The Occurrence of Leukemia in a Patient with Pulmonary Asbestosis

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A 77-year-old man, who had been a subway construction worker, was admitted to our hospital for surgical treatment of left cheek carcinoma and an examination for pancytopenia on November 17, 1986. Bone marrow aspiration revealed that 10% of the nucleated cells were blasts with morphological atypism. Bone marrow biopsy showed hypocellular marrow and a diffuse increase of argyrophil fibers with the presence of asbestos fibers was observed by microscope. A chest X-ray showed the findings of old tuberculosis and pulmonary asbestosis, and asbestos fibers were demonstrated in the broncho-pulmonary lavage fluid. He was diagnosed to have pulmonary asbestosis complicated with hypoplastic low percentage leukemia.

Key words: Asbestosis, Hypoplastic low percentage leukemia

It has been known that pulmonary asbestosis is complicated with various neoplasms, such as lung cancer, mesothelioma and gastrointestinal tumor. Regarding the mechanism of their relationship, immunological abnormalities or the direct effect of the asbestos have been considered. It is intriguing that neoplasms occur not only in the respiratory system but also in various other systems. The present case concerns pulmonary asbestosis complicated with hypoplastic low percentage leukemia. Moreover, asbestos bodies and/or fibers were detected in both the broncho-pulmonary lavage fluid and the bone marrow.

CASE REPORT

A 77-year-old man, who had been a subway construction worker for about 10 years, was admitted to Niigata University Hospital for surgical treatment of a left cheek tumor on November 17, 1986. His family history was not contributory. His past history showed that he had had an operation for a gastric ulcer at the age of 63. The tumor was noticed on his left cheek in April 1986 and had grown gradually until admission. A biopsy of the tumor revealed squamous cell carcinoma. Pancytopenia was simultaneously observed at a preoperative examination on November 17, 1986.

The physical examination showed ulcerative cheilitis at a right angle. There was no hepatosplenomegaly. Breathing was normal. Laboratory findings were as follows: erythrocyte sedimentation rate was 131 mm/h; Mantoux's test was negative; severe pancytopenia (RBC:1.32 x 10^6/μl, WBC:700/μl, Hb:5.2 g/dl, Plt:33 x 10^3/μl) was detected, CRP was 4+, RA 2+ and IgG 2,266mg/dl. In analysis of lymphocyte subsets, OKT-3 positive cells were 46.5%, OKT-4 14.7% and OKT-8 37.8% (OKT-4/OKT-8 = 0.39). Responses of lymphocytes to PHA and ConA were extremely low compared with control lymphocytes. The activity of natural killer cells was also decreased. Blood gas analysis was within the normal range.

Bone marrow aspiration showed hypocellular marrow and the smear preparation of marrow

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revealed the proportion of the blasts with morphological atypism to be 10% of nucleated cells (Fig. 1). Erythroid and granuloid cells were suppressed; the percentages among all nucleated cells being 19.4% and 23.2%, respectively. Lymphocytes and plasma cells were relatively increased to 35.8% and 6.0%, respectively. The blasts were negative for myeloperoxidase. The low percentage of the marrow

Fig. 1. The blasts with morphological atypism were observed on the marrow smear preparation stained with May-Giemsa (×1,500). The nucleus showed a fine chromatin configuration and the cytoplasm was basophilic.

Fig. 2. a: Argyrophil asbestos fibers (arrow) were observed in the bone marrow biopsy specimen by polarized microscope (×1,000). b, c: A bending rod-like asbestos body (b) and a needle-like asbestos fiber (c) were observed in the broncho-pulmonary lavage fluid by light microscope (×400). d: Asbestos bodies (arrow) were observed also in the cytoplasm of macrophages in the broncho-pulmonary lavage fluid by polarized microscope (×400).
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blasts made it difficult to characterize them. Cytogenetical analysis of bone marrow cells showed a normal karyotype. Bone marrow biopsy showed a diffuse increase of argyrophil fibers and hypo-

A chest X-ray showed the findings of old tuberculosis on bilateral pulmonary apices and shadows of pulmonary asbestosis over all lung fields (Fig. 3). $^{67}$Ga scintigraphy showed diffuse accumulation over all lung fields (Fig. 4). Bending rod-like asbestos bodies (Fig. 2b) and needle-like asbestos fibers (Fig. 2c) were demonstrated in the broncho-pulmonary lavage fluid by light microscope. Moreover, asbestos bodies were observed in the cytoplasm of macrophages by polarized microscope (Fig. 2d).

