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Sinus Histiocytosis with Massive Lymphadenopathy
- Multiple Skull Involvements -

Sinus histiocytosis with massive lymphadenopathy is a non-neoplastic self-limiting disease of the bone marrow stem cell origin. It is characterized by painless, bilateral cervical lymphadenopathy accompanied by fever, leukocytosis, elevated erythrocyte sedimentation rate and hypergammaglobulinemia. Extranodal involvement including bone is rare. The patient is a 45-year -old female with multiple punch out lesions on her skull. MRI findings included iso-signal intensity mass at the diploid space on T1 weighted image and on T2 weighted image, mild high signal intensity was obtained. Histologically, the lesion showed proliferation of histiocytes in the fibroblastic background with formation of reactive germinal centers and many plasma cells. The histiocytes show round nuclei and occasional nucleoli and abundant cytoplasms. In area, there is lymphocytophagocytosis. Immunohistochemically, the histiocytes were positive for S-100 protein and lysozyme.

Key Words : *Histiocytosis, sinus; Lymphatic diseases; Skull*

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INTRODUCTION

Sinus histiocytosis with massive lymphadenopathy (SHML) is a rare idiopathic histiocytic proliferative disorder and a distinct clinicopathologic entity (1, 2). It is usually a self-limited disease that characteristically manifests as a painless bilateral cervical adenopathy acccompanied by fever, leukocytosis, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia (1, 2). Most cases occur during the first or second decade of life, but any age group can be affected (1, 2).

The involved lymph nodes show a marked proliferation of sinus histiocytes often demonstrating lymphocytophagocytosis, so called emperipolesis. These histiocytes are large and contain vesicular nuclei, delicate nuclear membranes, distinct nucleoli , and voluminous pale cytoplasm. Also noted are numerous mature plasma cells and occasional neutrophils, and capsular and pericapsular fibrosis in the lymph nodes. Usually necrosis and eosinophil infiltration are absent.

Recently we have experienced SHML manifesting as multiple skull lesions on a 45-year-old female. We described clinical, radiographic, and pathologic features.

CLINICAL HISTORY

This 45-year-old female had had numbness in the right upper extremity and partial seizure for two months. There were no neurologic deficits. Laboratory findings including serum electrophoresis were normal.

Plain lateral view of the skull demonstrated multiple well-defined osteolytic lesions without sclerotic rim at the frontoparietal bone (Fig. 1). Axial view of the CT scan showed multiple lytic lesions at the diploic space of the frontal bone (Fig. 2A), which were more well delineated at the bone window image (Fig. 2B). T1 weighted sagittal image of the brain MRI revealed iso-signal intensity mass at the diploic space (Fig. 3A), which showed mild high signal intensity on T2 weight axial image (Fig. 3B), and homogeneous contrast enhancement on the Gd-DTPA enhanced T1 weight coronal image (Fig. 3C).

Under the impression of metastatic tumor or multiple myeloma, parietal bony lesion was resected. The lesion invaded both inner skull table and outer membrane of the dura.

The resected skull showed a round, well-defined bony defects filled with characteristic soft, yellow to white

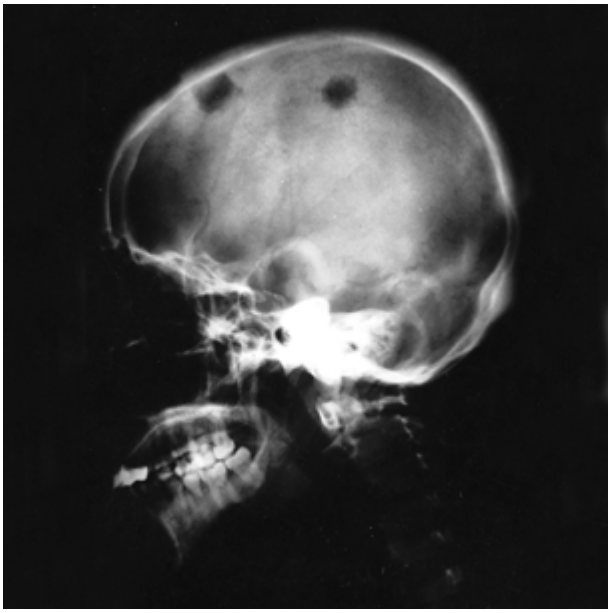

Fig. 1. Plain lateral view of the skull shows multiple well defined osteolytic lesions at the frontoparietal bone.

tumor tissue. There were no hemorrhage or necrosis (Fig. 4).

