Original Report

David D. Kidney[1]
Sara H. Kim

CNS Infections with Free-Living Amebas: Neuroimaging Findings

OBJECTIVE. The purpose of this report is to describe the clinical history, treatment, pathology, and imaging in two cases of rare CNS infection caused by free-living amebas. The *Naegleria fowleri* and *Acanthamoeba* species cause primary amebic meningoencephalitis and granulomatous amebic encephalitis, respectively. We describe the neuroimaging findings of a case involving a nonspecific cerebral edema pattern in primary amebic meningoencephalitis and a case involving focal enhancing lesions in granulomatous amebic encephalitis.

CONCLUSION. Primary amebic meningoencephalitis and granulomatous amebic encephalitis have a grave prognosis and, although rare, should be considered in the differential diagnosis for patients who present with appropriate histories and imaging findings, including nonspecific brain edema on CT in primary amebic meningoencephalitis and focal punctate enhancing lesions in the posterior cranial fossa on T1-weighted MR imaging in granulomatous amebic encephalitis.

Pathogenic free-living amoebas from the genera *Naegleria* and *Acanthamoeba* can cause CNS infections in humans. *Naegleria fowleri* causes primary amebic meningoencephalitis; several species of *Acanthamoeba* cause granulomatous amebic encephalitis [1–5]. These two disease entities have distinct epidemiologic patterns, clinical histories, pathologic features, and treatments. The imaging findings characteristic of both are described in this report.

Subjects and Methods

The neuroimaging studies (initial CT and MR imaging of the brain with two follow-up brain CT scans in the first patient and a single CT scan and MR image of the brain in the second patient) and medical records of two patients with free-living ameba infections were retrospectively reviewed. An autopsy was performed in one of the patients.

Results

Case 1

A 9-year-old boy presented with a 1-day history of frontal headaches, fever, nausea, and vomiting 1 week after visiting Mexico. The patient was initially alert, but he gradually became combative and had diminished pupillary response and eye deviation to the right. The patient had peripheral leukocytosis (15,400 WBC/mm^3 with left shift). CSF examination revealed a normal level of glucose (65 mg/dl), an elevated WBC (478 cells/mm^3 with 70% neutrophils), an elevated protein count (54 mg/dl), and gram-negative staining.

CT of the head at presentation showed no abnormalities. A contrast-enhanced MR image of the brain obtained the next day also showed no abnormalities. On the same day, the patient's right pupillary response fluctuated, and a repeat CSF examination showed further elevation of the WBC (1495 cells/mm^3). Treatment with cefotaxime and acyclovir was begun.

On hospital day 3, the patient could not follow commands or localize pain, and a second CT examination of the head showed acute onset of hydrocephalus, with compression of basal cisterns and evidence of nonspecific brain edema (Figs. 1A and 1B). Despite aggressive neurosurgical treatment with ventricular shunt placement and as-

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[1]Both authors: Department of Radiological Sciences, UCIMC, Rte. 140, 101 The City Dr., Orange, CA 92868-3298. Address correspondence to D. D. Kidney.

