the patient’s sister had also developed chronic HP from recurrent exposure to household birds. This case highlights recent studies implicating gene-exposure interactions in the development of HP.

1. Case

A previously healthy 36-year-old male non-smoker presented with rapidly worsening dyspnea during a home renovation in 2008. His family history included a sister with a diagnosis of chronic and progressive hypersensitivity pneumonitis (HP) secondary to a longstanding bird exposure in her home. Pulmonary function tests (PFTs) showed a borderline restrictive pattern with a forced vital capacity (FVC) of 83%-predicted and diffusion capacity of the lung for carbon monoxide (DLCO) of 52%-predicted. Chest computed tomography (CT) showed diffuse ill-defined, ground glass, centrilobular nodules (Fig. 1A). Bronchoscopy was negative for infectious and malignant etiologies, and transbronchial biopsies were non-diagnostic. There were 1% lymphocytes on bronchoalveolar lavage (BAL). Connective tissue disease serology and serum precipitins for Aspergillus were negative. A surgical lung biopsy confirmed a diagnosis of HP (Fig. 2A/B). He was treated with prednisone with near complete resolution of symptoms and normalization of physiological (FVC 106%, DLCO 88%) and radiological abnormalities (Fig. 1B). The patient denied exposure to mold, birds, hot tubs, and other likely antigens, with a clear underlying precipitant not identified.

He remained asymptomatic until 2015 when he presented with dyspnea and cough within several hours of his first visit to a friend’s ranch. FVC and DLCO had declined to 86% and 59%, respectively, and chest CT showed worsening diffuse centrilobular nodularity and mosaic attenuation (Fig. 1C). Bronchoscopy was negative for infectious etiologies and malignancy, with 85% lymphocytes on bronchoalveolar lavage (BAL). Endobronchial biopsies confirmed a diagnosis of HP (Fig. 2C). A precipitant was not identified at that time, but the patient was advised to not visit the ranch again. His symptoms and lung function improved following two weeks of prednisone 30mg daily with a subsequent 2-month taper.

He was referred to an interstitial lung disease (ILD) clinic as well as an allergist and immunologist after re-visiting the ranch on two subsequent occasions, with both episodes associated with worsening symptoms and physiology, and improvement with prednisone. He underwent skin testing, with no reaction to tree pollens or commercially available mold spores (Alternaria, Aspergillus, Cladosporium, Penicillium, or Fusarium). He experienced a third episode of worsening respiratory symptoms while camping at a location distant from the ranch and reported use of a down sleeping bag. Upon further questioning, he confirmed that he had used the same sleeping bag during all prior visits to the ranch.

2. Discussion

HP is characterized by inflammation of the lung parenchyma caused by exposure to an organic inhaled antigen [1]. The diagnosis of HP can
be challenging due to the lack of a diagnostic gold standard and the frequent inability to identify an underlying antigen [2,3]. Ground-glass, ill-defined nodules, and air trapping are seen on chest CT in acute and subacute HP, with reticulation, volume loss, and traction bronchiectasis present in chronic HP. HP is pathologically characterized by a bronchiolocentric granulomatous lymphocytic alveolitis, which can evolve into fibrosis in chronic cases [4]. Diagnostic models for HP using clinical and radiological variables have been proposed [5,6]; however, these models have not been adequately validated for clinical use in chronic HP. Patients with acute and subacute disease may fully recover with antigen avoidance and often corticosteroid therapy. Patients with chronic HP are frequently treated with systemic corticosteroids and additional immunosuppressive agents, but often have irreversible and progressive pulmonary fibrosis despite therapy [7].

Previous cohorts of familial HP have been reported, predominantly including Japanese patients with summer-type HP (SHP) with many of these individuals having a common home residence and exposure history [8,9]. SHP is the most common form of HP in Japan, typically occurring in the western part of Japan where summer temperatures and humidity are high [9]. In one recent publication, 50 Japanese patients with familial SHP from 23 families were reported between 1982 and 2011 [8]. All of these families lived in traditional Japanese wooden houses that were damp. 41 of 49 cases (84%) occurred in the summer of 2011 [8]. All of these families lived in traditional Japanese wooden houses that were damp. 41 of 49 cases (84%) occurred in the summer of 2011 [8].

