CASE REPORT

Malignant Peritoneal Mesothelioma Presenting with Polymyalgia Rheumatica-like Syndrome

Yuka Ide¹, Tsunetsugu Yuki², Yasuyuki Taooka¹, Yusuke Higashi¹ and Yoshiro Tachiyama³

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 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. After 6 years, he complained of a sudden high-grade fever and severe lower abdominal pain and was admitted to
hydrated antigen 19-9, and desmin. He was finally diagnosed to have the epithelial type of MPM.

To control the abdominal tumor, combination chemotherapy with pemetrexed (500 mg/m² day 1) and cisplatin (CDDP, 75 mg/m² 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 abdominoplasty for relief of the abdominal pain, and an 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 corticosteroids, 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.

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References
1. Sudanthiram R, Venmulapalli C, Raja A, Santhosam R, Joseph S. Malignant peritoneal mesothelioma presenting as a complex omental lesion. Radiology case reports 7 (2): 539, 2012.
2. Alexander HR Jr., Burke AP. Diagnosis and management of patients with malignant peritoneal mesothelioma. Journal of gastrointestinal oncology 7 (1): 79-86, 2016.
3. Gemb K, Fujimoto N, Aoe K, et al. Treatment and survival analyses of malignant mesothelioma in Japan. Acta oncotogica 52 (4): 803-808, 2013.
4. Lainakis G, Zagouri F, Kastritis E, et al. Systemic chemotherapy with pemetrexed and cisplatin for malignant peritoneal mesothelioma: a single institution experience. Tumori 97 (1): 25-29, 2011.
5. Ohya M, Kobayashi M, Suzuki T, Tanno H, Nakazawa K. Malignant peritoneal mesothelioma diagnosed 50 years post-radiotherapy for ovarian cancer in a patient with a history of multiple malignancies: An autopsy case. Molecular and clinical oncology 11 (4): 397-400, 2019.
6. Beck M, Stahl RA, von Pawel J, et al. Pemetrexed in the treatment of malignant mesothelioma: results from an expanded access program in Germany. Respiratory medicine 104 (1): 142-148, 2010.
7. Salvareni C, Gabriel SE, O’Fallon WM, Hunder GG. Epidemiology of polymyalgia rheumatica in Olmsted County, Minnesota, 1970-1991. Arthritis and rheumatism 38 (3): 369-373, 1995.
8. Bech C, Sorensen JB. Polynuropathy in a patient with malignant pleural mesothelioma: a paraneoplastic syndrome. Journal of thoracic oncology: official publication of the International Association for the Study of Lung Cancer 3 (11): 1359-1360, 2008.
9. Bojinca V, Janta I. Rheumatic diseases and malignancies. Maedica (Bucharest) 7 (4): 364-371, 2012.
10. Unemitsu A, Shinizu T, Iwamoto N, et al. Paraneoplastic Syndrome Presenting with Polymyalgia Rheumatica-like Accumulations on (18)F-fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography. Internal medicine 58 (6): 861-864, 2019.
11. Tabata M, Kobayashi T. Polymyalgia rheumatica and thyroid papillary carcinoma. Internal medicine 33 (1): 41-44, 1994.
12. Avina-Zubieta JA, Enkerlin HL, Galindo-Rodriguez G. Rheumatic manifestations of malignancy. Current opinion in rheumatology 8 (1): 47-51, 1996.

13. Muller S, Hider SL, Blecher J, Helliwell T, Mallen CD. Is cancer associated with polymyalgia rheumatica? A cohort study in the General Practice Research Database. Annals of the Rheumatic Diseases 73: 1769-1773, 2010.

14. Pfeifer EC, Crowson CS, Major BT, Matteson EL. Polymyalgia Rheumatica and its Association with Cancer. Rheumatology (Sunnyvale) Suppl 6: 2015.

15. Coelho S, Magalhaes H, Correia J, Magalhaes A, Lourenco P. Polymyalgia rheumatica and pulmonary adenocarcinoma: A case report and literature review. Porto Biomed J 2 (3): 93-95, 2017.

16. Carteni G, Manegold C, Garcia GM, et al. Malignant peritoneal mesothelioma-Results from the International Expanded Access Program using pemetrexed alone or in combination with a platinum agent. Lung cancer 64 (2): 211-218, 2009.

17. Janne PA, Wozniak AJ, Belani CP, et al. Open-label study of pemetrexed alone or in combination with cisplatin for the treatment of patients with peritoneal mesothelioma: outcomes of an expanded access program. Clinical lung cancer 7 (1): 40-46, 2005(in eng).

18. Abbas H, Rodriguez JC, Tariq H, Niazi M, Alemam A, Nayudu SK. Malignant Peritoneal Mesothelioma Without Asbestos Exposure. Gastroenterology research 12 (1): 48-51, 2019.

19. Shih CA, Ho SP, Tsay FW, Lai KH, Hsu PI. Diffuse malignant peritoneal mesothelioma. The Kaohsiung journal of medical sciences 29 (11): 642-645, 2013.

20. Spirtas R, Heineman EF, Bernstein L, et al. Malignant mesothelioma: attributable risk of asbestos exposure. Occupational and environmental medicine 51 (12): 804-811, 1994.

21. Chen LY, Huang LX, Wang J, Qian Y, Fang LZ. Malignant peritoneal mesothelioma presenting with persistent high fever. Journal of Zhejiang University Science B 12 (5): 381-384, 2011.

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