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Intraventricular neurocysticercosis: Presentation, diagnosis and management

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ABSTRACT

Neurocysticercosis is thought to be the most common helminthic infection of the central nervous system and its epidemiology is changing due to increasing travel and migration. Evidence to guide management of the intraventricular form is limited. We aimed to review the clinical presentation, diagnosis and treatment of intraventricular neurocysticercosis with reference to two recent cases seen at our institution. The intraventricular variant of neurocysticercosis is less common than parenchymal disease and usually presents with acutely raised intracranial pressure and untreated it progresses rapidly with high mortality. The diagnosis is based on imaging and serological tests but more invasive testing including histopathological examination of surgically acquired tissue specimens is sometimes required. Treatment is mainly surgical, using a neuroendoscopic approach if possible. Patients should also receive antihelmintic treatment with concomitant corticosteroids to reduce the incidence of shunt failure if a ventricular shunt is inserted and to treat viable lesions elsewhere.

1. Introduction

Neurocysticercosis is the most important helminthic central nervous system (CNS) infection worldwide and increasing travel and migration has led to a growing number of patients being diagnosed in non-endemic countries [1]. The majority of the published literature relates to the parenchymal form of the disease, and there is a paucity of epidemiological studies and high quality evidence to guide the management of the intraventricular variant.

Cysticercosis occurs when eggs from *Taenia solium (T. solium)*, the pork tapeworm, are ingested by humans who become dead-end intermediate hosts. Oncospheres migrate to various tissues, most commonly the CNS, eyes, muscles and subcutaneous tissues, and once fully developed as viable cysts, go through three consecutive distinct stages in the process of degeneration: colloidal, granular and calcified forms [2]. In intraventricular neurocysticercosis, the larvae reach the cerebral ventricles via the choroid plexus and cause symptoms either from obstructing CSF flow, ependymitis or both [3,4].

No recent population based prospective data is available on the frequency and pattern of intraventricular involvement in neurocysticercosis. Several studies, including the largest series available, were done prior to the introduction of MRI and CT scanning, and most were from non-endemic countries. The majority of recent publications are from neurosurgical journals, so significant referral bias can be expected since parenchymal neurocysticercosis is mainly managed medically and is less likely to involve surgical consultation. Intraventricular disease has been reported to occur in between 7.3% and 61.3% of cases of neurocysticercosis [3,5,6]. Cysts are most often found in the fourth ventricle (range 43%–70%) followed by the lateral (11%–43%) and third (1%–29%) ventricles with a minority in the Sylvean aqueduct (7%–9%) [3,5,7–9]. Compared to parenchymal neurocysticercosis, patients with intraventricular disease have a worse overall outcome and most deaths occur in this subgroup [10].

We report two cases of intraventricular neurocysticercosis that illustrate the natural history, diagnostic and management issues.

2. Case report 1

A 30 year old Indonesian female presented in 2004 with acute headache, fever and confusion. On examination she had neck stiffness with no focal motor or sensory deficits. She had a