This patient was diagnosed with recurrent acute HP associated with repeated exposures to a down sleeping bag, and in the context of a well-documented family history of chronic and progressive HP that was secondary to a longstanding bird exposure. While the 2008 VATS biopsy was typical of subacute HP, the 2015 bronchial biopsy showed an endobronchial granuloma, an uncommon finding in HP that may suggest an unusual degree of sensitization. This family may have a genetic predisposition to HP, but with different gene variants and/or exposures leading to recurrent episodes of acute HP in one sibling, and chronic HP in another. Future studies are needed to identify potential gene-environment interactions that predispose to HP in some exposed individuals and not in others.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmcr.2018.05.007.

References

[1] M. Selman, Hypersensitivity pneumonitis: insights in diagnosis and pathobiology, Am. J. Respir. Crit. Care Med. 186 (2012) 314–324.
[2] J.J. Mooney, Radiographic fibrosis score predicts survival in hypersensitivity pneumonitis, Chest 144 (2013) 586–592.
[3] P. Fernández, et al., Identifying an inciting antigen is associated with improved survival in patients with chronic hypersensitivity pneumonitis, Chest 144 (2013).
1644–1651.
[4] L.P. Hariri, Distinct histopathology of acute onset or abrupt exacerbation of hypersensitivity pneumonitis, Hum. Pathol. 43 (2012) 660–668.
[5] Y. Lacasse, M. Selman, U. Costabel, et al., Clinical diagnosis of hypersensitivity pneumonitis, Am. J. Respir. Crit. Care Med. 168 (2003) 952–958.
[6] K.A. Johansson, A diagnostic model for chronic hypersensitivity pneumonitis, Thorax 71 (2016) 951–954.
[7] J.J. Morisset, Use of mycophenolate mofetil or azathioprine for the management of chronic hypersensitivity pneumonitis, Chest 151 (2017) 619–625.
[8] N.N. Asai, Familial summer-type hypersensitivity pneumonitis: a review of 25 families and 50 cases in Japan, Intern. Med. 55 (2016) 279–283 (Tokyo, 1992).
[9] M.M. Ando, Japanese summer-type hypersensitivity pneumonitis, Geographic distribution, home environment, and clinical characteristics of 621 cases, Am. Rev. Respir. Dis. 144 (1991) 765–769.
[10] T. Okamoto, A familial history of pulmonary fibrosis in patients with chronic hypersensitivity pneumonitis, Respiration 85 (2013) 384–390.
[11] M.M. Ando, HLA-DQw3 in Japanese summer-type hypersensitivity pneumonitis induced by Trichosporon cutaneum, Am. Rev. Respir. Dis. 140 (1989) 948–950.
[12] A. Aquino-Galvez, A. Camarena, M. Montaño, et al., Transporter associated with antigen processing (TAP) 1 gene polymorphisms in patients with hypersensitivity pneumonitis, Exp. Mol. Pathol. 84 (2008) 173–177.
[13] A.A. Camarena, PSMB8 (LMP7) but not PSMB9 (LMP2) gene polymorphisms are associated to pigeon breeder's hypersensitivity pneumonitis, Respir. Med. 104 (2010) 899–894.
[14] Schaaf BM. Tumor necrosis factor-alpha -308 promoter gene polymorphism and increased tumor necrosis factor serum bioactivity in farmer's lung patients. Am. J. Respir. Crit. Care Med.; 163:379-382.
[15] B.B. Ley, The MUC5B promoter polymorphism and telomere length in patients with chronic hypersensitivity pneumonitis: an observational cohort-control study, Lancet Respir. Med. 5 (2017) 639–647.