Solitary Neurocysticercosis Presenting with Focal Seizure and Secondary Generalized Tonic-Clonic Seizure

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Conflict of interest: None declared

Patient: Male, 25-year-old
Final Diagnosis: Neurocysticercosis
Symptoms: Generalized tonic-clonic seizures
Medication: —
Clinical Procedure: Cyst removal under CT brain navigation with duraplasty
Specialty: Infectious Diseases • General and Internal Medicine • Neurology

Objective: Rare disease
Background: Neurocysticercosis is the most common central nervous system infection in developing countries. A wide array of clinical manifestations, ranging from asymptomatic to severe neurological symptoms, is observed in patients diagnosed with neurocysticercosis, depending on the number of lesions, cyst location, cyst stage, parasite genotype, and host immunity.

Case Report: We report the case of a 25-year-old Burmese man who presented with focal seizure and secondary generalized tonic-clonic seizure. Brain imaging studies revealed a 1-cm cyst, which showed rim enhancement, an eccentric scolex, and surrounding brain edema at the left superior frontal gyrus. His serum cysticercus antibody was positive. Thus, the patient was diagnosed with solitary neurocysticercosis based on clinical manifestations, neuroimaging findings, and positive serology. The patient received anti-parasitic and anti-seizure medications before surgical excision of the cyst via computed tomography (CT) scan navigation. Stereomicroscopic examination of the cyst revealed a parasite larva in a fluid-filled cyst, containing a scolex with hooks and 4 suckers, identical to that of Taenia solium. Molecular characterization of the parasite based on T. solium cytochrome c oxidase subunit 1 (COX-1) gene identified the species as being 99.7% identical to T. solium Asia genotype previously reported from pigs in Thailand.

Conclusions: Although the prevalence of neurocysticercosis seems to be declining, sporadic cases have been reported throughout the world and the prevalence may be underestimated. Differential diagnosis of neurocysticercosis in patients presenting with adult-onset epilepsy should be considered in disease-endemic areas.

Keywords: Cestode Infections • Cysticercus • Neurocysticercosis • Seizures • Taenia solium

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Background

Cysticercosis is a parasitic tissue infection caused by larval-stage cysticercus cellulosae of the tapeworm *Taenia solium* [1,2]. The disease is endemic in several regions of the world, including Asia, Central America, South America, and sub-Saharan Africa [1,2]. The presence of parasitic cysts of *Cysticercus cellulosae* in the central nervous system can cause a disease called neurocysticercosis, which is the most severe form of the disease [1,2]. Humans acquire neurocysticercosis by consuming food or water contaminated with *T. solium* eggs, which are shed from the stools of individuals with intestinal *T. solium* infection [1,2]. In developing countries, neurocysticercosis is the most common parasitic infection of the nervous system and it is the main cause of adult-onset epilepsy [1]. Neurocysticercosis is classified as either parenchymal or extraparenchymal, based on the location of the lesion [1,3]. In parenchymal neurocysticercosis, the parasitic cysts are localized in the brain and medullary tissues. In extraparenchymal neurocysticercosis, parasitic cysts develop in extraparenchymal locations, including the spine and intraventricular and/or subarachnoid spaces [1,3].

The clinical manifestations of patients with neurocysticercosis include a wide range of neurological abnormalities that vary according to the number, size, stage, and location of lesions, as well as individual host immune response and parasite genotype [1,4]. Parenchymal neurocysticercosis, which is the most common form of the disease, generally manifests with seizures and headaches [4,5]. Extraparenchymal neurocysticercosis, which has a poorer prognosis, is mainly associated with symptoms of increased intracranial pressure and hydrocephalus [4,5].

Here, we report a case of solitary neurocysticercosis in a patient who presented with a focal seizure and secondary generalized tonic-clonic seizure. An intact fluid-filled cyst containing a scolex with hooks identical to *T. solium* scolex was isolated from a lesion excised from our patient’s brain. Molecular characterization of the parasite based on *T. solium* cytochrome c oxidase subunit 1 (COX-1) gene identified the species as being 99.7% identical to *T. solium* Asia isolates, previously reported from pigs in Thailand.

Case Report

A 25-year-old Burmese man with an underlying medical history of thalassemia with unknown hemoglobin typing presented to the Emergency Department with a focal seizure and secondary generalized tonic-clonic seizure. One hour before arrival at the hospital, he started to feel numbness in his legs, and later developed right-sided clonus followed by generalized tonic-clonic seizure, salivary drooling, and unconscious for 30 seconds. He was then taken to the Emergency Department. After regaining consciousness, the patient still had a short episode of muscle contraction in his right leg. He reported having a severe headache twice a week with a pain score of 10 out of 10, which was relieved by over-the-counter painkillers, and had occasional non-projectile vomiting for 3 months. He was otherwise healthy with no history of head trauma, alcohol abuse, or drug abuse. Physical examination upon arrival showed vital signs within normal limits. He was oriented to person, place, and time, but appeared somnolent and slowly followed most commands. No focal neurological deficits were observed. Eye examination showed normal visual acuity, normal visual field, clear cornea, round pupils 3 mm in size, reactive to light both eyes, and no conjunctival lesions. Fundoscopic examination revealed a normal cup-to-disc ratio, no signs of papilledema, and no retinal lesion or detachment.

