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Case Report

Neurocysticercosis

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Neurocysticercosis (NCC), caused by the larval stage (cysticercus/cysticerci) of the tapeworm, *Taenia solium*, is one of the common parasitic diseases of the nervous system in human and constitutes a major public health problem. *T. solium* completes its lifecycle in pigs and humans.[1,2] The definitive host of *T. solium* is human who get the infection by eating pork contaminated with cysticerci, whereas the intermediate host is a pig that becomes infected by ingesting eggs or gravid segments of *T. solium* released from patients harboring adult tapeworms of *T. solium*.[2-4] Encystment of larvae can occur in almost any tissue. The most common location is the central nervous system (CNS) and known as NCC.[1,3,4]

The incidence of cysticercosis is increasing in developing countries. This disease is the main cause of neurologic disease in most non-moslem developing countries.[5] From various studies of autopsies in Mexico, NCC was discovered in 2.4-3.2% of adults and 0.5% of children.[6] In Asia, it has a focal distribution in China, India, Pakistan, and the Philippines. In Indonesia, the main endemic area with prevalent taeniasis/cysticercosis are Irian Jaya (42.7%), Bali (7.1%), Flores and Timor (7%), Northern Sumatera (2%), Lampung (1%), and Northern Sulawesi (0.4%).[7,8] This disease affects both sexes equally, occurs most frequently between the age of 20 and 50 years old, and in children, the mean age was 10 years, although manifestation could be detected since infancy[6,9]

The clinical manifestations of NCC depend on the number and localization of the cysts and the host immune response. Seizure is the most common clinical symptom occurring in 30-92% of patients with parenchymal cysts. Cysts may also be asymptomatic.[1,3,5] NCC should be suspected in patients coming from endemic areas with persistent headache or seizure, particularly in young adults. The varied presentations of NCC warrant different therapeutic approaches.[1,4,5] Since most forms of the disease are self-limiting, drug therapy of NCC is still controversial. Prevention of NCC depends on general, personal, food, and meat hygiene.[2,3]

In this paper we report a case of NCC in an 11-year old Balinese boy.

The case

DWS, an 11-year old Balinese boy came to the Outpatient Clinic, Department of Child Health, Sanglah Hospital of Denpasar on February 19, 2003 with a chief complaint of headache. This complaint had persisted for 6 months, and the symptom increased in the last one month. He suffered from frontal headache every morning when he woke up, without nausea and vomiting. Because of this, he often took analgesics (Paramex®). No complaint of abdominal pain, itchy on the anal region, and spontaneous excretion of flattened segments of *T. solium* per rectum. There was no history of trauma, fever, prolonged

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rhinorrhea, seizure, tachycardia, or disorders of activity or mental state. The patient often consumed undercooked pork/the traditional Balinese food called "lawar". The family had neither history of similar disease nor excretion of worm segments.

On physical examination, he looked alert, the blood pressure was 100/60 mmHg; pulse and heart rate were 92 beats/minute, equal, and regular; respiratory rate was 20 breaths/minute, and the body temperature was 36.5°C. The body weight was 55 kg and height was 138 cm. Body Mass Index for age Z score belonged to overweight (>2 SD to <3 SD).

The head circumference was 52 cm (within normal limits). There were no signs of anemia, jaundice, strabismus, and nystagmus on eyes examination. The pupil reflexes were positive and isocoric. The ENT and mouth were normal. No nodule was palpable on buccal mucosa. Neck stiffness was negative.

On inspection of the chest, there was no precordial bulging; ictus cordis was not visible, palpable at the fifth intercostal space and left mid-clavicular line and was not forceful. On auscultation, the first and second heart sounds were normal and no murmur was heard. The breath sound was vesicular, without rales, friction rubs or wheezing. Bowel sound was normal. The liver and spleen were not palpable. There was no muscle hypertrophy throughout the body. On examination of the extremities, the power, tones and reflexes were normal.

