Simultaneous Occurrence of Hodgkin’s Lymphoma and Langerhans Cell Histiocytosis of the Spine: A Rare Combination

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Hodgkin’s disease presenting with spinal cord compression owing to extradural and bone involvement is extremely unusual. A 48-year-old man presented with progressive lower extremity weakness resulting from spinal cord compression attributable to an epidural mass in the thoracic vertebrae. The patient underwent decompressive surgery, and was then treated with chemotherapy for Langerhans cell histiocytosis. However, the disease progressed, and we performed second decompressive surgery with stabilization. Subsequent histopathological investigations revealed Hodgkin’s lymphoma of the bone. Here, we describe an unusual case of spinal Hodgkin’s lymphoma and Langerhans cell histiocytosis to draw attention to this combination as a possible diagnosis in patients with mixed inflammatory cell infiltrate lesions in the spine.

KEY WORDS: Hodgkin’s disease, Lymphoma, Langerhans cell histiocytosis, Spinal cord compression.

INTRODUCTION

Non-Hodgkin’s lymphoma arises in the lymph nodes in approximately 60% of patients and at extranodal sites in about 40% of patients. In 90% of patients with Hodgkin’s lymphoma, the disease is thought to arise in the lymph nodes, whereas in 10% of patients the disease arises at other sites14. Although non-Hodgkin’s lymphoma can affect the central nervous system (CNS), such involvement is less common with Hodgkin’s disease4,10. Presentation with spinal cord compression arising from extradural and bone involvement in Hodgkin’s disease, without associated systemic lymphoma, is extremely rare. In the literature, there had been approximately 30 reports of patients with the coexistence of Langerhans cell histiocytosis (LCH) and Hodgkin’s disease3,8. We describe an unusual case of Hodgkin’s lymphoma and LCH of the thoracic spine.

CASE REPORT

History and examination

A 47-year-old man presented with a 6-month history of progressive motor weakness in the lower extremities, numbness below the midthoracic area, and spastic gait disturbance. His medical history indicated no abnormalities. Neurological examination revealed spasticity in the lower limbs with brisk deep tendon reflexes and grade 4/5 power in lower extremities that was worst in the hip flexors but did not preclude walking. There was a subjective decrease in pinprick sensation below the 4th thoracic dermatome. Computed tomographic (CT) scans of the thoracic spine showed a bone-destructive lesion in the second, third, and fourth thoracic vertebrae (Fig. 1A). A magnetic resonance imaging (MRI) scan demonstrated that the destroyed thoracic vertebrae had been replaced by an osteolytic mass and that the thoracic spinal cord was compressed by this mass (Fig. 1B and C). Routine blood analysis was normal. Skin tests using antigens to Candida, Trichomonas, and tuberculosis were negative. In a plain chest X-ray, no pro-
CT-guided needle biopsy of the anterior mediastinum and showed chronic inflammatory infiltrates with fibrosis. Bacterial, fungal, and tuberculosis cultures were negative. Analysis of a second percutaneous needle biopsy specimen yielded similar results.

First operation and postoperative course

The patient underwent surgery to obtain a diagnosis and to decompress the spinal cord. A fibrotic, compressive epidural mass that resembled fibrous and granulation tissue was partially removed by T3 laminotomy (Fig. 1E). Postoperatively, the patient made an uneventful recovery, he experienced strength improvement up to normal power in lower extremities. The tissue that was removed during surgery showed lymphoreticular cell proliferation, with lymphocytes, histiocytes, neutrophils, eosinophils, and Langerhans cells, consistent with Langerhans cell histiocytosis. Immunohistochemical staining for S-100 protein and CD1a was positive. Bacterial, fungal, and tuberculous cultures remained negative. Subsequently, the patient underwent chemotherapy with two cycles of cladribine. A combination of vinblastine and prednisone was administered weekly for 2 months. As maintenance therapy, seven cycles of vinblastine, 6-mercaptopurine, and prednisone were administered. After 6 months, a chest CT scan and a whole-body positron emission tomographic (PET) CT scan showed a decrease in tumor mass in the anterior mediastinum and no new lesions. One year after surgery, however, the patient developed recurrent progressive lower extremity weakness. MRI and a whole-body PET-CT scan demonstrated that the thoracic spine lesion had progressed with kyphosis but the mediastinal lesion had not changed (Fig. 2). There was abnormal enhancement of the 2nd to 4th thoracic vertebrae; these were expanded by a soft tissue mass that extended along the relevant portion of the thoracic spine. There was recurrent spinal cord compression and a more extensive prevertebral mass.

