Leptomyxid amebic meningoencephalitis mimicking brain stem glioma.

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Leptomyxid Amebic Meningoencephalitis Mimicking Brain Stem Glioma

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Summary: An 11-month-old infant presented with cranial nerve palsy and ataxia. MR revealed a large, enhancing pontine mass and small, nonenhancing parafalcial lesions; no organisms were seen in cerebrospinal fluid. After empiric treatment for brain stem glioma, the patient died. Autopsy revealed meningoencephalitis caused by leptomyxid amebae.

Index terms: Meningoencephalitis; Nervous system, infection; Children, central nervous system; Brain stem, neoplasms

Intracranial infection by opportunistic free-living amebae such as *Naegleria* and *Acanthamoeba* species is rare and may mimic cysticercosis or neoplastic disease (1). *Naegleria fowleri* penetrates the olfactory bulbs and produces an acute, fulminating meningoencephalitis. *Acanthamoeba* species produce a subacute or chronic granulomatous encephalitis often involving the contents of the posterior fossa and the base of the brain; the portal of entry is often unclear (2, 3). Soil-dwelling amebae of the order Leptomyxida may closely resemble *Acanthamoeba* species on light microscopy, and several previous cases of meningoencephalitis previously attributed to *Acanthamoeba* species have been shown by immunocytochemical studies to be caused by leptomyxid amebae (1, 4). We report a case of fatal intracranial infection by a leptomyxid ameba, which was mistaken clinically and radiographically for the more commonly encountered entity of brain stem glioma.

Case Report

An 11-month-old Hispanic girl from northeastern Texas presented with internal strabismus of the left eye, unsteady crawling, and difficulty grasping objects. There was no history of trauma or frequent or unusual infections. During recent travel to northern Mexico, the child had been given bottled water and was carefully supervised. On physical examination the child was afebrile and lacked nuchal rigidity. She had a left sixth nerve palsy, slightly decreased deep-tendon reflexes, and a Babinski sign on the left.

Cerebrospinal fluid analysis revealed normal protein and glucose content and a lymphocytosis (92 red blood cells per cubic millimeter, 60 white blood cells per cubic millimeter, 93% lymphocytes, and 7% monocytes and histiocytes). No malignant cells or organisms were seen on stained cytospin preparations, and cultures for bacteria, acid-fast bacilli, and fungus were negative.

Cranial magnetic resonance (MR) imaging was done in the sagittal and axial planes using short-repetition-time sequences (500/30/2 [repetition time/echo time/excitations]) before and after intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine. Nonenhanced proton-density and long-repetition-time/long-echo-time (2500/40, 80/2) images were acquired in the axial plane. The sagittal postgadolinium sequence revealed intense, homogenous enhancement within the pons (Fig 1A). The axial T2-weighted image revealed hyperintense signal within the pons and left brachium pontis (Fig 1B). On the proton-density image through the cerebral convexities, there were subtle areas of increased signal in a parafalcine location (Fig 1C), which did not enhance. There was no hydrocephalus or leptomeningeal enhancement.

The patient began receiving chemotherapy and radiation therapy for presumed pontine glioma. Approximately 3 weeks later, she presented with a new right hemiparesis and left seventh and ninth cranial nerve deficits. Repeat MR imaging showed an interval decrease in the pontine lesion. Contrast-enhanced computed tomography (Fig 1D) showed several new lesions in the left parietal lobe, which demonstrated peripheral enhancement. A biopsy of the cortical lesions was suggested but refused by the parents. The patient continued to deteriorate despite aggressive medical care, developed obstructive hydrocephalus, and died 7 days later. Consent was obtained for postmortem examination limited to the central nervous system.

Autopsy revealed symmetric enlargement of the basis pontis with focal softening and hemorrhagic discoloration