Based on the clinical manifestations, a working diagnosis of observation of chronic cephalgia was made. The differential diagnoses were space-occupying lesion on the central nervous system, chronic sinusitis, and lipid profile disorder.

The results of blood investigation were as follow: leukocyte count was 8330/μl with differential count of neutrophil was 4880/μl (58.6%), lymphocyte 2620/μl (31.5%), monocyte 340/μl (4.1%), eosinophil 460/μl (5.6%), basophil 30/μl (0.4%); hemoglobin 12.8 g/dL, hematocrit 35.0%, MCV 82.3 fl, MCHC 35.7 g/dL; and platelet count 334,000 K/μl. The lipid profile revealed total cholesterol level of 144 mg/dl, trygliceride 95 mg/dl, high-density lipoprotein 49 mg/dl, low-density lipoprotein 85 mg/dl. Electroencephalographic examination was in normal limit. Head CT scan examination showed small hyperdense areas on the frontal, right and left parietal regions, and vertex which also enhanced on contrast, which led to a conclusion of parasitic cyst (cysticercosis). The patient was consulted to the Department of ENT on March 3, 2003, but there was no sign of sinusitis. The patient was also consulted to the Department of Ophthalmology to evaluate the presence of ocular cysticercosis, but no sign of ocular cysticercosis was found.

From clinical manifestations, laboratory, and CT scan examinations, neurocysticercosis (NCC) was then established.

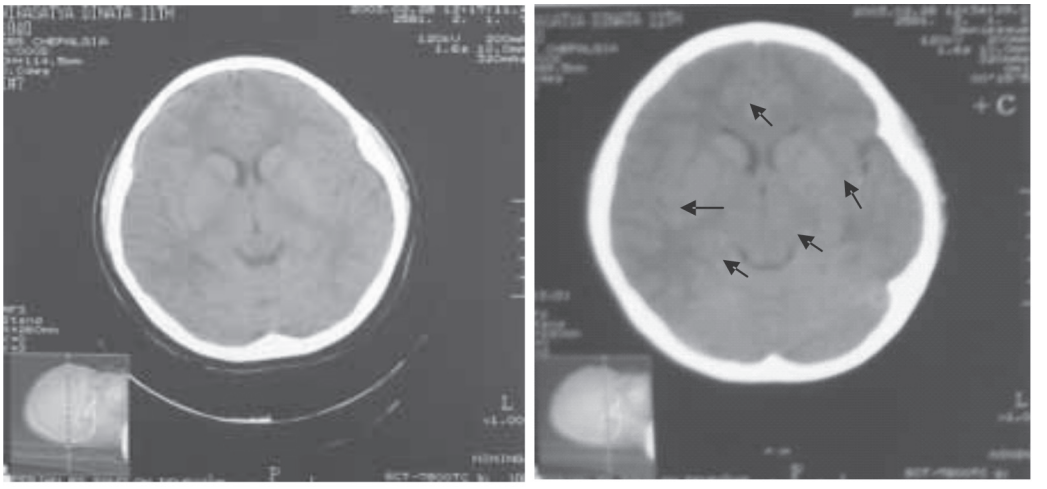

Figure 1. First head CT scan showed small hyperdense areas on the frontal, right and left parietal regions (left), which was also enhanced with contrast (right)

