Case Report

Langerhans Cell Histiocytosis Presenting as Adult Onset Epilepsy

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Abstract
A 37 year old man presented with recurrent secondarily generalized seizures from right partial onset since December 1999. MRI scan of brain (contrast study) revealed multiple enhancing lesions predominantly involving frontal, parietal and temporal regions. Left frontotemporal lesion was biopsied and histopathology confirmed it to be rare case of adult Langerhans cell histiocytosis. He was given short course of oral corticosteroids. Two years postoperative course on antiepileptic therapy alone is uneventful and repeat MRI brain and MR spectroscopy showed significant resolution of lesions.

Introduction
Langerhans cell histiocytosis (LCH) is rare in adults and CNS involvement is further a rarity. Clinical manifestations are variable, mostly affecting skin, lungs and bone although diabetes insipidus (DI) is fairly common. The MR imaging has improved the diagnosis of CNS abnormalities and classified the lesions. However CNS involvement in the form of multiple intracranial space occupying lesions is very uncommon.

A rare case of an adult presenting with secondarily generalized seizures is reported alongwith brief review of world literature.

Case Report
A 37 year old man presented with recurrent secondarily generalized seizures from right partial onset beginning from right upper limb since December 1999. There was history of mild to moderate generalized headache since the same time. He used to consume alcohol, cannabis and smoke 8-10 cigarettes per day for last many years. He denied history of vomiting, visual symptoms, fever, polyuria and tuberculosis. Fundus examination was normal. Neurological examination revealed short temperedness and impairment of recent memory. General physical and other systemic examination was unremarkable. In particular, there was no lymphadenopathy, hepatosplenomegaly, or any skin lesions.

Routine investigations revealed normal hemogram, ESR and blood chemistry. Serum HIV was negative. Chest and skull X-rays, and 99mTc bone scan did not show any abnormality. Ultrasonography of whole abdomen and water deprivation test were normal. CSF analysis was normal including cytology for malignant cells. Interictal EEG did not show any abnormality, MRI scan of brain (contrast study, September 2000; Fig. 1) revealed multiple enhancing lesions predominantly involving frontal, temporal and parietal...
regions with surrounding edema. A caudate nucleus lesion on left side showed peripheral enhancement on gadolinium administration while the central cystic - necrotic portion failed to enhance. Slight enhancement of ependymal and subependymal tissue adjacent to body of left lateral ventricle was seen. There was no meningeal enhancement and no abnormality was detected in pituitary region.

Left frontotemporal lesion was biopsied in October 2000.

**Histopathology**

Sections stained with hematoxylin and eosin (Fig. 2) showed cerebral tissue with diffuse and nodular, moderately dense cellular exudates with edema. There was marked capillary vascular proliferation, with diffuse eosinophilic infiltrate. Moderately dense perivascular lymphocytic infiltrate was also seen. In addition, there were multiple nodular aggregates of histiocytes with characteristic linear nuclear grooves, admixed with fair number of eosinophils in and around the nodular aggregate of histiocytes. PAS and GMS stained sections did not show any fungal bodies, larvae or adult parasite. On immunohistochemical study, histiocytes did not show staining for S-100 protein. Facility for electron microscopy was not available.

**Treatment and Follow-Up**

He was started on oral corticosteroids (prednisolone) along with antiepileptic (carbamazepine) therapy. Seizures were well controlled and headache got relieved. Repeat MRI brain (contrast study, February 2001; Fig. 3) three months after surgery showed reduction in edema and resolution of lesions. Steroids were gradually tapered off. Two years postoperative course on antiepileptic therapy alone is uneventful; and MRI brain (September, 2001; Fig. 4) and recent MR spectroscopy (June, 2002) confirmed significant resolution of lesions.

**DISCUSSION**

Langerhans cell histiocytosis (LCH) is a rare group of disorders with a wide spectrum of clinical presentations. The term LCH was introduced as an alternative to histiocytosis...
but less pronounced predilection for the cerebellum, especially the area of the dentate nucleus, has also been reported. Clinically, four groups of patients can be distinguished: 1. disorder of hypothalamic-pituitary system, 2. disorder of cerebellar-pontine pathway, 3. space-occupying lesions, 4. overlapping symptoms. Although lesions exerting a mass effect may arise from neighboring bone lesions, meninges or choroids plexus; discrete foci arising de novo in the cerebral substance and spinal cord have been reported. The exact incidence of mass lesions is not known.

When LCH presents in unusual sites such as the central nervous system, the diagnosis can sometimes be hampered by a low index of suspicion, by a clinical history that may point to an infectious etiology, or nonclassical histologic pattern. Electron microscopy, although helpful, is not always readily available. The MR imaging has improved the diagnosis of CNS abnormalities and classified the lesions. MR characteristics are not LCH-specific per se, however, the pattern of distribution together with signal and contrast enhancement in the appropriate clinical setting strongly suggest the diagnosis. In the present case, contrast MR study revealed multiple enhancing lesions predominantly involving frontal, temporal and parietal regions with surrounding edema and a left caudate nucleus lesion. The Table 1 lists the cases of mass lesion reported in world literature without diabetes insipidus or exophthalmos. There are only two cases of multiple masses reported so far by Geoffray A\(^6\) and by Goldberg R;\(^7\) in early childhood. To the best of my knowledge, this is the first case report of an adult having isolated multiple intracranial masses.

