Neurocysticercosis in central Saudi Arabia

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ABSTRACT

Neurocysticercosis is a disease endemic in pork breeding societies. It exhibits itself by the sudden development of seizures in an apparently healthy individual, a rather nonspecific symptom. In its own cultural circles, diagnosis is easy because of the higher incidence and prevalence of the ailment. However in cultures whose religion excludes the breeding of pork, such as Islamic countries, diagnosis depends on an often forgotten spiritual history, which we believe may have a place as the fourth epidemiologic criterion in the revised diagnostic criteria for neurocysticercosis.

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Neurocysticercosis (NCS) is not only the most common helminthic infection of the central nervous system (CNS), but also the single most common cause of acquired epileptic seizures in the developing world.[1,2] The encysted larval stage of the tapeworm *Taenia solium* was thought to have infested about 20 million people worldwide in a 1983 World Health Organization survey, with more than 1000 cases per year in the USA.[1] No information is available for Saudi Arabia which suffers from imported cases.[3] Here we present a typical case of NCS in a patient from the Indian subcontinent, the difficulties in its diagnosis, management and the benefits of careful history taking, including the often forgotten spiritual history.

Case Report. A 40-year-old Indian male presented to the accident and emergency department of Riyadh Medical Complex, Riyadh, Kingdom of Saudi Arabia after experiencing tonic-clonic convulsions followed by vomiting and culminating in irritability over a 12 hour period. His attendants informed us that he had come from India only 3 months ago. On initial physical examination his vital signs showed a temperature of 38.5 degrees celsius, a pulse of 88 beats/minute, respiratory rate of 22/minute and a blood pressure of 140/90 mm Hg. He was semiconscious, irritable and moving all limbs. There was no apparent injury to the head. No neck stiffness was found, and the right pupil was aphacic, the left one normal. Funduscopy did not reveal papilledema or other abnormalities. The neurological exam revealed a normal tone, power 3/5 and normal reflexes in all limbs. There was no clonus and the plantar responses were normal. He reacted to painful stimuli with withdrawal of the limb, but a formal test of his sensory system could not be carried out. Examination of the cardiovascular, respiratory and gastrointestinal systems, and the musculoskeletal system were normal. In the genitourinary system, it was noted that the patient was uncircumcised and had urinated involuntarily. Urinalysis revealed: 1+ glucose, 1+ acetone, 1+ bacteria. The patients generalized seizures needed to be controlled with repeated doses of the benzodiazepine Valium 10 mg of which 3 were administered and subsequently phenytoin intravenously in the conventional dosage. His agitation required a total of 15 mg of haloperidol. Thereafter the patient was commenced on ceftriaxone 2 grams intravenously (IV) 12 hourly and acyclovir 10 mg/kg IV 8 hourly with the presumptive diagnosis of a meningoencephalitis with secondary generalized tonic clonic seizures and appropriate investigations

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were initiated. Computed tomography scan (CT) of the brain plain and with contrast showed multiple scattered calcifications in both cerebral hemispheres at the gray white matter junction with a rim of hypo density representing the wall of a cyst, no enhancement noted on contrast injection (**Figure 1**). The differential diagnosis now included among others a possible toxoplasmosis infection in a case of advanced human immunodeficiency virus infection (HIV), but no further history could be obtained until the third hospital day, when the patient became conscious and told us that in his home place many people were suffering from repeated seizures. This lead the attending physician to inquire about his spiritual history in view of the previously noted uncircumcised genitalia, and it was established that he was a practicing Hindu and that he breed and consumed pork. Re-examination of the patient in the light of this new information and with the possibility of a case of NCS in mind, the treating team found palpable sub-cutaneous masses over the chest wall, in the right forearm and in the right lower limb. These areas were x-rayed and subcutaneous calcifications were visible. An excisional biopsy of one of the lesions was requested. Laboratory investigations showed a full blood count with white blood cells of 20.6, hemoglobin of 14.9 and a platelet count of 198. The erythrocyte sedimentation rate was 33 mm/hour. The malaria films thin and thick were negative. Serum electrolytes revealed a sodium of 147 mmol/L, potassium 4.3 mmol/L, urea 4.64 mmol/L, creatinine 98.9 µmol/L, amylase 64 u/L, calcium 2.25 mmol/L, phosphate 0.7 mmol/L, magnesium 0.88 mmol/l. Liver function tests and lipid profile were normal. *Brucella abortus* and *melitensis* titers were negative, so were screens for hepatitis B and C, and HIV 1 and 2. The cerebrospinal fluid (CSF) examination revealed a clear fluid with a total cell count of 18 with 95% lymphocytes and 3% monocytes, and 2% neutrophils. The CSF glucose was 5 mmol/l and lactate dehydrogenase 24 U/L, with a total protein content of 38.7 mg/dl. The latex test for bacteria was negative. The CSF gram stain, acid-fast bacilli stain and India ink stain were negative, so were polymerase chain reaction test for tuberculosis and culture for bacteria, tuberculosis and fungi. The CSF titers for Brucella, toxoplasma, Ebstein-Barr virus, cytomegalovirus and herpes simplex virus were negative. The electrocardiogram revealed normal sinus rhythm. In the radiological investigations, a chest radiograph was unremarkable. An ultrasound exam of the abdomen revealed multiple gallbladder stones with an enlarged fatty liver of 16 cm span. Magnetic resonance imaging of the brain revealed small discrete round lesions in both hemispheres mainly in the cortical and subcortical regions, each of the lesions shows iso to hyperintensity on T1, surrounded by a fluid intensity with thin capsule. No significant en-

