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Diagnosis Challenge of Neurocysticercosis in the Rural Area

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ABSTRACT

Neurocysticercosis (NCC) is caused by infection with the larvae of *Taenia solium* and is the leading preventable cause of adult-onset seizure worldwide. The most common route of transmission is by ingestion of *T. solium* eggs through the fecal–oral route. Common causes of this infection include consuming undercooked food, especially pork, water contaminated with *T. solium* or uncooked vegetables as well as poor hygiene habits. Epilepsy is the most common clinical manifestation of 70-90% in endemic areas. The case of a 45-years-old woman with history of 4 minutes episode of tonic-clonic seizure 30 minutes before go to the emergency department (ED). There is a history of 2 weeks of progressive headache and fevers with 3 day of acutely worsening headache, nausea and vomiting. Approximately 4-6 weeks earlier, the patient had begun to experience mild headache and fatigue. She was born and lived in East Nusa Tenggara and work as a farmer in Kupang. On physical examination, the patient had Babinski pathology reflexes is positive in left lower extremity. Patient have been head CT-Scan with contrast. Patients were treated with Albendazole, dexamethasone, phenytoin and omeprazole.

Keywords: Neurocysticercosis, diagnosis, rural area

INTRODUCTION

Neurocysticercosis (NCC) is caused by larval infection with *Taenia solium* and is a major preventable cause of stroke in adults worldwide. The most common route of infection is ingestion of *T. solium* eggs via the fecal-oral route. Common causes of this infection include consumption of undercooked food, especially pork, water contaminated with *T. solium*, consumption of undercooked vegetables, and poor hygiene practices.[1] Humans become 'accidental' intermediate hosts after consuming the parasite eggs, most often through food or water contaminated by infected human faeces. The larvae can encapsulate anywhere in the body, but are most commonly found in the muscles, eyes or brain. The larvae invade the nervous system causing NCC, the most severe form of the disease.[2] NCC is considered a worldwide public health problem and is not limited to endemic areas such as India, Latin America, Southeast Asia, China and Nepal.[1]

CASE PRESENTATION

A 45-years-old woman with history of 4 minutes episode of tonic-clonic seizure 30 minutes before go to the emergency department (ED). There is a history of 2 weeks of progressive headache and fevers with 3 days of acutely worsening headache, nausea and vomiting. Approximately 4-6 weeks earlier, the patient had begun to experience mild headache and fatigue. At the time of presentation, the headache was throbbing in nature and localised to the right posterior head. She denied visual changes, hallucinations, focal weakness, problems with coordination and difficulties with ambulation. The patient had no history of epilepsy, chronic cough, chronic diarrhea, weight loss or decreased appetite and had no history suggestive of diabetes, hypertension or tuberculosis. She was born and lived in East Nusa Tenggara and work as a farmer in

Kupang. She had not recently consumed raw or undercooked foods.

On physical examination, the patient was alert, conscious and cooperative, with a Glasgow coma scale of 15/15. Her temperature was measured at 36.7°C, heart rate was 75 bpm and blood pressure was normal. Neurological and fundoscopic examinations were normal, with no signs of meningeal irritation. Cranial nerves were intact, motor strength: within normal limits, sensory within normal limits, physiological reflexes within normal limits and Babinski reflexes is positive in left lower extremity. Sensory examinations were normal.

Initial laboratory evaluation revealed a white cell count (WCC) of 8.4×109 cells/L with neutrophilic predominance (6.19×109 cells/L), normal eosinophil count (0.08×109 cells/L) and normal basophils count (0.04×109 cells/L). Haemoglobin was 12.9 g/dL, sodium 140 mmol/L, serum creatinine 0.64 mg/dL and urea nitrogen was 13 mg/dL. Chest X-ray and electroencephalography study were normal. The patient refused to receive a lumbar puncture. An initial head CT contrast revealed abnormal hyperdense lesion with multiple calcification density in the right thalamus with the largest size being 1.2 cm which looks stung with contrast enhancement.