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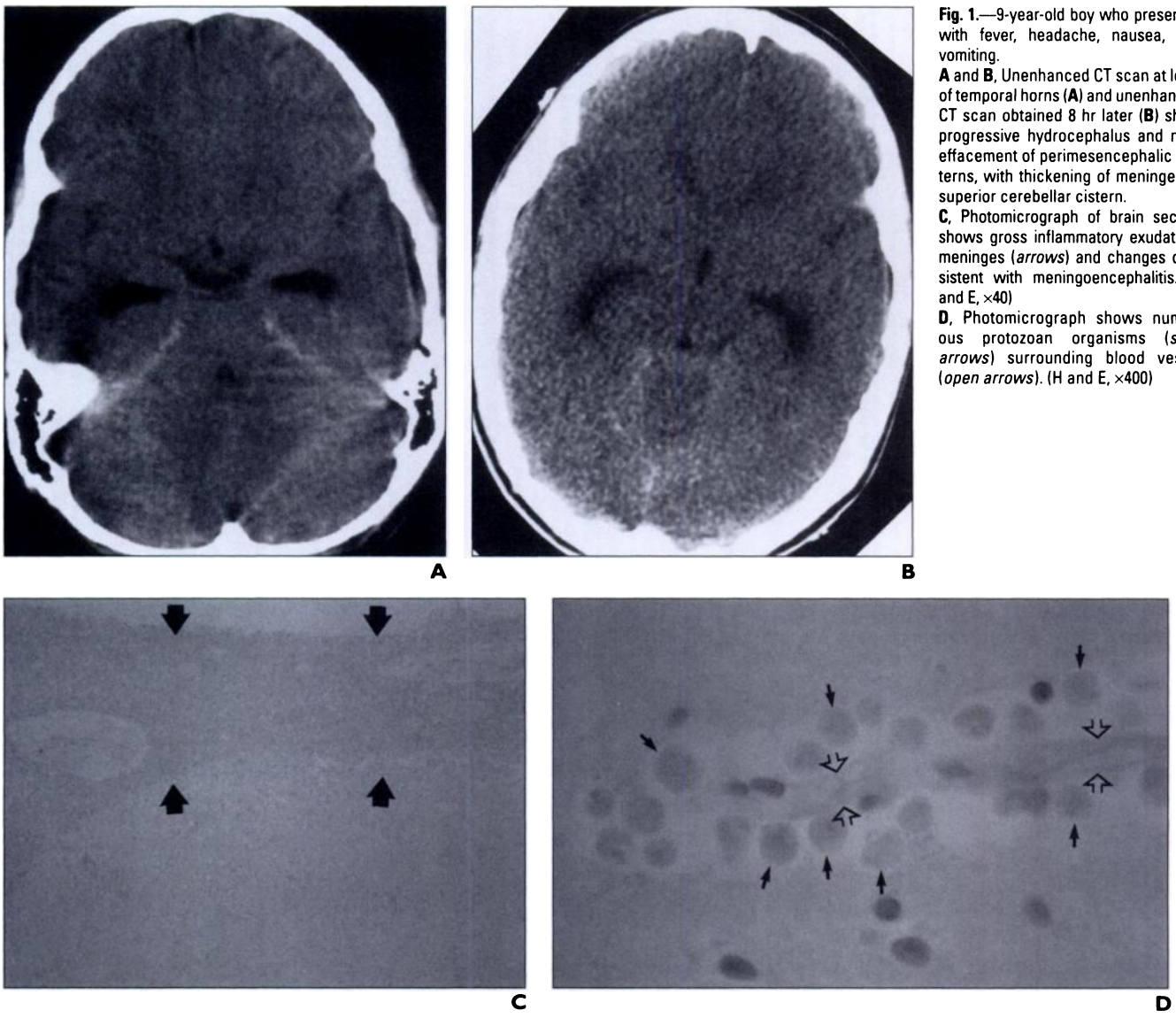

Fig. 1.—9-year-old boy who presented with fever, headache, nausea, and vomiting.
A and **B**, Unenhanced CT scan at level of temporal horns (**A**) and unenhanced CT scan obtained 8 hr later (**B**) show progressive hydrocephalus and near effacement of perimesencephalic cisterns, with thickening of meninges at superior cerebellar cistern.
C, Photomicrograph of brain section shows gross inflammatory exudate in meninges (*arrows*) and changes consistent with meningoencephalitis. (H and E, ×40)
D, Photomicrograph shows numerous protozoan organisms (*solid arrows*) surrounding blood vessel (*open arrows*). (H and E, ×400)

sisted hyperventilation, the patient died on hospital day 4.

At autopsy, the brain showed cerebral edema and mild uncal herniation. The base of the brain had a cloudy subarachnoid space with a tan–yellow exudate. On microscopy of H and E–stained sections, numerous protozoan organisms were seen within the meninges and perivascular areas at all levels of the gray matter of the cerebral cortex, brainstem, and cerebellum. These organisms were identified as *N. fowleri* trophozoites (Figs. 1C and 1D).

Case 2

A 43-year-old man with a medical history of schizophrenia and ulcerative colitis presented with a 2-week history of worsening difficulty in walking and complaints of nausea, vomiting, and headaches. On physical examination, the patient was alert and oriented and had no meningeal signs. Sensory function and cranial nerves I–XII were intact, but he had mild bilateral dysmetria. Examination of CSF revealed a normal level of glucose, an elevated protein count (209 mg/dl), and an elevated WBC (220 cells/mm^3 with 79% lymphocytes). An unstained wet preparation of CSF revealed amebic trophozoites with acanthopodia characteristic of *Acanthamoeba nigricans*. T1-weighted MR imaging of the brain performed after IV injection of gadolinium chelate contrast material showed multiple subtle punctate focal areas of contrast enhancement throughout the cerebellar hemispheres, with some scattered focal enhancement in the cerebral hemispheres and corpus callosum (Figs. 2A and 2B). These focal abnormalities were not visualized on a contemporary enhanced CT scan of the brain. Subsequently, the patient became unresponsive to verbal and tactile stimuli and went into a coma. Treatment with metronidazole and intrathecal amphotericin B brought about minimal neurologic improvement. At the time of transfer to a long-term care facility, the patient was only partially responsive to verbal commands and painful stimuli. The patient died 3 months after initial presentation.

