TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, VOL. 75, NO. 6, 1981

Cysticercus racemosus in an eosinophilic phlegmon in the brain

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Summary

Cysticercus racemosus in a tumour-like mass from the brain of a 30-year-old Canadian was identified by histological and specific immunofluorescent techniques. The patient possibly acquired the infection during her stay in India. She had a mild peripheral eosinophilia and complained of pounding headaches and convulsions. Examination of tissue sections revealed the larva enclosed in an eosinophilic phlegmon and the surrounding brain tissue infiltrated by histiocytes and eosinophils. Loss of microtriches and degenerative changes in the larva were apparent in areas with adherent eosinophils. With the appropriate reagents, both intracellular and interstitial specific immune complexes were detected in the biopsied tissue. The course of infection in the cystic and racemosus types of cysticercosis and the role of tissue eosinophilia in neurocysticercosis have been discussed.

Introduction

Endemic *Taenia solium* and *T. saginata* infections are unknown in Canada but two cases of neurocysticercosis in naturalized Canadians have been reported (OWEN & LENCZNER, 1956; ALI-KHAN *et al.*, 1979). The prospective diagnosis was based on (a) the demonstration of partially calcified encysted cysticerci in the subcutaneous tissue, (b) neurological symptoms without any family history of convulsion and epilepsy and (c) characteristic shadow by a computerized tomogram scanning of cerebral lesions.

The present report describes a case of neurocysticercosis and briefly reviews the complexity of the problems in the clinical and laboratory diagnosis of cerebral cysticercosis. To our knowledge this is the first report of racemosus cysticercosis from Canada. The histological features and clinical characteristics of racemosus cysticercosis are compared with the typical cystic form.

Materials and Methods

Five slides which contained nine tissue sections were submitted to the Institute of Parasitology and subsequently forwarded to us for further investigations. One slide was stained with haematoxylin-phloxine-saffron (HPS) and the others contained unstained paraffin sections.

Immunofluorescent staining: Two pieces (6 mm each) of formalin-fixed sparganum larva (ALI-KHAN *et al.*, 1973) were embedded in paraffin and sectioned at 4 μm. These and the brain sections of the patient were dewaxed and stained by the indirect fluorescent technique with varying dilutions of anticysticercus serum (ALI-KHAN *et al.*, 1979) and fluorescein-conjugated goat anti-human immunoglobulins (FGAHIg) with an F : P ratio of 2·7 (Behring Diagnostics, Montreal, Canada). The adsorption of the FGAHIg conjugate and method of staining have been described previously (SIBOO *et al.*, 1977; ALI-KHAN & SIBOO, 1981). The controls consisted of brain sections of the patient stained (i) with normal serum and FGAHIg conjugate, (ii) with FGAHIg conjugate only and

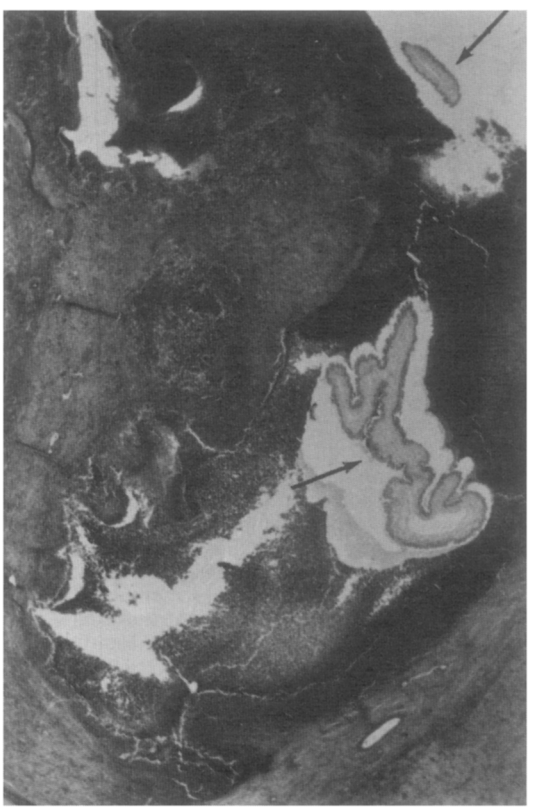

Fig. 1. Section of tumour-like mass in the brain parenchyma showing two longitudinal sections (arrows) of *Cysticercus racemosus* larva. HPS × 10.