When the disease begins as multifocal enhancing intracranial masses without hypothalamo-hypophyseal involvement, differential diagnosis includes tuberculoma, sarcoid granuloma, parasitic disease, mycotic infection, myeloproliferative disorder and a number of other lesions. Tissue diagnosis is mandatory in such a situation. Histopathologically, four stages described by Norman\(^9\)

### Table 1: Atypical cases reported in world literature without diabetes insipidus or exophthalmos

<table>
<thead>
<tr>
<th>Author</th>
<th>Age of onset</th>
<th>Clinical Presentation</th>
<th>Osteolysis</th>
<th>Neuropathology</th>
<th>S-100 staining</th>
<th>Birbeck granules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geoffray</td>
<td>2 years</td>
<td>Fever, otitis media</td>
<td>-</td>
<td>Multiple mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goldberg R(^7)</td>
<td>33 months</td>
<td>ICP(^\uparrow)</td>
<td>+</td>
<td>Multiple mass</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Sivlingam(^6)</td>
<td>9 years</td>
<td>Epilepsy</td>
<td>-</td>
<td>Temporal mass</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Moscinski LC(^10)</td>
<td>30 years</td>
<td>Epilepsy</td>
<td>-</td>
<td>Frontotemporal mass</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Cerda-Nicolas(^11)</td>
<td>35 years</td>
<td>Epilepsy</td>
<td>-</td>
<td>Epilepsy</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Kepes(^12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>12 years</td>
<td>ICP(^\uparrow), hemiparesis</td>
<td>?</td>
<td>Temporal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 2</td>
<td>11 years</td>
<td>ICP(^\uparrow), hemiparesis</td>
<td>?</td>
<td>Temporal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 3</td>
<td>9.5 years</td>
<td>ICP(^\uparrow)</td>
<td>?</td>
<td>Temporal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 4</td>
<td>26 years</td>
<td>Hemiparesis, ICP(^\uparrow)</td>
<td>?</td>
<td>Frontal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greenwood(^13)</td>
<td>14 years</td>
<td>Epilepsy, ICP(^\uparrow)</td>
<td>?</td>
<td>Frontoparietal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waldron(^14)</td>
<td>34 years</td>
<td>Epilepsy, ICP(^\uparrow)</td>
<td>+</td>
<td>Frontoparietal mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Khan A(^15)</td>
<td>26 months</td>
<td>Epilepsy</td>
<td>-</td>
<td>Multiple</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present case</td>
<td>37 years</td>
<td>Epilepsy</td>
<td>-</td>
<td></td>
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include hyperplastic - proliferative stage, granulomatous stage, xanthomatous stage, and a stage of fibrosis. The hallmark is the presence of Langerhans' cells by light microscopy. The lesions in LCH may consist of either pure histiocytic infiltrates or mixed, histiocytic/eosinophilic lesions. Presence of Birbeck granules in the LCH cell cytoplasm near the nucleus seen by electron microscopy is pathognomonic of LCH. Birbeck granules rarely are found in cells of the liver, gastrointestinal tract, or brain, even when those organs are clinically involved in the disease process. Immunohistochemical phenotyping shows that they react positively for S100, CD1, CD11 and CD14 antigen. Histopathological findings in our case included multiple nodular aggregates of histiocytes with characteristic linear nuclear grooves, admixed with fair number of eosinophils.

Positive S-100 staining has been reported only in cases of Moscinski LC,10 and Goldberg R.7 In our case, S-100 staining was negative. Unfortunately, we could not demonstrate Birbeck granules due to non-availability of electron microscopic but only three cases with Birbeck granules have been reported so far.7,8,11

The patients in the LCH-CNS2 with mass lesions as the only CNS pathology were free from disease without neurologic defects after surgery or treatment with steroids or chemotherapy. In general, mass lesions respond well to treatment, with minimal or even no residual defects.7,11

The present case received a short course of oral corticosteroids for three months. Two years postoperative course on antiepileptic therapy alone is uneventful which is further confirmed by repeat MRI brain study (Fig. 4), and recent MR spectroscopy (June, 2002) showing significant resolution of lesions. The case described here besides being a rare disease entity, revealed several unusual features such as:

* Isolated CNS involvement in the form of multiple intracranial masses in an adult presenting with secondarily generalized seizures.

* Absence of osteolytic lesions and diabetes insipidus.

* Two years postoperative course is completely seizure free and repeat MRI brain, and MR spectroscopy shows significant resolution of lesions.

## References