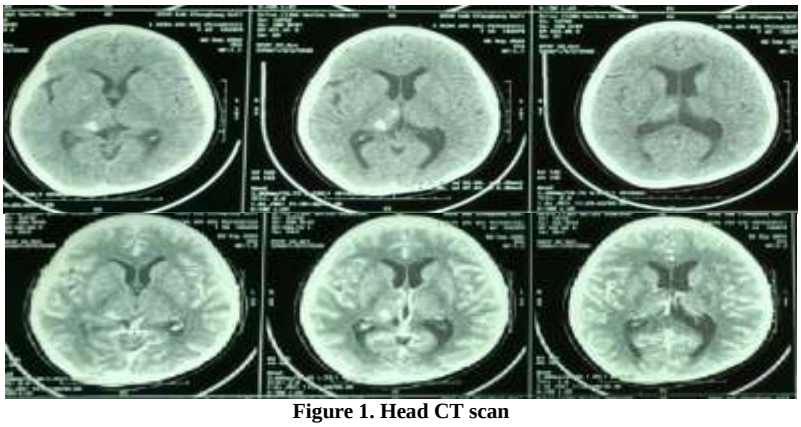

Figure 1. Head CT scan

Treatments for this patient is infusion NaCl 0,9% 1500mg/24 hours, albendazole 15mg/kg/day for 2 weeks, phenytoin injection 3x100mg for the seizure, dexamethasone injection 3x10mg and omeprazole injection 2x40mg. The author reports a case of NCC from East Nusa Tenggara who presented with generalized tonic–clonic seizure. This case argues that NCC should be considered as a differential diagnosis in patients presenting with seizures, even if the patient does not have initial symptoms indicative of NCC and resides in an area where the condition is rarely reported, and especially if the patient is from a disease-endemic country.

DISCUSSION

NCC is the most common brain parasitic infection, with an increasing prevalence outside endemic areas such as Latin America, Asia, and sub-Saharan Africa.[2] Neurocysticercosis is the most common helminthic infection of the central nervous system worldwide and contributes to 30% of epilepsy in endemic countries. Common causes of this infection include eating undercooked food, especially pork, water contaminated with *T. solium* or undercooked vegetables, and poor hygiene habits.[1] Notably, there is significant variability among the stages of cyst development in NCC patients who are asymptomatic.[3] Calcified lesions of NCC, which often develop late in the disease, are more likely to be associated with seizures than any other larval stage.[4] Although the mechanism underlying convulsions in NCC is still poorly understood, it has been hypothesized that these seizures are related to the inflammatory response associated with cystic degeneration.[4]

Recognition of NCC in the acute setting is complicated by clinical polymorphisms and the incubation period after exposure, which can persist for many years. This case highlights the diagnostic challenge associated with this emerging infection, which can manifest outside of endemic regions without a clear exposure history.

Most cases of NCC are asymptomatic; however, the clinical presentation can be very variable depending on the number, location and size of calcified cysts. The patient's immune status also plays a role in the clinical presentation of NCC. Convulsions were considered the most common presentation, followed by severe and persistent headache.[5] Focal neurological signs typically follow a subacute course similar to other space-occupying lesions. Less commonly, acute focal deficits can occur when inflammatory changes in penetrating arteries result in ischaemic stroke.[6] Signs of increased ICP occur in over 10% of patients. All other manifestations, including chronic meningitis, encephalitis, vision changes, nerve root pain, or sensory changes, occurred in <10% of patients.[7] In this patient's case, her history of seizures and episodic headache could be attributed to parenchymal lesions distal to the NCC, particularly from neuroimaging calcifications. In addition, cyst calcification, which produces periungual edema, can significantly affect the duration of infection. The form of NCC varies in severity depending on the location of the lesion (intraventricular, subarachnoid or spinal).[8] The subarachnoid larva, responsible for a rare but serious form of the disease, may have a typical scolex form or a less obvious racemose form, consisting of multiple agglomerated membranes. The giant form may consist of a cluster of sacs and membranes or a single large cyst, usually located in a sylvian fissure.[8]

Established methods for the diagnosis of NCC include detailed clinical examination, serologic testing, and neuroimaging. Each method has advantages and disadvantages, some of which are more effective in diagnosing NCC infections at different stages (cystic, cystic calcification). Definitive classification provided by Del Brutto et al. (Table 1), and Carpio et al. (Table 2).[9,10]

Definitive
- Histological demonstration of the parasite from biopsy of a brain or spinal cord lesion
- Evidence of cystic lesions showing the scolex on neuroimaging studies
- Direct visualization of subretinal parasites by fundoscopic examination