Pre-contrast computed tomography (CT) of the brain revealed a 1-cm well-defined cystic lesion with wall hyperdensity, with a tiny intraslesional eccentric calcification, and perilesional edema at the left superior frontal gyrus (Figure 1A, 1B). After contrast media injection, this lesion showed faint enhancement of the wall (Figure 2A, 2B). Magnetic resonance imaging (MRI) of the brain revealed a 1-cm cyst with a thick enhancing wall and perilesional edema at the left superior frontal gyrus. The cyst content showed hypointensity on T1-weighted image and hyperintensity on T2-weighted image, similar to that of cerebrospinal fluid (CSF). The cyst with dot sign representing the parasitic cyst with an eccentric scolex was recognized on T2-weighted imaging (Figure 3A-3D). These imaging findings were compatible with a diagnosis of neurocysticercosis. His lumbar puncture yielded a normal opening CSF pressure, a normal white blood cell count (2 cells/mm³), and elevated red blood cells (2000 cells/mm³) due to traumatic puncture. The concentrations of glucose and total protein in the CSF were 75 mg/dL and 58 mg/dL, respectively. The patient was positive for serum cysticercus IgG antibody as assessed by cysticercous IgG enzyme-linked immunosorbent immunoassay (ELISA) kit (IBL International Corp, Hamburg, Germany). His peripheral blood showed anemia (Hb 9.8 g/dl), but no eosinophilia (total eosinophil count 29 cells/µl). CSF culture for bacteria, modified acid-fast stain, and polymerase chain reactions (PCR) for *Mycobacterium tuberculosis* complex and non-tuberculous Mycobacteria were all negative. Serum IgM and IgG for *Toxoplasma gondii* were undetectable. Chest X-rays were normal. His stool direct examination revealed no ova or parasites.

He was diagnosed with neurocysticercosis and was prescribed albendazole 200 mg BID, praziquantel 1200 mg TID, phenytoin 300 mg daily, and dexamethasone 4 mg TID for 1 month. Despite receiving medical treatment, he still had occasional focal seizures as right leg jerks, but otherwise unremarkable. One month after the follow-up MRI of the
brain showed a mild increase in lesion size (from 0.65×1 cm to 0.95×1 cm), an increased thickness of the enhancing wall, and an increased degree of perilesional edema. The patient was referred to Siriraj Hospital for further management. Due to the location and number of the cyst, an operation for cyst removal was performed. The patient underwent a small craniotomy with cyst removal under CT brain navigation with dura-plasty. The intraoperative finding was a thick-walled abscess at the left posterior central gyrus with a size of approximately 1 cm in diameter. The lesion was completely removed and sent for histopathology. Gross examination of the lesion showed a round intact cyst containing translucent fluid, approximately 1 cm in diameter (Figure 4A). Dissection of the cyst under a stereomicroscope revealed an invaginated scolex with rostellum and hooks with 4 suckers, which is compatible with the scolex of *T. solium* (Figure 4B). Histological examination of the
Figure 3. Axial T1-weighted image (A), axial T2-weighted image (B), axial T1-weighted image with contrast media (C), and coronal T1-weighted image with contrast media (D) demonstrated a 1 cm cyst with thick enhancing wall and perilesional edema at the left superior frontal gyrus. The cyst content showed hypointensity on T1-weighted image, and hyperintensity on T2-weighted image similar to that of cerebrospinal fluid. The cyst with dot sign was recognized on T2-weighted image.
surrounding tissue revealed mildly increased cellularity without specific findings. DNA extraction was performed from the tissue using the QiAamp DNA Mini Kit (Qiagen, Hilden, Germany) following the manufacturer’s protocol for isolating DNA from tissue samples. Molecular identification of the scolex was performed by PCR using primers specific for the *T. solium* COX-1 (cytochrome c oxidase subunit 1) gene using a multiplex PCR protocol as previously described, followed by DNA sequencing [6]. In brief, the multiplex PCR reaction was set up using primers targeted for COX-1 gene of *T. solium*; Tsol/Asia-Fwd 5’-GGATTGTTATAATTTTTGATTACTAAC-3’, Tsol/Amer-Fwd 5’-GGGGTAGATTTTTTAATGTTTTCTTTT-3’, and Tsol-common-Rev 5’-GACATAACATAATGAAAATGAGC-3’.

