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【 CASE REPORT 】

Malignant Peritoneal Mesothelioma Presenting with Polymyalgia Rheumatica-like Syndrome

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Abstract:
A 30-year-old man was admitted to our hospital because of pain in his proximal extremities. The pain mimicked polymyalgia rheumatica (PMR) and it temporarily improved by a low dose of glucocorticoids, but his symptoms relapsed many times. After six years of glucocorticoid treatment, he developed abdominal pain and ascites, for which he was diagnosed with malignant peritoneal mesothelioma (MPM). His PMR-like symptoms improved with cytoreductive surgery and chemotherapy for MPM. Finally, we diagnosed this PMR-like syndrome to be paraneoplastic syndrome with MPM. Although cases of MPM complicated by PMR-like syndrome are rare, MPM should be taken into account in the differential diagnosis.

Key words: asbestos, malignant peritoneal mesothelioma, polymyalgia rheumatic, paraneoplastic syndrome

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Introduction

Malignant peritoneal mesothelioma (MPM) is a rare and aggressive neoplasm that arises from the mesothelial lining of the peritoneum (1-4), and it accounts for approximately 15% to 33% of all mesothelioma cases (3, 5, 6). The population in Japan is aging and the number of patients with malignant mesothelioma has been increasing annually (5). Polymyalgia rheumatica (PMR) is a common inflammatory rheumatic disease in elderly patients and it is characterized by symmetrical pain and stiffness of the proximal extremities (7). PMR-like syndrome is a type of paraneoplastic syndrome that can present with atypical symptoms of PMR. Paraneoplastic syndrome is known to include the signs and symptoms of tumors that are located distant from the primary site or metastatic lesion and can sometimes be the first sign of the presence of tumors (8, 9). Few cases of paraneoplastic syndrome in MPM have so far been reported (8). We herein report a case of MPM presenting with PMR-like syndrome in a 30-year-old man with no asbestos exposure history.

Case Report

A 30-year-old man presented to our hospital with left abdominal pain and persistent severe pain and morning stiffness in the neck, bilateral shoulders, and bilateral hip joints with an acute onset that had lasted for a few weeks. There were no headaches, claudication or cutaneous lesions. A contrast-enhanced computed tomography (CT) scan of the abdomen and upper and lower gastrointestinal endoscopy were unremarkable. Although his symmetry pain and morning stiffness that lasts for over an hour of the extremities were characteristic of PMR, his age did not meet the 2012 American College of Rheumatology/European College of Rheumatology (ACR/EULAR) classification criteria for PMR. Initially, non-steroidal anti-inflammatory drugs and acetaminophen were prescribed for pain relief, but these had no effect. Based on a consideration of undifferentiated connective tissue disease, low-dose glucocorticoid treatment with prednisolone (PSL) at 10 mg daily was initiated and it led to rapid but temporary relief of symptoms. Over a 6-year period, his muscular symptoms relapsed many times and he required low-dose glucocorticoid (PSL 3-5 mg daily) for symptom control.

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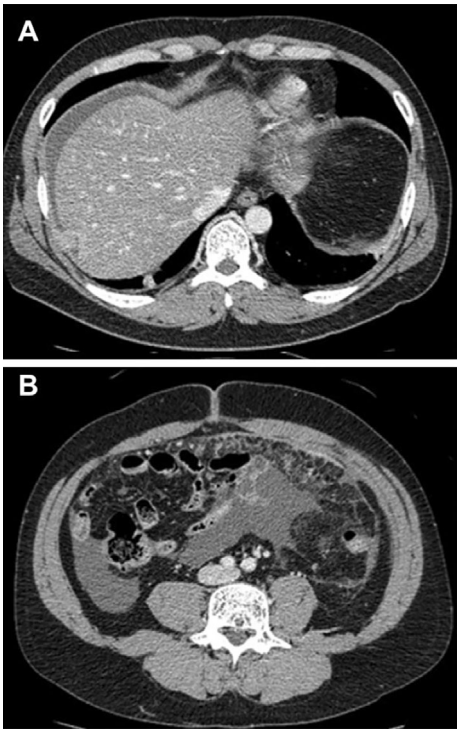

Figure 1. Computed tomography (CT) of the abdomen on first admission. A: There was ascitic fluid with a mean density of+18 CT units (compared with the 0±4 CT units for a water phantom around the liver). B: There was ascitic fluid similar to A in the abdominal cavity.

