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Atypical image of pulmonary alveolar proteinosis — a case report

The authors declare no financial disclosure

Abstract

Pulmonary alveolar proteinosis is a very rare interstitial lung disease caused by abnormal intra-alveolar surfactant accumulation. Usually, it appears as a „crazy-paving” pattern on high-resolution computed tomography. The image is so typical, that together with the characteristic bronchoalveolar lavage examination with presence of Periodic Acid Schiff positive substance is sufficient for establishing diagnosis, without histological confirmation. We present the case of the young woman with severe dyspnoea suspected of acute hypersensitivity pneumonia. The computed tomography showed numerous intralobular nodules uniformly distributed throughout the lungs. Treatment by corticosteroids had no clinical effect and next computed tomography showed progression. Despite the high risk of complications (patient had a respiratory failure), a surgical lung biopsy was performed and the histopathological diagnosis of pulmonary alveolar proteinosis was made. The whole lung lavage procedure performed twice caused regression of radiological lesions and respiratory failure.

Key words: respiratory failure, pulmonary alveolar proteinosis, computed tomography, whole lung lavage

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Introduction

Pulmonary alveolar proteinosis (PAP) is a rare disease with a prevalence of 3.7–6.2/1 000 000. There are three main forms of PAP: hereditary, secondary and autoimmune, but common to all is impaired clearance of surfactant by alveolar macrophages, resulting its retention in the terminal airway and in the alveolar space [1]. A chest computed tomography (CT) commonly showing a „crazy-paving” pattern, is a major tool in the diagnosis of PAP. The image is so typical, that together with the characteristic bronchoalveolar lavage (BAL) examination with presence of Periodic Acid Schiff (PAS) positive substance is sufficient for establishing diagnosis [2]. We present the case of the young woman with severe dyspnoea and radiological image suggesting hypersensitivity pneumonia (HP). The final diagnosis of PAP was

established basing on the histological examination of surgical lung biopsy specimens.

Case report

A 31-year-old caucasian woman admitted to National Research Institute of Tuberculosis and Lung Diseases with a 1 month history of worsening dyspnoea and cough, without fever. She was non-smoker and reported exposure to chemical compounds — last 6 months she worked on the production of car mats (exposure to lead, zinc, solvents) and she had a contact with the pigeons, but it was an accidental exposure. Before her admission she had been treated by empirical antibiotics and bronchodilators without improvement.

On admission she was in severe general condition. Respiratory rate was 28 breaths per min, heart rate 120 beats per min, and oxygen

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saturation was 68% on room air. Chest examination showed good air entry with no abnormal sounds. Her full blood count, C-reactive protein, antinuclear antibodies and complement levels were normal, but she had a raised lactate dehydrogenase (LDH) concentration of 1123 U/L (normal 200–384 U/L). Pulmonary function tests showed reduced diffusing capacity of the lung for carbon monoxide (DLCO) to a severe degree (35% N). Chest radiograph showed bilateral non-specific disseminated lesions and high resolution computed tomography (HRCT) appeared numerous intralobular nodules uniformly distributed throughout the lungs (Figure 1). Based on the HRCT image together with the exposure to the pigeons' antigens in medical history, HP was strongly suspected. Patient received 30 mg of prednisone without clinical improvement and respiratory failure remained ($\text{PaO}_2 = 32\text{--}40$ mm Hg). She required oxygen supplementation 3–5 L/min, despite increased dose of corticosteroids (CS) to 60 mg daily. Control HRCT showed a progression of the intralobular opacities with the appearance of the discrete „septal thickening”. Bronchoscopy with transbronchial lung biopsy (TBLB) was performed, but histological examination was not conclusive. All cultures were negative. Patient underwent bronchoalveolar lavage, but the procedure had to be stopped, because of severe dyspnoea with decrease of the oxygen saturation. After 3 weeks of corticotherapy without marked improvement, surgical lung biopsy was performed to determine the diagnosis. The histopathological