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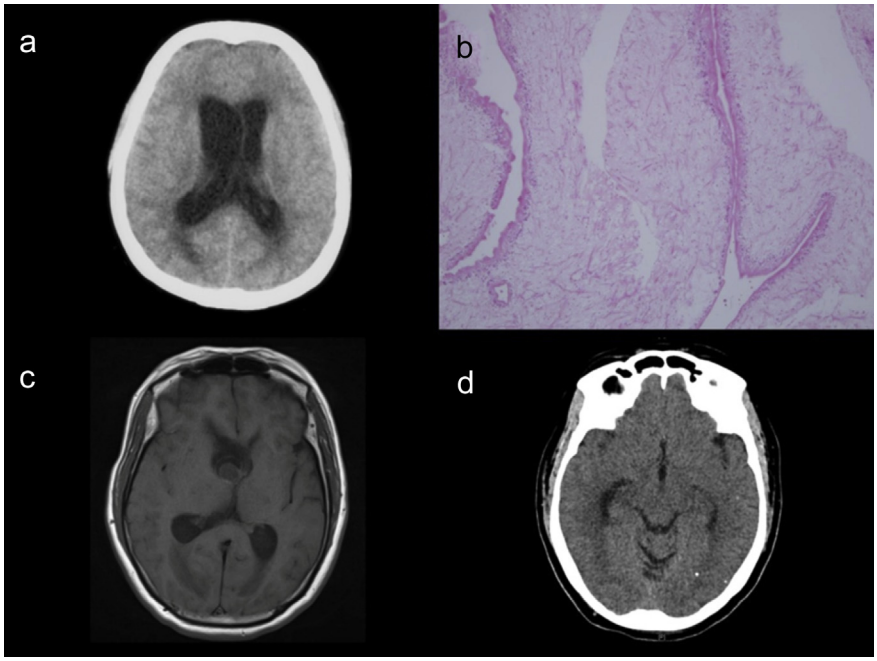

Figure 1. Findings on imaging and histopathology in two cases of neurocysticercosis.
A: CT scan of brain (Case 1) demonstrating dilated lateral and third ventricles as well as effaced cerebral sulci; B: Histopathological examination, haematoxylin and eosin stain at magnification ×100 (Case 1) showing three distinct layers consistent with a *T. solium* cyst: a cuticular layer with hair-like microtrichia, a middle cellular layer and an inner reticular layer with focal calcification; C: MRI brain (Case 2) identifying a bilobed cyst in the foramen of Monro and severe obstructive hydrocephalus; D: CT scan of brain (Case 2) after relief of hydrocephalus showing multiple tiny calcifications throughout both hemispheres.

leucocytosis of 18×10^9 white cells per litre, of which 17×10^9 were neutrophils, and blood tests including HIV serology were otherwise unremarkable. A CT scan showed moderate dilatation of lateral and third ventricles, a normal sized fourth ventricle and effacement of all cerebral sulci (Figure 1a).

Empiric treatment for bacterial meningitis was started and emergency external ventricular drains were inserted into both lateral ventricles. CSF collected at the time of drain insertion contained 6×10^6 white cells per litre of which 5×10^6 were polymorphonuclear cells and no organisms were identified on Gram stain or standard bacterial culture. The CSF levels of glucose and protein were 4.4 mmol/L and 0.09 g/L respectively.

The patient's symptoms improved after drain insertion and a subsequent MRI scan showed mild residual dilatation of the lateral ventricles but the third and fourth ventricles were normal in size and CSF flow studies were normal. A post-operative lumbar puncture showed a mild pleocytosis of 33×10^6 white cells per litre, with 78% lymphocytes. The glucose concentration was normal at 3.6 mmol/L and protein was normalising at 0.44 g/L. Culture for bacteria, fungi and mycobacteria were all negative.

On endoscopic third ventriculostomy a large cyst with a white membranous wall was found protruding through the foramen of Monro. Histopathological examination of the cyst was consistent with cysticercosis (Figure 1b). Serum testing for cysticercosis IgG with an enzyme-linked immunosorbent assay (ELISA) was negative (Diagnostic Automation Inc., California, USA).

3. Case report 2

A 50 year old female from Punjab, India was admitted in 2013 with two days of headache, nausea, irritability and confusion. She was afebrile without focal neurological deficits and blood tests including full blood count, liver and renal functions were normal.

The patient had been living in Australia for 30 years with frequent trips to India to visit family. Twenty years previously she had been diagnosed with parenchymal cysticercosis and had a viable cyst in the right biceps muscle which was removed. She had a brief period of dysphasia and left arm weakness at the time of diagnosis, but these symptoms resolved.

