Pulmonary Aluminosis Diagnosed with In-air Microparticle Induced X-ray Emission Analysis of Particles

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Abstract

We herein present a case of pulmonary aluminosis diagnosed with in-air microparticle induced X-ray emission (in-air micro-PIXE) analysis. The diagnosis of pulmonary aluminosis was supported by the occupational exposure to aluminum, ground glass opacity and ill-defined centrilobular nodular opacities seen in high resolution CT, and respiratory bronchioles accompanied by pigmented dust by histological examination by in-air micro-PIXE analysis of the lung tissues. The possibility of developing this rare condition should not be underestimated in workers at high-risk jobs. This is an important report showing the usefulness of an in-air micro-PIXE analysis for the early diagnosis of aluminosis.

Key words: aluminosis, in-air microparticle induced X-ray emission analysis, pneumoconiosis, elemental analysis

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Introduction

Inhalation exposure to dust containing aluminum particles or its compounds leads to progressive pulmonary fibrosis, called aluminosis. Although lung fibrosis induced by aluminum dust is rare under today’s working conditions, it is important to distinguish aluminosis from idiopathic interstitial pneumonia. In-air microparticle induced X-ray emission (in-air micro-PIXE) analysis is a method for elemental analysis of materials by irradiation with a proton microbeam. Here we presented a case of pulmonary aluminosis diagnosed with aluminum detection in a lung specimen by an in-air micro-PIXE analysis.

Case Report

A 70-year-old man was referred to our hospital with a month-long history of cough. He had been working in an aluminum processing factory for 25 years. A chest X-ray abnormality had been pointed out four years before the consultation. Physical examination revealed fine crackles in the bilateral lower lungs, and his oxygen saturation by pulse oximetry was 96% on room air. Laboratory findings (Table 1) demonstrated elevated serum levels of Krebs Von den Lungen 6 (1,856 U/mL [normal, <500 U/mL]), and surfactant protein D (157.3 ng/mL [normal, <110 ng/mL]). Antinuclear antibodies and each autologous antibody were all negative. His chest radiograph showed diffused ground glass opacity, and the CT scan demonstrated predominantly ill-defined centrilobular nodular opacities (Fig. 1). The mediastinal lymph nodes were highly attenuated (Fig. 1B). A pulmonary function test suggested a restrictive ventilatory pattern (vital capacity (VC) 2.6 L, % expected VC 75.5%) and a diffusion impairment [diffusing capacity of lung for carbon monoxide (DLCO) 15.7 mL/min/mmHg, % expected DLCO 84.5%].
Table 1. Laboratory Findings and Other Clinical Data.

| Laboratory findings          | BAL  |
|-----------------------------|------|
| WBC 6,100 /μL              |      |
| Neutrophil 56 %            |      |
| Lymphocyte 39.3 %          |      |
| Basophil 0 %               |      |
| Eosinophil 0.4 %           |      |
| Monocyte 4.3 %             |      |
| RBC 508 ×10^6/μL           |      |
| Pt 28.2 ×10^6/μL           |      |
| ESR 25 mm/h                |      |
| BAL 157.3 ng/mL            |      |

PFT BAL

VC 2.6 L
%VC 75.5 %
FVC 2.62 L
%FVC 77.8 L
FEV1.0 2.26 L
%FEV1.0 83.6 %
%DLCO 84.5 %
%DLCO/VA 102 %
6MWT (room air) CD4/8 5.1
SpO2 96%—93%
6MWD 525m

Bronchoalveolar lavage with a recovery rate of 59.3% from the right middle lobe bronchial revealed the elevation level of lymphocyte 66%, and the CD4/CD8 ratio was 5.1. Video- 

Discussion

Pulmonary aluminosis is defined as pneumoconiosis caused by the inhalation of dust containing aluminum into the lung tissue (1). It is caused by chronic exposure to aluminum or its compounds under diverse occupational circumstances and factors. Over 70-80 years, pulmonary disease caused by exposure to aluminum and its compounds have been sporadically reported in association with pulmonary fibrosis, asthma, alveolar proteinosis, lung cancer, granulomatosis, and bronchiolitis (2).

In Japan, 17 cases of aluminosis have been reported (Table 2). All patients were men and the median age was 52 [range 32-70] years old. The duration of exposure to aluminum varied from two months to 27 years, and the longest period between the last exposure and the onset of the disease was 55 years. The patient’s susceptibility to aluminum is supposed to have an individual difference. At least 9 out of 10 patients whose pathological examinations were documented in the reports had pathologically pulmonary fibrosis.

Among the aluminium-related lung abnormalities, pulmonary fibrosis has been the most frequently discussed. In the advanced stages, severe pulmonary fibrosis with honeycombing is described. Occupational exposure was thought to be a risk factor for interstitial pulmonary fibrosis. In addition, the frequency of pulmonary fibrosis in metalworkers was reportedly 1.26%, which was significantly higher than the other occupations (3). The other case-control study based on the questionnaire showed that exposure to metal dust was related to 9.55-fold increase risk in fibrosis. Addi-
Figure 1. (A) Chest radiograph on admission reveals diffuse ground glass opacity. (B) Chest CT image at the tracheal carina level shows ill-defined nodular shadow and ground glass opacity. Mediastinal lymph nodes were highly attenuated (arrows).