Neuroimaging criteria:
Major neuroimaging criteria:
- Multilobulated cystic lesions in the subarachnoid space
- Typical parenchymal brain calcifications

Confirmative neuroimaging criteria
- Resolution of cystic lesions after cysticidal drug therapy
- Spontaneous resolution of single small enhancing lesions
- Migration of ventricular cysts documented on sequential neuroimaging studies

Minor neuroimaging criteria
- Obstructive hydrocephalus (asymmetric or asymmetric) or abnormal enhancement of basal leptomeninges

Clinical/exposure criteria
Major
- Evidence of lesions highly suggestive of neurocysticercosis on neuroimaging studies
- Positive serum immunoblot for the detection of anticysticeral antibodies or cysticeral antigens by well-standardised immunological tests
- Resolution of intracranial cystic lesions after therapy with albendazole or praziquantel
- Spontaneous resolution of single small enhancing lesions
- Cysticercosis outside the central nervous system
- Evidence of contact with *T. solium* infection

Minor
- Evidence of lesions compatible with neurocysticercosis on neuroimaging
- Presence of clinical manifestations suggestive of neurocysticercosis
- Positive CSF ELISA for the detection of anticysticeral antibodies or cysticeral antigens
- Evidence of cysticercosis outside the central nervous system
- Individuals coming from or living in an area where cysticercosis is endemic

Epidemiological
- Individuals coming from or living in an area where cysticercosis is endemic
- History of travel to disease-endemic areas
- Evidence of household contact with *T. solium* infection

Degrees of diagnostic certainty
Definitive
- Presence of one absolute criterion
- Presence of two major plus one minor and one epidemiological criteria
- Two major neuroimaging criteria plus any clinical/exposure criteria
- One major and one confirmative neuroimaging criteria plus any clinical/exposure criteria
- One major criterion plus two clinical/exposure criteria (including at least one major clinical/exposure criterion) together with the exclusion of other pathologies producing similar neuroimaging findings

Probable
- Presence of one major neuroimaging plus two minor clinical/exposure criteria
- Presence of one major plus one minor and one epidemiological criterion
- Presence of three minor and one epidemiological criterion
- One minor neuroimaging criteria plus at least one major clinical/exposure criteria

Diagnostic criteria from 2001 (in black) and changes from Del Brutto et al. (2017) (in red). Criteria moved or deleted from the original are in blue. CSF, cerebrospinal fluid; ELISA, enzyme-linked immunosorbent assay.

Table 1. Diagnostic criteria by Del Brutto [6]

Parenchymal neurocysticercosis

Definitive parenchymal neurocysticercosis, one of the following:

1. Parenchymal cyst with pathological diagnosis
2. Single or multiple active parenchymal cysts, with at least one cyst with scolex on CT or MRI
3. Multiple parenchymal vesicles without scolex associated with at least one of the following:
   a. Seizures: focal or generalized tonic–clonic
   b. Positive serum or CSF immunological test (ELISA, EITB)
4. Any combination of the parenchymal cysticercus in different evolutive stages: vesicular with or without scolex, degenerative (colloidal or nodular), and calcified

Probable parenchymal neurocysticercosis, one of the following:

1. Single parenchymal calcification or vesicle (without scolex) or degenerating cyst(s), establishing differential diagnoses with other etiologies, associated with at least two of the following:
   a. Seizures: focal or generalized tonic–clonic
   b. Subcutaneous or muscle cysts location confirmed by biopsy
   c. Positive serum or CSF immunological test (ELISA, EITB)
   d. Plain X-ray films showing "cigar-shaped" calcifications
   e. Individual who lives or has lived in or has traveled frequently to endemic countries
2. Multiple parenchymal calcifications in an individual who lives or has lived in or has traveled frequently to endemic countries and in whom clinical state excludes other etiologies of calcifications

Extraparenchymal neurocysticercosis (intraventricular/basal subarachnoid)

Definitive extraparenchymal neurocysticercosis, one of the following:

1. Extraparenchymal cyst with pathological diagnosis
2. One or more extraparenchymal cysts on MRI special sequences with scolex in at least one of them
3. One or more extraparenchymal cysts on MRI special sequences without scolex associated with at least two of the following:
   a. Hydrocephalus
   b. Inflammatory CSF
   c. Positive CSF immunological test (ELISA, EITB)
   d. Presence of single or multiple calcifications or parenchymal vesicular or degenerative cyst

Parenchymal and extraparenchymal neurocysticercosis

Combination of the above definitive parenchymal and definitive extraparenchymal criteria

CT, computed tomography; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; ELISA, enzyme-linked immunosorbent assay; EITB, enzyme-linked immunoelectrotransfer blot.

