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CASE REPORT

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Hodgkin's lymphoma initially presenting with polymyalgic symptoms: a case report

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Abstract The association of polymyalgic symptoms and lymphoma is a rare event whose pathogenesis remains to be clarified. Here, we describe a case of a 75-year old man with Hodgkin's lymphoma, who had presented with polymyalgic symptoms suggesting polymyalgia rheumatica. An intensive investigation with respect to malignancy was initially negative. Corticosteroid treatment was administered first and a dramatic clinical improvement was achieved. Four months later, when the corticosteroid treatment was tapered off, the initial manifestations reappeared. After the development of lymph node enlargement, the patient was diagnosed by lymph node biopsy as having Hodgkin's lymphoma. The lymphadenopathy and musculoskeletal manifestations all responded well to chemotherapy. Hodgkin's lymphoma should be considered in the differential diagnosis of PMR. These musculoskeletal syndromes should alert the physician to possible paraneoplastic manifestations of an evolving neoplasm.

Key words Hodgkin's lymphoma · Paraneoplastic syndrome · Polymyalgia rheumatica

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Introduction

Determining whether musculoskeletal symptoms are cause by a rheumatic disease or a malignancy is complex and intriguing. The musculoskeletal system may be either directly or indirectly associated with malignancy, or with a paraneoplastic syndrome, particularly those of the hematological type.[1,2] Cutaneous vasculitis, seronegative arthritis, and polymyalgia rheumatica (PMR) are the most common findings associated with myelodysplastic syndromes and lymphoid malignancies. Polymyalgia rheumatica is a relatively common disorder characterized typically by morning stiffness and aching of the shoulder and hip girdles, neck, and torso in patients over the age of 50 years.[3,4] In the present case, we report a patient with polymyalgic symptoms associated with Hodgkin's lymphoma. To our knowledge, the association between Hodgkin's lymphoma and polymyalgic symptoms has never been reported.

Case report

A 75-year-old man presented with a 3-week history of progressive pain and moderate stiffness in his shoulder, cervical and hip girdles, limitation of mobility, and bilateral swelling of wrists and knees. Medical history revealed a weight loss of 10 kg within 3 months. There was no history of headache, visual changes, or jaw claudication. Physical examination revealed a temperature of 37.6°C, tenderness and limitation of shoulder movement, and synovitis of the wrist. There were no signs of temporal arteritis. Laboratory data showed that erythrocyte sedimentation rate (ESR) was 81 mm/h, C-reactive protein (CRP) of 90 mg/dl, white blood cell (WBC) count of 9000/mm^3, hemoglobin 11.9 g/dl and platelet count of 302 000/mm^3. Renal and liver hepatic profiles were normal. In differential diagnosis of chronic infections, PMR, collagen diseases, and paraneoplastic syndrome were suspected. Rheumatoid factor and antinuclear antibodies were negative. There was a mild polyclonal gammopathy in protein electrophoresis. Serological tests and blood cultures

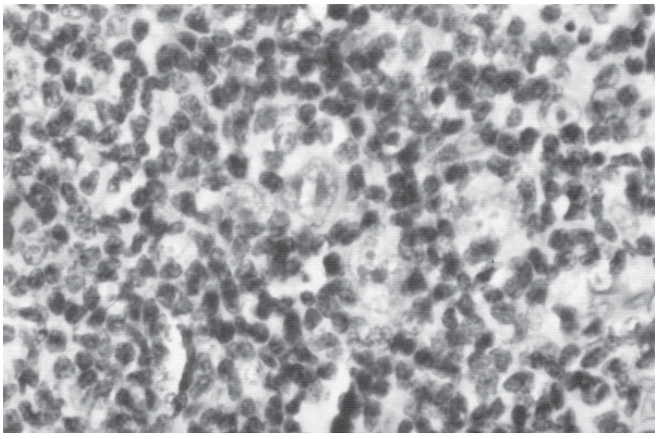

Fig. 1. Typical Reed–Sternberg cells in Hodgkin's lymphoma (hematoxylin–eosin, ×400)

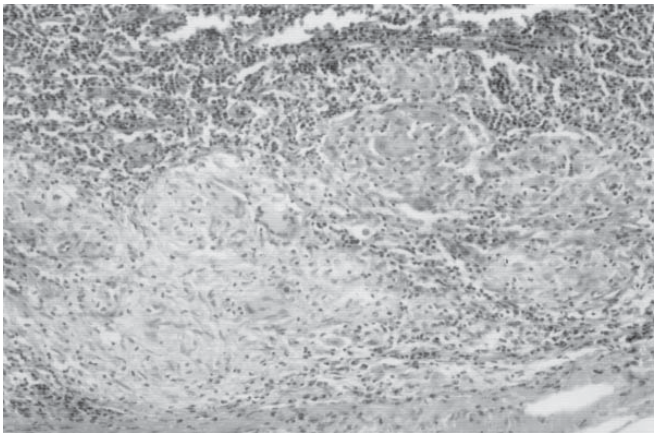

Fig. 2. Granulomas with giant cells in Hodgkin's lymphoma (hematoxylin–eosin, ×200)