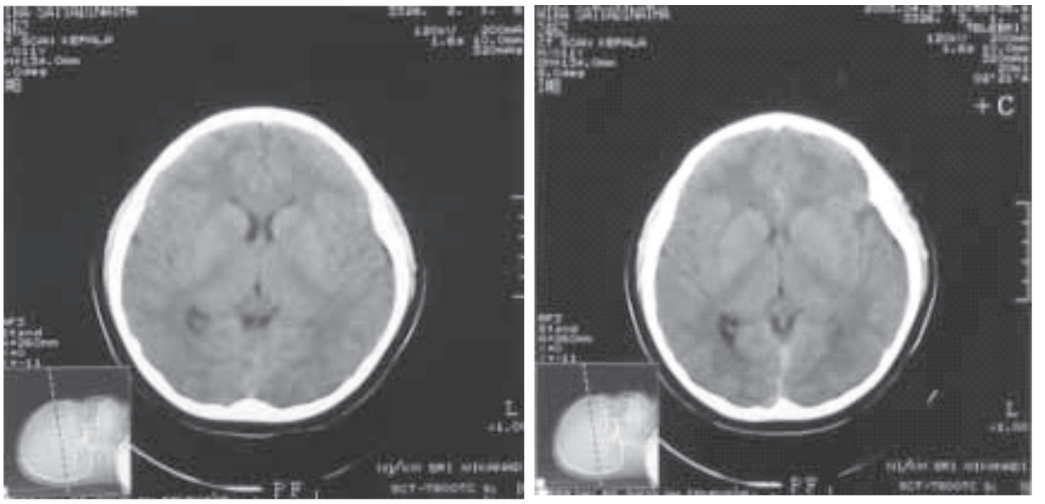

Figure 2. Head CT scan reevaluation 2 months after treatment showing no cyst and calcification

On March 6, 2003 the patient was admitted for evaluation and treatment. The patient was then consulted to the Department of Neurosurgery, there was no surgical intervention needed. The patient was managed conservatively with praziquantel 900 mg 3 times a day (50 mg/kg/day) for 2 weeks. Steroid (prednison) was administered 20 mg 3 times a day, started 3 days before the praziquantel administration. The stool examinations were done every 3 days after the administration of praziquantel; ova and proglotids of *T. Solium* were not found. During hospitalization, there was no history of seizure, but he suffered from severe headache on the fourth day. On day 7, the headache attenuated and on March 12, 2003 he was discharged and followed up at the outpatient clinic.

For screening, stool of family members was examined after the administration of a single dose praziquantel 10 mg/kg. The results of these examinations showed that his father had positive ova and proglotids of *T. solium*. Two months after treatment, there was no complaint of headache and the patient's physical activities were normal. The patient no longer consumed pork and followed our suggestion to eat thoroughly rinsed vegetable and well-cooked meat. Head CT scan reevaluation showed no cyst and calcification.

Discussion

Human is the only known host harboring the adult cestode parasite, *Taenia solium,* in the intestine. Infection is acquired by ingesting undercooked pork infected with *Taenia* larvae (i.e., cysticerci). The cysticerci evaginate into the intestines where they mature into adult worms. The worm consists of a scolex, which attaches itself to the intestinal wall, and numerous proglottids i.e., segments. Proglottids and eggs are shed intermittently into the stool.

There are many symptoms of adult tapeworm infection including spontaneous discharge of flattened segments (proglottids) per rectum, abdominal pain, nausea, weakness, loss or decreased appetite, headache, constipation, dizziness, diarrhea, and pruritus ani. Abdominal pain and nausea occurred most commonly in the morning and were characteristically relieved by food.[2] In our patient, there were no signs and symptoms of adult tapeworm infection.

The intermediate host that is the pig, is infected by ingesting parasite eggs or proglottids containing eggs (i.e., porcine cysticercosis). The oncospheres escape from the eggs, penetrate the intestinal mucosa, migrate through the bloodstream, and lodge in the tissues. After weeks to months, they evolve into larvae that enlarge and mature into cysticerci. The life cycle is completed when human ingest pork contaminated with the cysts. Human cysticercosis is acquired after eating food contaminated with fertilized eggs excreted in the feces of *Taenia* carriers. In human, the most common route of infection is the ingestion of *T. solium* eggs from contaminated food. Rarely, autoinfection by fecal-oral route or regurgitation of gravid proglottids into the stomach from the intestines can happen.[1,3,10]

Some reports indicated that only 20% of patients with cysticercosis have a history of intestinal tapeworm.[2] Even though the yield is low, patient with NCC should have stool examinations for *T. solium*. Family members should also be screened.[2] In our case, because neither ova nor *Taenia sp*. were visible on repeated stool examination, it was impossible that autoinfection had occurred. The presence of positive proglottids and ova of *Taenia sp* in the father's stool strongly suggested that cross-infection had occurred.

