Intracranial xanthogranuloma of the dura in Hand-Schüller-Christian disease

Case report

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The authors describe a 37-year-old man with the classic clinical features of Hand-Schüller-Christian disease. He presented with symptoms of increased intracranial pressure due to obstructive hydrocephalus secondary to a huge xanthogranuloma involving falx cerebri and tentorium cerebelli. Immunohistochemical and ultrastructural studies failed to demonstrate Langerhans histiocytes, however. The implication of this finding is discussed in light of the recent relevant literature.

KEY WORDS • Hand-Schüller-Christian disease • Langerhans cell • Weber-Christian disease • xanthogranuloma

Intracranial xanthogranulomas are rare and may represent an incidental finding or a manifestation of a variety of pathological processes. Kepes' distinguished 12 different conditions that may give rise to intracranial xanthomatous lesions. The exact nature of such lesions, whether neoplastic, inflammatory, or metabolic, remains controversial in most cases. Consequently, the nomenclature and the distinction of the different lesions continue to be unclear.

We report the case of an extensive intracranial xanthogranuloma of the dura in a patient with symptoms of Hand-Schüller-Christian disease. The immunohistochemical and ultrastructural findings of the dural lesion are described, and the difficulties of differential diagnosis of the underlying disorder are discussed.

Case Report

This 37-year-old man, father of three children, presented to the neurosurgical division of King Khalid University Hospital with a 3-year history of headache and progressive bilateral proptosis associated with blurring of vision and diplopia. He was diagnosed 11 years earlier as having diabetes insipidus, which was well controlled with chlorpropamide and chlorothiazide. His family medical history was negative.

Examination. The patient was in a good general condition. Multiple xanthelasmas were seen on both eyelids, as well as mild bilateral exophthalmos. In addition, ophthalmological examination revealed chronic bilateral papilledema, enlargement of the blind spots, and bilateral partial sixth nerve palsy. There were several small, whitish cutaneous nodules on the flanks and buttocks.

Computerized tomography (CT) revealed a large, diffusely enhancing lesion between the occipital lobes, extending anteriorly to the pineal region and causing obstructive hydrocephalus. In addition, there was marked bilateral thickening of the optic nerves (Fig. 1). On magnetic resonance imaging, the lesion emitted a low signal intensity on both T1- and T2-weighted images, with a rim of enhancement around the lesion following gadolinium injection (Fig. 2). Cerebral angiography showed the mass to be avascular. A 99mTc bone scan revealed multiple foci of intense uptake in the skull, facial bones, and the femur and tibia of both legs. The following investigations were normal: skull and chest roentgenograms, abdominal ultrasound studies, and iliac bone marrow aspirate. Laboratory findings (including electrophoresis of plasma protein, lipoprotein, and immunoglobulin) and cerebrospinal fluid
lesion formed and the region presented a mass involving the occipital lobe. CSF examination revealed papilledema to diabetes insipidus. The patient was not asymptomatic. The patient’s course was unchanged. On surgery, the patient was not asymptomatic and there was no change in his diabetes. The postoperative course was uneventful.

Postoperative Course. The patient’s condition remained unchanged. He received a course of radiotherapy to the intracranial tumors (300 cGy over 10 days), but no chemotherapy was given. One year after surgery, he is asymptomatic apart from mild bilateral ptosis and diabetes insipidus, which is controlled with desmopressin acetate, and has returned to his previous office work. Postoperative CT showed no significant change in the size of the dural lesions.

Pathological Examination. The intracranial lesion was subjected to cytological, histological, ultrastructural and immunocytochemical study. On cytological examination, smears prepared from fresh tissue revealed two types of histiocytes: some with moderate amounts of amphiphilic cytoplasm and a reniform or indented nucleus, and others which were larger and xanthomatous, with a finely vacuolated cytoplasm and a round nucleus. Multinucleated giant cells were also present, which exhibited a central or peripheral cluster of nuclei surrounded by foamy cytoplasm, so-called “ Touton giant cells,” with scattered polymorphs.

Histological examination of lesion sections showed sheets of large xanthomatous cells with a finely vacuolated cytoplasm and interspersed Touton-type giant cells. Focal aggregates of smaller histiocytes with eosinophilic or amphiphilic cytoplasm and a lobulated or indented nucleus, similar to those seen in the smear, were also noted. Modest numbers of inflammatory cells consisting of polymorphs, eosinophils, lymphocytes, and fibroblasts were also present, separating groups of xanthomatous cells (Fig. 3).

On ultrastructural study, membrane-bound lipid droplets were seen within the cytoplasm of the histiocytes (Fig. 4). In spite of an exhaustive search, no Birbeck granules were detected. Immunocytochemical stains showed both foamy and nonfoamy histiocytes positive for α1-antitrypsin, α1-antichymotrypsin, and lysozyme; however, there was negative reactivity for S-100 protein (Fig. 5).

The biopsy material from the small nodular lesions in the skin showed a xanthogranulomatous lesion consisting of small clusters of lipid as well as nonlipid-laden histiocytes admixed with other inflammatory cells in the dermis. Ultrastructural and immunohistochemical studies were not performed.