This patient was diagnosed as pulmonary asbestosis complicated with hypoplastic low percentage leukemia. After the removal of skin squamous cell carcinoma, the treatment for leukemia was started on January 5, 1987, with gamma-interferon (GI-3; Toray, Tokyo, Japan). A dose of $0.3-0.6 \times 10^6$ IU of gamma-interferon was injected subcutaneously daily for 54 days, for a total amount of $28.2 \times 10^6$ IU. Although it was not effective in improving pancytopenia, the percentage of marrow blasts decreased to 2.6% after the treatment with gamma-interferon, but the suppression of blasts by gamma-interferon was transient. Though he was treated with vitamin D$_3$ at an outpatient clinic, anemia progressed and transfusions of packed red cells were required until January 1989, when this paper was written.

**DISCUSSION**

It has been reported that pulmonary asbestosis can be complicated with various neoplasms such as mesothelioma, lung cancer, ovarian tumor, gastrointestinal tumor, renal tumor or hematological malignancies (1–5). But there have been few published reports on asbestos-related hematological malignancies (1, 3–8). Gerber reported five asbestosis-related hematological malignancies (multiple myeloma in 2 patients, myeloproliferative disorders in 2, and Waldenstrom’s macro-globulinemia in one), and he showed that the incidence of this association was higher than the incidence of such disorders in the corresponding age group of patients without asbestosis (4). Lieben reported 21 cases with asbestos-related neoplasms,
and recognized hematological malignancies in 5 of these 21 cases (lymphatic leukemia in 2 cases, malignant lymphoma in 1, multiple myeloma in 1, and type undetermined acute leukemia in 1) (3). In his paper, he showed that the incidence of malignancy in patients with asbestosis was eight times higher than in the general population (3). Other investigators, however, reported that the mean latent period between the onset of exposure and diagnosis of asbestosis-related neoplasm was about 25 years (2). This long interval would make it difficult to establish the actual relationship between asbestos and various neoplasms.

Regarding the prognosis, some reports showed that the average interval between initial exposure to asbestos and death in lung cancer is about 35 years (4). Goldsmith analyzed the causes of death of 1,845 cases with pulmonary asbestosis in 1982 and demonstrated that death was caused by lung cancer in 42% of the patients with pulmonary asbestosis, mesothelioma 17%, gastrointestinal cancer 7%, and other neoplasms 10% (9). But the precise incidence and prognosis of asbestos-related hematological malignancies remains uncertain.

It is intriguing that malignancies associated with pulmonary asbestosis occur not only in the respiratory system but also in various other systems. Kobayashi et al and Auerbach et al demonstrated asbestos fibers in esophagus, spleen, pancreas, thyroid gland and bone marrow in the autopsied specimens of patients with pulmonary asbestosis (10-13). In the present patient, the presence of asbestos fibers was demonstrated not only in the broncho-pulmonary lavage fluid but also in bone marrow and in cytoplasm of macrophages. Some investigators suggest the possibility that asbestos fibers become widely disseminated by the blood and lymphatic stream throughout the human body (4, 10, 11, 14).

The complication of neoplasms in patients with pulmonary asbestosis is reported to be related to impaired immunological mechanisms, especially T cell dysfunction, or to the carcinogenicity of asbestos (1, 15, 16). In this patient, immunological dysfunction was suggested from the laboratory data (negative Mantoux’s test, inverted ratio of OKT-4/OKT-8, low response of lymphocytes to PHA and Con A, and decreased activity of natural killer cells), but an actual relationship between this dysfunction and the onset of low percentage leukemia was uncertain.

In this case, hypoplastic low percentage leukemia was demonstrated in the bone marrow sample, in which asbestos fibers were present. Therefore, the present case suggests the association of asbestos bodies and the onset of hypoplastic low percentage leukemia.

REFERENCES