(iii) with fluorescein-conjugated rabbit anti-goat IgG (FRAGIgG) only. As "normal controls" brain sections from two persons who had died of non-parasitic infections were stained either with anti-cysticercus serum (1 : 20) and FGAHIg conjugate or with FGAHIg conjugate only.

History and Clinical Observations

A 30-year-old Canadian woman was admitted to Hôpital du Sacre-Coeur, Montreal, in December 1979. Before admission the patient had two episodes of generalized convulsions. She complained of pounding headaches, nausea and vomiting. Her physical examination was normal; no sensory or motor deficiency was noted by the neurosurgeon. The patient had been a vegetarian for the last four years. She spent 13 months in India and had several bouts of diarrhoea which were treated with antibiotics. She denied ever having any parasitic infections.

On 22nd December, 1979, the patient underwent surgery. The right cerebral hemisphere was found oedematous. A firm tumour-like mass approximately 2 cm in diameter, in the brain parenchyma and extending to the duramater was removed for histological examinations. The patient was discharged three weeks after surgery.

Neurological Examination

The echo-encephalogram showed a midline shift of 6 mm to the left. Skull X-ray revealed a 6 mm pineal shift. Brain scan indicated under perfusion of the right hemisphere and inferior displacement of the left middle cerebral artery; increased uptake

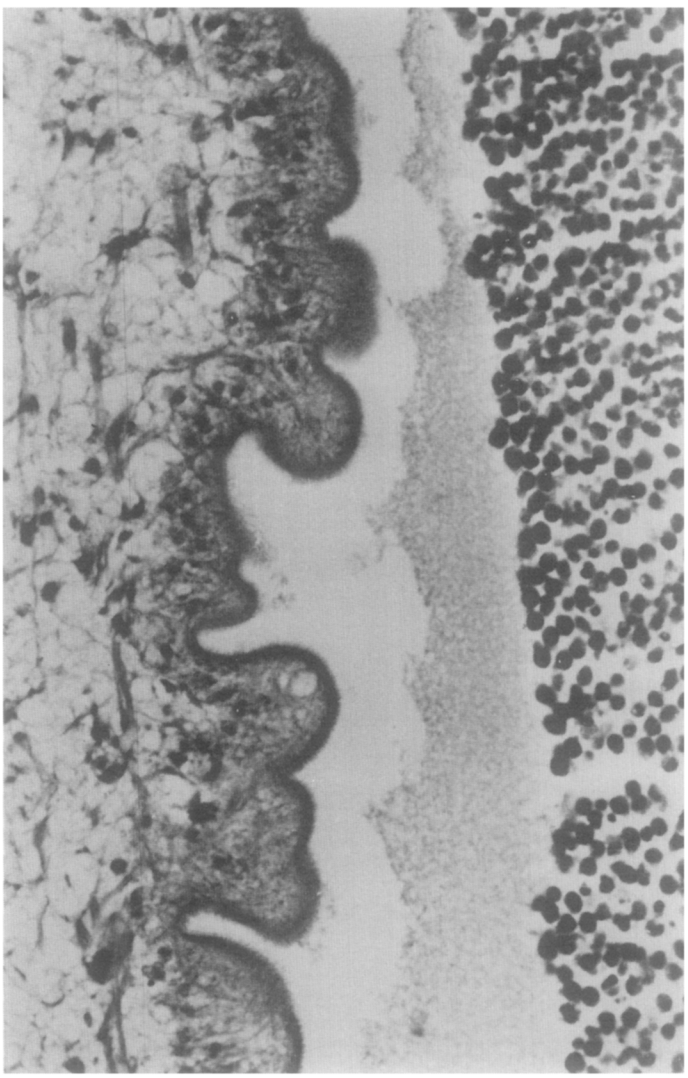

Fig. 2. Enlarged view of the convoluted body surface of the larva showing microtriches, distal cytoplasmic layer, subepidermal cells and mesenchymal tissue; note mainly eosinophils opposite to the larva. H.P.S. × 250.

in the right frontoparietal area was suggestive of a tumour. Carotid angiography confirmed an infiltrating right parietal tumour.

Laboratory Investigations

The urinalysis, electroencephalogram, haemogram and blood chemistry were normal. The differential blood count showed mild peripheral eosinophilia (3-5%). Three stool examinations were negative for parasites.