Microscopically, there were polymorphous cellular infiltrates consisting of large histiocytes, lymphocytes and abundant plasma cells. In area, these cells formed a reactive germinal center (Fig. 5). The characteristic histiocytes showed vesicular round to oval nuclei with smooth contours and distinct, small nucleoli. The cytoplasm was abundant and vacuolated. In some areas, emperipolesis by the histiocytes were found (Fig. 6). Background stromal tissue of the lesion showed prominent fibroblastic component with storiform growth pattern. Immunohistochemical stainings for the S-100 protein and lysozyme were done to reveal the nature of histiocytes. There were strong S-100 protein positive cells (Fig. 7) and lysozyme positive cells in the reactive germinal centers.

DISCUSSION

In 1969 Rosai and Dorfman first described this rare disease that affects mainly children and young adults (1, 2). It is a rare self limited non-neoplastic histiocytic proliferation characterized by painless bilateral cervical lymphadenopathy (95% of cases) as well as other nodal involvements (3, 4).

Foucar et al. noted that the condition has occurred both congenitally and in a 74-year-old patient. The mean age was about 20 years, and most patients were in their first or second decade of life (5).

The most common sites of extranodal disease are skin (6, 7), upper respiratory tract (8), and bone (9-12) followed by the genitourinary, lower respiratory tract, oral cavity, and soft tissues (5).

Osseous involvement occurs in less than 5-10% of cases and is nearly always associated with nodal and non-osseous disease (3). Bony lesions are often multiple (70%)

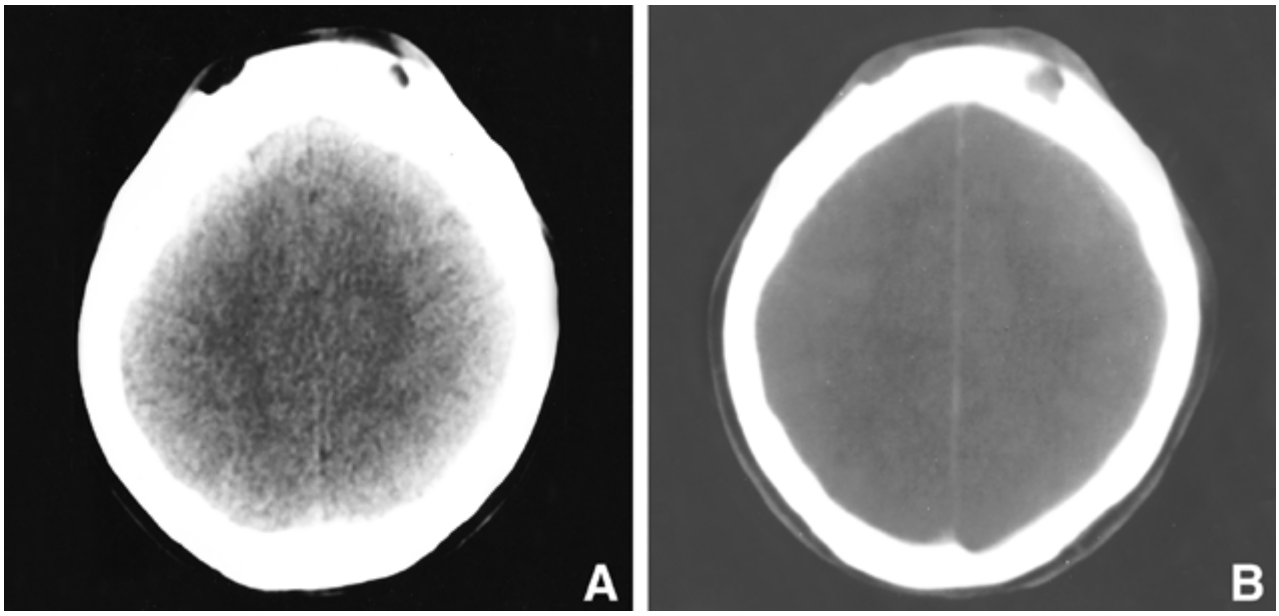

Fig. 2. Brain CT scan demonstrated multiple osteolytic lesions at the diploic space (A), which is more well-delineated at the bone window image (B).

