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ORIGINAL PAPER

Cysticercosis of the Fourth Ventricle Causing Sudden Death: A Case Report and Review of the Literature

Tibor Hortobágyi · Ali Alhakim · Olaf Biedrzycki · Vesna Djurovic · Jeewan Rawal · Safa Al-Sarraj

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Abstract A 15 years old girl of African origin was admitted with a history of headaches and a generalised tonic seizure. Her clinical examination including fundoscopy was normal. She claimed she had been assaulted. Within a few hours of her admission she was found dead in her bed during the ward round. Cardiopulmonary resuscitation was unsuccessful. At *post-mortem*, the major organs showed no pathological changes and neck dissection showed no abnormality. Neuropathological examination after formalin fixation revealed a cystic lesion in the fourth ventricle, ependymitis and acute hydrocephalus. Histology showed parts of the parasite *Taenia solium* and the diagnosis was neurocysticercosis. This case highlights the need for forensic and general pathologists as well as forensic medical examiners and paediatricians to be aware of neurocysticercosis as a possible cause of sudden death in the presence of normal clinical findings and negative autopsy, especially in patients from Asian, African or South American countries. As cysticercosis is the commonest cause of seizures in the developing world, neurocysticercosis needs to be considered as a cause of sudden and unexpected death in any patient with a history of headaches and/or seizures.

Keywords Cysticercosis · Neurocysticercosis · Sudden death · *Taenia solium*

Tibor Hortobágyi and Ali Alhakim are first authors who contributed equally to this work.

T. Hortobágyi · S. Al-Sarraj (✉)
Department of Clinical Neuropathology, King's College Hospital,
Denmark Hill,
London SE5 9RS, UK
e-mail: safa.al-sarraj@kch.nhs.uk

T. Hortobágyi
NIHR Biomedical Research Centre for Mental Health,
The South London and Maudsley NHS Foundation Trust and
Department of Clinical Neuroscience, Institute of Psychiatry,
London, UK

T. Hortobágyi
Department of Histopathology, University of Szeged,
Szeged, Hungary

A. Alhakim
Department of Histopathology, East Surrey Hospital,
Surrey, UK

O. Biedrzycki
Institute of Pathology, Royal London Hospital,
London, UK

V. Djurovic
Forensic Pathology Services,
London, UK

J. Rawal
Oldchurch Hospital, BHR NHS Trust,
Romford, Essex, UK

Introduction

Cysticercosis is a parasitic infestation that results from ingestion of eggs from the adult pork tapeworm, *Taenia Solium* (*T. Solium*). Neurocysticercosis results from hatching of larval forms in the digestive tract, which then penetrates the gut wall and spread via the bloodstream to encyst in the central nervous system (CNS). The resultant symptoms and pathology vary with the final resting site of the cysts in the CNS. Sudden death, although rare, has been recognised by clinicians as a potential complication for a long time [1–3], and may result from mechanisms such as raised increased intracranial pressure, hydrocephalus and acute encephalitis/meningitis. In addition more unusual examples of sudden death due to neurocysticercosis such

as a reaction to antilarval drugs [4], and sudden cyst rupture secondary to trauma [5] have also been reported.

Forensic medical examiners are often involved in the investigation of such cases and must be alert to the possibility of this condition as a potential cause of sudden death, especially in the immigrant population who are more likely to have been exposed to the organism.

We present a highly unusual case of sudden death due to neurocysticercosis with a prior confounding history of assault in an adolescent girl. The case highlights the need to exclude all possible causes of death and the crucial importance of formal examination of formalin fixed brains by specialist neuropathologists. We believe that this is the first reported case of sudden death in a child due to cerebral cysticercosis in the UK; although two children with neurocysticercosis have been previously reported, both remained well and seizure-free without treatment [6].

