Focal eosinophilic granuloma of the temporal lobe

Case report

SELVADURAI SIVALINGAM, M.D., GUY CORKILL, M.D., WILLIAM G. ELLIS, M.D., AND JOHN R. CLAICHE, M.D.

Departments of Neurological Surgery and Pathology, University of California, Davis, Sacramento Medical Center, Sacramento, California

The authors describe the clinical, pathological, and therapeutic aspects of a case of focal temporal lobe eosinophilic granuloma, presenting with otitis media and meningitis, and evolving subsequently into a temporal lobe mass. This triad, otitis media, meningitis, focal cerebral lesion with systemic manifestations of inflammation, eosinophilia of blood and cerebrospinal fluid, should suggest eosinophilic granuloma in the differential diagnosis. The lesion is sensitive to relatively small doses of radiation.

KEY WORDS • eosinophilic granuloma • temporal lobe • Hand-Schüller-Christian • Letterer-Siwe • histiocytosis-X • radiotherapy

EOsinophilic granuloma in its well recognized classical form is a benign reticuloendothelial proliferation manifesting as a solitary lytic lesion of bone. Histologically indistinguishable lesions have been described as primarily involving the lungs, skin, stomach, and spinal cord. There is confusion in nomenclature, however. The histopathological characteristics between Hand-Schüller-Christian disease, Letterer-Siwe disease, and eosinophilic granuloma are similar, leading to the concept that these diseases are basically identical in nature, and therefore describable under a single nosological heading “histiocytosis-X,” in spite of the strikingly different clinical pictures. It is for this reason that many clinicians and pathologists no longer accept the unitarian concept implied by “histiocytosis-X.” The spectrum of this disease complex ranges from a localized form of eosinophilic granuloma treatable with local excision and radiation compatible with normal life span, to a fatal systemic form in which cytotoxic agents are palliative only. The potential hazard to patients of grouping eosinophilic granuloma, Letterer-Siwe, and Hand-Schüller-Christian disease entity for treatment purposes is apparent. To our knowledge there has been no previously reported case of a solitary eosinophilic granuloma located in the temporal lobe; all previously reported cases have been localized in the hypothalamus and/or pituitary gland (Gagel’s granuloma). Extra-hypothalamic cerebral lesions histologically compatible with eosinophilic granuloma have been reported in the temporal lobe, but these have been autopsy
studies and had documented multiple organ involvement.6

This report concerns a patient who at the age of 9 years underwent three consecutive craniotomies for apparent cerebral infarction of the brain. This disease process, initially a diagnostic and therapeutic dilemma, was subsequently diagnosed as focal cerebral necrosis with eosinophilia, and was controlled eventually by the use of small doses of radiation. Even though there was clinical evidence of systemic involvement, extensive search revealed no further histological evidence of dissemination.

Case Report

This 9-year-old boy presented to his family doctor with a several-day history of headache, malaise, sore neck, abdominal discomfort, and low-grade fever. Examination revealed inflamed tympanic membranes, and ampicillin was prescribed for otitis media. Symptoms persisted and 1 week later he developed a right-sided Jacksonian seizure. He was admitted to a local hospital where a lumbar puncture revealed clear cerebrospinal fluid with an opening pressure of 210 mm H₂O, protein 26 mg%, glucose 57 mg%, and 200 lymphocytes.

Examination. Physical examination on transfer to the University Medical Center revealed low-grade fever, lethargy, ataxia, dysphasia, nystagmus, bilateral clonus, and mild weakness of the right upper extremity. There was no papilledema or cranial nerve palsies. Admission white blood cell (WBC) count was 5900 with 10% eosinophils; Hg was 10.2 gm. A diagnosis of viral meningoencephalitis was considered most likely. The patient began to improve and was transferred back to his local hospital at the family's request. He was readmitted because of persistent low-grade fever. Repeat lumbar puncture showed 67 WBC's, 91% mononuclear, 9% eosinophils, and a protein of 57. Spinal fluid, anaerobic, aerobic, viral, fungal, and tuberculous cultures were all negative. Acute and convalescent titers were negative. Tuberculosis, coccidiodomycosis, Casoni, toxicara, and Ascaris tests were negative. A computerized tomography (CT) scan was normal. He remained stable until the 15th hospital day when increased lethargy, progressive disorientation, and increasing right arm weakness was noted. Further rapid deterioration and bradycardia led to a repeat CT scan and an arteriogram which showed a left temporal lobe mass with significant left-to-right shift.

