Cerebral Cysticercosis as a Common Cause of Epilepsy in Gurkhas in Hong Kong

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ABSTRACT: A prospective study of Nepalese adults (Gurkhas) based in Hong Kong who presented with adult-onset epileptiform seizures determined that cerebral cysticercosis was causative in 7 out of 8 cases. The relative roles of specific cysticercal serology and computerised axial tomography in diagnosis are discussed. Serum IgE levels were found to be raised in all patients with cerebral cysticercosis in the absence of other parasitic infection and reverted to normal after the patients were treated with praziquantel. Evidence suggests that the Gurkhas acquired their cysticercal infections in Nepal.

Introduction

Cerebral cysticercosis was considered a possible cause of adult onset epileptiform seizures in Nepalese soldiers and their wives (Gurkhas) in Hong Kong. The case notes of sixteen adult Gurkhas referred to the British Military Hospital, Hong Kong with fits of recent onset in the years 1981 to 1986 were traced. It is possible that not all cases were identified. During this period six patients were thought to have had cerebral cysticercosis on the basis of computerised axial tomographic (CT) scanning and exclusion of other causes. A prospective study was therefore undertaken to determine the importance of cysticercosis as a cause of adult-onset seizures in Gurkhas in Hong Kong.

Patients and Methods

From January 1987 all Gurkha patients presenting with epileptiform seizures with no previous history of fits were investigated as in-patients at the British Military Hospital, Hong Kong. The following investigations were performed: a full blood count, white blood cell differential and erythrocyte sedimentation rate, urea and electrolytes, liver function tests, fasting calcium, glucose and IgE levels. Three separate stool samples were examined by a concentration-flotation method for evidence of bowel infestation with *Taenia solium* or other parasites. Each patient had a chest x-ray, skull x-ray and x-rays of the limb girdles looking for evidence of calcified soft-tissue cysticerci. An electroencephalogram (EEG) was performed after the immediate post-ictal period.

All patients had a cerebral CT scan within one week of presentation using a GE 8800 scanner with 10mm contiguous cuts from base to vertex, both non-enhanced and enhanced with 60 mls of urografin 60%. Those with CT appearances suggestive of cerebral cysticercosis were subjected to lumbar puncture and their cerebrospinal fluid (CSF) examined for cells and the CSF protein and glucose concentrations measured.

Serum and CSF samples collected from patients were tested for the presence of antibodies against *Cysticercus cellulosae* by an indirect enzyme-linked immunosorbent assay (ELISA) for IgG antibodies using homogenised

whole cysts of *C. cellulosae* collected from muscle of infected pigs as antigen and by an indirect fluorescent antibody test (IFAT). For each test reference positive and negative controls were included.

Those patients diagnosed as having cerebral cysticercosis were treated with praziquantel 50 mg per Kg daily in three divided doses for fifteen days. Dexamethasone 2 mg three times daily was started two days prior to praziquantel treatment, the dosage being tapered off during therapy, to suppress possible exacerbation of symptoms associated with treatment. A cerebral CT scan, EEG, IgE levels and cysticercal serology were repeated two months after completion of treatment.

Results

Eight Gurkha adults with recent onset epileptiform seizures presented in an eighteen month period. Seven had abnormal CT brain scans with a ring-enhancing lesion and adjacent oedema characteristic of cerebral cysticercosis (Figs 1 & 2).

On physical examination no patients were found to have evidence of subcutaneous cysticercal cysts. All patients had normal haematology, a normal white cell count and differential and erythrocyte sedimentation rate. Liver function tests and fasting calcium and glucose levels were all normal. Stool examination for evidence of intestinal parasites was negative in all patients. There was no radiological evidence of intracranial or soft tissue calcified cysticerci. No cells were found in any CSF samples and CSF levels of glucose and protein were normal.

An initial EEG was reported as abnormal in only three of the seven patients with cerebral cysticercosis. One showed a very active discharging focus in the right frontal lobe and two demonstrated reduced alpha activity and some general increase in theta activity but no evidence of epileptiform activity. Electroencephalograms recorded two months after treatment were normal in all seven patients.

Immunoglobulin E levels were raised in all 7 patients with cerebral cysticercosis being greater than 800 Ku/

Fig. 1. The unenhanced CT scan shows an area of oedema (white arrows) in the right frontal region.

Fig. 2. After contrast enhancement a 6mm ring lesion (black arrow) is shown in the cortex.

in six. Two months post treatment serum IgE levels had fallen to below 400 Ku/L in all cases. Pre and post treatment ELISA and IFAT serology was negative on all patients excepting one. In this patient the pre-treatment ELISA was positive on serum and CSF and the IFAT positive 1:20 on serum. Two months after treatment both ELISA and IFAT were negative.

A CT scan repeated two months after treatment showed that the perifocal oedema had resolved completely in all 7 patients. Four patients had entirely normal scans whilst in 3 patients the ring-enhancing lesion was considerably smaller and in 2 of these patients early calcification of the lesion was visible on the unenhanced scan.

To date all 7 patients have remained well, free of seizures and have not required anticonvulsant drug therapy.

Discussion

The clinical manifestations of cerebral cysticercosis are varied depending on the number of larvae, their location and the host response(2). Clinical manifestations include fits, focal deficits, increased intracranial pressure secondary to communicating and noncommunicating hydrocephalus and meningitis(3). Focal Jacksonian or generalised seizures occur in up to 92% of patients(4).