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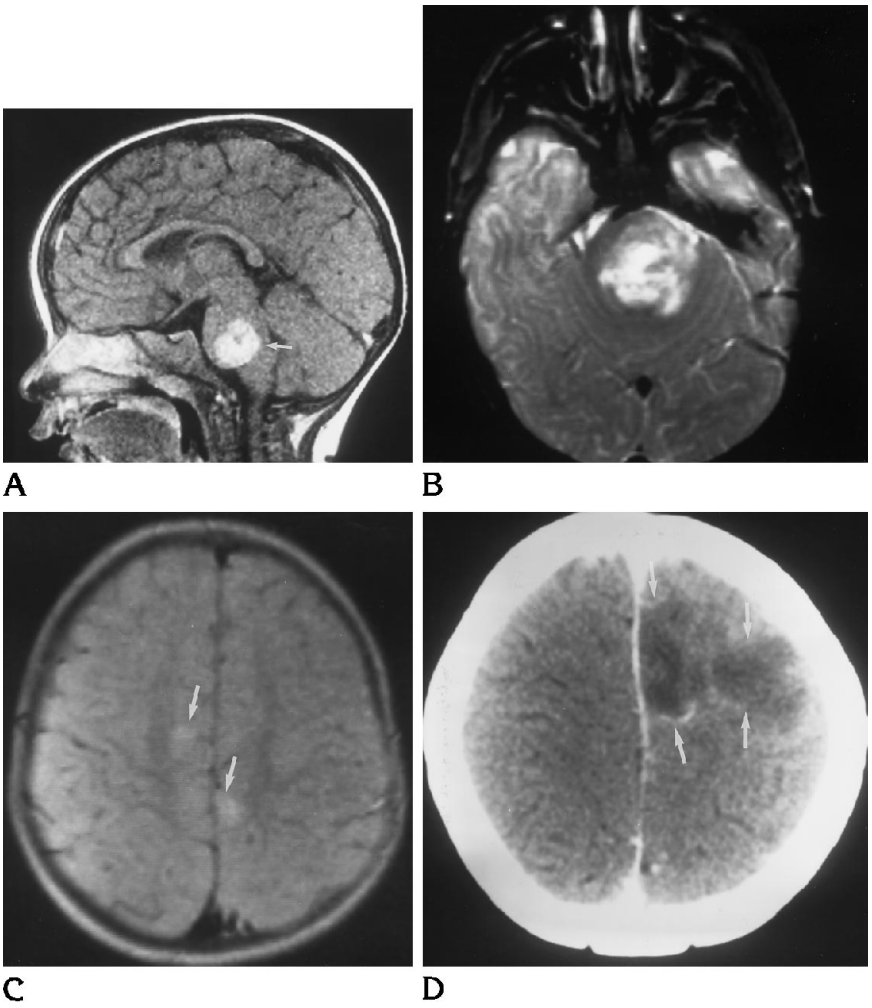

Fig 1. *A*, Sagittal postgadolinium T1-weighted (500/30/2) (*arrows*) image shows an enhancing lesion within the pons.

B, Axial T2-weighted image (2500/80) shows inhomogeneous hyperintense signal with the brain stem.

C, Proton-density image (2500/40/2) shows areas of increased signal within right and left parietal cortex (*arrows*).

D, Contrast-enhanced computed tomogram obtained shortly before death shows large areas of cortical edema with peripheral enhancement (*arrows*).

of the left and right superior parietooccipital convexities (Fig 2). Axial sections of the cerebellum and the brain stem revealed expansion of the basal pons by a soft, hemorrhagic, necrotic mass, which infiltrated the middle cerebellar peduncles and extended into the left cerebellopontine angle cistern and the fourth ventricle with obstruction of the aqueduct. Circumscribed, necrotic lesions were present within the left cingulate gyrus and the parietooccipital cortex bilaterally.

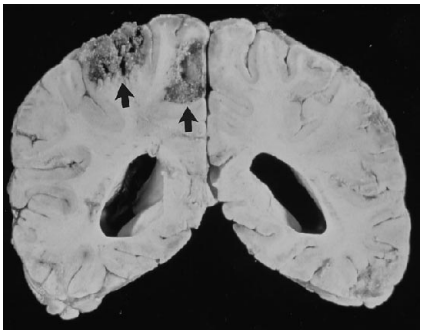

Fig 2. Coronal section of cerebral hemispheres showing necrotic lesions involving the right cerebral cortex (*arrow*).

Microscopic examination revealed extensive parenchymal necrosis, accompanied by numerous amebic cysts and trophozoites within and surrounding the larger vessel walls (Fig 3). Trophozoites were round to ovoid and averaged 23 μm in diameter, with a single eccentric nucleus, a prominent central nucleolus, and a perinucleolar halo. No erythrophagocytosis or cytoplasmic glycogen was identified. Cysts averaged 14 μm in diameter and possessed a refractile bilayered wall with periodic acid-Schiff–positive cytoplasm. Indirect immunofluorescence stains revealed immunoreactive Leptomyxida-related antigens in tissue cysts and trophozoites. No immunoreactivity was demonstrated, in contrast, in sections incubated with anti-*Acanthamoeba* sera.

