Malignant Lymphoma Involving the Penis Following Malignant Pleural Mesothelioma

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A 74-year-old man who had been diagnosed with malignant mesothelioma developed malignant lymphoma of B-cell origin involving the penis. He had a history of occupational exposure to asbestos as a construction worker. The association of malignant mesothelioma with lymphoma is rare, and the possibility of asbestos exposure as a common etiology is discussed. The intense stimulation of B lymphocytes and decreased T lymphocyte activity in asbestos-exposed populations may result in development of B-cell malignancies. Though the relationship between asbestos exposure and malignant mesothelioma is firmly established, the relationship between asbestos exposure and lymphoma remains to be investigated.

Introduction

The association between asbestos exposure and malignant mesothelioma was clearly established in 1960 (1). Asbestos exposure is also related to lung cancer and laryngeal cancer. In addition, epidemiologic studies suggest a relationship between asbestos and cancers at other sites, including the gastrointestinal tract, kidney, liver, pancreas, ovary and hematopoietic systems (2). Several studies have examined the connections between asbestos exposure and the development of malignant lymphoma. Ross et al (3) have reported an excess of large-cell lymphomas primary to the gastrointestinal tract and oral cavity in an asbestos-exposed population.

However, the association of malignant mesothelioma and malignant lymphoma has been described only twice (4, 5). We report a patient with occupational exposure to asbestos in whom malignant mesothelioma was followed subsequently by malignant lymphoma involving the penis.

Case Report

A 74-year-old man who had been diagnosed with malignant mesothelioma was admitted to the hospital in July 1993 because of penile pain. He was a former construction worker and had a history of occupational asbestos exposure.

The patient had been in stable health until twenty months earlier, when dyspnea on exertion developed and a chest radiograph revealed a right pleural effusion. Laboratory results and findings from thoracentesis and pleural biopsy specimens were not conclusive. A tuberculin skin test was positive. With a presumptive diagnosis of pleural tuberculosis the patient was started on therapy with three anti-mycobacterial drugs, but the right pleural effusion increased gradually. In May 1992 pleural biopsy was repeated, with examination of the specimen revealing malignant mesothelioma of the epithelial type (Fig. 1). Long, slender microvilli were noted on electron microscopic examination (Fig. 2). In June 1992 chemical pleurodesis was performed because of the recurrent pleural effusion. Two weeks prior to the reported admission, penile pain developed and he noticed swelling at the base of his penis.

Physical examination revealed decreased breath sounds over the base of the right lung and swelling at the base of the penis, but no lymphadenopathy. Laboratory findings included an elevated erythrocyte sedimentation rate and serum lactate dehydrogenase (635 U/l). A chest radiograph (Fig. 3) showed a large pleurally based tumor in the right apical region, as well as decreased breath sounds over the right base of the lung and swelling of the penis.
as a blurred right costophrenic angle. Gallium scintigraphy (Fig. 4) showed marked accumulation at the root of the penis and in the left upper abdomen and right chest. Abdominal computed tomography (CT) revealed enlarged para-aortic and splenic hilar lymph nodes.

A biopsy specimen from the penile tumor revealed malignant lymphoma of diffuse mixed type (Fig. 5). Immunohisto-
Association of malignant lymphoma with mesothelioma has been reported only twice. Efremidis et al. (4) described a 61-year-old patient with a diffuse, poorly differentiated lymphocytic lymphoma who developed malignant mesothelioma of the epithelial type 9 years later. Tondini et al. (5) described a 58-year-old patient in whom malignant mesothelioma of the epithelial type and plasmacytoid lymphocytic non-Hodgkin's lymphoma developed simultaneously. Efremidis et al. (4) described several possible explanations for the combined occurrences: coincidence; increased susceptibility to cancer due to malignant lymphoma; radiation or chemotherapy for the first neoplasm increasing the likelihood of the second; and a common etiology such as asbestos exposure. Tondini et al. (5) emphasized the intense stimulation of B lymphocytes and decreased T lymphocyte activity seen in asbestos-exposed populations (6) as possibly resulting in development of B cell malignancies, and described other B-cell proliferations, including one previously reported case of multiple myeloma (7), plasmacytoma (8), and chronic lymphocytic leukemia (4) associated with malignant mesothelioma. Kagan and Jacobson (9) have described two IgG-secreting multiple myelomas coexisting with malignant mesothelioma in among 13 lymphoplasmacytic neoplasms with asbestos exposure, stating that the fortuitous occurrence of these two neoplasms seemed unlikely.