Case Report

Case History

A 15-year-old girl from Rwanda, Africa, with no known significant past medical history presented to her family doctor with a 2-week history of headaches and vomiting. The family doctor diagnosed acute migraine and treated her for the same with Migraleve (paracetamol + codeine + buclizine). Her headache had worsened over one week, when she presented to accident and emergency department with history of an episode of generalised tonic convulsion lasting for two minutes on the same day. She was admitted in the children's ward, for neuro-observations and subsequent neuroimaging. Her neurological examination and fundoscopy were normal. She was alert, orientated and haemodynamically stable. Her neuro-observation was normal. She had her breakfast at 8 am, after which she had gone to sleep again. A few hours after, during the morning ward round, she was found dead. All attempts of resuscitation were unsuccessful.

Autopsy Findings

Macroscopic Findings

The body of a well-nourished adolescent girl was examined at autopsy. The main finding on external examination was a 0.3 cm scar with rolled edges present over the left forehead. This was interpreted as an old injury and was the only potentially significant finding on external examination. The scalp showed no evidence of bruising and there were no skull fractures. A detailed layered neck dissection was unremarkable. All major organ systems, apart from the brain, showed no macroscopic abnormality and all organ weights were within normal ranges.

The brain (1494 g) was fixed in paraformaldehyde. Neuropathological examination revealed swelling with flattening of the gyri, no herniation but bulging of both unci. Coronal sections showed dilatation of the third and fourth ventricles, the latter being hugely dilated. A small cystic nodule was loosely attached to the floor of the inferior part of the fourth ventricle (Fig. 1A). The nodule measured 6×4×4 mm, contained a greyish and gelatinous content and lied just beside the exit foramen. The lining of the ventricular system was shaggy and granular with a greyish appearance, consistent with ependymitis. The cortex showed no focal lesions or haemorrhage. Oedematous changes were present in the white matter, around the hypothalamus and above the optic chiasm. The remainder of the brain showed no pathological changes.

Microscopic Findings—Histology and Immunohistochemistry

Histological examination of the cyst revealed three histologically distinct layers: an outer cuticular layer, a middle cellular layer with pseudo-epithelial appearances and an inner reticular or fibrillary layer. Some of the layers had hazy appearances, probably due to death of the parasite and autolysis. The dead but still relatively well-preserved parasite had a scolex containing muscular sucker and hooklet (Fig. 1b). The appearances were those of cysticercosis. There was a marked ependymitis consisting of a lymphocytic infiltrate in a perivascular distribution, as well as oedema (Fig. 1c) and associated lymphocytic inflammation of the basal leptomeninges (Fig. 1d). The inflammation affected the third and fourth ventricles, the aqueduct and the lateral ventricles. In some areas, the oedema and inflammation of the subependymal area had occupied most of the ventricular lumen. Mild vacuolation and shrunken neurons, consistent with ischaemia, were present in the cerebral cortex and hippocampal formation. No other histopathological changes were observed and, in particular, no changes to suggest head injury were demonstrated using immunohistochemistry for beta-amyloid precursor protein.

Toxicological Findings

Toxicological examination of *ante mortem* blood sample showed no evidence of drugs or alcohol.

Discussion

Neurocysticercosis is the leading cause of epilepsy in the developing world [7], as well as being the commonest