Discussion

We report a case of amebic encephalitis secondary to infection with a leptomyxid ameba mimicking a brain stem glioma in a presumably

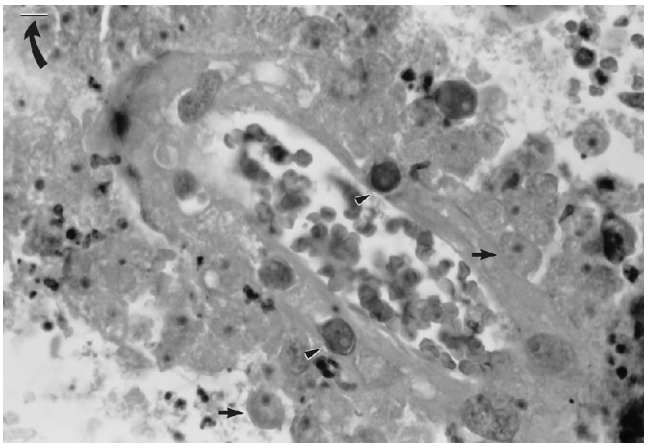

Fig 3. Periodic acid-Schiff stain, cysts (*arrowheads*) and trophozoites (*arrows*) of leptomyxid amebae in vascular walls and perivascular tissue of the brain stem. The *bar* in the upper left corner equals 10 μm.

immunocompetent child. Eight of 17 previously reported cases of encephalitis caused by this organism have also occurred in children who ranged in age from 4 months to 23 years (1, 4–6). Immunodeficiency has not clearly played a role in these pediatric cases, although an adult with acquired immunodeficiency syndrome and Leptomyxid amebiasis has been reported (7). A previous report from Texas by Matson et al (1) described an 11-year-old Hispanic girl with presumed neurocysticercosis who deteriorated after administration of antihelminthics and steroids.

Involvement of the cerebrum, the cerebellum, and the brain stem have been documented in patients with leptomyxid encephalitis at autopsy, and multifocal disease in common. In contrast to infection with *Naegleria* organisms, leptomyxid amebiasis often has a more indolent course, as seen in the case reported herein. However, with rare exception, central nervous system infection with free-living amebae is fatal, because consistently efficacious treatment has yet to be developed (5, 8).

Encephalitis caused by *Acanthamoeba* species has clinical and radiologic characteristics similar to those noted in leptomyxid encephalitis. Despite major biological differences, such as variable in vitro growth requirements, the similar light-microscopic appearance of the tissue stages of *Acanthamoeba* species and leptomyxid amebae precludes specific identification without the aid of immunocytologic studies. Immunofluorescence, immunoperoxidase, and modified indirect *Staphylococcus* protein A coagglutination have been successfully used to speciate members of the genus *Acanthamoeba* (9, 10) and, more recently, to identify Leptomyxid amebae (4). The isolation of specific agglutinating antibodies from a patient infected with *Acanthamoeba culbertsoni*, although in low titer, suggests that serologic studies may also be of use in diagnosis of some cases of amebic encephalitis (11).

The computed tomographic appearance of amebic encephalitis is described as low-density cortical lesions, which may have peripheral calcification and which demonstrate variable enhancement (1). There may be regional subcortical edema and hydrocephalus. In the early stages of encephalitis, computed tomography may be negative, whereas MR may show focal nonspecific increased T2 signal in the cerebral cortex (1). Pathologic changes include focal necrosis accompanied by a predominantly mononuclear inflammatory infiltrate, prominent vascular changes ranging from amebic invasion of the vessel wall to arteritis, fibrinoid necrosis, thrombosis, and an overlying exudative leptomeningitis (7, 12). The mild nature of the inflammatory infiltrate in the present case may have been caused by the antineoplastic treatments administered.