After 6 years, he complained of a sudden high-grade fever and severe lower abdominal pain and was admitted to our hospital. He was a professional bus driver and had not been exposed to asbestos. His home was wooden and asbestos was not used in his bus brakes. He did not have any remarkable past medical history, other than a fatty liver. Body temperature was 37.0°C, blood pressure was 139/89 mmHg, heart rate was 95/min, and respiratory rate was 24/min. Physical examination revealed stiffness and rebound tenderness of the lower abdomen. A blood examination showed a white blood cell count of 8,000/μL, hemoglobin of 15.2 g/dL, platelet count of 292,000/μL, creatine kinase of 74 IU/L, creatine of 0.7 mg/dL, C-reactive protein of 8.4 mg/dL, and antinuclear antibody titers of less than 1:40, rheumatoid factor of 15 U/mL and anti-cyclic citrullinated peptide antibody of less than 0.6 U/mL. Contrast-enhanced CT of the abdomen showed a moderate volume of retained ascites, a thickening of the omentum in the left lower quadrant, and a tumorous lesion measuring 18 mm in diameter in the right subphrenic space (Fig. 1). Upper gastrointestinal endoscopy was unremarkable. Cytological examinations of the ascitic fluid revealed an increased number of atypical mesothelial cells. Exploratory laparotomy was performed, and histological examination of the tumorous lesion in the right subphrenic space revealed a proliferation of mesothelial cells with tubular and papillary formation (Fig. 2). Immunohistochemistry of the omental tissue was positive for calretinin, D2-40, Wilms' tumor gene product, epithelial membrane antigen, cytokeratin (CAM5.2), and epithelial antigen (Ber-EP 4), but it was negative for carcinoembryonic antigen, carbohydrate antigen 19-9, and desmin. He was finally diagnosed to have the epithelial type of MPM.

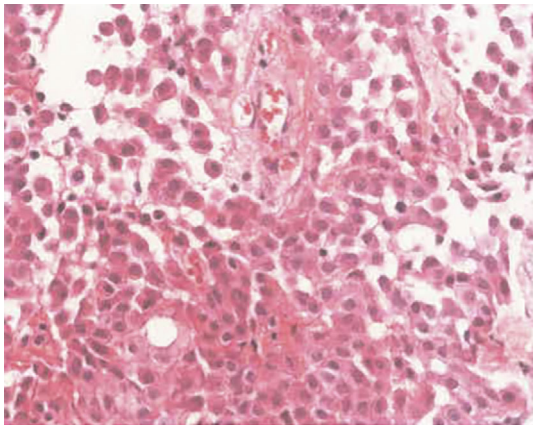

Figure 2. Laparoscopic biopsy specimen from a tumorous lesion in the right subphrenic space shows that the tumor is composed of atypical mesothelial cells arranged in a papillary and tubular pattern. (Hematoxylin and Eosin staining, ×40)

To control the abdominal tumor, combination chemotherapy with pemetrexed (500 mg/m^2 day 1) and cisplatin (CDDP, 75 mg/m^2 day 1) every 3 weeks was started and carried out for a total of 10 cycles. At the same time, PSL was discontinued, because the polymyalgia resolved after the excision of the thick omental lesion. After 1 year, contrast-enhanced magnetic resonance imaging showed a residual tumor in the right subphrenic space and this tumor was extracted. Although his muscle symptoms were relieved for a few months, there was recurrence of lower abdominal pain after 6 months. He underwent abdominocentesis for relief of the abdominal pain, and am ascitic fluid analysis detected mesothelioma cells. The MPM had relapsed, and he agreed to restart chemotherapy, but the dose of CDDP was reduced to 33% of the full dose and was nonscheduled because of renal dysfunction. During the clinical course, PSL returned and his muscular symptoms gradually worsened. Fifteen months after restarting chemotherapy, CT proved the presence of peritoneal and intrathoracic dissemination, indicating that the MPM was in the terminal stage. Two years later, he discontinued chemotherapy because of his poor performance status. Palliative therapy was continued, and he died 6 months later.