Figure 2. Low- and high-power views of the lung specimens in surgical biopsy. Histopathological study shows particles deposited around the bronchiole with peribronchial fibrosis. The presence of large amounts of particles, visible as pale staining crystals on the Hematoxylin and Eosin staining and brightly birefringent material with polarized light indicated that this is a pneumoconiosis.
Figure 3. Elemental analysis: The intensity of the element materials in lung tissue is shown by gray scale. White dots indicate the location of elements in the lung specimen. (A) This case, (B) Idiopathic pulmonary fibrosis without occupational inhalation. Phosphorus was markedly observed in both lungs from the patient and from control. Aluminum was prominently localized only in the patient’s lung. Silicon was slightly detected in the patient’s lung.

tional adjustment for the years of smoking did not change the association (4). An elemental analysis for hilar lymph node of autopsy specimens reported that the deposits of inorganic particles such as aluminium and silicon had significantly higher concentration in idiopathic pulmonary fibrosis patients (adjusted odds ratio 57.84; 95%CI 1.45-2,306.19 and 2.99, 95%CI: 1.29-6.85, respectively) (5).

Since the industrial importance and use of aluminium continues to rise, lung damage from exposure to aluminum particles should not be overlooked and should be monitored and prevented. It is desirable to detect the early stages of the disease using a high resolution CT (HRCT) and to diagnose it with state-of-the-art methods such as in-air micro-PIXE analysis.

In the previous study, the HRCT findings in aluminium powder workers with or without aluminosis were reported as parenchymal changes characterized by small rounded opacities predominantly in the upper lobes (24.2%), with thickening of the interlobular septum (5%) (6). Microscopically, aluminosis is characterized by diffuse alveolar septal fibrosis associated with aggregates of brown-black dust particles (7). In some cases, multinuclear giant cells and macrophages were present suggesting a foreign body type reaction (8). The histopathological study in this case revealed all those pathological findings above. Based on the histopathological and radiological findings, we could suspect pulmonary aluminosis and proceed with the elemental analysis.

An in-air micro-PIXE analysis enables visualizing of the spatial distribution and quantitation of the various elements with higher sensitivity in a smaller amount of samples. No specific chemical treatment is necessary when preparing the samples. An accelerated 3.0 MeV proton beam is usually employed in the analysis, and the characteristic X-ray peaks from irradiated samples are specific for each element. The X-ray peaks distinguish up to 40 elements with lower background noise, and could be used to quantitate the content of each element, especially the heavy elements (9). The electron beam method, which is currently the most widely used, performs elemental analysis by irradiation with an electron beam, at approximately 2,000 times lighter than proton microbeam. Because the mass of electron is small, the electron is easily curved by atomic nucleus and generates braking radiation, resulting in increased background noise and decreased sensitivity. With this advantage, the in-air micro-PIXE analysis has been adopted to detect the intercellular and intracellular distribution of the particles in clinical samples (10).

This method has been applied for the diagnosis of asbes-
Table 2. Reported Cases of Pulmonary Aluminosis in Japan.

| Reference year | Age | Gender | Occupation | Years after exposure | Fibrosis | Element Analysis | Complications | Outcome | Cause of death |
|----------------|-----|--------|------------|----------------------|----------|------------------|---------------|---------|----------------|
| 12 1956        | 39  | M      | Grinder/8y | 8                    | +        | TB,PTX           | Death         | PTX     |                |
| 13 1956        | 32  | M      | Welder/3y  | 3                    | +        | TB                | Death         | RF      |                |
| 14 1970        | 32  | M      | Grinder/3y | 3                    | +        | TB/PTX           | Death         | RF      |                |
| 14 1970        | 39  | M      | Recycler/10y| 8                    | +        | TB/PTX           | Death         | PTX     |                |
| 14 1970        | 52  | M      | Recycler/3y | 3                    | +        | TB                | Death         | RF      |                |
| 14 1970        | 66  | M      | Grinder/10y| 8                    | +        | EDXA             | Death         | RF      |                |
| 14 1970        | 42  | M      | Recycler/3y | 10                   | Unknown | TB                | Unknown       | -       |                |
| 14 1970        | 57  | M      | Recycler/5y | 3                    | Unknown | TB                | Unknown       | -       |                |
| 14 1970        | 57  | M      | Grinder/25y| 10                   | +        | EDXA             | TB/PTX        | Death   | PTX            |
| 15 1989        | 70  | M      | Grinder/27y| 55                   | +        | EDXA             | TB/PTX        | Unknown |                |
| 16 1989        | 62  | M      | Grinder/10y| 25                   | +        | EDXA             | TB            | Unknown |                |
| 17 1991        | 60  | M      | Grinder/12y| 12                   | + (UIP)  | Not performed    | -             | Unknown |                |
| 18 1992        | 52  | M      | Recycler/18y| 18                   | -        | Not performed    | PTX           | Unknown |                |
| 19 1997        | 63  | M      | Stone worker/5y| 0                   | + (UIP)  | Not performed    | ICP           | RA      | Unknown        |
| 20 1999        | 43  | M      | Grinder/18y| 0                    | + (UIP)  | EPMA             | -             | Unknown |                |
| 21 2000        | 67  | M      | Grinder/2m  | 30                   |          | EDXA             | MPA           | Unknown |                |
| 22 2010        | 39  | M      | Processor/18y| 1                    | +        | EPMA             | PTX           | Unknown |                |
| This case      | 2014| 70     | Processor/25y| 3                    | +        | In-air micro-PIXE| -            | Alive   |                |

TB: tuberculosis, PTX: pneumothorax, RF: respiratory failure, UIP: usual interstitial pneumonia, EDXA: Energy dispersive X-ray analysis, ICP: Inductively Coupled Plasma Atomic Emission Spectroscopy, EPMA: electron probe microanalysis, in-air micro-PIXE: In-air microparticle induced X-ray emission analysis

This case

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The authors state that they have no Conflict of Interest (COI).

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