Spontaneous Regression of Malignant Pleural Mesothelioma

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We describe the spontaneous regression of a malignant pleural mesothelioma with left pleural effusion, chest pain, and a high fever (38° to 39°C) in a 37-year-old man. The patient was referred to us because multiple nodules were seen on his chest radiograph after he was successfully treated with thoracocentesis and conventional antibiotic therapy for pleural effusion. Our diagnosis was malignant pleural mesothelioma, based on histologic findings in a biopsy specimen obtained during thoracoscopy. Interestingly, the tumors markedly regressed without treatment, and the patient was doing well more than 5 months after the cancer was diagnosed. The spontaneous regression of malignant pleural mesothelioma is rare, and this may represent the first case report.

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INTRODUCTION

Malignant mesothelioma is a rare tumor arising most commonly from the pleura (approximately 80%), followed by the peritoneum. It is well-known that the risk of mesotheliomas has increased with the increasing use of asbestos; asbestos exposure has been reported in 60% to 90% of the patients with this disease.[1,2] Although surgery, chemotherapy, radiotherapy, or a combination of these therapies have been used in the treatment of patients with mesotheliomas, the incidence of complete recovery remains low, with few long-term survivors.[3] We report a recent case of spontaneous regression of malignant pleural mesothelioma in a 37-year-old Japanese man.

CASE REPORT

A 37-year-old Japanese man noted the onset of a fever (38° to 39°C) and chest pain in his left side on July 25, 1994. A chest radiograph obtained on this date, at his presentation at a local hospital, disclosed a moderate pleural effusion in the left thorax. Thoracocentesis revealed a clear, yellowish fluid without evidence of infiltration by abnormal cells. The levels of adenosine deaminase, hyaluronidase, and lactate dehydrogenase in the pleural effusion were not assessed. The patient was treated with conventional antibiotic therapy, consisting of 2 g/day of cefoperazone sodium/sulbactam and 1 g/day of imipenem/cilastasin sodium, resulting in resolution of the pleural effusion within 3 weeks of treatment. One month later, multiple nodules along the left pleura were visible on a follow-up chest radiograph. The patient was referred to us on September 30, 1994 for further examination. His work history included the gas analysis of chemical products including carbon dust, zinc, and iron for 10 years, but no history of asbestos exposure. He had smoked 20 to 40 cigarettes a day for 20 years.

During the physical examination the basal area of the left thorax was dull to percussion with diminished breath sounds. Neither systemic lymphadenopathy nor hepatosplenomegaly was found. Laboratory findings on admission included elevations of the C-reactive protein concentration (3.2 mg/dL), erythrocyte sedimentation rate (104 mm/h), and sialyl Lewis X concentration (72 U/mL). Other laboratory findings, including a complete blood cell count, blood chemistry values, immunoglobulin levels, and tumor marker concentrations (carcinoembryonic antigen, squamous cell carcinoma-related antigen, and neuron-specific enolase), were normal. Multiple nodules developing along the pleura of the left lung were visible on the chest radiographs (Fig. 1A) and computed tomography scans (Fig. 2A).

On the 27th hospital day, these nodules were con-

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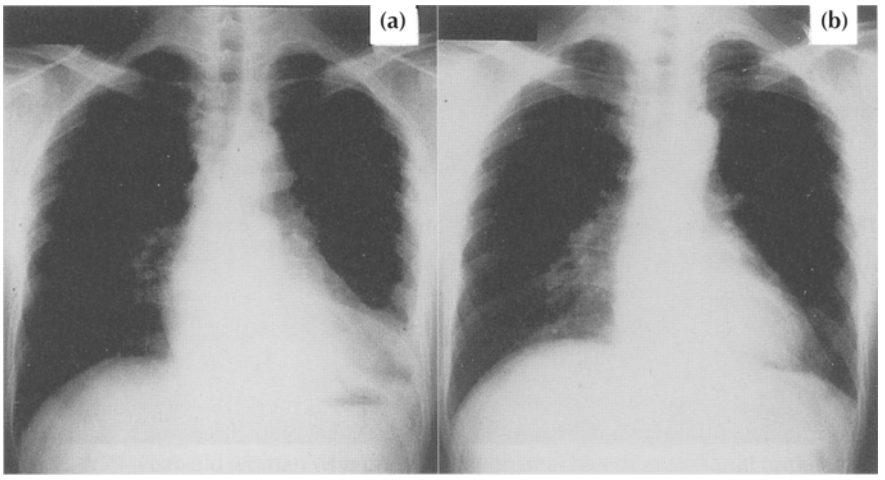

Fig. 1. (**a**) Chest radiograph obtained at time of referral to the authors (September 30, 1994) of a 37-year-old man with symptoms of fever and pain in his left chest. Multiple nodular lesions are visible in the left lung field. (**b**) Chest radiograph obtained the following March 10 (approximately 22 weeks later) shows almost complete regression of lesions.