Second operation and postoperative course

The patient underwent a second surgical procedure to obtain a diagnosis, decompress the spinal cord, and stabilize the spine. The patient underwent decompressive laminectomies from T2 to T4 with partial removal of the tumor, and
operations grew neither visit. Final cultures from specimens obtained during the two patient was able to walk independently at the last follow chemotherapy. Lower extremity strength improved, and the mycin, bleomycin, vinblastine, and dacarbazine (ABVD) patient was treated with oral dexamethasone and adria site in the sternum, anterior mediastinum, and spine. The no evidence of Hodgkin's disease other than at the primary and CT scanning of the neck, abdomen, and pelvis showed ture, a whole (PCR) and a weakly positive T bulin H gene rearrangement by polymerase chain reaction the tumor cells. The cells showed a germ nase (Fig. 3B and C). Epstein Barr virus was not detected within the tumor cells. The cells showed a germ-line immunoglobulin H gene rearrangement by polymerase chain reaction (PCR) and a weakly positive T-cell receptor-γ gene rearrangement by PCR-heteroduplex analysis. The morphological and immunological phenotypes were consistent with Hodgkin's disease. The tissue from the first operation was reexamined immunohistochemically for the presence of Hodgkin's disease. However, the previous tissues were immuno-reactive for S-100, CD1a, and CD30, but not for leucocyte common antigen, CD3, CD15, CD20, CD45, CD68, CD79A, CD138, CD4, CD5, CD8, CD10, CD163, CD138, CD56, CD117, CD34, activin receptor-like kinase-1, myeloperoxidase, B-cell lymphoma 6, or cytokeratin (Fig. 3B and C). Epstein-Barr virus was not detected within the tumor cells. The cells showed a germ-line immunoglobulin H gene rearrangement by polymerase chain reaction (PCR) and a weakly positive T-cell receptor-γ gene rearrangement by PCR-heteroduplex analysis. The morphological and immunological phenotypes were consistent with Hodgkin's disease. The tissue from the first operation was reexamined immunohistochemically for the presence of Hodgkin's disease. However, the previous tissues were immuno-reactive for S-100, CD1a, and CD30, but not CD15, CD30.

Analysis of cerebrospinal fluid drawn via lumbar puncture, a whole-body gallium scan, a bone marrow biopsy, and CT scanning of the neck, abdomen, and pelvis showed no evidence of Hodgkin's disease other than at the primary site in the sternum, anterior mediastinum, and spine. The patient was treated with oral dexamethasone and adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy. Lower extremity strength improved, and the patient was able to walk independently at the last follow-up visit. Final cultures from specimens obtained during the two operations grew neither Mycobacterium tuberculosis nor any other organism.

**DISCUSSION**

Wood and Coltman estimated that primary extranodal presentation of Hodgkin’s disease occurs in no more than 0.25% of patients. Most patients with Hodgkin’s disease with CNS involvement present with concurrent neurological and nodal disease or develop neurological disease after diagnosis of Hodgkin’s disease. Spinal cord compression secondary to lymphoma is not rare, although in most patients this occurs when the disease is well established. Fifty (5%) of 1,039 patients with non-Hodgkin’s lymphoma in one series developed CNS involvement. Only 5 (0.5%) of the 50 patients had CNS involvement at the time of initial presentation. Compared with non-Hodgkin’s lymphoma, spinal cord compression occurs much less often in Hodgkin’s disease. Sapozink and Kaplan reported that none of 2,185 patients with Hodgkin’s disease presented with spinal cord compression. In summary, spinal cord compression due to Hodgkin’s disease is very rare and usually develops in the setting of diffuse, undiagnosed disease or at some time after initial diagnosis. To our knowledge, our case is the first report of a patient with both Hodgkin’s disease and LCH who presented with spinal cord compression arising from epidural and spinal disease.