Cysticerci may be found in almost any tissues. The most frequent location is the central nervous system (CNS), and less frequent in the skeletal muscle, skin, oral cavity, heart and eye.[1,2,10] In the central nervous system, *T. solium* is deposited in the cerebral parenchyma, meninges and spinal cord.[10] In our case, on CT-scan we found cerebral parenchyma cysticercosis.

Clinical manifestations of NCC are mostly variable and depend on the inflammatory response around cysticerci, size, number, and location of the cyst, and age of the patient.[4,5,9] It may remain asymptomatic during life and be incidentally discovered at autopsy. The time of onset of symptoms after infection may vary from less than a year to even up to 30 years.[4] The presence of viable, living cysticerci in the CNS usually does not cause symptoms. In contrast, inflammation around degenerating cysticerci may have severe consequences, including focal encephalitis, edema, and vasculitis.[1] Involvement of brain parenchyma is common. Ventricular and subarachnoid cysts are also found. NCC can cause a wide variety of clinical symptoms due to either a mass effect or, particularly in racemose disease, raised intracranial pressure.[1,10] Such various clinical features necessitate further investigations to make a diagnosis before treatment.[3] A study reported that approximately 80% of children diagnosed with NCC presented with seizures, mostly focal in nature. Increased intracranial pressure causes other common clinical symptoms including headache, nausea, and vomiting.[1] Less common presentations include hemiparesis, visual changes, progressive obtundation, sciatica (from cauda equina involvement), and sensory disturbances.[1] A study by Vanijanonta *et al*[11] found that the clinical features included epilepsy (80%), headache (56%), focal seizure (48%), and mild degree of dementia (16%). A study on 753 children in Chicago found that none presented with fever.[1] In our case, the patient came to the pediatric outpatient clinic because of his persistent headache for 6 months which increased in the last one month with unresponsiveness to pain medication. The location of the headache was on front of the head. On physical findings we did not find any specific neurologic disorders.

Laboratory studies of cysticerci only play an adjunctive role in the diagnosis of cysticerci. On blood investigation, peripheral eosinophilia usually is not present but sometimes the eosinophil may account for 10-15% of white blood cells.[1,2] Immunoserologic assays may be useful. Currently, the ELISA is the most frequently used diagnostic method to detect cysticercus antibodies in both serum and cerebrospinal fluid.[1,2] This test can be highly sensitive, but it may cross-react with other helminth antibodies, especially *Echinococcus*. The enzyme-linked immunoelectrotransfer (i.e., Western blot) has proven to be highly specific and sensitive, although sensitivity has been shown to decline when individuals have fewer than two parenchymal cysts.[1,2,12] In our patient, blood investigation showed no peripheral eosinophilia. We could not perform both ELISA and Western blot examination because there was no facility in the hospital.

On imaging studies, skull radiographs can be performed, though they are rarely helpful. Occasionally, separation of the cranial sutures can be observed, which indicates increased intracranial pressure; soft tissue radiograph may show calcifications of inactive cysts.[10,13] The only reliable standard for diagnosing NCC is pathologic confirmation through biopsy or autopsy[10] despite the obvious morbidity (and possibly mortality) associated with this procedure. Nevertheless, even without definitive scientific data, CT scan and MRI are considered to be the main tools for the diagnosis of NCC.[1,10] Multiple calcifications disseminated in the parenchyma accompanied with viable cysts and transitional stage lesions is the typical finding of imaging studies in NCC.[10,13] The relation between imaging studies and the anatomopathologic changes had been well described. It can be summarized with the following recommendations:[10] (1) Brain CT scan should be obtained as a first imaging study. CT is more widely available, less expensive, and has a faster imaging time than MRI; contrast and noncontrast studies should be obtained. (2) Non-contrast studies will show calcification of inactive cysts, which is the most common disease

form at presentation. (3) Contrast studies will show ring enhancement, signifying edema surrounding the involuting live cysticercus.