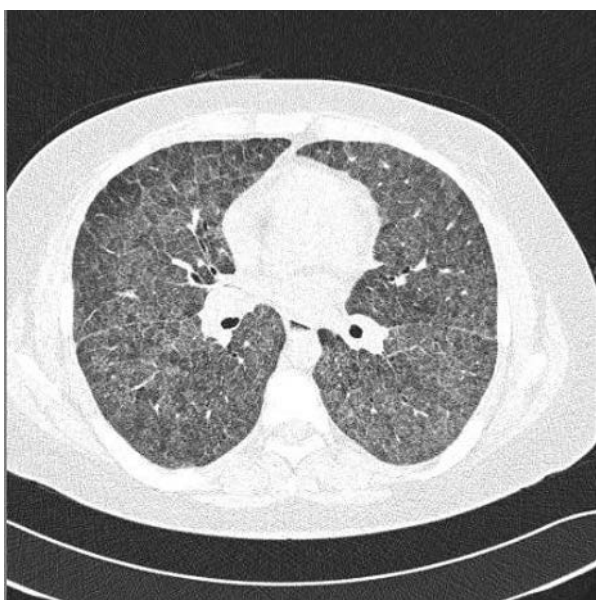


Figure 1. High-resolution computed tomography scan showing atypical image of PAP — numerous diffuse intralobular nodules

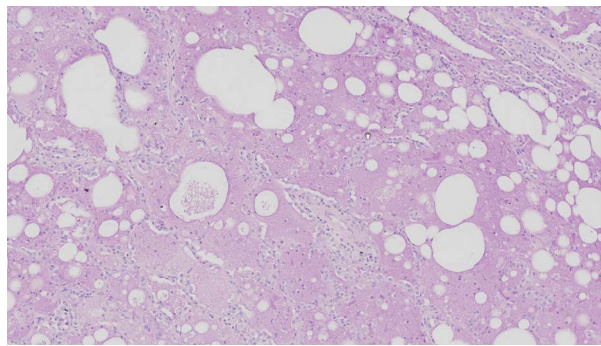


Figure 2. Surgical biopsy photomicrograph — alveoli filled with PAS-positive staining substance (original $\times 400$)

examination revealed alveoli and terminal bronchioles filled with an eosinophilic proteinaceous material that stained pink with PAS — the diagnosis was PAP (Figure 2). Anti-granulocyte macrophage — colony stimulating factor (anti-GM-CSF) antibody concentrations — the gold standard for diagnosis of autoimmune PAP — is not available in Poland. The CS were gradually eliminated and stopped and whole lung lavage (WLL) with 10 L of 0.9% saline was performed (in the operating room under general anaesthesia). Directly after one procedure, the clinical improvement was observed. At last follow-up after 6 weeks, the patient was asymptomatic and chest radiograph showed regression of the disseminated lesions (Figure 3A, B).

Discussion

PAP is a rare syndrome characterized by the accumulation of surfactant — like substance in pulmonary alveoli resulting in varying degrees of respiratory insufficiency and myeloid cell dysfunction resulting in increased risk of infection [1]. Autoimmune PAP occurs, when anti — GM-CSF antibodies block activation of alveolar macrophages. It is the most common type of PAP and accounts for 90% cases. Congenital PAP is caused by mutations in surfactant proteins genes B or C, ABCA3 and a chain of the GM-CSF receptor. Secondary PAP is an acquired defect of malignancies, inhalation of inorganic agents or opportunistic infections [3]. Our patient had exposure to chemical compound, like lead, zinc and solvents during last 6 months, which may suggest the secondary type of the disease, but recent studies showed, that a history of chemical substances inhalation may be strongly associated also with the autoimmune form of PAP [4]. A Differentiating factor could be examination of the