Operation. A decompressive fronto-temporal craniotomy was performed with a left temporal polar lobectomy. The meninges appeared grossly normal. The cortex over the superior temporal gyrus appeared somewhat pale, and the gyri were widened. When the cortex was incised, a hemorrhagic necrotic area involving cortex and extending into white matter was encountered. The infarcted brain tissue was excised.

Histological Findings. The most striking and consistent histological feature of the excised brain tissue was a dense polymorphous perivascular infiltrate associated with focal necrosis (Fig. 1). In the area of greatest involvement the infiltrate was confluent and sheet-like. This process primarily involved the cerebral cortex and white matter, although

![Fig. 1. Perivascular cellular infiltrate forms a sleeve around the branching artery in the cerebral cortex. Note that the vessel lumen is narrowed or obliterated in several areas. H & E, X 75.](image)
Fig. 2. Perivascular cellular infiltrate made up of pale histiocytes (arrows), lymphocytes, plasma cells, and numerous eosinophilic polymorphonuclear leukocytes that appear as dark black granules. Note the gemistocytic astrocytes (G) on the adjacent disrupted brain tissue. H & E, X 235.

Fig. 3. Computerized tomography scan before third operation showing finger-like areas of reduced density and ventricular displacement.

small numbers of lymphocytes and other mononuclear cells were present around the leptomeningeal vessels. The cerebral infiltrate was composed of histiocytes, lymphocytes, plasma cells, and numerous eosinophils (Fig. 2). The histiocytes were moderately large and had rounded or indented vesicular nuclei, small nucleoli, and fairly abundant pale eosinophilic cytoplasm. No phagocytosis of erythrocytes or mononuclear cells were noted. Mitotic activity up to three mitoses per high-power field was seen in some areas. Most of the mitotic cells appeared to be histiocytes. The cellular infiltrate encased the blood vessels as they passed through the cerebral cortex and entered the superficial white matter. The lumina of many vessels were narrowed or completely obliterated. Endothelial cells of the involved vessels were swollen and hyperplastic. Foci of subacute necrosis in the subjacent white matter contained lipid-filled phagocytes and were surrounded by large bizarre-appearing gemistocytic astrocytes. Cerebral cortical neurons were relatively well preserved even in areas immediately adjacent to the perivascular infiltrates. Special stains and serial sections of the entire specimen revealed no parasites, micro-organisms, or viral inclusions. The subsequent two biopsy specimens qualitatively showed the same changes but had more vascular proliferation and fewer eosinophils.

Postoperative Course. The patient's neurological status improved postoperatively but during the following week he developed hepatomegaly with ascites. A liver scan showed no focal deficits and needle biopsy of the liver revealed only mild fatty metamorphosis. Cytological examination of the ascitic fluid was negative. The boy showed significant improvement in neurological status and was discharged home.

Within a few days he returned with depressed conscious level and progressive right hemiparesis. Repeat CT scan confirmed the presence of a mass lesion in the left temporal lobe. A second craniotomy was performed, with further resection of the infarcted brain, and the patient was discharged home with an uneventful postoperative course. He returned yet again with recurrent symptoms and marked mass effect on the left temporal lobe confirmed by CT scanning (Fig. 3). He was treated with further excision of swollen
S. Sivalingam, G. Corkill, W. G. Ellis and J. R. Claiche

temporal lobe. By this time review of the histology had led to two opinions that this was focal cerebral necrosis or a manifestation of eosinophilic granuloma, and it was decided therefore to treat the boy with radiotherapy and steroids. The patient had received 2000 rads of radiation when further review of the literature led us to believe that the lesions should be sensitive to low doses of radiation. Thus further radiation was discontinued. Three months later he was admitted for elective cranioplasty. At this time eosinophilia was no longer present, and his only neurological sequela was a right superior homonymous quadrantanopsia. He has remained well at 18 months post-radiotherapy.