excluded common viral and bacterial infections. Chest radiography and two-dimensional echocardiography were normal. Purified protein derivative test was negative. Abdominal ultrasonography and computerized tomography (CT) scan were normal. Gastric, duodenal, bone marrow, and prostate malignancies were ruled out by their biopsies. The initial diagnosis was considered to be PMR, and the patient was prescribed 25 mg prednisolone daily. A week later, he felt well, and his pain and stiffness had apparently regressed. Erythrocyte sedimentation rate was reduced to 55 mm/h. While the dose of corticosteroids was being tapered off, polymyalgic symptoms reoccurred. Afterwards, the patient could not be controlled regularly. Four months after discharge, he presented again with similar complaints and also with right inguinal tenderness and fatigue. It was learned that the patient was no longer on steroids. On physical examination, weight loss, pallor, pain and limitation of shoulders and wrists, enlarged posterior cervical (2 × 2 cm in size), right inguinal (2 × 2 cm in size), and left inguinal lymph node (2 × 1.5 cm in size) were observed. There was no hepatosplenomegaly. Laboratory data showed that the WBC count was 8100/mm^3, hemoglobin level 11.8 g/dl, platelet count 233 000/mm^3, ESR 67 mm/h, and CRP 102 mg/dl. Analysis of blood chemistry revealed that his hepatic and renal functions within normal limits, except an elevated lactate dehydrogenase level (533 IU/l). Chest X-ray was normal. Abdominal CT revealed enlarged multiple lymph nodes near the external iliac, internal iliac, and left-right inguinal areas and also multiple para-aortic lymph nodes with a maximum diameter of 11 cm. Right and left inguinal lymph node biopsies revealed microgranulomas with Hodgkin's lymphoma, mixed cellular type (Figs. 1 and 2). Immunohistochemical staining was positive for CD30 but negative for CD15, CD20, CD45, and CD68. Subsequent staging CT of thorax showed pulmonary small nodules but no mediastinal or axillary lymphadenopathy. Bone marrow biopsy showd no involvement. The Ann Arbor clinical staging was IIIB. The patient was treated with six courses of chemotherapy comprising doxorubicin 25 mg/m^2, bleomycin 10 mg/m^2, vincristine 6 mg/m^2 and dacarbazine 375 mg/m^2 given on days 1 and 15 repeated every 4 weeks (ABVD therapy). The musculoskeletal complaints diminished by the third course of chemotherapy. The patient was symptom-free for 7 months after the completion of therapy. Disease remission was achieved. One year later, he is still in remission.

Discussion

This case was interesting with respect to its presentation with polymyalgic symptoms. Polymyalgic symptoms appeared prior to the symptoms of Hodgkin's lymphoma. The patient's presentation and good response to corticosteroid treatment led us to believe the diagnosis of PMR was current.[5] The final diagnosis was delayed, as long as 8 months. These unusual manifestations accounted for this delay, but even in more typical cases a delay can also occur because of the indolent course of the Hodgkin's lymphoma.

New-onset proximal muscle pain and/or stiffness in elderly people are most often caused by PMR, but polymyalgic pain can also be present in a wide variety of disorders, such as malignant neoplasms, endocarditis, different vasculitic disorders, and connective tissue diseases.[3] This case and the accompanying literature call into question a dogmatic approach that precludes making a diagnosis of PMR in the presence of a malignancy. These two diseases can also occur together by chance, and a pathologic association is unlikely.[6,7] A careful history and physical examination can lead to the diagnosis of PMR in patients with malignancy. Treatment of PMR as well as the malignancy may greatly improve the patient's functional status and quality of life. Although information on the reversibility of symptoms associated with PMR in the other malignancies are unknown, as it was in our patient, polymyalgic symptoms may be reversible after treatment. Our patient had completed the treatment successfully and he was disease-free on follow-up, albeit for only 7 months after completing the treatment.

On the other hand, diverse rheumatological manifestations have been reported in patients with lymphoma including bone pain, monoarthritis, polyarthritis, and spinal cord involvement.[8] In reviewing the literature, these manifestations are more frequent with non-Hodgkin's lymphoma, but are found to be rare with Hodgkin's lymphoma.[8] In a recent study, Varoczy et al.[9] reviewed 940 patient charts with malignant lymphomas to assess the rate of associated autoimmune diseases and reported that an associated autoimmune disease occurred in 45 (8.6%) out of 519 Hodgkin's lymphoma patients. Polymyalgia rheumatica was not reported in any patient.

Our patient subsequently developed lymph node enlargement. His disease was then diagnosed as Hodgkin's lymphoma on the basis of lymph node biopsy. Malignant lymphomas associated with granulomas in the bone marrow, liver, or spleen are frequently found in the advanced stage of the disease.[10] There are case reports of sarcoid-like granulomas in the lymph nodes, which were interpreted as epithelioid forms of Hodgkin's lymphoma, particularly a subvariant of the mixed-cellularity type.[11–13] We proposed the hypothesis that granulomatous reaction occurring as a result of immune dysregulation may predispose to a lymphoid malignancy as reported in the literature.[13] Moreover, just as in our case, the disease may have an unusual clinical history that delays the diagnosis and management. In our patient, 8 months had passed before Hodgkin's lymphoma was diagnosed from findings of the lymph node biopsy specimens taken after the development of generalized lymphadenopathy.

In conclusion, musculoskeletal complaints may dominate in the early course of an unrecognized malignancy. Hodgkin's lymphoma should be considered in the differential diagnosis of PMR or polymyalgic symptoms. It should be borne in mind, however, that some patients may exhibit granuloma formation in their lymph node with Hodgkin's lymphoma, as in the case presented here. We suggest that a thorough initial medical examination in patients with suspected PMR can exclude most of the cases with an underlying pathology.

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