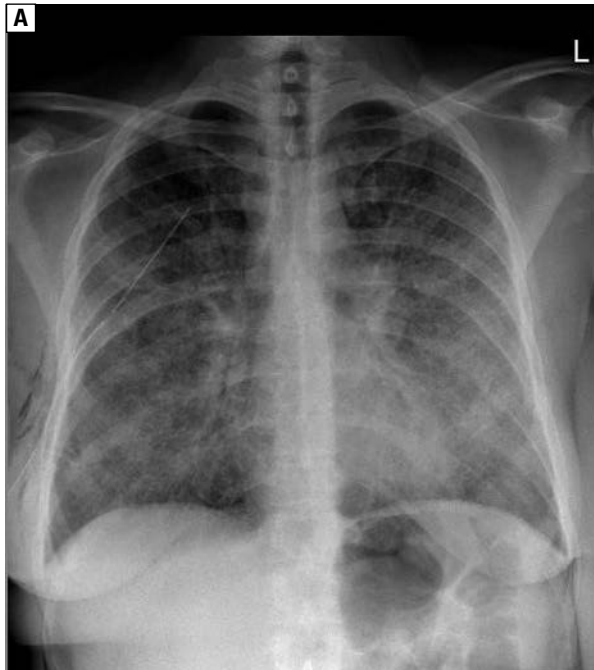


Figure 3A. Chest radiograph before whole lung lavage — visible disseminated lesions in the lungs

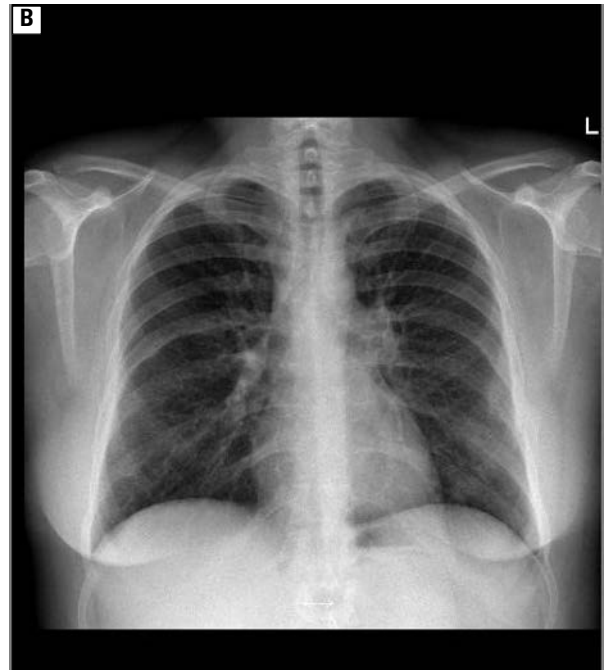


Figure 3B. Chest radiograph after whole lung lavage — complete regression of lesions

anti-GM-CSF antibody concentration in patient's serum, but in Poland it is not available. On the other hand, autoantibodies are detected also in secondary PAP, but are much less common [5]. IgG anti-GM-CSF have been described in a patient with PAP secondary to exposure to indium [6].

The most often symptoms of PAP are dyspnoea and cough (39–79%), which are common, but non-specific symptoms seen by medical practitioners [3]. An important examination for the diagnosis of PAP is HRCT, which shows lesions in the form of ground-glass opacities with visible polygonal structures — the so-called „crazy paving” pattern. The areas of filled alveoli are usually separated from the normal lung parenchyma making a geographical pattern (Figure 4) [7]. Vrielynck et al. evaluated the accuracy of chest CT in the differential diagnosis of chronic infiltrative lung disease in children. Among a cohort of 59 patients with nine disorders, PAP was the most frequently properly diagnosed (72%), showing that the HRCT appearance of PAP is suggestive of the disease [8]. Current guidelines imply, that characteristic image of HRCT together with a typical results of the examination of BAL are sufficient criteria for establishing diagnosis, without histological confirmation [2, 7]. Unfortunately, in our patient we have not received material from BAL, because of severe respiratory failure. On the other hand, HRCT showed multiple intralobular nodules uncharacteristic for PAP and in this

