Respiratory Medicine CME 3 (2010) 90–92

Contents lists available at ScienceDirect

Respiratory Medicine CME

journal homepage: www.elsevier.com/locate/rmedc

Case Report

Diffuse alveolar hemorrhage with chronic thyroiditis in an advanced-age adult

Masanori Fujii, Nobuaki Miyahara*, Yasushi Tanimoto, Nagio Takigawa, Masahiro Tabata, Arihiko Kanehiro, Katsuyuki Kiura, Mitsune Tanimoto

Department of Hematology, Oncology, Allergy and Respiratory Medicine, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical sciences, Okayama, Japan

ARTICLE INFO

Article history:
Received 4 March 2009
Accepted 1 April 2009

Keywords:
Diffuse alveolar hemorrhage
Chronic thyroiditis
Corticosteroids

ABSTRACT

Idiopathic pulmonary hemosiderosis (IPH) is one of the rare causes of diffuse alveolar hemorrhage (DAH), and usually occurs in children. The mechanism underlying this disease development has not been defined. During the acute phase, death due to massive alveolar hemorrhage and subsequent severe respiratory failure with multiple organ failure often occurs. We report a case of IPH which occurred in an advanced-aged adult during following thyroidectomy for chronic thyroiditis. Following surgery this 83-year-old male developed acute onset dyspnea and pulmonary hemorrhage. In a search for underlying causes, no disorders were found and the only finding was the presence of anti-thyroid antibody. Systemic corticosteroid therapy was effective and he fully recovered. To our knowledge, this is the second documentation of IPH in association with chronic thyroiditis.

1. Introduction

Idiopathic pulmonary hemosiderosis (IPH) is a rare disease that causes diffuse alveolar hemorrhage (DAH),[1] characterized by recurrent episodes of hemoptytis and diffuse pulmonary infiltrates. Previous reports suggest that some appear to be associated with cow's milk allergy,[2] and celiac disease,[3] and most cases reported were in children.[1] Death may occur suddenly from acute pulmonary hemorrhage or progressive respiratory failure.[4] The exact etiology of this disease is not defined, and there are no specific treatments. Some observational studies suggest that corticosteroids or corticosteroids in combination with other immunosuppressive agents are effective for either exacerbations or maintenance therapy of IPH.[1,4] These clinical findings indicate that an immunologic cause may be involved in the development of IPH.

Here, we present a rare case of IPH occurred which in an advanced-aged adult during the follow-up of chronic thyroiditis, and rescued by systemic steroid therapy.

2. Case report

An 83-year-old man with a history of chronic thyroiditis underwent a thyroidectomy. Within a month he presented with hemoptysis. The patient stated that before the onset of these symptoms, he was in his usual state of health, denying recent fever, chills, chest pain, or weight loss. The patient had a history of laryngectomy for laryngeal cancer several years earlier. He became aware of increasing bloody sputum, so laryngoscopy was performed, but it showed no significant abnormality. However, the persistence of hemoptytis, together with shortness of breath gradually led him to revisit the hospital. A repeat laryngoscopy was performed, but no abnormalities were discovered. He was referred to the Division of Respiratory Medicine.

Physical examination on admission revealed his temperature of 36.2 °C, blood pressure 108/72 mm Hg, pulse 78/min, and respiratory frequency 15/min. On auscultation, diffuse fine crackles were heard in the both lungs, and no systolic or diastolic murmurs were detected. A chest X-ray revealed alveolar and interstitial infiltrates of both lungs (Fig. 1). A CT scan of the chest also demonstrated scattered ground-glass areas in both lung fields (Fig. 2). Arterial blood gases (room air) were pH 7.43, PaO_2 73.8 mm Hg, and PCO_2 35.4 mm Hg. Pulmonary function could not be measured because of breathlessness. An echocardiogram demonstrated normal cardiac function. Regarding laboratory findings, renal and liver function tests were normal.

The patient was evaluated for the intra-alveolar hemorrhagic syndromes. Among the tests, serum IgG, IgA, and IgM levels, and C3 and C4 levels were normal. Perinuclear anti-neutrophil cytoplasmic antibodies and cytoplasmic anti-neutrophil cytoplasmic antibodies were negative. Anti-nuclear antibodies, anti-ds DNA and anti-glomerular basal membrane antibodies were negative. Other

* Address for Correspondence: Department of Hematology, Oncology, Allergy and Respiratory Medicine, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical sciences, 2-5-1 Shikata-cho, Okayama 700-8558, Japan. Tel.: +81 86 235 7227; fax: +81 86 232 8226.
E-mail address: miyahara@md.okayama-u.ac.jp (N. Miyahara).