At the time of the recent presentation a MRI scan revealed a 16 mm × 18 mm bilobed cystic lesion in the foramen of Monro, with minimal surrounding enhancement and severe obstructive hydrocephalus. No scolex was seen (Figure 1c). The cyst was removed endoscopically, an external ventricular drain was inserted and her symptoms resolved. Cerebrospinal fluid sampled at the time of surgery contained no white cells. Histopathological examination showed three distinct layers consistent with cysticercosis. No serological tests were performed on serum or cerebrospinal fluid as a conclusive histopathological diagnosis was made. A post-operative CT scan demonstrated resolution of the hydrocephalus and multiple tiny calcifications scattered throughout cerebral and cerebellar hemispheres bilaterally consistent with calcified cysts (Figure 1d).

4. Discussion

Management of intraventricular neurocysticercosis is distinct from the parenchymal form for which most evidence has been published [11,12]. Guidelines have not been validated in this subgroup of patients and as a consequence, management is mostly based on smaller case series and expert opinion.

As exemplified by our cases, intraventricular neurocysticercosis commonly presents with acute obstructive hydrocephalus secondary to either cyst entrapment in narrow foramina or ependymitis [3,4]. Headache is reported in nearly all patients

and other common presentations include nausea, vomiting, decreased visual acuity, altered mental status and cranial nerve palsies [3,5,7–9].

The diagnosis of intraventricular neurocysticercosis is most often made radiologically and MRI is considered the most useful modality although no direct comparison has been made with other techniques. Increased T1 and T2 signal of the cyst wall is usually seen, although cysts are sometimes missed as seen in Case 1 [3,7]. The visualisation of a scolex is diagnostic [12]. Enhancement with gadolinium and increased intensity of cyst content on a T1-weighted sequence indicates cyst involution in either the colloidal or granular stage which is often associated with ependymitis [3]. A disadvantage of MRI scanning is that its sensitivity for calcified lesions is poor compared to CT as seen in Case 2 where these were only apparent on a CT scan after removal of the intraventricular cyst. In the absence of a visualised scolex, intraventricular cysticercosis can be mistaken for a benign colloid cyst as was the case in Case 2. If a MRI scan does not reveal a cyst and there is suspicion of neurocysticercosis, CT ventriculography or neuroendoscopic exploration may be warranted. This was illustrated in Case 1, where the cyst only became apparent during endoscopy.

The inflammatory process in neurocysticercosis varies markedly with parasite location [13]. The interpretation of biochemical and serological tests on blood and CSF in intraventricular disease is therefore problematic since most evidence for their use come from studies in patients with parenchymal lesions.

The current antibody test of choice is an immunoblot assay using *T. solium* antigens on serum or CSF samples [14]. The performance of this test in patients with intraventricular disease has not been adequately studied, although the sensitivity is likely around 80% based on the analysis of small subgroups of patients in the original studies [15]. It is unclear if the test performs differently on serum and CSF samples and a major drawback of antibody tests is the inability to distinguish between active or past infection in patients who typically come from high-prevalence regions [14].

Direct detection of *T. solium* antigen has the advantage of being associated with active infection (viable, colloid and granular stages) and disease severity, and the best studied method is an ELISA using a monoclonal antibody against the *Taenia saginata* (beef tapeworm) HP10 antigen [14]. Studies on both serum and CSF have shown a high specificity for viable cysts although some have reported a lower sensitivity (21.4%–94.1%) compared to antibody assays [16,17]. In addition, antigenaemia predicts the presence of viable cysts in patients who only have calcified lesions on CT making it useful in settings where MRI is not available [18]. In intraventricular neurocysticercosis the antigen levels are often higher, specificity is close to 100% and serial monitoring with the HP10 assay is a useful way of confirming the disappearance of viable cysts with treatment [17]. Applying the antigen detection assay to CSF is unlikely to result in better sensitivity and specificity than when used on serum [17].

Detection of *T. solium* specific DNA in CSF by polymerase chain reaction has been studied in a small number of patients with intraventricular neurocysticercosis where it had variable sensitivity (71%–97%) using different primers [14,16]. Larger studies are still needed to confirm its use in intraventricular disease, and its use is limited by cost in most endemic areas.

