Disseminated human neurocysticercosis
A morphologic analysis of two cases

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Summary. This study was based on two cases of disseminated human neurocysticercosis from India. The material available was examined grossly, and by light microscopy, histochemistry, immunomorphology and electron microscopy. The results showed that the parasites commonly embolized to the anatomically discernable gray-white matter junction of the brain and were located in cavities, the walls of which were dilated vascular channels. The parasite-nutrition process was through endocytosis and microtrichal activity. To camouflage themselves from the host-defense mechanisms, the parasites apparently covered themselves with host-tissue-like material. Host reactivity to the parasite was heralded morphologically by the physical anchoring of the parasite by activated endothelial cells, loss of the host-tissue-like cover and an acute polymorphonuclear leucocytic response.

Key words: Neurocysticercosis — Pathogenesis — Histochemistry — Immunohistochemistry — Electron microscopy

Cysticercus cellulosae are the larval forms of the tape worm, Taenia solium. While the adult tape worms are found in the small intestine of Man, the definitive host, the larval forms are found in the skeletal muscle of the intermediate host, the pig [1—6]. To develop cysticercosis, man has to replace the pig in the Taenia solium life cycle and the eggs must mature within the human small intestine as they do in the pig's. Entry of the eggs into the human small intestine may occur to two ways: by autoinfection or by ingestion or inhalation of egg-contaminated food or water [4, 7].

Mahmood and Thomas [7], on parallel studies performed on human and pig skeletal muscle Cysticerci, found that Cysticerci occurring in pigs killed in abattoirs showed no pericysticercal host-tissue inflammatory changes. On the other hand, all human tissues removed at biopsy showed Cysticerci measuring 0.5—0.8 cm with an outer focal macrophagic granulomatous inflammation. An intense acute inflammatory response could be detected in the immediate vicinity of some Cysticerci.

The inflammatory responses could be graded [7] and related to parasitic viability. Such viability was gauged morphologically using two criteria: intraparasitic vacuoles containing histochemically demonstrable neutral fat, glycogen, calcium and carbonate; and the external parasitic bilaminate structure status. With increases in the inflammatory response, the parasite vacuole count gradually decreased with fragmentation and, finally, total dissolution of this structure [7]. As these criteria of loss of viability increased, an acute inflammatory response, possibly of an allergic hypersensitivity Type 1 reaction, set in [11]. Mahmood and Thomas [7] surmised that in some way the parasite was able to prevent the host from recognizing it as being “foreign”, thereby allowing growth in a relatively unpimped manner. The morphological evidence of parasite death is related to the acute inflammation and the clinical symptom of a “painful lump”, that brought the patient to the operating surgeon [7]. These results [7] stimulated certain questions: how could a tape worm embryo of about 20 μm grow and mature into a Cysticercus measuring 0.7—0.8 cm (7000—8000 μm) without being recognized as “foreign” to the human organism? How did the Cysticercus behave in an environment like the brain, believed to be normally immunologically non-reactive?

The purpose of this present study has been, therefore, to examine disseminated human intracerebral neurocysticercosis grossly, histochemically, immunohistomorphologically and ultrastructurally.
Material and methods

The brain tissue for this study was obtained from two 45-year-old Indian males. The first patient was diagnosed at autopsy and the second at surgical intervention.

Case 1

This patient was admitted to the psychiatric ward with altered behaviour, principally irrelevant talking and emotional disturbances. He also had a history of vomiting, headache and progressive deafness of 3-month duration. Physical examination showed no deficits but the patient, although well oriented, continued to talk irrelevantly. The clinical impression was of depression or occult malignancy. On the 6th day after admission the patient suddenly became deeply unconscious and all limbs were flaccid. He died the same day.

At autopsy all systems appeared normal except the brain. This organ weighed 1400 g and showed evidence of raised intracranial tension. Many cysts measuring between 0.7–0.8 cm were situated throughout the brain and were notably at the gray-white matter junction. All cysts showed a demonstrable “white spot”.

Case 2

This male reported to Neurosurgery with symptoms and signs of raised intracranial tension suggesting a neoplastic process. At operation, many cysts measuring between 0.7–0.8 cm were visible, impinging themselves on the meninges. One such cyst was biopsied and showed a “white spot”.