Discussion

Clinical Presentation

Cerebral involvement by a form of reticuloendotheliosis in its classical form involving the hypothalamus, that is, when it presents with the clinical triad of calvarial defect, exophthalmos, and diabetes insipidus, is well recognized. When the disease begins as a tumor in the central nervous system without apparent hypothalamic involvement, diagnosis is difficult. The presence of a focal cerebral lesion associated with systemic manifestation of inflammation and eosinophilia of the blood and CSF should suggest a reticuloendothelial form of disease involving the central nervous system. Illness similar to otitis media is a recognized form of onset of this disease. Also, the simulation of bacterial meningitis by these conditions should be recognized. Nevertheless, no frequent characteristic pathognomonic presentation exists.

Histopathological Assessment

The diagnosis of eosinophilic granuloma can be confirmed only by histopathological examination. The classical microscopic pattern is that of focal accumulation of histiocytes and eosinophils in varying proportions. The histiocytes are described as moderately large with a medium-sized round or indented vesicular nucleus that contains a small central nucleolus. The cytoplasm varies in amount and is usually finely granular and eosinophilic. Phagocytosis may or may not be present. Scattered lymphocytes and plasma cells are most often noted, and neutrophils may occur around foci of necrosis. The latter tend to be central and are sometimes associated with cholesterol clefts, multinucleated giant cells, and foamy histiocytes. In lesions involving the brain a prominent perivascular arrangement of the cellular proliferation has been described along with a proliferating vascular component made up of newly formed capillaries surrounded by a loose network of reticulin. Variable astrocytic gliosis and nonspecific inflammation of the overlying leptomeninges are generally present.

The histopathological changes found in the temporal lobe lesion in this case conform well to previously described eosinophilic granulomas of the brain. Several consulting neuropathologists felt that the microscopic appearance could be a reaction to parasitic infestation of the brain. However, an intensive search for parasitic disease including serological tests, skin tests, and serial sections of all available tissue was negative. In addition, this lesion should be differentiated from other conditions such as pilocytic astrocytoma, microgliomatosis, tuberculoma, and sarcoid granuloma.

Since some aspects of the clinical course, namely, protracted fever, eosinophilia, and transient hepatomegaly with ascites, are not usual manifestations of solitary eosinophilic granuloma, the possibility of multisystem involvement, that is, Hand-Schüller-Christian disease, is considered. Search for other areas of involvement including liver biopsy and bone marrow were negative. Despite significant organ enlargement, chemical tests of liver function may be normal; no information is available as to the diagnostic value of needle biopsy of the liver. Bone marrow studies are also not significant unless aspiration of a lesion localized by x-ray film is obtained.

Although solitary lesions of this type involving the hypothalamus are well documented (Gagel's granuloma), extrahypothalamic cerebral involvement has been reported only in the multifocal or systemic well differentiated reticuloendotheliosis commonly known as Hand-Schüller-Christian disease and Letterer-Siwe disease. There have been at least 24 reported cases of cerebral involvement in patients with Hand-Schüller-Christian disease, not all of which
Focal temporal lobe eosinophilic granuloma

were confirmed histologically. Generalized microfocal "meningoencephalitic" involvement of the brain has rarely been described in cases of Letterer-Siwe disease. In one patient with this condition, the histiocytic infiltrates were localized to one temporal lobe.

Treatment

A combination of decompressive craniotomy, which included resection of the temporal pole, dural graft, and leaving the bone flap out, and steroid and radiotherapy was successful in arresting the disease process. The operative approach was not only lifesaving, but also provided tissue diagnosis which was not suspected on clinical grounds.

This case seems noteworthy for several reasons. This may be the only recorded surviving patient with antemortem histological diagnosis of a solitary eosinophilic granuloma of the temporal lobe. The clinical manifestations of a meningoencephalitic process with progressive temporal lobe involvement suggested a differential diagnosis of 1) herpes virus hominis encephalitis, 2) partially treated bacterial meningitis with secondary brain abscess, and 3) parasitic infestation of the brain. The presence of an enlarging temporal lobe mass that required decompression raised the possibility of a malignant neoplastic process. However, the possibility of a primary reticuloendothelial process was not considered until the involved brain tissue was histologically examined. Therefore this case illustrates that solitary eosinophilic granuloma of the brain might be considered when the usual causes of meningoencephalitis with localizing mass effect have been excluded.

References


Address reprint requests to: Selvadurai Sivalingam, M.D., Department of Neurological Surgery, University of California, Davis, School of Medicine, 4301 X Street, Sacramento, California 95817.