Observations

The worm: Two pieces of the worm were present in the abscess (Fig. 1). The large piece was branched and measured 2·5 mm + 0·2 to 0·4 mm. The tegument of the worm was crested irregularly and the crests were spaced roughly 9 μm apart (Fig. 2). The clefts were either shallow or deep (27 to 54 μm). The distal cytoplasm was 2 μm in thickness and was covered uniformly by microtriches 2 μm long (Figs. 2 and 3). Scolex and bladder wall were not seen in any sections of the worm. Eosinophils and granular eosinophilic concretions were trapped in the narrow spaces between the crests (Fig. 3). In these areas, the microtriches were either absent or appeared disrupted and the outline of the plasma membrane was fuzzy or mildly crenated. A few eosinophils were present in the parenchyma and among subepidermal cells which were either round or elongated and arranged mostly in single file. The calcareous corpuscles and longitudinal muscle fibres were rare in the parenchyma which was vacuolated and criss-crossed by tubules.

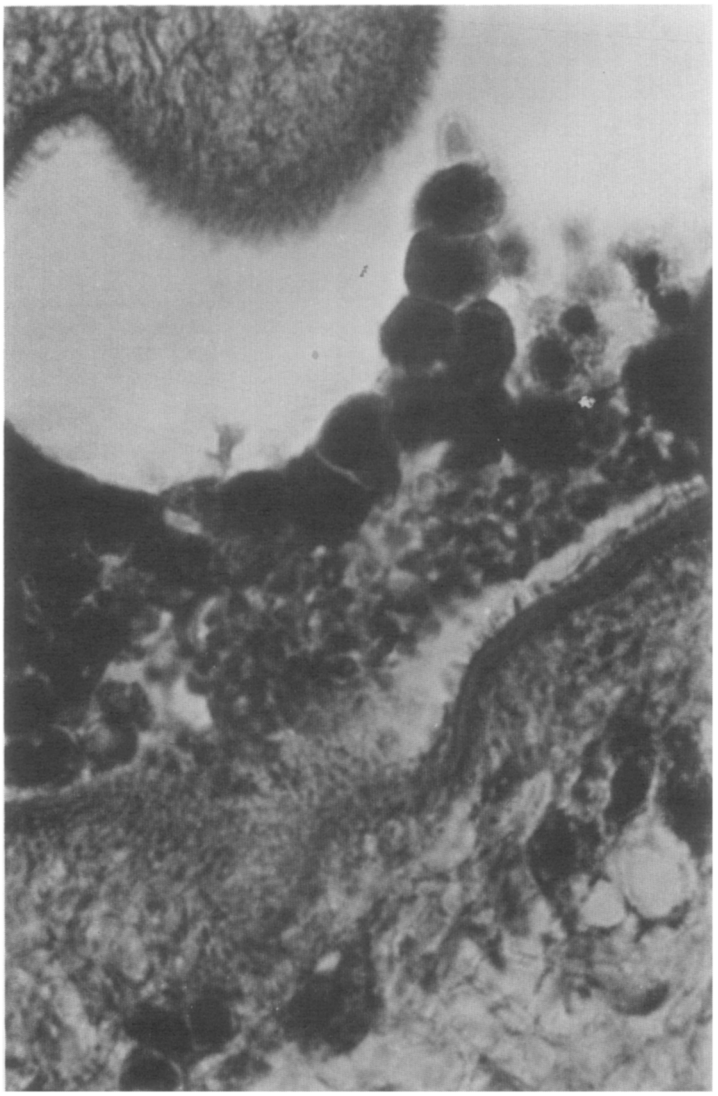

Fig. 3. Section showing degenerative changes in the distal cytoplasmic layer and microtriches adjacent to the eosinophils and eosinophilic granules. H & E ×1000.

