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CASE REPORT

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Primary cervical epidural malignant lymphoma with rheumatoid arthritis: a case report

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Abstract We report a case of primary cervical epidural malignant lymphoma with rheumatoid arthritis. Because of the acute progression of paralysis in both legs, surgical decompression and stabilization of the cervical spine were performed. The resected specimen showed proliferation of lymphoblastic cells diagnosed as malignant lymphoma. Four series of chemotherapy were administered after surgery, and the patient recovered from paralysis.

Key words Cervical spine · Malignant lymphoma · Methotrexate · Rheumatoid arthritis · Surgical treatment

Introduction

Malignant lymphoma forms in many organs, but primary epidural lymphoma is less common, representing 0.9%–6.5% of all non-Hodgkin's lymphoma.[1] As patients usually have no symptoms until severe pain or the development of neurological deficit, it is very difficult to make an appropriate and prompt diagnosis for malignant lymphoma. The incidence of paralysis, sensory disturbance, and walking disorder because of spinal cord compression by lymphoma is not very frequent; it is reported in up to 7% of cases.[2] This relatively low incidence of neurological symptoms makes the appropriate diagnosis of primary malignant lymphoma of the spine very difficult.

Primary epidural lymphoma might have a better outcome with prompt diagnosis and treatment.[3] When neurological deficits such as paralysis and urinary dysfunction are present, emergency surgery for compression of the spinal cord is required. As malignant lymphoma is reported to be remarkably sensitive to radiation or chemotherapy, the recovery of neurological symptoms is far better than with other tumors such as metastatic carcinomas.[3]

Here, we report a case of primary cervical epidural malignant lymphoma in a patient with rheumatoid arthritis. As acute neurological deficits by compression of spinal cord were present, the patient underwent spinal surgery and then received chemotherapy. The patient recovered from the neurological deficits after surgery and could walk with a cane in 1 year and 2 months after the surgery.

Case presentation

A 65-year-old woman had received medication for rheumatoid arthritis for 9 years. She was taking 7.5 mg of predonisolone daily and 4 mg of methotrexate (MTX) weekly to control arthritis of multiple joints. She had undergone hip arthroplasty 3 years earlier and bilateral resection arthroplasty for deformity of the toes 4 months earlier. The patient was re-admitted to our hospital for conservative treatment of superficial infection of the right toes. Seven days after admission, the patient began to feel muscle weakness in both legs. The muscle weakness of the lower extremities and numbness of the bilateral extremities rapidly progressed in a few days. The disturbance of dexterity and the muscle weakness of the fingers also progressed. Neurological examination showed slight motor weakness of both hands above the C5 level and severe impairment of both hands below the C6 level. Gradually, the motor strength of the right leg weakened to trace level. Hypesthesia was present in the all upper and lower extremities. Deep tendon reflexes of bilateral patellar and Achilles' tendon showed hyperreflexia. Left Babinski's reflex was also present. Ranawat criteria for pain and neural assessment were Grade 2 and Class IIIB.

Blood analysis showed slightly increased values of transamylase and rheumatoid factor (GOT 94 IU/l, GPT

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Fig. 1. Magnetic resonance imaging (T2-weighted imaging) shows compression and heterogeneously high-intense change of the spinal cord by atlanto-axial subluxation, spinal compression from C5 to C6 by spinal tumor (*arrow*). Low-intense change of C5 vertebral body is also recognized

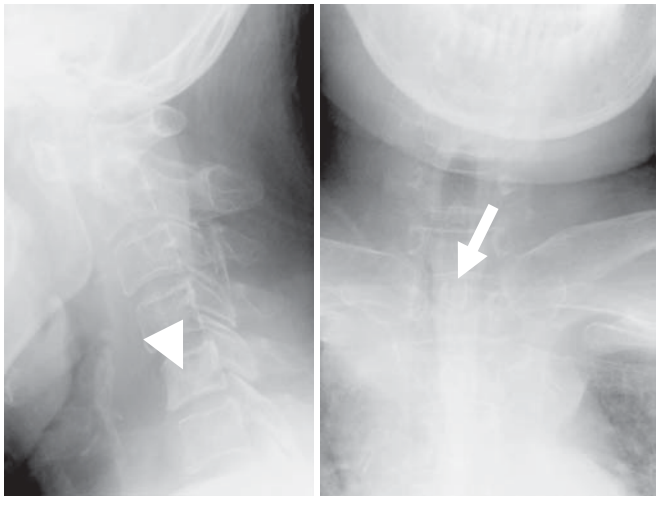

Fig. 2. Myelography of cervical spine shows the interruption of contrast medium at C6 (*arrow*), osteosclerotic change of C5 vertebral body (*arrowhead*), and atlanto-axial subluxation

108 IU/l, and RF 27 IU/l). Other data were almost within normal limits.

Cervical T2-weighted images on magnetic resonance imaging (MRI) revealed a tumor that was compressed from behind the cervical spine from the C5 to C6 level. The C5 vertebral body and its lamina were heterogeneously isointense on T2 images (Fig. 1). Myelography of the anteroposterior view showed that the flow of contrast medium was interrupted at the C6 level (Fig. 2). On the basis of these findings, an epidural tumor at C5 level was suspected. Additionally, the lateral view of the cervical spine also showed subluxation of the atlanto-axial joint which was thought to be caused by rheumatoid arthritis. The atlanto-dental interval was extended to 14 mm.