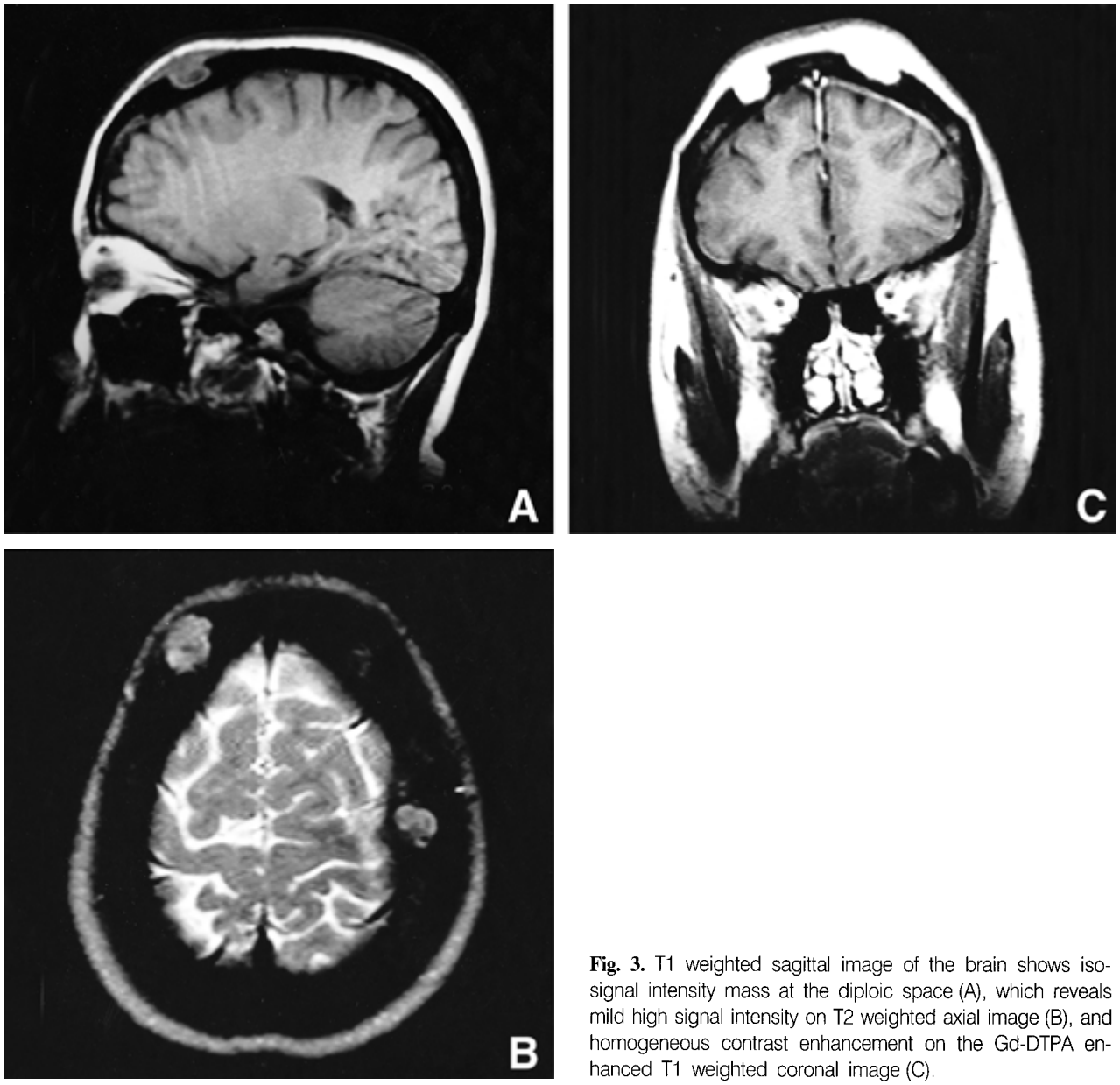

Fig. 3. T1 weighted sagittal image of the brain shows iso-signal intensity mass at the diploic space (A), which reveals mild high signal intensity on T2 weighted axial image (B), and homogeneous contrast enhancement on the Gd-DTPA enhanced T1 weighted coronal image (C).

and may involve any bone. Involvement of the skull, facial bones, vertebrae, sacrum, long bones, phalanges, and ribs are common. Long bone lesions may be metaphyseal, diaphyseal, or epiphyseal, often with multiple lesions in the same bone (13). Radiographically, osseous lesions are typically lytic lesions with poorly or sharply defined margins, but blastic and mixed blastic/lytic examples have been described (14). Involvement is usually within the medullary cavity, with occasionally cortical defects (9, 14). Periosteal reaction and intralesional calcification have not been reported (9). The MRI appearance in SHML shows inhomogenous low signal intensity of T1-weighted images and bright on T2-weighted images (12). The skeletal radiographic differential diagnosis includes histiocytosis X, metastatic malignant tumor, sarcoidosis, lipid storage disease and neurofibromatosis (3, 9).

Microscopically, the lesion showed cellular infiltrates similar to those found in the lymph nodes. The main differential diagnosis lies between histiocytosis X and SHML. The histiocytic cells of SHML lack the irregular nuclear contours, grooves and indentations of Langerhans cells. Both cells of SHML also express S-100 protein, but the cells of SHML also contain lysozyme, alpha-1-antitrypsin, alpha-1-antichymotrypsin, and stained with Mac-387 and Leu-22 markers which are lacking in histiocytosis X (15). In our case, we demonstrated S-100 protein and lysozyme positive cells in the resected lesion.