Discussion

In this case of a 30-year-old man without asbestos exposure, a PMR-like syndrome presented as a paraneoplastic syndrome of MPM, before the diagnosis of MPM. The patient received cytoreductive surgery and chemotherapy but died 6 years after the MPM diagnosis. This case was remarkable for three reasons, including the appearance of PMR-like symptoms before the diagnosis of MPM, the long-

term survival, and the absence of prior asbestos exposure.

PMR is a disorder affecting older adults >50 years of age and manifests with pain and stiffness of the shoulders, hip girdle, and neck; fatigue; anemia of chronic disease; and an elevated erythrocyte sedimentation rate. This condition responds promptly to low doses of prednisone (7, 9, 10). In contrast, the characteristics of PMR-like syndrome include age <50 years old, resistance to low doses of corticosteroid, and asymmetric pain; (8, 9) this case had these three features and did not meet the criteria for any of the collagen diseases, except PMR. Moreover, the PMR-like signs and symptoms resolved after starting treatment for MPM and without the use of corticosteroids. He was finally diagnosed with PMR-like syndrome which is a paraneoplastic syndrome of MPM. There have been case reports on PMR-like symptoms presenting as paraneoplastic syndromes in various malignant tumors, such as those in the kidney, lung, colon, and esophagus, and multiple myeloma (9, 10). Furthermore, a previous study described that paraneoplastic syndromes can be observed in MPM (8). MPM presenting with PMR-like syndrome has not, however, been reported previously (2, 10-12). The association of PMR and malignancy remains controversial. On the one hand, Muller et al. found a 69% increase in the risk of cancer in patients with PMR within the first 6 months after a PMR diagnosis (13). On the other hand, a population-based cohort study found no difference in the cumulative risk of malignancy after 10 years of follow-up in patients with PMR compared with comparator subjects (14). This association seems to be particularly true in patients presenting with atypical PMR (15).

For this case, we selected a combination of cytoreductive surgery and systemic chemotherapy for MPM therapy. The systemic chemotherapy regimen was the pemetrexed-cisplatin combination, following the regimen for malignant pleural mesothelioma. This patient survived for 5 years after starting the treatment for MPM. The reported median overall survival of patients with MPM was 4.7 months (3). It is of note that no standard treatment for MPM has yet been established in Japan, because there have been few reports on the treatment strategies and their contributions to survival in patients with MPM (3, 5). Systemic chemotherapy with contemporary pemetrexed-based regimens for MPM can achieve response rates that are comparable to those for malignant pleural mesothelioma and they are now commonly incorporated into the treatment algorithm (6, 16, 17). Moreover, pemetrexed in combination with cisplatin has been shown to improve survival in patients with MPM (16, 17). Considering these facts, we believe that our treatment regimen allowed the patient to achieve a relatively long-term survival.

This patient was a bus driver and had no history of asbestos exposure, which is the most common cause of malignant mesothelioma, particularly in men, possibly because of occupational risks (3, 18, 19). Asbestos exposure is evident in 80% of malignant pleural mesothelioma cases but in only 33% to 50% of MPM cases. (18-20) Because the clinical symptoms of abdominal pain, abdominal distension, weight loss, and fever are not specific to MPM (21), MPM in the early stages is difficult to diagnose, especially in the absence of any risk factors.

In summary, this report described an extremely rare case of PMR-like syndrome as a paraneoplastic syndrome of MPM. Upon encountering a patient with atypical features of PMR, clinicians should search carefully for presence of any malignancies, including MPM.

Informed consent was obtained from the patient's family for publication of this study.

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

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