The PCR reactions were set up in a volume of 20 µl containing 2 µl of 2X AccuStart II PCR SuperMix kit (Quantabio, Beverly, MA, USA), 0.4 µl of each primer, 10 ng of DNA, and H₂O up to 20 µl. The PCR cycling included initial denaturation at 95°C for 5 min; 10 cycles of touchdown PCR (95°C for 30 s, 52°C to 42°C for 30 s, 72°C for 1 min); and 30 cycles of PCR (95°C for 30 s, 42°C for 30 s, 72°C for 1 min); and 72°C for 5 min. The PCR product specific for *T. solium* Asia genotype with approximately 987 bps was observed.

The PCR product underwent sequencing, which showed it was 99.7% identical to *T. solium* Asia genotype previously reported from pigs in Thailand (GenBank accession number AB066487.1) [7]. The sequence was submitted to NCBI under GenBank accession number OK398427. The patient recovered well postoperatively and continued to receive albendazole and praziquantel for 15 additional days. The anti-seizure medication was tapered off until discontinued. He had no further seizures for 9 months upon the latest follow-up period. However, he still had numbness in his right leg.

**Discussion**

Neurocysticercosis is the most common parasitic infection of the central nervous system in developing countries [1,2]. The disease is endemic in areas with a high prevalence of *T. solium* or immigrants from endemic areas. Humans acquire the infection by consuming food or water contaminated with *T. solium* eggs. In humans, the eggs further develop into cysticerci in human tissue. The disease is categorized into 2 main forms, either parenchymal or extraparenchymal, depending on the location of the cysticerci [1,3]. The parenchymal form is found in more than 60% of cases, and approximately 75% of patients with this form present with adult-onset seizures. For the extraparenchymal form, cysticerci are mainly located in the cerebrospinal fluid circulation pathway, including intraventricular regions and subarachnoid spaces. The main clinical manifestations in this group include nausea, vomiting, hydrocephalus, and signs of increased intracranial pressure [5]. A definite diagnosis of neurocysticercosis is made based primarily on clinical manifestation, patient history, physical examination, brain imaging, and cysticercus antibody, as described in detail by Del Brutto et al in 2007 [8]. Neuroimaging remains a good diagnostic tool with high sensitivity and lower false-positive rate compared to serological testing in disease non-endemic areas [3,9]. Based on neuroimaging findings, neurocysticercosis is classified into the following 5 stages: non-cystic, vesicular, colloidal vesicular, granular nodular, and calcified nodular. Patients may have multiple cysts with various stages of development and different degrees of inflammation within their brains [1,3,9]. Solitary ring-enhancing lesions are the most common findings in patients with neurocysticercosis [10]. According to the radiological findings of our patient, his lesion was likely in the colloidal vesicular stage of intraparenchymal...
neurocysticercosis, which is the stage that is highly associated with clinical symptoms.

Immunological assays can aid the diagnosis of neurocysticercosis but cannot distinguish between an active or previous infection [1,8]. Moreover, patients with solitary lesions or calcified lesions may show as seronegative [11]. The enzyme-linked immunoelectrotransfer blot (EITB) technique, which identifies specific antibodies to the lentil lectin purified glycoproteins (LLGP-EITB) antigen of *T. solium* cysts, has almost 100% sensitivity for detecting parenchymal or extraparenchymal neurocysticercosis, but the sensitivity decreases to 60-70% in patients with calcified lesions [12]. However, the LLGP-EITB method was not commercially available, so cysticercus ELISA was performed instead, with a positive result. The CSF profile in the patients with parenchymal neurocysticercosis is mostly inconclusive. Our patient was diagnosed with neurocysticercosis using the diagnostic criteria for neurocysticercosis proposed by Del Brutto et al in 2017 [8], before the patient underwent surgery. The diagnosis was based on the neuroimaging criteria, the presence of the cyst in the colloidal vesicular stage, and positive detection of cysticercus antibody. The diagnosis of patients with solitary neurocysticercosis by neuroimaging is particularly challenging since the lesion may be similar to other diseases that present with intracerebral ring-enhancing lesions, including primary or secondary neoplasm, intracerebral infections that cause abscess or granuloma, and demyelinating lesions. Unless a scolex within a fluid-filled cyst (dot sign) is observed in neuroimaging studies, the diagnosis of neurocysticercosis cannot be made [3,8].