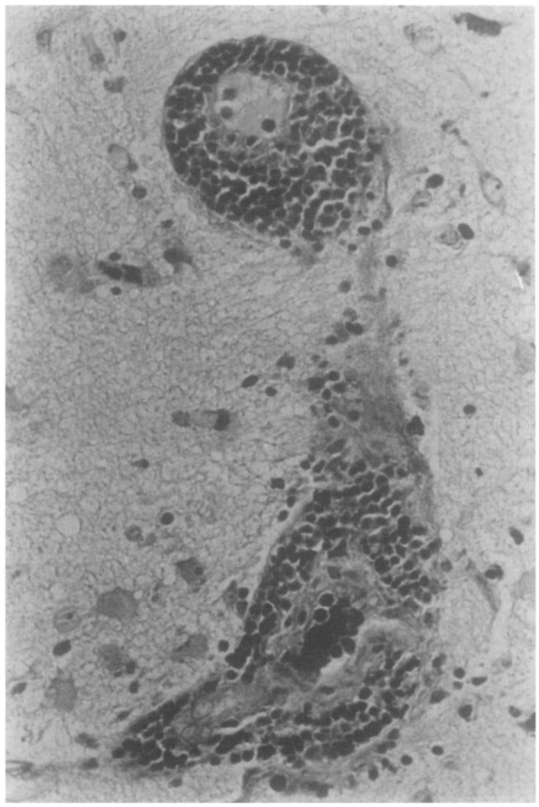

Fig. 4. Virchow-Robin spaces and brain parenchyma infiltrated by histiocytes and eosinophils. Giemsa × 250.

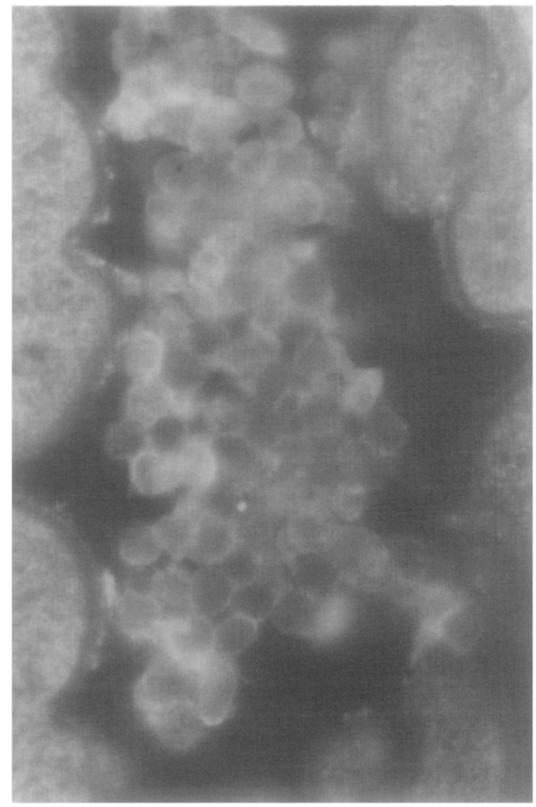

Fig. 5. Brain tissue treated with human anti-cysticercus serum and stained with fluorescein conjugated goat anti-human Igs; note fluorescence of the subepidermal cells and the parenchyma of the cysticercus. Membrane and intracellular fluorescence is also observed in approximately one of four inflammatory cells (see text for detail). × 650.

Tissue Pathology: The larva was contained in a fibrinous eosinophilic phlegmon which was surrounded by granulation tissue (Fig. 1). Approximately one half of the eosinophils in the phlegmon was partially degranulated; histiocytes and neutrophils were rare. The granulation tissue forming the wall of the abscess had a narrow inner zone of fibrohistiocytes which was infiltrated densely by eosinophils and plasma cells. The outer zone of fibrotic tissue merged with the cerebral parenchyma and had at least five necrotic foci filled with exudates. The cerebral parenchyma adjacent to the abscess was infiltrated by eosinophils, had an increased number of glial cells and the expanded Virchow-Robin space contained lymphocytes, eosinophils and foamy histiocytes (Fig. 4).

Immunofluorescent studies: The anti-cysticercus serum did not specifically stain the sparganum sections above a dilution of 1 : 20 but it did specifically stain (4+) the cysticercus larva at a dilution of 1 : 80. Specific fluorescence was detected only in the subepidermal cells, parenchyma (Fig. 5) and the epithelial lining of the excretory tubules of the cysticercus. All the controls were negative.