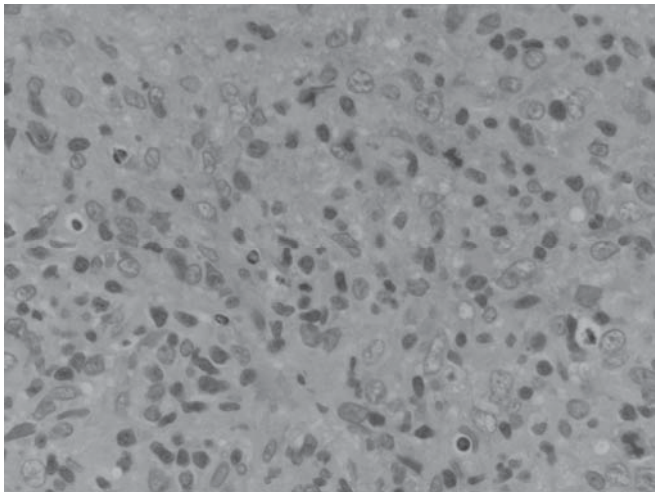

Fig. 3. Histopathological analysis of resected tumor shows diffuse increase of anaplastic tumoral cells

The patient underwent emergency surgery for acute neurological deficits. Cervical laminectomy from C4 to C6 with partial resection of the tumor was performed. Because the purposes of this surgery were decompression of the spinal cord and histological diagnosis of the tumor, instrumental fixation of the cervical spine was not performed. For the remaining instability of the cervical spine after the surgery, a halo orthosis was applied to help immobilize the cervical spine. Histopathological analysis of the resected specimen showed diffuse proliferation of lymphoblastic cells (Fig. 3). Immunohistochemical characterization of the tissue specimen showed that the cell membrane was stained with CD20 and CD79a. On the basis of these findings, the tumor was diagnosed as malignant lymphoma of diffuse large B-cell type. As swelling of the superficial lymph node was not recognized and gallium scintigram did not show any abnormal uptake except in the cervical spine, the tumor was diagnosed as primary cervical epidural malignant lymphoma.

The muscle strength of the upper extremities and right leg improved to the 4/5 level from the day after surgery. Ranawat criteria improved to Grade 1 and Class IIIA. Two weeks after surgery, after the results of histopathological and immunohistochemical analyses were obtained, the patient underwent posterior stabilization by instrumental spondylodesis from C1 to C7 for the instability of the middle-lower cervical spine and atlanto-axial subluxation. In the second surgery, the atlanto-axial subluxation was reduced and the C1 vertebral body was fixed with screws. Pedicle screws were used in C2, C6, and C7 for spondylodesis. Articular facet screws were also used for the instability at C4/C5 facets (Fig. 4).

After the second surgery, the patient received four series of chemotherapy involving cyclophosphamide, hydroxydaunomycin, oncovin, and predonisolone (CHOP regimen) with full and half dosages. One year and two months after the second surgery, although slight numbness of the bilateral hands and legs remained, the patients could walk a short distance with a cane.

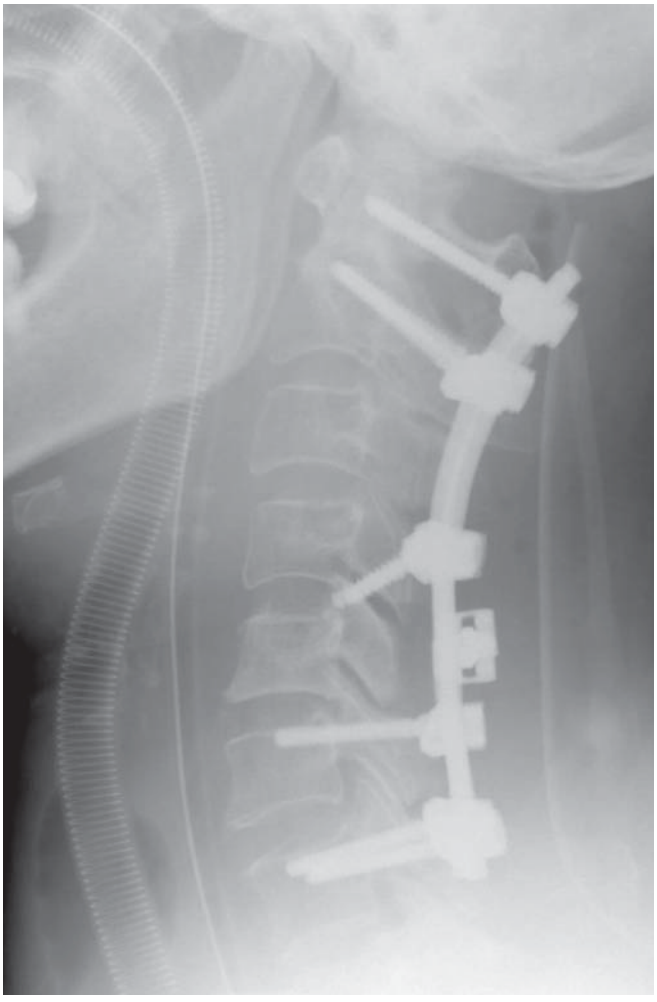

Fig. 4. Lateral radiograph of cervical spine after surgical stabilization shows the reduction of atlanto-axial subluxation and solid spondylodesis from C1 to C7