At presentation, the MR characteristics of the posterior fossa lesion were consistent with brain stem glioma. The MR appearance of brain stem glioma is variable. Pontine gliomas frequently have prolonged T1 and T2 relaxation times but may have areas of subacute hemorrhage and gadolinium enhancement (13). The differential diagnosis includes encephalitis and tuberculoma, but in view of the rarity of these diagnoses and the patient's clinical status, pathologic confirmation was not obtained. Although some centers recommend routine biopsy of brain stem tumors, the role of routine biopsy in patients with endophytic brain stem gliomas remains somewhat controversial, because of the inherent risks associated with brain stem biopsy and interpretive problems related to the small sizes of such biopsies (14). The MR study was atypical for the presumed diagnosis with respect to the parasagittal lesions, the significance of which was not appreciated until the patient presented with neurologic deterioration 3 weeks after the initiation of therapy, at which time there was extensive cortical and leptomeningeal disease. Although multifocal cerebral astrocytomas are known to occur, noncontiguous dis-

semination in association with a brain stem glioma is distinctly uncommon (15). Mantravadi et al analyzed the extent of tumors at autopsy in 25 patients with brain stem glioma and found that meningeal involvement was limited to the pia-arachnoid in the region of the tumor mass, and contiguous spread along the long tracts of the brain stem and midbrain was common, but noncontiguous spread into the cerebral hemispheres or remote leptomeninges did not occur.

This case highlights a known pitfall in MR diagnosis, that is, the inability to distinguish malignant tumors from inflammatory disease processes in the brain stem. Familiarity with the MR appearance of amebic encephalitis may result in a heightened level of suspicion for nonneoplastic disease potentially amenable to antimicrobial therapy, although treatment for this entity is currently unsatisfactory.

Acknowledgments

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References

1. Matson DO, Rouah E, Lee RT, Armstrong D, Parke JT, Baker CJ. *Acanthameba* meningoencephalitis masquerading as neurocysticercosis. *Pediatr Infect Dis J* 1988;7:121–124
2. Martinez AJ, Garcia CA, Halks-Miller M, Arce-Vela R. Granulomatous amebic encephalitis presenting as a cerebral mass lesion. *Acta Neuropathol (Berl)* 1980;51:85–91
3. Visvesvara GS, Martinez AJ, Schuster FL, et al. Leptomyxid ameba, a new agent of amebic meningoencephalitis in humans and animals. *J Clin Microbiol* 1990;28:2750–2756
4. Martinez AJ, Sotelo-Avila C, Garcia-Tamayo J, Moron JT, Willaert T, Stamm WP. Meningoencephalitis due to *Acanthamoeba* SP. *Acta Neuropathol (Berl)* 1977;37:183–191
5. Wessel HB, Hubbard J, Martinez AJ, Willaert E. Granulomatous amebic encephalitis (GAE) with prolonged clinical course: CT scan findings, diagnosis by brain biopsy, and effect of treatment. *Neurology* 1990;30:442–447
6. Popek EJ, Neafie RC. Case 4. Granulomatous meningoencephalitis due to Leptomyxid ameba. *Pediatr Pathol* 1992;12:871–881
7. Anzil AP, Rao C, Wrzolek MA, Visvesvara GS, Sher JH, Kozlowski PB. Amebic meningoencephalitis in a patient with AIDS caused by a newly recognized opportunistic pathogen: Leptomyxid ameba. *Arch Pathol Lab Med* 1991;115:21–25
8. Lowichik AL, Siegel JD. Parasitic infections of the central nervous system in children, I: congenital infections and meningoencephalitis. *J Child Neurol* (in press)
9. Willaert E, Stevens AR. Indirect immunofluorescent identification of *Acanthamoeba* causing meningoencephalitis. *Pathol Biol* 1976; 24:545–547
10. Culbertson CG, Harper K. Pathogenic free-living amebae: immunocytologic demonstration and species identification. *Am J Trop Med Hyg* 1984;33:851–856
11. Willaert E, Stevens AR, Healy GR. Retrospective identification of *Acanthamoeba clubertsoni* in a case of amoebic meningoencephalitis. *J Clin Pathol* 1978;31:717–720
12. Popek EJ, Neafie RC. Case 4: granulomatous meningoencephalitis due to Leptomyxid ameba. *Pediatr Pathol* 1992;12:871–881
13. Barkovich AJ. *Pediatric Neuroimaging,* 2nd ed. New York: Raven Press, 1995;321–437
14. Russell DS, Rubenstein LJ. *Pathology of Tumours of the Nervous System.* Baltimore: Williams & Wilkins, 1989;86:221–223
15. Mantravadi RVP, Phatak R, Bellur S, Liebner EJ, Haas R. Brain stem gliomas: an autopsy study of 25 cases. *Cancer* 1982;49: 1294–1296