Neurocysticercosis is caused by the larval stage of the tapeworm *Taenia solium* that inhabits the small bowel of an infected human host. Initial clinical manifestations of central nervous infection include seizures, focal neurologic deficits, and mental status changes.\(^1\) With cysticidal treatment, the natural history of the infection is accelerated.\(^2\) A successfully treated lesion rapidly progresses from an inert cyst with a live scolex to involution and calci®cation. During the process of cyst death the host mounts an in¯ammatory response to released larval proteins, accompanied by a cellular in¯ltrate and edema. Although seizures may persist after treat-ment, patients with calcified lesions are assumed to be cured of active disease.\(^2\)

We report a case of neurocysticercosis in which a patient who was assumed to be cured of active infection presented with sudden onset of headache, associated with in¯ammation and edema around lesions previously shown to be calcified.

A 37-year-old woman, originally from Ecuador and with a known history of neurocysticercosis, presented to the emergency department of The Toronto Hospital on January 7, 1997. The patient was well until early December 1996, when she developed a self-limited flue-like illness consisting of malaise, fever, and sore throat. Two weeks later, fever recurred along with erythema nodosum (her third recurrence since 1989) for which she was admitted to hospital for five days and treated with solumedrol and amoxicillin. One week after discharge from the hospital her headaches began. The headaches were frontal in location and occurred intermittently, associated with vomiting, slowed mentation, and episodic visual scintillations.

Her medical history revealed that in 1987 she had been diagnosed with neurocysticercosis when she presented with severe headaches and grand mal seizures. Her computed tomo-graphy (CT) scan had shown numerous active cystic lesions and hydrocephalus. The patient underwent ventriculoperitoneal (VP) shunt placement in 1988 and cysticidal treatment with albendazole in 1991. Subsequently, she remained relatively asymptomatic, receiving phenobarbital for seizure control. Over several years, on repeat imaging studies, numerous parenchymal lesions were noted to evolve from early cystic stages to involution and complete calcification. Although several calcified lesions continued to exhibit minimal circumferential contrast-enhancement visible only by magnetic resonance imaging (MRI), from a clinical perspective she was considered to be cured of any active disease in 1993 (four years prior to this presentation).

On examination, she appeared to be ill; she was drowsy but arousable and had normal results on a mental status ex-amination. There were no focal neurologic abnormalities. The results of a funduscopic examination were normal.

The patient was admitted and investigated for presumed VP shunt malfunction. Laboratory ®ndings revealed a he-moglobin level of 128 g/L and a normal white blood cell count and differential cell counts. Her electrolyte levels, re-nal function, and blood glucose level were also normal.

A CT scan of the brain, performed on the day of admission, showed numerous densely calcified lesions located bi-laterally in the cerebral parenchyma. Several of these lesions were surrounded by a hypodense area consistent with edema (Figure 1). In particular, edema was evident around two le-sions in the right frontal white matter, one in the wall of the left lateral ventricle, and one located superiorly in the right parietal lobe. None of these lesions had associated edema on a routine follow-up CT scan obtained three months earlier.

Three days after admission, unenhanced and enhanced MRI showed focal areas of hypointensity throughout the brain parenchyma on spin-echo T1- and T2-weighted images consistent with the densely calcified lesions seen on the CT. On T2-weighted spin-echo images, high signal intensity, consistent with increased extracellular water, surrounded all of the lesions exhibiting edema on the CT and was most marked around the lesion in the right frontal lobe (Figure 2A). The edema seen by MRI was not seen on a previous routine follow-up scan obtained three months earlier (Figure 2B). Several additional lesions exhibited edema not seen on the CT, including a lesion posterior to the occipital horn of the left lateral ventricle and a lesion in the right parietal white matter. Compared with the previous MRI three months earlier, contrast-enhanced T1-weighted images revealed ring-enhancement around many of the same lesions (Figure 3A), but the degree of enhancement was considerably greater (Figure 3B). In addition, all lesions that exhibited edema had been seen on the previous study to have persistent contrast-enhancement.