The brain sections from the patient when treated with FGAHIg only stained some of the inflammatory cells present in the fibrohistiocytic stroma, astrocytes and the enlarged endothelial cells of blood capillaries in the cerebral parenchyma and approximately one of every four inflammatory cells in the phlegmon. This conjugate, however, did not stain the cysticercus larva. This indicated that the inflammatory cells contained immune complexes which bound the FGAHIg conjugate as shown in Fig. 5. The specificity of the fluorescence was confirmed by treating the patient's brain sections with FRAGIgG conjugate and "normal" brain sections with anti-cysticercus serum and FGAHIg conjugate; the results were negative in both cases.

Discussion

In patients with frequent episodes of headache, vomiting and signs of neurological disorders the presence of cysticerci in the extraneural tissues may suggest cerebral involvement (ASENJO, 1961; BICKERSTAFF *et al.*, 1952, 1956; ALI-KHAN *et al.*, 1979). However, LEPE & CASTRO (1961) and ARRIAGADA *et al.* (1961) found that neither radiological examinations nor any specific clinical symptoms are pathognomic for cerebral cysticercosis. Similarly, eosinophilia is also an incon-

sistent finding (ARRIAGADA *et al.*, 1961; BICKERSTAFF *et al.*, 1952). In the present case no cysticerci were detected in the skeletal tissues and since the patient had lived most of her life in Canada except for a brief visit to India where the infection might have been acquired (DIXON & LIPSCOMB, 1961; BICKERSTAFF *et al.*, 1952), cerebral cysticercosis was not included in the differential diagnosis.

In the light of the morphological and immunological evidence, it can be stated with certainty that the pieces of worm present in the abscess are portions of *Cysticercus racemosus* and not sparganum. *Sparganum*, probably *S. proliferum*, also is reported to cause cerebral lesions (TASHIRO, 1924). However, it differs histologically (BRATEN, 1968) but shares some common antigens with cysticercus (MUELLER & COULSTON, 1941). Except for a marked eosinophiloencephalopathy and the absence of obliterative endarteritis, the histological findings of the worm and brain lesions were similar to reports by other investigators (BICKERSTAFF *et al.*, 1952; BIAGI *et al.*, 1961; MARTINEZ, 1961).

The cystic and racemosus cysticerci in humans differ from each other in form, behaviour and clinical course. The differentiation of the oncosphere into the cystic form or the multilobulated racemosus form, is determined by the compactness of the surrounding host tissue. The cystic form is small in size, relatively short lived, invariably encapsulated and is detected on X-ray or at autopsy. They may cause epileptic episodes as a result of space-occupying lesions in the brain. On the other hand oncospheres localized in the cerebrospinal pathways develop into a multibranched long-lived racemosus form (BICKERSTAFF *et al.*, 1952, 1956). Although histologically similar to the cystic type, the racemosus larva is thin-walled and lacks a scolex. The absence of delimiting host tissues around the developing oncosphere favours branching and contributes to the expanding brain lesion which may culminate in obstructive or necrotic types of cerebral cysticercosis.

Of considerable significance, however, is the eosinophilic phlegmon and immune complex present in the brain lesion of this patient. These events might have occurred due to a sudden release of antigen from the damaged cysticercus as reported in hydatidosis (KERN *et al.*, 1979) and cysticercosis (BICKERSTAFF *et al.*, 1952).

In conclusion, it is interesting to speculate that the severity of eosinophilia and damage to the surrounding tissue may be linked to the integrity of *Cysticercus* in the brain tissue. Arginine-rich major basic protein released by activated eosinophils is believed to damage non-specifically both metazoan parasites and mammalian cells (BUTTERWORTH *et al.*, 1979). The comments of BICKERSTAFF *et al.* (1956) regarding his cases of cerebral cysticercosis appear to be quite pertinent, "In none of these cases was there a marked eosinophilia until after surgical exploration". Two of five of his patients showed over 1000 eosinophils per mm^3 in blood and CSF after surgery and died 10 days to three weeks later. The release of antigen during surgical removal of the larvae was considered to be the cause of eosinophilia.

Acknowledgements

We wish to thank Dr. J. Knaack, Department of Pathology, McGill University, for providing us with the human brain sections used in this study as normal controls in immunofluorescence studies. This investigation was supported by a grant (MA-7023) from the Medical Research Council of Canada. Research at the Institute of Parasitology is supported by the Natural Sciences and Engineering Research Council of Canada and the Formation des Chercheurs et d'Action Concertée du Ministère de l'Education du Quebec.

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Accepted for publication 10th February, 1981.