Table 2. Definitive diagnostic criteria for symptomatic neurocysticercosis by Carpio et al.

A definitive diagnosis is rarely achieved and is only made by autopsy, biopsy, or visualization of the scolex specifically on imaging.[5] In most endemic countries, CT is done and is usually diagnostic, although it may miss posterior fossa lesions. MRI is more sensitive than CT in detecting scolex and in diagnosing extraparenchymal NCC. It can sometimes miss small calcified lesions.[11] Neuroimaging can determine the location and stage of the lesion. The appearance of parenchymal cysts progresses from no enhancement (if the lesion is alive with little host inflammatory response) to ring enhancement (when the cyst degenerates and activates an immune response) to nodules. calcified or completely gone.[5] CT is more sensitive for the most common lesions (calcifications) and is more widely available in endemic countries, but MRI is more sensitive for all non-calcified forms of the disease.

There are four main stages (also known as Escobar's pathological stages) : vesicular stage, colloidal vesicular stage, granular nodular stage, nodular calcified stage. vesicular stage, colloidal vesicular stage, granular nodular stage are 3 active stages of NCC and the calcified nodular stage is an inactive stage. In the vesicular stage, parasite (scolex) is viable with intact membrane and therefore no host reaction. In the colloidal vesicular stage, parasite dies within 4-5 years, untreated or earlier with treatment and the cyst fluid becomes turbid. As the membrane becomes leaky edema surrounds the cyst. This is the most symptomatic stage. In the granular nodular stage, edema decreases as the cyst retract further; enhancement persists. The nodular calcified is end-stage quiescent calcified cyst remnant with no edema.[12]

Serological methods can detect specific anti-*T. solium* antibodies or *T. solium* antigens in blood, urine, and CNS.[13] The enzyme-linked immunoelectrotransfer blot (EITB) is preferred due to the high specificity (100%) and sensitivity (94–100%), if performed on serum. The EITB has much lower sensitivity for calcified cysts, particularly if a single lesion is present.[6] Another test that can be used is enzyme-linked immunosorbent assay (ELISA) detection of T. solium antibodies using crude or purified parasitic antigen extracts uses IgG as the target

immunoglobulin; however, Ab-ELISAs generally have a lower specificity and sensitivity of EITB.[14] In this patient, the diagnosis of NCC depends on brain imaging, which is expensive where there is no magnetic resonance imaging device (only CT scan) and patient do not have access to this examination. The head CT contrast of this patient shows us that is in the nodular calcified stage. As for the serology, the family and the patient refuse to receive lumbar puncture.

The goals of treatment for NCC include control of symptoms, eradication of parasites with antiparasitic drugs, and reduction of host inflammation. Seizures are typically responsive to first line antiepileptic drugs (phenytoin, carbamazepine or valproic acid).[9] The ideal duration of seizure prophylaxis is unknown, but expert consensus recommends treatment for at least 2 years after the last seizure, followed by dose reduction (except in patients with patient has a self-healing lesion without calcification).[15] Other therapies to consider for symptom relief include anti-inflammatory drugs, analgesics, and agents or interventions to control intracranial hypertension. Albendazole (at 15 mg/kg/day by mouth for 8–15 days) is slightly more efficacious than praziquantel (at 50–75 mg/kg/day by mouth for 15 days).[15] The ideal treatment regimen for a single lesion remains unclear, but antiparasitic therapies appear to slightly improve radiographic imaging and reduce seizure recurrence.[16] Experts recommend adjuvant corticosteroid therapy, a practice supported by preliminary studies showing that it reduces the recurrence of attacks and increases the likelihood of lesions resolving.[17] Dexamethasone (0.1 mg/kg/day) is the first-line treatment, initiated 1 day before antiparasitic therapy and continuing for 1–2 weeks followed by a slow tapering off.[18]

Declaration by Authors

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