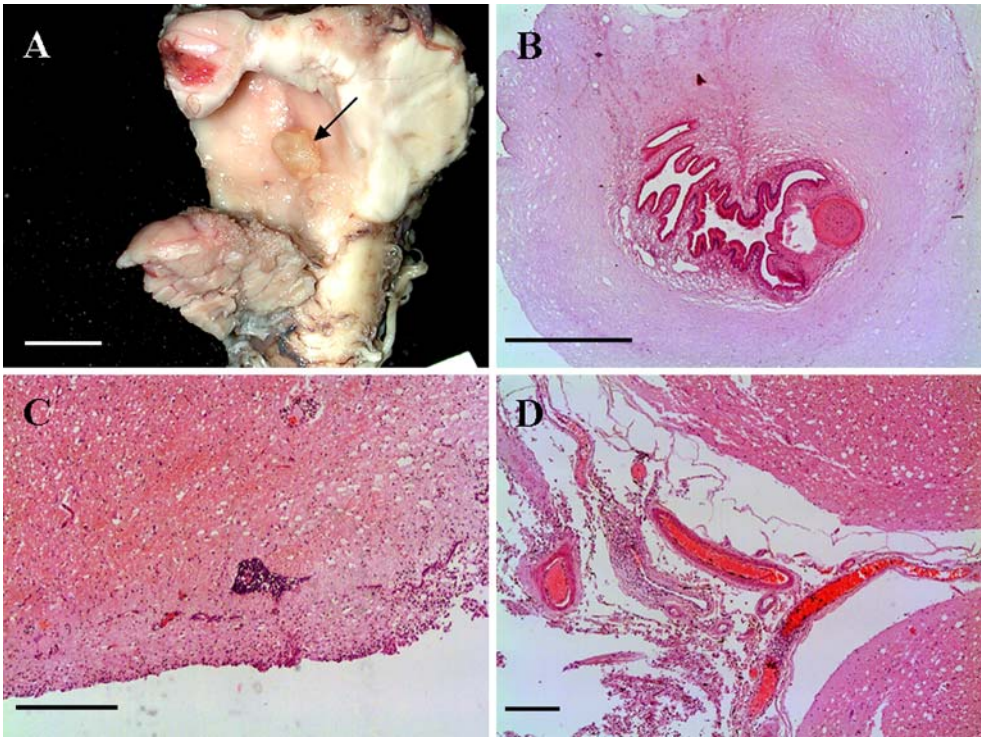

Fig. 1 (**A**) The dilated fourth ventricle contained a 6 mm nodule attached to the wall at the exit foramen. (**B**) Histology revealed a relatively well-preserved and encysted part of the dead helminth *Taenia Solium* with the apparent mouth organ (scolex). (**C**) The wall of the ventricle had an uneven surface lacking the normal ependymal cell lining with oedema and mainly perivascular lymphocytic inflammation and macrophages of the subjacent brain tissue, consistent with granular ependymitis. (D) The leptomeninges at the base of the brain showed scanty infiltration by lymphocytes as a sign of a reactive inflammatory change [Calibration bar lengths: 1 cm (**A**); 1 mm (**B**); 0.1 mm (**C**, **D**)]

parasitic infestation of the central nervous system [8, 9]. Although a disease of developing world [9], emigration of people from endemic to non-endemic areas and ease of travel across the world has increased its prevalence in developed countries as well [9]. The prevalence of neurocysticercosis in one centre in the United States of America has been quoted as 6 cases out of over 45,000 autopsies (0.013%) [10] and is on the increase mainly owing to an influx of immigrants from endemic areas such as many parts of Asia [11], Latin America and Africa [12]. No studies examining the prevalence in the UK exist but with the large numbers of immigrants and asylum seekers arriving each year, patients with undiagnosed neurocysticercosis and its complications will continue to present. Many paediatricians may expect cerebral cysticercosis to present with seizures in children and may not be aware of its potential cause of sudden death.

The organism responsible for the disease is *T. solium*, a pork tapeworm, whose permanent host is a man. The adult organism lives in the small intestine; four suckers and two rows of hooklets attach it to the intestine's wall. Intermediate host animals or humans ingest eggs excreted in the faeces, when eating food contaminated with viable eggs or the adult tapeworm. In the intestines, the ova penetrate the wall and are carried away by the circulation potentially to all organs, including the brain, where they develop a cyst in about two months. The cysts take several forms. In most cases they remain small, sequestrated and eventually die.