Discussion

Primary Amebic Meningoencephalitis (Case 1)

N. fowleri is a free-living ameba that causes primary amebic meningoencephalitis, first described in 1965 [1]. Primary amebic meningoencephalitis typically has an acute onset with severe headache, anorexia, nausea, vomiting,

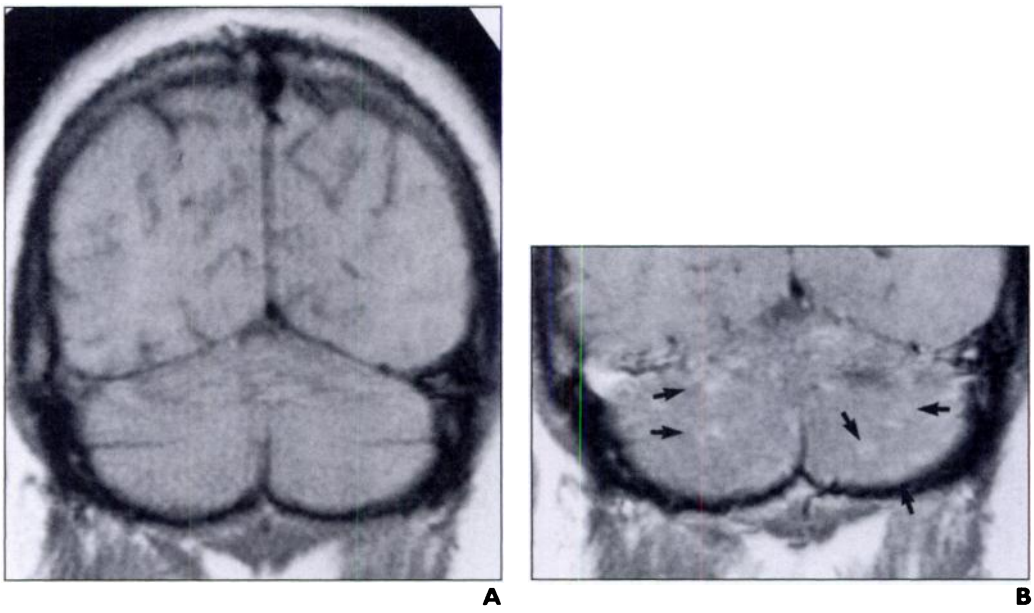

Fig. 2.—43-year-old man with 2-week history of nausea, vomiting, headache, and difficulty in walking. **A** and **B**, Unenhanced (**A**) and gadolinium-enhanced (**B**) coronal MR images (TR/TE, 750/16) show multiple subtle foci of enhancement bilaterally in cerebellar hemispheres (*arrows*, **B**).

fever (39–41°C), ataxia, diplopia, stiff neck, and coma with rapid progression to death. It affects healthy children and young adults who swim in a stagnant freshwater lake or swimming pool contaminated with the thermophilic organism or who inhale dust or soil containing amebic cysts. *N. fowleri* ascends directly along the olfactory tract to the brain [2, 6]. We postulate that our patient was infected while swimming in a freshwater lake in Mexico.

Pathologically, our case is typical of the described macroscopic appearance of primary amebic meningoencephalitis, with cerebral edema, uncal herniation, and a meningeal exudate. Microscopically, a purulent leptomeningeal exudate, hemorrhages, and necrosis can occur throughout the cerebral hemispheres, brainstem, cerebellum, and upper parts of the spinal cord [2]. In our case, the exudate was confined to the base of the brain, the caudal surface of the optic nerve, the pituitary infundibulum, and the upper segments of the spinal cord.