In our patient, the first head CT scan examination showed small hyperdense areas on the frontal, right and left parietal regions, and vertex, which were also enhanced on contrast.

Although NCC is a common helminthic infection of the CNS but its diagnosis remains difficult. Clinical manifestations are non-specific, most neuroimaging findings are not pathognomonic, and some serologic tests have low sensitivity and specificity. Del Brutto *et al*[14] proposed diagnostic criteria for NCC based on objective clinical, imaging, immunologic, and epidemiologic data.

Interpretation of these criteria permits two degrees of diagnostic certainty:[14] 1) *definitive diagnosis*, in patients who have one absolute criterion or in those who have two major plus one minor and one epidemiologic criteria; and 2) *probable diagnosis*, in patients who have one major plus two minor criteria, in those who have one major plus one minor and one epidemiologic criteria, and in those who have three minor plus one epidemiologic criteria.

In our patient, the definitive diagnosis was established because we found two major criteria including lesions highly suggestive of NCC on CT scan and resolution of intracranial cystic lesions after praziquantel treament; one minor criterion that is clinical manifestations suggestive of NCC; and one epidemiologic criterion i.e., evidence of a household contact with *T. solium* infection/living in an endemic area of cysticercosis. It is known that Bali is an endemic area for cysticercosis/ taeniasis.

Once NCC is diagnosed, treatment may be necessary.[5] Anthelminthic agents are the mainstay of definitive treatment. Controversy exists as to whether or not antiparasitic treatment is necessary. Therapy is recommended for children with active cyst or ring-enhancement lesions. Many believe that it is preferable to treat all children rather than waiting for the natural resolution of the cyst, although some studies recommended that children should be treated only if they are symptomatic.[1,2] In the encephalitic or disseminated forms, cysticidal therapy must be used with great caution for fear of the effects of accelerated brain inflammation.[1,5]

Drug therapy is less effective for chronic arachnoiditis. NCC is treated with praziquantel 50 mg/kg/day in three divided doses for 14 days. Controlled studies showed that it was successful in reducing the number of cyst and CNS symptoms.[9,11] The mechanism of action is by increasing cell membrane permeability in susceptible worms resulting in loss of intracellular calcium, massive contractions, paralysis of musculature, vacuolization, and disintegration of schistosome tegument.[2] This is followed by the attachment of phagocytes to parasite and death.

About 2-3 days after treatment, a strong inflammatory reaction may be initiated with increased protein and cells in the CSF, edema around the lesions, and worsening of symptoms such as headache. This process lasts for 2-3 days, but can be suppressed with steroid i.e., prednisone, 1-3 mg/kg/day, started 2 to 3 days before therapy.[9] Clinical improvement is seen 2-3 months after treatment.[1,9,11] For this reason NCC should be assessed by follow-up imaging. Finally, repeating the CT scan or MRI can clarify the diagnosis.[10] Albendazole given for eight days has also been used as treatment.[2,3] However, it is usually not used in combination with steroid because steroid may decrease the effectiveness of the drug.[1]

Surgical treatment should be restricted to the removal of parasites located in the subarachnoid (racemose form) or ventricular area and to ventriculoperitoneal shunting for the treatment of decompensated hydrocephalus. Surgery should not be considered for parenchymal cysts without regard to location, size, or stage of evolution, because this form of NCC can be controlled only by symptomatic treatment (or presumably by etiologic treatment).[1,10] In addition, surgical sequelae could result in more brain damage than the parasite itself. In our patient, praziquantel 900 mg three times a day (50 mg/kg/day) for 2 weeks and prednison 20 mg three times a day started 3 days before praziquantel therapy were given. Clinical improvement occurred on day 7. The patient did not need neurosurgical intervention. CT scan reexamination was done about 2 months after the treatment and the result was negative for cyst and calcification.