1755-0017/$36.00 © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rmedc.2009.04.006

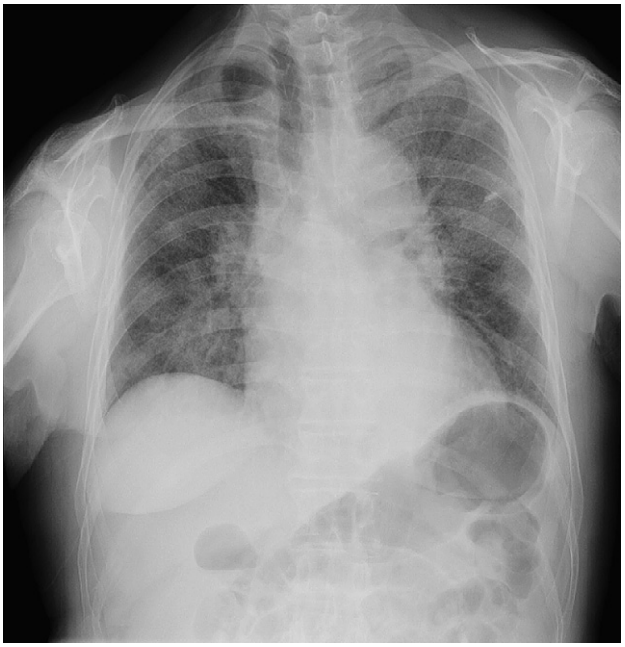

Fig. 1. An X-ray film of the chest on admission showed alveolar and interstitial infiltrates of both lungs.

auto-antibodies except for anti-thyroid antibodies were negative. Only anti-thyroglobrin antibodies and anti-thyroid peroxidase antibodies were highly elevated (Table 1).

On the third day of hospitalization, a bronchoscopy was performed, and revealed a hemorrhagic return from the distal alveoli consistent with diffuse alveolar hemorrhage. Bronchial alveolar lavage (BAL) demonstrated abundant haemosiderin-laden macrophages (Fig. 3). Culture of the BAL fluid was sterile.

On the basis of these findings, the patient was diagnosed as IPH and was begun on a regimen of high dose corticosteroids (1000 mg/day) that was tapered gradually to 5 mg/day. The patient's condition, as well as CT findings, improved progressively and he regained strength gradually. He became asymptomatic and no recurrence occurred.

Table 1
Autoimmune antibody panel.

P-ANCA (EU)	<10	(<19)
C-ANCA (EU)	<10	(<10)
Anti-GBM (EU)	<10	(<9)
Anti-TG (IU/ml)	403.3	(<13.5)
Anti-TPO (IU/ml)	117.0	(<3.1)

P-ANCA: perinuclear anti-neutrophil cytoplasmic antibodies. C-ANCA: cytoplasmic anti-neutrophil cytoplasmic antibodies. Anti-GBM: anti-glomerular basement membrane antibodies. Anti-TG: anti-thyroglobulin antibodies. Anti-TPO: anti-thyroid peroxidase auto-antibodies.

3. Discussion

We describe a very rare case of IPH associated with chronic thyroiditis in an elderly male. To the best of our knowledge, only one case of IPH in association with chronic thyroiditis has been previously reported.[5] Diffuse alveolar hemorrhage (DAH) is characterized by widespread hemorrhage from the microvasculature of the lung into the alveolar spaces. Such pulmonary hemorrhage, although it is uncommon, can occur in association with a wide variety of clinical disorders, many of which have overlapping features of glomerulonephritis, immune complex disease, and anti-glomerular basement membrane disease.[6] In our case, however, renal function was normal and serum anti-glomerular antibodies were negative. He also had no evidence of systemic vasculitis, collagen vascular disorders, infection, cancer, pulmonary embolism or other conditions, which may be associated with DAH.

Alberda et al. previously divided DAH into six categories.[6] This classification is shown in a Venn diagram that classifies DAH into categories based on association with renal disease (usually glomerulonephritis), and two immunologic mechanisms: anti-GBM antibodies or immune complexes. Based on this classification, our case is categorized as idiopathic pulmonary hemosiderosis (IPH). However, from a clinical point of view and the favorable response to high dose corticosteroid, an immunopathological mechanism may have been involved in this unusual case of IPH. Previous reports also showed that appropriate immunosuppressive therapy without delay may be effective in IPH.[1]

It was notable that chronic thyroiditis was also present. Rabec et al. reported a case of DAH, neither capillaritis nor diffuse alveolar damage, in association with inflammatory bowel disease and chronic thyroiditis.[5] On the one hand, association between DAH

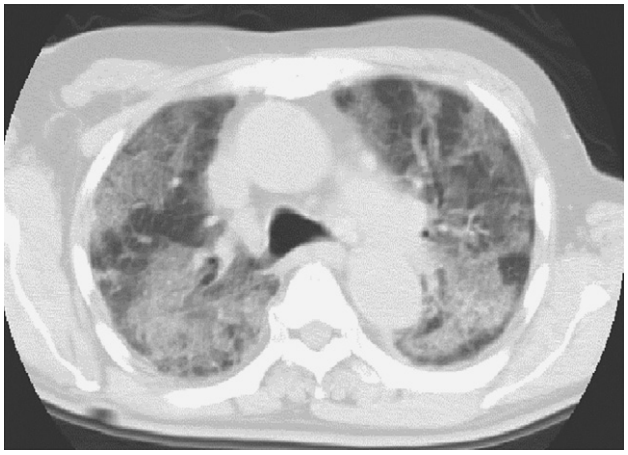

Fig. 2. A CT scan of the chest demonstrated areas of ground-glass attenuation and a reticular micronodular appearance in both lung fields. High dose corticosteroids led to diffuse ground-glass attenuation.