The isolated presentation in our case contributed to difficulty in diagnosis. Our initial diagnosis was LCH. The clinical presentation of spinal cord compression arising from extradural mass lesions is more likely related to metastatic tumors than to hematological disorders. However, Hodgkin’s disease, or disease of the non-Hodgkin’s variety, rarely presents with extradural spinal cord compression. Our patient seemed to have extranodal Hodgkin’s disease. Several mechanisms of pathogenesis have been suggested. Hodgkin’s disease may arise outside the lymph nodes after hematogenous dissemination from mediastinal nodal sites or it is possible that lesions originate primarily in bony structures.

![Fig. 3.](image) (A) Scanning power view shows irregular osteolytic fibrous lesion with extensive inflammation (original magnification, ×20, H&E stain). (B) High power view shows cellular lesion composed of a mixture of histocyte, Langerhans cells, eosinophils, and fibroblasts in the densely sclerotic background (original magnification, ×400, H&E stain). Inset : The Langerhans cells stain positively with S100 and CD1a. (C) Adjacent area shows numerous Reed-Sternberg cells, with their characteristic bi-lobed mirror image nuclei containing owl-eyed nucleoli among small lymphocytes, and plasma cells (original magnification, ×400, H&E stain). Inset : Immunostain for CD30 (Ki-1 antigen).
into the epidural space, or perhaps into bone, may also occur. In the patient described here, the disease may have arisen from mediastinal lymphatic tissue and subsequently spread to the contiguous spine. Several authors have suggested that small lymphatic elements in the epidural space may give rise to lymphoma.\textsuperscript{2,11}

It seems that an association of LCH with malignant lymphomas occurs more often than might be expected by chance, and Hodgkin’s disease is the lymphoma most frequently associated with LCH.\textsuperscript{3,8} To the year 2000, there had been approximately 30 reports of patients with co-diagnoses of LCH and Hodgkin’s disease.\textsuperscript{3,8} Most often, Hodgkin’s disease either preceded LCH (11 cases) or was diagnosed at the same time (17 cases).\textsuperscript{3,8} Infiltration by Langerhans’ cells took the form of localized foci and/or extensive multifocal involvement within dilated cortical and medullary sinuses, with no evidence of posterior systemic spread.\textsuperscript{18,9} It seems that nodal LCH represents a process with a benign clinical course, as demonstrated in the literature.\textsuperscript{5} This is, however, curious, if we consider the old hypothesis of a malignant change in cells of the monocyte-histiocyte system as the origin of “classic” Hodgkin’s disease. In our patient, as in previously reported cases, there was no histological evidence for conversion of one form of lesion into the other. To summarize, we report the unusual coexistence of two hematological disorders, but the significance of this association remains unknown.

It should be mentioned that the role for extensive tumor resection via attempted gross total resection and vertebrectomy. This patient underwent initial surgery to obtain a diagnosis and to decompress the spinal cord. It is possible that due to a relatively conservative surgery, representative tissue showing Hodgkin’s lymphoma might have been missed during first surgery.

**CONCLUSION**

LCH may show a complex association with Hodgkin’s lymphoma. LCH may precede, occur with, or follow Hodgkin’s lymphoma. This is the first time that the coexistence of these two hematological disorders in the spine has been reported. Here, we describe an unusual case of mixed spinal Hodgkin’s lymphoma and LCH to draw attention to this combination as a possible diagnosis in patients with diverse inflammatory cell infiltrate lesions in the spine.

**References**