A CSF pleocytosis, which is absent in up to one third of cases, is usually below 500×10^6 cells per litre and consists mainly of lymphocytes and infrequently eosinophils [5]. These changes have been found to be more marked when measured by lumbar puncture compared to sampling directly from ventricles.

Histopathological demonstration of *T. solium* cysts is an absolute diagnostic criterion in parenchymal neurocysticercosis and although these criteria are not validated for intraventricular disease, this was how the diagnosis was confirmed in both our cases [12]. If only the membranous structures are found, they include an outer eosinophilic layer, a middle cellular layer with between one and three rows of lymphocyte-like cells and finally an inner reticular layer. Because the scolex and membrane lose their distinct features during the degeneration process, a histopathological diagnosis is limited to the viable stage.

The treatment of neurocysticercosis includes antihelmintic drugs and surgical resection of lesions as well as symptomatic treatment with analgesia, anti-inflammatory drugs and anti-epileptics.

Surgical intervention is usually warranted acutely in intraventricular neurocysticercosis to relieve pressure and remove cysts [4]. Traditionally, treatment comprised of emergency shunt placement and cyst removal by open craniotomy allowing for antihelmintic treatment, which generally has poor efficacy. Neuroendoscopic cyst resection with ventriculostomy with or without placement of an external ventricular drain or permanent shunt has now become the surgical treatment of choice, resulting in less complications and higher cure rates and this may be curative without anthelmintic [5,6,8,9]. Ventriculostomy at the time of procedure is often enough to relieve hydrocephalus without external drainage which carries a risk of bacterial infection, although it is still needed in patients with extensive disease and ependymitis. When a shunt is placed there is a high risk of shunt failure by blockage and administration of antihelmintic therapy reduces this.

No trials or guidelines are available on the antihelmintic treatment of the intraventricular form of neurocysticercosis and it has not been determined if its use improves outcome when added to surgery. Although medical therapy alone has been reported to lead to resolution of mild cases without significant hydrocephalus, repeat courses are often necessary. Most clinicians follow the guidelines for parenchymal neurocysticercosis from the American Academy of Neurology which recommends albendazole (15 mg/kg/d for 8 d) and either dexamethasone or prednisolone [11]. Praziquantel 50 mg/kg/d for 15 d is an alternative. Although prolonged treatment with albendazole has not been shown to improve efficacy, increasing the dose to 30 mg/kg/d was safe and more effective in a small randomised trial in patients with extraparenchymal disease but these results need confirmation in larger studies [19].

Treatment with anthelmintic may lead to a paradoxical worsening of symptoms or unmask previously undiagnosed neurocysticercosis if treatment is given for another helminthic infection. Treatment should therefore be given under observation in hospital with concomitant corticosteroid administration and in this setting it is thought to be safe [20]. Moderate doses of either dexamethasone (0.1 mg/kg/d) or prednisolone (1 mg/kg/d) are usually given for the duration of antihelmintic treatment but the dose and duration may have to be increased in cases with marked symptoms or a large number of viable cysts. Corticosteroids have been shown to reduce the plasma level of praziquantel supporting the preferential use of albendazole.

5. Conclusions

Intraventricular disease occurs in a significant minority of patients with neurocysticercosis, which is no longer an infection that is restricted geographically to resource-poor regions. The presentation is with features of raised intracranial pressure and the untreated the mortality is high. The diagnosis is based on imaging with MRI, but serological tests, PCR, histopathology and direct surgical visualisation are important supplementary diagnostic tools. Treatment is mainly surgical, preferably using a neuroendoscopic technique, but patients should receive anti-helmintic treatment with concomitant corticosteroids to reduce incidence of shunt failure if a ventricular shunt is inserted and to treat undiagnosed viable lesions elsewhere.

Conflict of interest statement

We declare that we have no conflict of interest.

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