There are several clinical presentations of the disease. The underlying pathological processes include inflammation around the cyst, space occupation, impaired cerebrospinal fluid flow, meningeal inflammation and vasculitis [13, 14]. The far most common presentation is seizure (in 70–90% of patients)[15]. In 10%-20% symptoms are non-specific, as nausea, vomiting, headache, ataxia and confusion due to ventricular cysts. Hydrocephalus, vasculitis and stroke can be a presentation of cysts of the basal cisterns. Rarer manifestations, like altered mental state, spinal cysticercosis with radicular pain, parasthaesiae, progressive cord compression, ophthalmic cysticercosis, migraine headaches, neurocognitive deficits, and cerebral oedema which is common in young girls [15]. The commonest pathological presentations are degenerating or calcified cyst (52%), followed by leptomeningitis (48%), which is most often basal and may cause hydrocephalus. In intraventricular forms, the 4th ventricle is most frequently involved; the cyst may attach to the ventricular wall. In cerebrovascular form vasculitis with or without thrombotic occlusion may ensue. In the rare encephalitic type, mainly affecting children, the dead helminths evoke an inflammatory reaction. The least frequent forms are the disseminated, dementing and spinal forms [16, 17]. Our patient had the intraventricular form with additional mild basilar leptomeningeal involvement presenting with headaches, vomiting, and seizure.

The prognosis is influenced by the location of the cyst(s), with the intraventricular and meningobasilar forms being the least responsive to therapy.

The definite diagnosis of cysticercosis is based on histological identification of the helminth, although neuroimaging is the mainstay investigation. Characteristic neuroimaging features include the scolex appearing as a hyperintense nodule ("hole-with-dot" imaging) and punctuate calcification. Single or multiple ring-like (starry sky), or nodular enhancing lesions, are seen in patients with cysticerci in the acute phase [18]. Our patient, unfortunately, died before the neuroimaging could be arranged. Most serologic assays have limited value because of poor sensitivity and specificity. EITB (enzyme linked immuno-electro-transfer blot) has been found to be more specific and sensitive.

The differential diagnosis includes other cystic lesions in the brain. To this end, recently we had a case with similar history and sudden death in an 11 years old girl, where neuropathological examination revealed a colloid cyst of the third ventricle [19].

The mechanism of death in present case was consistent with rapidly developing acute hydrocephalus due to obstruction of the ventricular system. There was nothing to suggest trauma, which could result in rupture of the cyst with subsequent death, as described previously [5]. Since neurocysticercosis was diagnosed *post-mortem* therefore the patient did not receive any anti-larval treatment, a reaction to anti-larval drugs as a cause of death is not relevant in our case. This, however, has been described previously [4]. Another potential mechanism of sudden death, recently described in relation to colloid cyst of the third ventricle, is the 'neurogenic stunned myocardium' [20]. It has been proposed that sudden elevation of intracranial pressure, with subsequent decreased cerebral perfusion pressure, induces a vigorous cerebro-protective neuroendocrine system activation that can lead to the stunned myocardium; this mechanism may be operating as the mode of death rather than frank cerebral herniation [20]. Although in the present case—given the lack of evidence of frank uncal herniation or pontine haemorrhages and the catastrophic speed the final demise—this remains a hypothetical possibility the authors favour the acute hydrocephalus as the main mechanism leading to sudden death.

The consensus guidelines for treatment of neurocysticercosis by the international panel of experts [21] suggest, that (*1*) treatment must be tailored in terms of number, site, and viability of parasite. (*2*) Growing parasite must be treated with antiparasitic drugs or surgery. (*3*) Seizures need antiepileptic drug treatment. (*4*) Treatment of raised intracranial pressure must take priority before considering other forms of therapy. The raised intracranial pressure or hydrocephalus due to cyst located in ventricular system, as in our case, should be relieved surgically by neuroendoscopic resection and shunt [21].

In summary, neurocysticercosis remains a potentially preventable cause of sudden death in at risk patients. With the numbers of migrant population increasing, paediatricians, general and forensic pathologists should bear this rare diagnosis in mind when faced with sudden death in an apparently healthy child and an apparently negative autopsy. Formalin fixation of the brain with subsequent neuropathological examination is not only vital to reach the diagnosis but also for medico-legal, epidemiological and infection control purposes.

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