Primary amebic meningoencephalitis is diagnosed by obtaining a culture of free-living ameba from CSF or by observation of *N. fowleri* trophozoites in brain tissue from biopsy [2–4]. The drug of choice for treating primary amebic meningoencephalitis is amphotericin B, which is most effective when given early in the course of the illness. Without early treatment, the disease progresses to death within weeks despite administration of amphotericin B [6–8]. To date, to our knowledge, only three surviving patients have been reported [6, 7].

Brain CT findings in primary amebic meningoencephalitis have rarely been described and are typically nonspecific, with evidence of brain edema [9]. Our patient showed dramatic interval change, brain edema, obliteration of the basal cisterns, and acute hydrocephalus seen on CT; an enhanced MR image of the brain obtained just 17 hr earlier showed normal findings. Our imaging findings are similar to the earlier description of primary amebic meningoencephalitis and correlate well with the pathologic process of the disease. Furthermore, our case illustrates the acute and fulminant course of primary amebic meningoencephalitis, which to our knowledge has not been documented heretofore.

Granulomatous Amebic Encephalitis (Case 2)

The *Acanthamoeba* and *Leptomyxa* genera can cause a granulomatous amebic encephalitis. Granulomatous amebic encephalitis, caused by a species of *Acanthamoeba*, has a slow clinical onset with focal neurologic symptoms and a chronic prolonged clinical course [2, 8]. *Acanthamoeba* species are found in all types of environments: air, soil, tap water, chlorinated water in swimming pools, and even in dialysis units. Most recently, *Acanthamoeba* has been associated with an amebic keratitis from contaminated contact lens solutions [10]. Despite this organism's prevalence in the environment, relatively few infections occur because several host defense mechanisms exist [4].

Granulomatous amebic encephalitis typically occurs in patients who are debilitated, chronically ill, or immunocompromised (e.g., by AIDS, chemotherapy, or iatrogenic steroid therapy) [11, 12]. Our patient with granulomatous amebic encephalitis had a history of ulcerative colitis and previous treatment with steroids but was not clinically immunosuppressed at the time of presentation. *Acanthamoeba* spreads hematogenously from a primary lung, skin, or eye infection called acanthamoeba keratitis [10]. Our patient was not a contact lens wearer and did not have any skin lesions; we postulate that his inflamed bowel may have been the portal of entry.

Pathologically, the macroscopic appearance of granulomatous amebic encephalitis includes mild focal edema of the cerebral hemisphere. The posterior cranial fossa structures, diencephalon, thalamus, and brainstem are the sites of predilection. Trophozoites and cysts are found in the lesions, and chronic granulomatous reaction with multinucleated giant cells is characteristic. However, some patients who are severely immunologically suppressed may exhibit no granulomatous reaction [11].

Granulomatous amebic encephalitis is diagnosed by identifying *Acanthamoeba* trophozoites or cysts in the CSF or on brain biopsy. A culture of brain tissue or CSF can also reveal *Acanthamoeba* [1]. No proven effective treatment exists for granulomatous amebic encephalitis, and to our knowledge only three survivors have been reported [3]. In treating some *Acanthamoeba* species infections, ketoconazole and clotrimazole have been effective in vitro. Sulfadiazine has been used but is less effective [3].

The brain CT findings of granulomatous amebic encephalitis have been described as resembling space-occupying lesions [1]. One reported case had multifocal areas of signal in-

tensity abnormality in the left parietal and left occipital lobes on unenhanced MR imaging of the brain. Another case showed ringlike areas of contrast enhancement of discrete lesions in the parietal and occipital regions on gadolinium-enhanced MR imaging of the brain [12, 13]. In our case, gadolinium-enhanced T1-weighted MR images of the brain showed multiple punctate focal areas of enhancement bilaterally throughout the cerebellar hemispheres, with some scattered foci supratentorially. These lesions may represent focal cerebritis or microabscesses. Because of the patient's age and clinical course, vasculitis, infective processes, and multiple sclerosis comprised the initial differential diagnosis.

In conclusion, free-living amebas of the genera *Naegleria* and *Acanthamoeba* cause life-threatening CNS infections that differ from each other in history, clinical course, pathology, radiographic features, and treatment. On CT of the brain, primary amebic meningoencephalitis shows a nonspecific brain edema pattern, and MR imaging of granulomatous amebic encephalitis shows a multifocal process. It is important to be aware of these disease entities and their associated neuroimaging characteristics so that amebic encephalitis is considered in the differential diagnosis of a patient with a suggestive clinical history, atypical neurologic presentation, and similar radiographic findings.

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