Although the patient’s clinical symptoms resolved spon-
FIGURE 1. Unenhanced computed tomography scan of the patient at presentation. There are numerous densely calcified lesions, located bilaterally in the cerebral parenchyma, as well as one less densely calcified lesion in the wall of the left lateral ventricle. There is edema around several of these lesions (black arrows). The edema is most marked around the lesion in the right frontal lobe and causes a slight degree of mass effect (white arrow).

Simultaneously within several days, she received a 28-day course of albendazole, cimetidine, and dexamethasone with subsequent resolution of her cerebral edema. No further symptoms have occurred since completion of therapy.

DISCUSSION

We report a unique case of reactivation of neurocysticercosis in a patient who presented with sudden onset headache associated with marked inflammation and edema surrounding numerous calcified parenchymal lesions. Based on their previous imaging characteristics of complete involution and calcification, these lesions had been assumed to be inactive as a result of previous cyst (larval) death. Therefore, the patient’s presentation represents a reactivation of neurocysticercosis.

According to the Escobar classification, the natural history of neurocysticercosis infection is thought to follow four identifiable stages. Initially, the lesion exists as an inert cystic structure with a scolex. With treatment-induced or spontaneous larval death, the cyst degenerates, releasing antigens and inciting an inflammatory response. Subsequently, the cyst fluid gradually disappears and the lesion involutes. At this stage the inflammation and edema associated with the degenerating lesion are markedly decreased. With time, the involuted lesion undergoes complete calcification or resorption. At this stage, the infection is no longer considered to be active.
Recent evidence suggests that mild inflammation may persist in the calcified stage in some cases, and may be associated with an increased risk for ongoing seizures.\(^6\) However, to our knowledge, recurrence of inflammation with edema at the site of long-standing calcified lesions has not been described previously. Our report raises the interesting possibility that parenchymal neurocysticercosis does not necessarily resolve after lesions becomes completely calcified. Our findings suggest that persistence of inflammation surrounding some lesions, visible only on contrast-enhanced MRI, may be predictive of a patient’s risk for reactivation. This hypothesis is supported by the fact that on the reactivation images, edema was only seen around lesions that had previously exhibited persistent contrast-enhancement.

There are several hypotheses that might explain this apparent relapse of disease. Cerebral edema may have resulted from the death of parasites that were viable and incompletely calcified. Alternatively, antigen release from several dead and involuted, calcified parasites might have produced cerebral edema. However, it is difficult to understand why numerous parasites would have died or released antigen simultaneously. A more plausible hypothesis is that a spontaneous increase in immunity, possibly triggered by the release of antigen from a live or dying parasite, led to an intense immune response to antigen at the site of a calcified lesion. Alternatively, another unrelated event, the immunologic reaction causing her erythema nodosum, might have led to a generalized enhancement of cellular immunity, which in turn was directed against cysticercal antigen associated with several dead calcified lesions. This upgrading of immunity would be analogous to the treatment-induced or spontaneous enhancement of cell-mediated immunity associated with the reversal reaction of leprosy,\(^7,8\) the lymphadenitis of Mycobacterium tuberculosis,\(^9\) and in patients infected with human immunodeficiency virus, the lymphadenitis due to M. avium complex (Kaplan MH, unpublished data) and ocular lesions of cytomegalovirus (Torriani F, unpublished data). This phenomenon might help to explain why several calcified lesions might simultaneously develop a surrounding inflammatory response associated with edema.

Regardless of the explanation, clinicians and radiologists must now be made aware of the fact that patients with calcified lesions assumed to be resolved may present with late-onset symptoms associated with marked inflammation and
edema around these lesions. In retrospect, re-treatment with an anthelmintic was probably unnecessary in this case, whereas corticosteroid therapy should have sufficed.

Addendum: Since the completion of this report, we have come across a paper by Del Brutto in which he makes reference to five patients whose CT scans showed an area of brain swelling surrounding previously inactive calcifications. He postulates that the edema could be directly related to a breakdown in the blood-brain barrier around the epileptogenic focus.

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