Discussion

The incidence of malignant lymphoma in patients with rheumatoid arthritis is reported to range from 0.19% to 0.41%.[4,5] On the other hand, the incidence of malignant lymphoma in the whole population is reported to be 0.005%.[4] On the basis of the difference in these rates of incidence, the occurrence of malignant lymphoma in patients with rheumatoid arthritis is thought to be far higher than that in the whole population. Several reports have suggested an increased risk of lymphomas in patients with rheumatoid arthritis treated with MTX.[3,4,6] Although the reason for the higher rate of incidence has not been clearly investigated yet, immunosuppressive therapy may play a significant role in the development of lymphoma. The suppression of cellular immune response may tend to induce viral infection. Blood analysis of the virus antibody might prove the immunosuppressive effect of MTX. The occurrence of metastasis and the recurrence of malignant lymphoma may decrease by suspending MTX medication on the basis of reports of patients who stopped MTX medication and had a curative course.[7] In this case, as curative therapy for malignant lymphoma, we suspended MTX therapy following partial resection of the tumor.

Lymph nodes are the most common lesion of primary malignant lymphoma. Primary lymphoma in bone is less common, representing only 1.8%–4.7% of all extra nodular lymphomas.[3,8] Primary malignant lymphoma located in the spinal bone is reported in only about 1% of malignant lymphomas.[9] Primary epidural malignant lymphoma is estimated to be more uncommon. On the basis of these reports, our case of primary epidural malignant lymphoma is very rare.

It is reported that epidural malignant lymphoma has two theories of origin. The first theory is that lymphoma develops from the epidural space, and the other is that the lymphoma extends to the epidural space from vertebral or paravertebral lesions.[9] In this case, because osteolytic lesions of both lamina and vertebral bodies were recognized, it was difficult to identify the origin. The symptoms of epidural malignant lymphoma usually begin with local pain. Patients whose symptoms begin with low back pain account for 80% of the cases of epidural malignant lymphoma.[5] It was reported that approximately 40% of cases show urinary dysfunction and 30% of cases show paralysis of legs at the time of diagnosis of malignant lymphoma.[5] Most malignant lymphoma in the spine presents with paralysis of extremities and urinary dysfunction after a few days at earliest or 3 months on average. In the clinical latent period, hematological and biochemical laboratory data usually show normal values; therefore, the diagnosis of malignant lymphoma in the early stages is difficult. In this case, blood analysis showed normal values, except GOT, GPT, and RF, similar to other reports. The tumor could not be identified from these laboratory data, and was recognized when neurological deficits developed.

The treatment of lymphoma depends on the location and clinical stage. Radiation therapy is one method for the inoperable patients with local pain and paralysis. Symptoms such as pain and paralysis were improved by surgery in this case. Although the combination of radiation therapy and chemotherapy was another choice after the first surgery in this case, posterior stabilization by instrumental spondylodesis was selected for the remaining instability of the cervical spine, and chemotherapy was thought to be sufficient for disease control.

A roentgenogram of primary malignant lymphoma of the cervical spine shows many patterns of osteolytic or osteosclerotic changes.[10] As differential diagnosis on plane radiograph, metastatic spinal tumor, spinal abscess, and primary epidural tumor should be considered. The radiographs of this case showed an osteosclerotic lesion at the C5 vertebral body. In general, most tumors with osteolytic change on plane radiograph or computed tomography (CT) scan usually show poor prognosis, whereas most tumors with osteosclerotic change usually show slow progression and better prognosis.[10] Lymphomas usually show homogeneous intensity on the CT scan, and give a higher signal than muscle and slightly lower signal than fat on MRI images (T1- and T2-weighted imaging).[11] Lymphomatous tissue ap-

pears homogenously hypointense on MRI, and lymphoma usually shows the same signal as lymphomatous tissue.

In this case, we performed atlanto-axial joint reduction and fixation in addition to middle-lower posterior stabilization of the cervical spine because the paralysis of the extremities might have been affected by severe atlanto-axial dislocation.

In most treatments of malignant lymphoma, chemotherapy is administrated with the CHOP regimen. Radiation therapy is also performed according to the size and location of the tumor. This is sometimes applied before surgery, and then the tumor is resected after tumor shrinkage. It is important to start the treatment as early as possible, because the prognosis of lymphoma depends on the clinical stage.

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