While the relationship between asbestos exposure and malignant mesothelioma is firmly established (1), the relationship between asbestos exposure and malignant lymphoma remains uncertain. Several studies have sought to connect asbestos exposure to the development of malignant lymphoma. Robinson et al. (10), following a cohort of 3,276 asbestos workers, documented 7 deaths from malignant lymphoma, while only 3 would have been expected. Ross et al. (3) documented a previous history of asbestos exposure in 24 of 28 large-cell lymphomas primary to the gastrointestinal tract and oral cavity, but in only 8 of 28 matched controls. Although an increased incidence of malignant lymphoma was not demonstrated, Bengtsson et al. (11) documented 12 (10.2%) asbestos-exposed subjects among 109 patients with non-Hodgkin's lymphomas. Olsson et and Brandt (12) also found 10 patients (20%) with confirmed asbestos exposure in 50 large-cell lymphoma cases. Kagan and Jacobson (9) and Roggli et al. (13) each reported one case of malignant lymphoma with a history of asbestos exposure. Using a bleach digestion method (14), we have demonstrated 104 and 605 asbestos bodies per gram (unpublished observation) in the lung tissues of two autopsy cases of malignant lymphoma with parietal pleural plaques, which are regarded as a significant indication of exposure to asbestos (15).
In experimental studies, Wagner et al (16) produced 8 occurrences of lymphoma or leukemia in 713 rats exposed to aerosolized asbestos with 2 instances observed in controls, a difference not attaining significance. However, Ozsemi et al (17) produced 52 (16.5%) malignant mesotheliomas and 42 (13.3%) malignant lymphomas, with 11 instances of both developing in the same host, in 321 mice receiving intraperitoneal injections of fibrous zeolite, a material similar to asbestos. These findings were statistically significant compared to animals receiving only talc or saline solution.

Inhaled asbestos fibers are transported via the lymphatics and the bloodstream to various organs. Roggli and Benning (18) demonstrated asbestos bodies in pulmonary hilar lymph nodes, and Dodson et al (19) also detected asbestos fibers in tracheal lymph nodes. Auerbach et al (20) identified ferruginous bodies in the spleen and other organs remote from the lung in asbestos workers, while Kishimoto (21) detected asbestos fibers in the bone marrow of patients with acute leukemia. Although malignant lymphoma involving the penis is very rare (22), and we lack information regarding asbestos content of penile tumor tissues, an asbestos association cannot be denied on the basis of remoteness of the site.

While malignant lymphoma in this case may conceivably have resulted from a cause other than asbestos, asbestos remains a major problem in environmental medicine. A careful history of occupational, environmental, or familial exposure to asbestos should be obtained in patients with lymphoid neoplasms to provide more useful epidemiologic data.

Malignant mesothelioma is unresponsive to conventional therapy. Its prognosis is poor, with a median survival of 6 to 12 months (23). Roggli et al (24) stated that the frequency of a second primary cancer in patients with pleural mesothelioma does not differ from the general rate of second cancer occurrence when they reported 4 cases of dual primaries in a series of 129 consecutive pleural mesotheliomas. This finding actually raises the possibility of an increased incidence of second cancers with malignant mesothelioma relative to the short life expectancy of these patients. Patients with malignant mesothelioma who do show a longer survival (25) should be followed carefully for second occurrences of cancer including malignant lymphoma.

Acknowledgements: We are grateful to Drs. Samuel J. Pierce and Gerald R. Christensen of the Naval Hospital at Yokosuka, for reviewing the manuscript.

References