Mortality from cysticerci is minimal and generally limited to cases complicated by encephalitis, increased intracranial pressure secondary to edema, and/or hydrocephalus and cerebrovascular accidents.[1] In simple NCC, prognosis is excellent.[1,2] Treatment with anthelminthics results in complete

resolution or significant regression in 80-90% of patients.[2] Usually, seizures are easy to control, and most children can be weaned from their anticonvulsants within 1-2 years.[1] The majority of children remain free of seizures. In our case, the patient had a good prognosis.

References

1. Kossof EH, Kumar A, Konop R, Barton LL, Tolan RW, Steele R. Neurocysticercosis. Available from: URL: http: www.emedicine.com/ped/topic 1573.htm.
2. Wittner M. Taeniasis and cysticercosis. In: Rudolph AM, Hoffman JIE, Rudolph CD, Sagan P, editors. Rudolph's pediatrics. 20th ed. Stamford Plaza: Prentice Hall International; 1996. p. 734-37.
3. Blanoton R. Cestodiasis. In: Behrman RE, Kliegman RM, Arvin AM, editors. Nelson textbook of pediatrics. 15th ed. Philadelphia: WB Saunders; 1996. p. 993-5.
4. Singhal BS, Ladiwala U, Singhal P. Neurocysticercosis in the Indian context (with special reference to solitary parenchymatous cyst). Neurology India [serial online] 1997 Jul-Aug. Available from: URL: http://www.Neurologyindia.com/vol45-4/laravi 001.shtml.
5. Commentaries: controversies in the management of cysticercosis. Emerg Infect Dis 1997;3:1-3
6. Aguilar RF. The profile of neurocysticercosis in Mexican children [abstract]. Available from: URL: http:// www.imbio-med.com.mx/Circiruj/Ccv66n3/ english/ Zcc83-02.html.
7. Sutisna P, Fraser A, Kapti N, Rodriguez-Canul R, Widjana DP, Craig PS, *et al*. Community prevalence study of taeniasis and cysticercosis in Bali, Indonesia. Trop Med Int Health 1999;4:288-94.
8. Margono SS, Subahar R, Hamid A, Wandra T, Sudewi R, Sutisna P, *et al*. Cysticercosis in Indonesia: epidemiological aspects. Southeast Asean J Trop Med Public Health 2001;32:79-84.
9. Weiss LM, Wittner M. Cysticercosis. In: Gellis SS, Kagan BM, editors. Current pediatric therapy. 13th ed. Philadelphia: WB Saunders; 1990. p. 585-6.
10. Carpio A, Ugalde J, Lorenzo N, Hulihan JF, Talavera F, Thomas FP, *et al*. Neuroimaging in neurocysticercosis. Available from: URL: http:// author.emedicine.com/ NEURO/topic 654.htm.
11. Vanijanonta S, Bunnag D, Riganti M. The treatment of neurocysticercosis with praziquantel. Southeast Asean J Trop Med Public Health 1999;16:275-78.
12. Theis JH, Goldsmith RS, Flisser A, Koss J, Chioino C, Plancarte A, *et al*. Detection by immunoblot assay of antibodies to *Taenia solium* cysticerci in sera from resident of rural communities and from epileptic patients in Bali, Indonesia. Southeast Asean J Trop Med Public Health 1999;25:464-68.
13. Ong S, Talan DA, Moran GJ, Mower W, Newdow M, Tsang VCW, *et al*. Neurocysticercosis in radiographically imaged seizure patients in US. Emergency Departments. Emerg Infect Dis 2002;8:608-13.
14. Del Brutto OH, Rajshekhar V, White AC Jr, Tsang VCW, Nash TE, Takayanagui OM, *et al*. Proposed diagnostic criteria for neurocysticercosis. Am Acad Neurol 2001;57:177-83.