Computerised tomographic scanning is useful in the diagnosis of cerebral cysticercosis and several patterns have been described(5). Parenchymal lesions are most commonly found(6,7,8). Small [2–6 mm] round or oval calcifications represent dead calcified cysticerci(7). The number of calcifications and distribution in the brain is variable. Calcified lesions show no perifocal oedema and in post-contrast studies, no enhancement(8). Cysticerci in the form of cysts can be demonstrated with the CT

scan. These range from 0.5 to 3.0 cm in size and are of low attenuation(9). They may be associated with perifocal oedema and ring enhancement after administration of contrast material(7). In adults lesions are usually few in number(7) and when associated with seizures perifocal oedema is invariably noted(8). It is likely that there is little if any reaction of the brain to the cysticerci prior to their death(6). Ring enhancement has been noted to develop after therapy with praziquantel, a larvicidal drug, suggesting this is a manifestation of an inflammatory response to the dying larva(10). It would appear that the death of a larva provokes an inflammatory reaction with perifocal cerebral oedema and that this may provoke an epileptiform seizure(9,11). In this study a single ring-enhancing lesion with surrounding oedema was found in six of the patients, there being two such lesions in the seventh. A single, small [less than 1 cm] ring enhancing lesion has been reported in 26% of enhanced CT scans in Indian patients with seizures(12). In other recent series of fifteen Indian patients with seizures and a single enhancing lesion on CT scanning excision biopsy of the lesion was performed and revealed evidence of cysticercosis in twelve and non-specific inflammatory changes in the remaining three cases(13).

Several serologic tests have been developed for detection of antibodies as a diagnostic procedure in cysticercosis with varying degrees of success in the diagnosis of human cysticercosis(14). Most are beset by the problems of antigen specificity and sensitivity(15,16). Recent studies(17,18,19,20) have shown that the performance of an ELISA method is superior to that of other serologic techniques, giving higher levels of specificity and sensitivity. However all immunologic tests, including the ELISA, for cysticercosis so far reported are suboptimal in that a

significant number of patients known to have cerebral cysticercosis have false negative tests(20). In this series of Gurkhas with cerebral cysticerci the ELISA and IFAT was positive in one patient only. It has been postulated(21) that these false negative serologic results are not necessarily due to insensitive methodology but to an insignificant humoral response of the host to the parasite. This may be particularly true when there are only small numbers of intracerebral cysticerci present(22). Positive serum serologic tests for cysticerci do not *per se* demonstrate cerebral involvement but positive serologic tests on CSF do, however, imply CNS involvement(23).

Serum IgE was elevated in all seven patients with cerebral cysticercosis in the absence of an absolute eosinophilia or any evidence of intestinal parasites. Treatment with praziquantel resulted in a reduction in IgE levels measured two months after completion of treatment. Raised IgE levels provide indirect evidence suggesting a possible diagnosis of cerebral cysticercosis in patients with ring-enhancing lesions demonstrated on CT brain scans.

Electroencephalographic abnormalities suggesting a focal lesion were found in only one patient and electroencephalography appears to be a poorly sensitive method of localising lesions in cerebral cysticercosis.

Praziquantel was first reported as a treatment for cysticercosis in pigs in 1978 and in man in 1980(24). Sotello et al(10) provided objective evidence that treatment with praziquantel can reduce the number and size of cysticercal cysts. The dramatic host reaction that develops around the cysts during treatment can lead to the development of increased symptoms and severe intracranial hypertension(10). Dexamethasone should be used in conjunction with praziquantel to reduce cerebral oedema and its sequelae(25). In this and other reported series of patients post treatment CT scans have demonstrated the complete resolution of the ring-enhancing lesion or the appearance of calcification at the site of the original lesion(26). Although spontaneous resolution of contrast enhancing cerebral cysticerci has been demonstrated without specific treatment(9) the rationale for treatment in patients who on CT scans appear to have few cerebral cysticerci is to kill any live cysticerci present which may have escaped detection by the CT scan under the control of the inflammatory suppressant action of dexamethasone.

The problem of cerebral cysticercosis is not new to the British Army. MacArthur(27) whilst working at the Queen Alexandra Military Hospital, Millbank noted that "a considerable number of men previously healthy and coming of sound nervous stock developed epilepsy in adult life during or after service abroad". This was attributed to cerebral cysticercosis and evidence pointed to the patients being infected in India. A continuation of Sir William MacArthur's original work was published by Dixon and Lipscombe(4) reporting a total of 450 cases of epilepsy caused by cerebral cysticercosis among

troops who served at some time in India. Worldwide cysticercosis is the most common parasitic infection of the CNS(23). Large series of cases attest to its frequency in Eastern Europe(28), China(29), India(30), Mexico(31), South America(32) and Africa(20). There have been sporadic cases of cysticercosis involving the CNS and striated muscle of man in Hong Kong(33,34) although a low prevalence of *Taenia solium* has been reported in the Chinese population of Hong Kong(35). The average interval from initial infection to onset of symptoms is approximately five years, with a range of a few months to thirty years(4,36). Pig rearing is common in rural areas of Nepal and human defaecation remains indiscriminate. It is likely that the cysticercal infections in Gurkhas were acquired in Nepal. A diagnosis of cerebral cysticercosis should be considered in adults presenting with epileptiform seizures who have spent time in an area where cysticercosis is known to be endemic.

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