Histiocytosis-x of the spinal cord

Case report

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The authors present a case in which there was direct invasion of the spinal canal and its contents by a granuloma of histiocytosis-x, and emphasize the importance of considering this condition as a cause of spinal cord and cauda equina syndromes.

KEY WORDS • histiocytosis-x • spinal cord • cauda equina • reticuloendotheliosis • spinal canal • granuloma

HISTIOCYTOSIS-X is a relatively rare disorder of the reticuloendothelial system involving the proliferation of histiocytes, granulation tissue, and inflammatory cells in many different organ systems of the body. Its protean manifestations usually present in the form of one of three clinical entities (Hand-Schüller-Christian disease, Letterer-Siwe disease, and eosinophilic granuloma) with varying degrees of overlap. Involvement of the nervous system is uncommon and usually occurs by means of contiguous extension, as in eosinophilic granuloma of the skull, for example. Recent reports have described cases arising intracranially within the substance of neural tissue. Histiocytosis-x has also been reported associated with various meningoencephalitic and demyelinating processes of uncertain causality.

In reviewing the literature, we have found that direct involvement of the spinal cord is exceedingly rare. Only two cases of documented intramedullary and dural granulomas are on record to these we add a third case of epidural spinal histiocytosis-x and review the various spinal cord presentations of this unusual condition.

Case Report

First Admission

In February, 1972, this 17-year-old girl was admitted because of progressive confusion, increasing drowsiness, generalized weakness, polyuria, polydipsia, irregular menses, and a low-grade fever. A brain scan revealed a left-sided parasellar mass. When examined, she was somnolent and poor at calculations; visual acuity was 20/100 bilaterally. Other cranial nerve findings were normal. Arteriography revealed distortion of the third ventricle by an intraventricular mass. A pneumoencephalogram (PEG) was compatible with an anterior third ventricular tumor. A clinical diagnosis of low-grade hypothalamic astrocytoma was made and radiotherapy was instituted. Tests of endocrine
function revealed subnormal levels of T4, luteinizing hormone, and ACTH. Visual acuity improved to between 20/30 and 20/40 bilaterally and the patient was discharged on a regimen of hormonal replacement therapy.

Second Admission
She was readmitted in November, 1972, because of anterior thigh pain, pain in the right ankle, and episodes of chills with persistent low-grade fever. Her temperature was 100.2°F; there were palpable lymph nodes in the left axilla, and in both cervical and inguinal regions. The thighs were tender, but normal motor strength, sensation, and reflexes were present in the legs. A repeat PEG demonstrated involvement of the interpeduncular cistern; her course was complicated by the development of rage-like behavior. Following radiotherapy, lymph node biopsy was carried out in December, 1972; the pathological diagnosis of histiocytosis-x was made at this time (Fig. 1), and the patient was begun on Cytoxan.

Third Admission
She was readmitted in March, 1973, because of difficulty in walking for 1 month. The cervical and inguinal nodes were palpable; there was tenderness over both the liver and the spleen, and loss of pubic hair. She was lethargic, and showed impaired memory; her visual acuity was 20/30 bilaterally. She had a shuffling gait and was poor at heel and toe walking. Straight leg raising was positive at 40° bilaterally. Strength in the legs was symmetrically diminished proximally as well as distally. There was a symmetrical hyporeflexia but no sensory impairment. Myelography revealed an extradural block at L-1 (Fig. 2) and other epidural lesions at T-4 and T-7. An emergency laminectomy was carried out from T12-L2, and a ventrally placed, vascular tumor at L-1 was biopsied. The primary specimen contained histiocytes, multinucleated giant cells, and acute inflammatory cells (Fig. 3); the histological picture was similar to that found in the previously biopsied lymph nodes (Fig. 1).

Discussion
The etiology of histiocytosis-x is unknown. At one time the disease was classified as a

Fig. 1. Photomicrograph of the lymph node biopsy. Note the large numbers of multinucleated foreign body cells and the small, darkly staining nuclei of inflammatory cells. Throughout the field are masses of large histiocytes with lightly staining or vacuolated cytoplasm and small, round nuclei. H & E, X 120.