Methods

All relevant available material was fixed using either buffered 4% formaldehyde or 3% glutaraldehyde depending on whether further processing was for paraffin sectioning or electron microscopy. Special care was taken to avoid artefactual distortion as far as possible.

The following routine stains were performed on paraffin sections using standard techniques: hematoxylin-eosin; periodic-acid Schiff (PAS) reaction for glycogen and neutral mucosubstances; Klüver-Barrera for myelin and Nissl substance; Elastic van Gieson for elastic tissue and collagen; Masson-Goldner stain for collagen; reticulin stain for reticulin fibres; and von Kossa stain for calcium carbonate. Frozen sections were stained by Sudan IV for neutral fat. Immunocytochemical reactions were carried out using a triple layer (polyclonal antisera) or a four-step (monoclonal antibodies) peroxidase-antiperoxidase (PAP) technique according to Sternberger et al. [10] on 5-μm paraffin sections of routinely processed autopsy material. The following primary antibodies were used: rabbit antisera against glial fibrillary acidic protein (GFAP; 1:200), against lysozymes (1:100) and against immunoglobulins G, M and A (Ortho, Neckargemünd, FRG; undiluted) as well as monoclonal antibodies against vimentin (clone V9; Dako, Hamburg, FRG; 1:50), GFAP (clone GF-2; Dako, Hamburg, FRG; 1:100), muscle specific actin (clone HHF35; Euro Biochem, New York; 1:1000), myelin basic protein (Camon, Wiesbaden, FRG; 1:400), common leucocyte antigen (CLA, clone T200; Camon, Wiesbaden, FRG; undiluted), B lymphocytes (clone L26; Dako, Hamburg, FRG; 1:200) and T lymphocytes (UCHL1; Dako, Hamburg, FRG; 1:100).

Rabbit anti-mouse (Dianova, Hamburg, FRG; 1:50) and swine anti-rabbit (Dako, Hamburg, FRG; 1:20) antisera as well as the PAP complex (Dako, Hamburg, FRG; 1:100) were used as further antibodies. Amino ethylcarbazole was employed as enzyme substrate. All antibodies were incubated for 30 min in a moist chamber. Negative controls were made by omitting the first antibody.

Tissue blocks for electron microscopy were post-fixed in 1% osmium tetroxide in pH 7.3 phosphate buffer, dehydrated in ethanol and propylene oxide and embedded in Araldite. Thin sections were made from blocks after study of stained thick sections. They were stained with uranyl acetate and lead citrate and examined with the Zeiss EM-9-S-2 electron microscope at an accelerating voltage of 60 kV.

Results

Gross characteristics

All relevant material available from these two cases was examined and measured with the aid of a dissection microscope. In general, intracerebral Cysticerci occurred at the junction between the gray and white matter and tended to project more into the gray matter than into the white matter. The cysts measured between 0.7–0.8 cm in diameter and had a semitransparent membrane through which the parasite content could be viewed. The only solid structure visible was the “white spot” which appeared to float in a clear, watery fluid. The transparent membrane sometimes had a focal thin deposit of white, cheesy material on its external host aspect and the parasite could be dislodged as a whole from its cavity with ease. The brain tissue forming the cavity was smooth and showed no irregularity (Fig. 1a, b).

Light microscope appearances

Several parasites were examined in situ with surrounding brain tissue using the hematoxylin-eosin stain. All parasites satisfied the morphological criteria used by Mahmood and Thomas [7] to identify them as being Cysticercus cellulosae. These criteria included a well-formed head or scolex with suckers and a refractile rostellum of hooklets (Fig. 1c), intracorporal vacuoles and a thick peripherally located undulating eosinophilic ribbon-like zone on which fine hair-like processes could be discerned.

All parasites examined lay free within tissue cavities or “cysts”, with only a few showing the external bilaminar surface with hair-like processes to come into contact with the host cyst wall. While most parasites showed the head to be invaginated within itself, some had exvaginated heads.

The cavity occupied by the parasite was always round and its inner aspect usually smooth. This inner surface was lined by compressed spindle-shaped cells resembling endothelial cells, more peripheral to which the walls of the cavities varied in thickness and were pink and hyaline. Only an occasional identifiable ves-