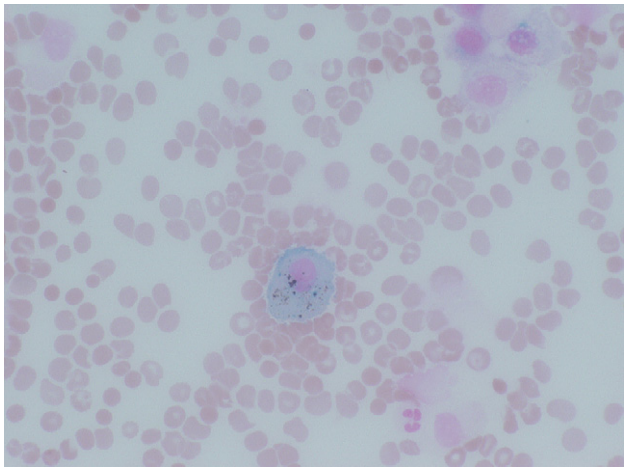

Fig. 3. Iron stain performed on bronchial alveolar lavage (BAL) specimens, highlighting the abundant intra-alveolar siderophages.

and inflammatory bowel disease including celiac disease (CD) has previously been reported. On the other hand, although an association between chronic thyroiditis and DPH has not been proved, there is evidence of a strong association with CD and several immune-mediated diseases, including autoimmune thyroid disorders.[7] Previous reports have revealed that some of these conditions share HLA haplotypes and non-HLA alleles, e.g., cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), which may underlie their pathogenesis.[7] Indeed, some reports have previously shown that a small number of patients with autoimmune thyroiditis were found to have CD and villous atrophy.[7–10] These reports suggest that chronic thyroiditis as well as CD may trigger DAH through as yet unknown mechanisms.

In the present case, one might consider the possibility that a history of chronic thyroiditis and the eventual thyroidectomy triggered DAH which set off the disease as seen in patients with celiac disease. Although DAH associated with chronic thyroiditis is very rare, and has been reported only once before, a search for anti-thyroid antibodies may be warranted in cases of DAH where the initiating event is unclear.

In conclusion, we describe the possible association of DAH with chronic thyroiditis and/or thyroidectomy.

Conflict of interest

The authors have no financial conflict of interest.

References

1. Ioachimescu OC, Sieber S, Kotch A. Idiopathic pulmonary haemosiderosis revisited. *Eur Respir J* 2004;**24**:162–70.
2. Heiner D. Primary pulmonary hemosiderosis with sensitivity to cow's milk. In: Kending EL, Chernick V, editors. *Disorders of the respiratory tract in children*. Philadelphia: W.B. Saunders; 1990. p. 505–6.
3. Reading R, Watson JG, Platt JW, et al. Pulmonary haemosiderosis and gluten. *Arch Dis Child* 1987;**62**:513–5.
4. Saeed MM, Woo MS, MacLaughlin EF, et al. Prognosis in pediatric idiopathic pulmonary hemosiderosis. *Chest* 1999;**116**:721–5.
5. Rabec C, Barcat J, Ray D. Alveolar hemorrhage associated with intestinal inflammatory disease and Hashimoto thyroiditis. *Arch Bronconeumol* 2004;**39**:283–5.
6. Albelda SM, Gefter WB, Epstein DM, et al. Diffuse pulmonary hemorrhage: a review and classification. *Radiology* 1985;**154**:289–97.
7. Ch'ng CL, Jones K, Kingham JGC, et al. Celiac disease and autoimmune thyroid disease. *Clin Med Res* 2007;**3**:184–92.
8. Cucco L, Certo M, Jorizzo RA, et al. Prevalence and early diagnosis of celiac disease in autoimmune thyroid disorders. *Ital J Gastroenterol Hepatol* 1999;**31**:283–7.
9. Berti I, Trevisiol C, Tommasini A, et al. Usefulness of screening program for celiac disease in autoimmune thyroiditis. *Dig Dis Sci* 2000;**45**:403–6.
10. Volta U, Ravaglia G, Granito A, et al. Coeliac disease in patients with autoimmune thyroiditis. *Digestion* 2001;**64**:61–5.