Fig. 2. Myelogram demonstrating complete block at L-1. Anteroposterior (left) and lateral (right) views. Note that the bulk of the lesion arises ventrally.
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normocholesterolemic variant of xanthomatosis on the basis of lipid accumulation within the histiocytes. It is more precise to group histiocytosis-x with other nonspecific reticuloendothelioses. Involvement of the nervous system in cases with generalized visceral involvement is rare and histiocytosis most commonly presents as an isolated eosinophilic granulomatous lesion of the skull. Intracranial involvement proceeds by direct extension or, in rare cases, through the proliferation of reticuloendothelial cells within the cerebral substance. Histiocytosis localized to the hypothalamus and to the region of the optic chiasm have both been recently reported. In addition, several rare pathological entities, including granuloma infiltrates of the hypothalamus, Ayala’s disease and Gagel’s hypothalamic granuloma, have been identified as being identical to intracerebral histiocytosis-x. Finally, there has also been a report of a meningoencephalitic type of acute (Letterer-Siwe) histiocytosis.

In the spinal cord, histiocytic involvement may proceed along one of three general lines. First, there may be eosinophilic granulomas in the vertebrae, compromising the spinal canal and its contents, without direct attachment to the spinal cord or its coverings. This mechanism is analogous to the contiguous compression of the intracerebral contents by lesions arising in the bones of the skull and is well documented. Second, there are syndromes which arise from intraspinal processes loosely associated with histiocytosis-x elsewhere in the body, and which do not in any way conform to the pathological picture of the disease. In these cases the cord was involved with demyelinating plaques. The association of an extremely rare disease with the lesions of a much more common condition, for instance, multiple sclerosis, is not unexpected. Furthermore, the remote effects of neoplastic processes on muscle and nerve are well known and the contribution of such paraneoplastic syndromes to these cases of “spinal” histiocytosis remains undefined.

The spinal cord may also become involved either by metastatic spread from other loci of histiocytosis or through the de novo appearance of a disease focus in the cord or its coverings. Ezrin, et al., reported the case of a 43-year-old man who initially presented with hypothalamic disease and then, 4 years later, developed back pain with paraparesis. Postmortem examination revealed that the spinal cord was involved by epidural, subdural and intramedullary granulomas which resembled those in other locations. Originally, the clinical impression had been a nonspecific granulomatous lesion of the cord, possibly Hodgkin’s disease.

Miller and Ramsden reported the case of a 29-year-old man suffering from nausea and vomiting. Eight months after his initial presentation, he returned because of exophthalmos with extensive bony defects in the skull and orbital ridges. An orbital biopsy revealed sclerosing xanthoma. Apparently, the patient never had complaints referable to lesions of the spinal cord and these were only picked up during the postmortem examination, 4 years after onset. Plaques and nodules were found on the extradural surfaces in the cervical, thoracic, and lumbar regions. There

Fig. 3. Photomicrograph of the operative biopsy. The specimen is from the ventral lesion demonstrated at L-1 in Fig. 2. Histiocytes, inflammatory cells, and giant cells are all present within the surrounding stroma of connective tissue. H & E. × 150.
were no intradural lesions, but the cord showed some areas of demyelination and neuronal degeneration. These processes were thought to be secondary to epidural cord compression.

Our case is instructive in several respects. The diagnosis was made in life; thus it is important to keep in mind the possible diagnosis of histiocytosis-x in a patient presenting with paraparesis or some form of cauda equina syndrome. This is especially true, despite the rarity of spinal cord involvement, in cases in which the disease has been found in other locations. In the two symptomatic cases, motor function was more involved than sensory, and the spinal symptoms presented well after the intracranial onset of the disease. Moreover, our case illustrates the manner in which the diagnosis of a histiocytic process gradually evolves through the exclusion of other neoplastic, infectious, or granulomatous conditions. Although isolated eosinophilic granulomas are best treated by local curettage, there is no universally agreed upon or thoroughly effective therapeutic approach to widespread visceral histiocytosis. Our patient was treated with radiotherapy and surgery, as well as with Cytoscan. Other chemical agents, such as vinblastine, are also receiving clinical trials against this rare and baffling disease. Rational treatment of patients with central nervous system involvement obviously depends on prompt and accurate diagnosis.

References

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