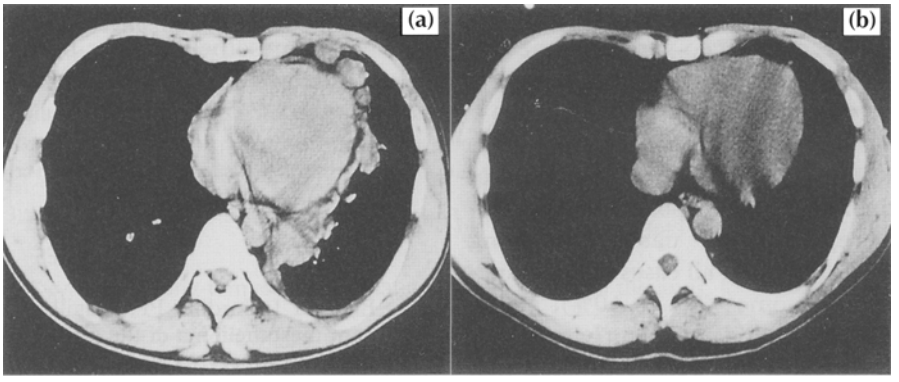

Fig. 2. (**a**) Contrast-enhanced, chest computed tomography scan in the patient described in Fig. 1, and also taken at the time of referral, shows multiple nodular lesions in contact with the pleura of the left lung. (**b**) Contrast-enhanced computed tomography scan of the chest in the same patient obtained the following March 10 shows an almost complete regression of the pleural lesions.

firmed by thoracoscopy as being present on the parietal pleura. The histologic diagnosis of the biopsy specimens was epithelial-cell diffuse malignant pleural mesothelioma (Fig. 3A). Mucoid deposits digested with hyaluronic acid showed Alcian blue stain on the cell membranes and cytosol (Fig. 3B). The patient was considered to have stage I disease, because all of the tumors were confined to the left pleural cavity. Intensive chemotherapy, which was scheduled for initial treatment of the patient, was postponed because follow-up computed tomography of the chest obtained 3 weeks after thoracoscopy revealed substantial regression of the nodules. A chest radiograph (Fig. 1B) and computed tomographic scan (Fig. 2B) obtained on March 10 showed almost complete resolution of the pleural nodules. At his most recent follow-up, on March 17, 1995, the patient was doing well and had no evidence of recurrence.

DISCUSSION

Although exposure to asbestos has been considered the major etiologic factor in this condition, our patient had no history of direct asbestos exposure. However, an environmental exposure to asbestos may be associated with this occurrence of mesothelioma, because the patient had lived in the vicinity of a large shipyard for 20 years. In fact, the highest incidence of mesothelioma has been reported in cities with shipyards and asbestos plants.[1,2]

Survival rates in patients with malignant pleural mesothelioma are generally low.[1,2] Thus far, treatment modalities have included pleuropneumonectomy, hemithoracic radiotherapy, and cisplatin-based chemotherapy.[3] When patients are treated with pleuropneumonectomy,[1,2,4] the median survival time is 9 to 10

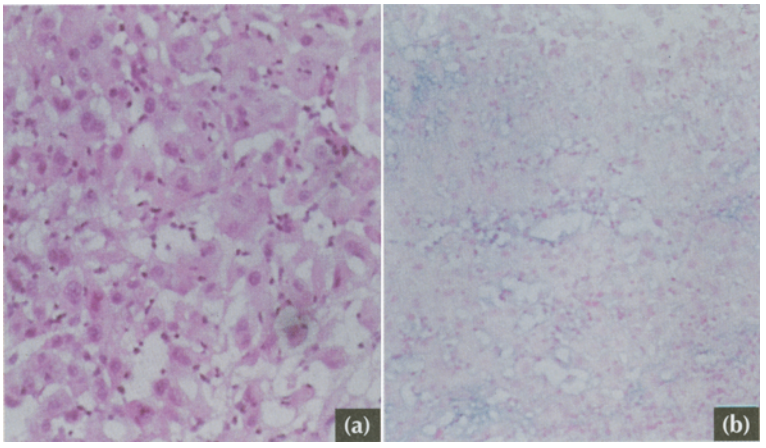

Fig. 3. (**a**) Histologic section of biopsy specimen taken during thoracoscopy 27 days after the patient described in Fig. 1 was referred to the authors shows diffuse infiltration into the pleura of pleomorphic cells that have clear nucleoli. (**b**) The hyaluronic acid digestion test shows mucoid deposits stained with Alcian blue on cell membranes and cytosol.

months, and the 3-year survival rate is 15%. Almost identical results have been achieved with radiotherapy and chemotherapy.[1–4] No standard treatment for prolonging survival has been established.

The spontaneous regression of cancer is defined as the partial or complete disappearance of a tumor without antineoplastic treatment.[5] Rates for spontaneous regression have been reported in cases involving hypernephromas (10% to 15% of all cases of spontaneous regression), neuroblastomas (5% to 10%), malignant melanomas (5% to 20%), and malignant lymphomas (15% to 20%).[6] However, it has been estimated that spontaneous regression of cancer occurs in no more than 1 in 60,000 to 100,000 afflicted patients.[7] A variety of mechanisms, such as immunologic and hormonal factors, have been proposed to explain the spontaneous regression of cancer. For instance, hormonal manipulation causes complete or partial regression in about 50% of prostatic cancers, 30% to 40% of breast cancers, and 30% of endometrial cancers.[8] Surgical procedures such as resection and biopsy also appear to be a factor. For example, in a number of cases, surgery intended to treat a primary tumor or metastasis has been reported to result in the regression of the remaining tumors.[6–8] In these cases of surgery-related regression, the reduction of the tumor burden presumably allows the host's immune system to affect the remaining tumor.[7] In our case, the exact mechanism of spontaneous regression of the tumor remains unknown. The tumors demonstrated modest progression until the time of biopsy, and then spontaneous regression occurred after biopsy. Thus, trauma related to the biopsy procedure may have played a role in inducing immunologic modulation by producing cytokines such as interferon, interleukin,[2] and tumor necrosis factor, which eventually led to spontaneous tumor regression.[9,10]

Only 1 case of spontaneous regression of a malignant peritoneal mesothelioma has been reported thus far.[11] To our knowledge, ours is the first published report of spontaneous regression of a malignant pleural mesothelioma.

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