The parasite larva recovered from our patient’s excised cyst showed a typical pattern of cysticercus cellulose, which is characterized by the larval stage of the parasite within a fluid-filled cyst containing a scolex with hooks and 4 suckers. Molecular characterization of the parasite was performed using the *T. solium* cytochrome c oxidase subunit 1 (COX-1) gene, which identified the species as *T. solium*, Asian genotype. Two main *T. solium* genotypes were found: the Asian and African/American genotypes. The Asian genotype is mostly reported in humans and pigs in Asia and some parts of Madagascar, while the African/American genotypes are primarily found in Africa, South America, and some parts of Madagascar [13]. Molecular characterization of the causative species is essential for understanding the disease epidemiology and association of the genotype with clinical manifestations. A few studies have proposed that the genetic diversity of the parasite contributes to the heterogeneity of disease manifestations [14]. It has been previously reported that neurocysticercosis caused by the Asian genotype, but not the African/American genotype, is typically associated with subcutaneous cysticercosis [13]. Our patient had no observed history of a subcutaneous mass or nodule, which may present in subcutaneous cysticercosis. However, due to cost limitations, whole-body imaging was not performed to rule-out subcutaneous cysticercosis in our patient.

In addition, a study has proposed that genetic variation of the parasite genotypes is associated with distinct parasite antibody recognition patterns [14]. However, further studies are required to confirm the association between the parasite genotypes and the clinical manifestations and severity of disease.

In Thailand, the prevalence of cysticercosis is underestimated. The prevalence of taeniasis, including *T. solium* and/or *T. saginata* infection, was reported to be lower than 1% during 2000-2005 [15]. Fewer than 500 cases neurocysticercosis were reported during 1965-2005 based on diagnostic criteria that did not include serological diagnosis [15]. A study conducted to determine the cysticercus antibody using in-house immunoblot testing among Thai patients suspected of having neurocysticercosis during 2000-2005 yielded positive results in approximately 42% of the patients [16]. To date, only 6 patients with extraparenchymal cysticercosis who presented with racemose cysts have been reported in Thailand [15].

Neurocysticercosis was reported to be most prevalent in the Northern region of Thailand, followed by the Central, Northeastern, and Southeastern regions [16]. The actual prevalence of cysticercosis in Burma (Myanmar) is inconclusive. However, a few studies reported seropositive in approximately 5.5% of Burmese refugees in Thailand and 23.2% of Burmese refugees in the United States [17,18]. In Thailand, the prevalence of neurocysticercosis and taeniasis seems to have decreased due to the improvements in latrine sanitation, regular anti-helminthic administration in closed-system farm-raised pigs, and elimination of pork containing cysticercosis during market pork quality control. There is an increased risk of cysticercosis when close family members or residents in the community have taeniasis solium or cysticercosis [19]. Studies found that people who live close to people with neurocysticercosis have a 3 times increased risk of being found seropositive for cysticercosis [19]. It is thus recommended that these at-risk people be screened for taeniasis and cysticercosis by fecal examination and serological examination.

Treatment of neurocysticercosis depends on the patient’s clinical manifestations, the severity of the disease, and the numbers, locations, and stages of the cysts. Anti-parasitic drugs have been shown to accelerate viable cyst degeneration, diminish seizure risk, and reduce recurrent hydrocephalus [20]. However, the use of anti-parasitic drugs can trigger subsequent inflammatory reactions of degenerating cysts, especially in patients with multicystic lesions [21]. Thus, corticosteroids should be given before and in conjunction with anti-parasitic drugs to reduce inflammation and subsequent seizures [21]. Single-use albendazole should be given to patients with solitary viable or degenerating neurocysticercosis; however, the combination of albendazole and praziquantel should be the drug treatment of choice in patients with multiple viable or degenerating cystic lesions [21]. Surgical removal of cystic lesions can be performed...
with minimally invasive procedures in locations that are easily reached and in intraventricular cysts [1,21]. The standard treatment guideline for patients with solitary neurocysticercosis, as in our patient, includes administration of an anti-parasitic agent, preferably albendazole with or without steroids, and anti-seizure medication until the lesion is resolved on neuroimaging, which can take months to years. Surgical removal of the lesion is not initially recommended. However, our patient did not seem to respond well to the medications given since the follow-up neuroimaging showed an increase in the size of the lesion and the persistent focal seizures in his right leg. After discussion with the patient about the treatment choices, risks, and benefits, he preferred to undergo surgery. He recovered well after surgery and no recurrent seizure was observed up to 9 months during the follow-up period. Minimally invasive surgery had a favorable outcome in our patient and can reduce long-term use of anti-seizure medications.

Conclusions

Although the prevalence of neurocysticercosis seems to be declining, sporadic cases have been reported throughout the world, and the prevalence may be underestimated. To make a definite diagnosis of neurocysticercosis, several criteria, including histological data, neuroimaging findings, and clinical exposure history, must coincide to ensure diagnostic certainy. Since the disease presentation and neuroimaging findings of neurocysticercosis are similar to those of other more common diseases, neurocysticercosis is mostly misdiagnosed or underdiagnosed, especially in the disease non-endemic areas. It will, therefore, be difficult to eradicate this disease even though humans are the only definitive host of this parasite.

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Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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