Fig. 4. Cut surface of the resected skull shows well-defined yellow white tumor tissue.

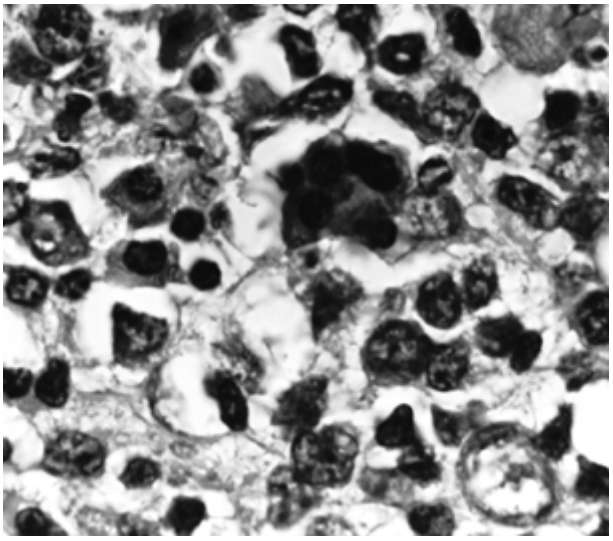

Fig. 6. There is lymphocytophagocytosis characterized by well-preserved lymphocytes and plasma cell located within cytoplasmic vacuoles (H&E, ×1,000).

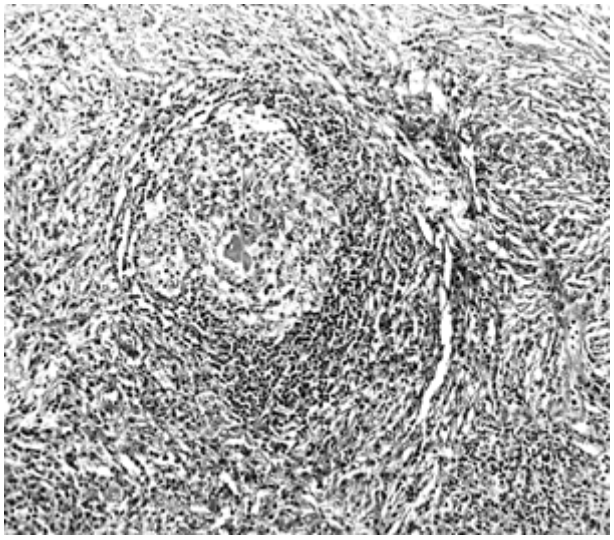

Fig. 5. Phtomicrograph of the lesion shows inflammatory infiltrates composed of lymphocytes, plasma cells and some histiocytes. Also noted are surrounding fibrosis with storiform pattern (H&E, ×100).

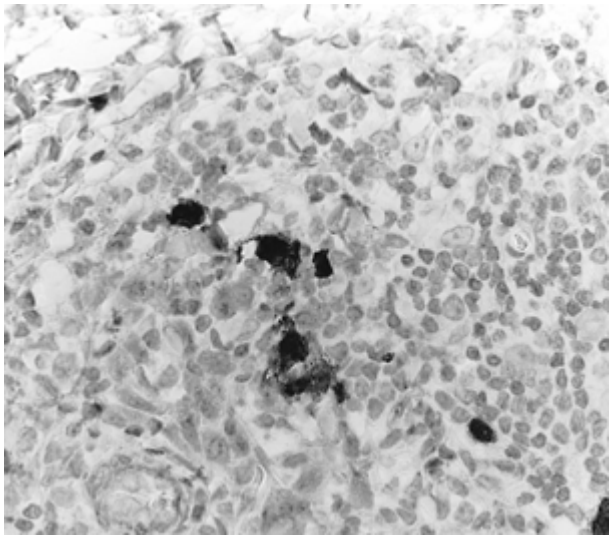

Fig. 7. There are strong S-100 protein positive cells in the reactive germinal center (Avidin Biotin immunoperoxidase staining, ×100).

Also there are many processes that may exhibit collections of foamy histiocytes admixed with lymphocytes and other inflammatory cells, usually as an expression of focal secondary degeneration. Other conditions include fibrous dysplasia, fibrous histiocytoma, so-called solitary xanthoma of bone, and a variety of benign and malignant bone neoplasms (9).

Most patients require no therapy because the disease is usually self-limited and characterized by spontaneous regression (16). Patients who have osseous manifestations of SHML do not show any significant difference from the total group of patients having this disease. The bone lesions tend to regress spontaneously, albeit slowly, along with the lymphadneopathy. This is consistent with the natural history observed in associated with lesions at other sites of extranodal involvement.

In this report, we dealt with a 45-year-old female who had a lesion on her skull with multiple involvements of sinus histiocytosis with massive lymphadenopathy.

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