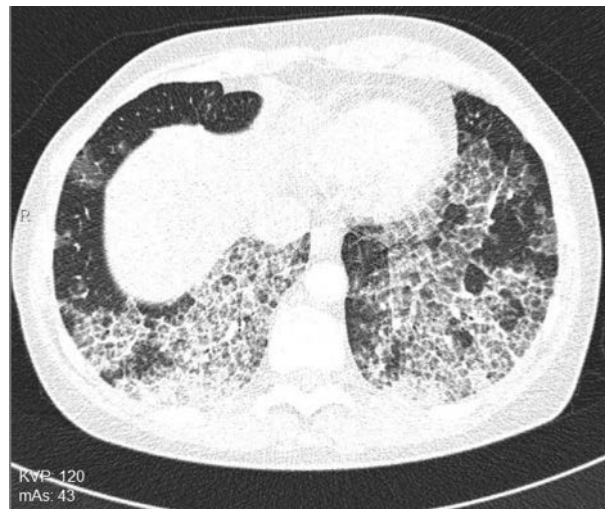


Figure 4. High-resolution computed tomography scan showing typical image of PAP: ground-glass opacities with visible polygonal structures — the so-called „crazy paving” pattern (from own collection of the Third Department of Pneumology, National Research Institute of Tuberculosis and Lung Diseases)

situation typical BAL examination could not be sufficient for diagnosis of PAP. Clinical course of disease was against of HP diagnosis and surgical lung biopsy was necessary. Perhaps, the decision to proceed surgical biopsy could be taken at the time the lack of therapeutic effect of 30 mg of prednisone, but patient was in a serious condition with respiratory failure and we wanted to take the

opportunity of optimal treatment, before deciding on the invasive procedure. Our case shows, that HRCT image of PAP can be atypical and uncharacteristic, which may hinder correct diagnosis. Intralobular nodules observed in our patient conform an unusual and occasional manifestation of PAP. In the Holbert's et al study investigating the HRCT features of PAP in a group of 27 patients, intralobular lesions were found only in two cases (7.4%) [9], while Berteloot et al found intralobular nodules only in one case of PAP (4.2%) [10]. In the material of Fijolek et al., among the 17 patients with PAP, in 4 cases another interstitial diseases were considered, but PAP was also taken into account [11]. Although the nodular appearance of PAP on HRCT could not be clearly explained, the appearance of such pattern may suggest very early PAP in patients.

There are no firm criteria for initiation of therapy of PAP, but according to the majority of authors, the treatment is necessary in case of hypoxaemia ($\text{PaO}_2 < 65 \text{ mm Hg}$ or $< 60 \text{ mm Hg}$) or saturation below 90%, the growth of alveolo-capillary gradient of oxygen partial pressure above 40 mm Hg, pulmonary shunt exceeding 10–12% and/or dyspnoea limiting daily activities of the patient [12, 13]. Still the most effective and safe method of treatment is WLL, which removes surfactant-like material from the alveoli [7, 11, 14]. The improvement starts within days and is sustainable in many. Usually, oxygenation improves first, chest imaging shows varying degrees of resolution, but complete resolution of opacities is uncommon. Our patient met the eligibility criteria for treatment and improvement was quickly observed — few days after WLL blood gases normalized, and follow-up HRCT image performed 6 weeks later showed almost complete regression of the disease.

In conclusion, radiological image of PAP at HRCT is usually typical and it is decisive for diagnosis, but sometimes HRCT is not characteristic and may suggest other disease. Bilateral diffuse intralobular nodules can be caused by infection, panbronchiolitis, vasculitis and vascular metastases, respiratory bronchiolitis-interstitial lung disease, HP and pneumoconiosis [15]. Our case shows, that in case of disseminated intralobular nodules in CT, PAP — although extremely rare — should be taken into consideration in differential diagnosis. Our conclusion is, that in cases of undiagnosed diffuse pulmonary disease, espe-

cially in young patients the surgical lung biopsy should be performed. The precise diagnosis is necessary to implement appropriate treatment, without exposing the patient to the inadequate therapy and its possible side effects.

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Conflict of interest

The authors declare no conflict of interest.

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