Discussion

Choroid Plexus Xanthogranuloma

Intracranial xanthogranulomas arise most commonly in the choroid plexus, being almost uniformly located in the trigone of the lateral ventricle. They are usually asymptomatic and discovered incidentally in 1.6% to 7.0% of autopsies. Only a few cases of symptomatic choroid plexus xanthogranuloma were reported in the literature, the majority of which were located in the third ventricle resulting in CSF obstruction and hydrocephalus. Generally, there has been no demonstrable relationship between choroid plexus xanthogranuloma and sex, race, or systemic disorders such as hypercholesterolemia, athroscerosis, or diabetes. Because most of the affected subjects were aged in their 70’s, these lesions are thought to result from a normal aging process. However, bilateral choroid plexus xanthogranulomas have been documented in a child with Hand-Schüller-Christian disease.

Dural Xanthogranuloma

In contrast, dural xanthogranulomas are rare and
Intracranial dural xanthogranuloma

Fig. 3. Photomicrograph showing granulomatous tissue consisting of fibroblasts and inflammatory cells on the left side and sheets of xanthomatous cells on the right. H & E. × 125.

Fig. 4. Electron micrograph revealing lysosomes, phagolysosomes, and membrane-bound lipid droplets in the cytoplasm of a histiocyte. × 3350.

Fig. 5. Immunohistochemical study showing positive staining of xanthomatous cells for α1-antichymotrypsin. × 200.

Hand-Schüller-Christian Disease

Our patient fulfilled fully the classical triad of Hand-Schüller-Christian disease, namely diabetes insipidus, exophthalmos, and multiple osseous lesions (on bone isotope scan). He also showed cutaneous involvement which may occur in about one-third of patients with this disease. The long interval of 11 years between the manifestation of diabetes insipidus and the development of exophthalmos in this patient, although remarkable, is not completely unusual in the course of Hand-Schüller-Christian disease. Kepes and Kepes9 reported two cases in which diabetes insipidus preceded the other manifestations of the disease by 6 and 7 years.

Intracranial involvement in Hand-Schüller-Christian disease is not uncommon and consists typically of intracerebral perivascular histiocytic infiltration or a granulomatous mass, particularly in the hypothalamic region which accounts for the diabetes insipidus.9 Intracerebral lesions may develop by direct extension from neighboring bone, usually the base of the skull, or the process may originate in the brain, presumably from adventitial cells of the blood vessels. Meningeal involvement in histiocytosis X is rare and usually associated with either skull lesions or purely parenchymal lesions.4 The dural lesions may remain circumscribed to the dura, or they may infiltrate the underlying brain parenchyma.7 Their size may range from a small isolated nodule to large masses covering broad areas of dura, falx, and/or tentorium, as in the present case. While small dural lesions usually remain asymptomatic, the large ones tend to produce symptoms of increased intracranial pressure either by virtue of their mass or by obstruction of CSF pathways.

Histopathology

The pathognomonic feature of the lesions in Hand-Schüller-Christian disease (and histiocytosis X in general) is a special histiocyte, the Langerhans cell.14 This cell represents a specific subpopulation of the mononuclear phagocytic system and is normally present in the skin. It is distinguished from other histiocytes by
staining positive for S-100 protein and the presence of Birbeck granules on electron microscopy. Recent data suggest that Langerhans cells are involved in antigen processing and presentation to T lymphocytes.

The causes of the proliferation of Langerhans cells in histiocytosis X are unknown. Three basic mechanisms have been discussed: 1) normal Langerhans cells are activated by an "unknown" external antigen, producing a physiologically appropriate but clinically pathological reaction; 2) normal Langerhans cells respond to an abnormal immune system signal (a number of distinct immunological abnormalities have recently been identified in patients with histiocytosis X; most importantly, perhaps, a deficiency of suppressor cells); and 3) the Langerhans cell itself is inherently abnormal, reacting pathologically to physiological stimulation.

The absence of Langerhans cells in the dural lesions in this case is interesting and raises a number of speculations. Recently, Miyachi, et al. reported similar immunohistochemical and ultrastructural results from a large dural mass lesion in a patient with systemic xanthogranulomatosis. They concluded that the condition was unrelated to histiocytosis X and represented, in spite of the absence of skin involvement, a variant of systemic Weber-Christian disease. The assumption in our patient of an underlying disorder other than histiocytosis X would, in view of the typical clinical presentation as a Hand-Schüller-Christian disease, have serious implications. It would suggest that the Hand-Schüller-Christian disease is a clinical syndrome that can be produced by disorders of different histocytes, not only of the Langerhans cells. To date, there is no clinical or pathological evidence to support such an assumption. We are, therefore, more inclined to believe that the immunohistochemical and ultrastructural criteria suggested by Miyachi, et al., do not allow a clear distinction between Weber-Christian disease and histiocytosis X. It is also possible that the two conditions are related, which would account for such overlapping results.

References


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