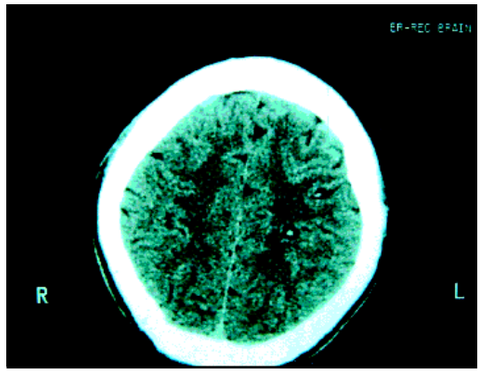

Figure 1 - Computed tomography scan of brain without contrast showing calcified lesions of neurocysticercosis.

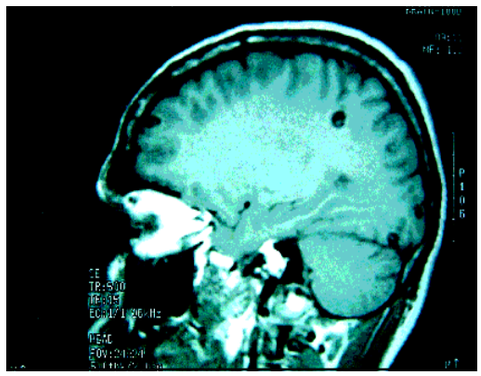

Figure 2 - Sagittal TI weighted magnetic resonance images of brain revealing multiple cysts of neurocysticercosis.

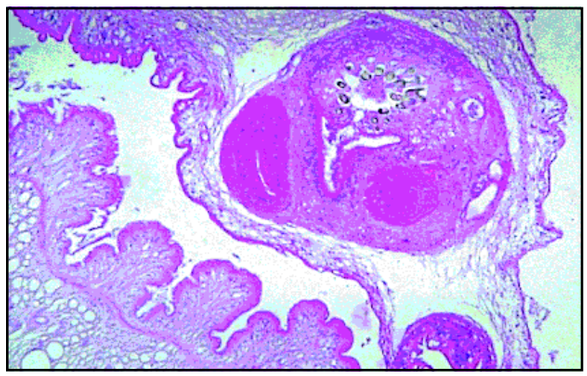

Figure 3 - Chest wall skin biopsy showing scolex equipped with suckers and hooks of cysticercus cellulosae.

hancement or perifocal edema was seen. The centers of most of the lesions show dot like calcifications as seen on the CT scan. The ventricles were normal in size, no gyral or cisternal enhancement. Two small nodular lesions which were hypo-intense on T1 (**Figure 2**) and hyper-intense on T2 were seen in the upper neck muscles on the right side and a similar lesion was seen under the scalp on the right occipital region. In conclusion, the lesion location and appearance suggest NCS representing vesicular as well as granulomatous stage. Excisional biopsy was reported as cysticercus cellulosae. (**Figure 3**). On the fifth hospital day the patient was started on dexamethasone 4 mg IV 8 hourly in conjunction with anti-helminthic therapy in the form of praziquantel 2400 mg per day for a total of 14 days, thereafter steroids were tapered off. The patient was returned to an active life, while on anti-epileptic medications, and subsequently was lost to follow-up.

Discussion. The larval stage of *Taenia solium* "the pork tapeworm" is called cysticercus cellulose and the corresponding infection in humans is known as cysticercosis cellulosae.[4] Rare in our society in Saudi Arabia, it is a common ailment in pork consuming nations, especially in the developing world, where it is the most common cause for acquired late-onset epilepsy, however, it should be noted that the real source of infection of cysticercosis for humans and pigs is the ingestion of food contaminated with human feces from *Taenia solium* carriers.[2,5] Once eggs of the parasite have been ingested, infective oncospheres expelled invade, within 2 hours, the sub-mucosal blood and lymphatic vessels and migrate to internal organs and become larval cysts which can locate anywhere in the body, but usually lodge in the brain, muscles or subcutaneous tissues.[2,3] The reason for these sites of predilection are not clear.[3] While modulating the host's immune mechanisms they evade destruction and mature in size in approximately 3 months.[2] Invasion of the nervous system is termed NCS, and is divided into parenchymal and extra-parenchymal NCS.[2,3] A racemous form occurs in the ventricles and basal cisterns, and although leading to the dissolution of the parasite is associated with abnormal growth of its cystic membranes, with a resultant inflammatory reaction leading to cases of hydrocephalus, which are difficult to manage.[2,3] Eventually, the parasite degenerates and calcifies, with or without clinical consequences for his host in the form of seizures, the only clinical manifestation in most patients with parenchymal NCS.[3] Depending on the number and location of the parasites and host’s immune response, various neurological syndromes have been described, including brainstem dysfunction, cerebellar ataxia, sensory deficits, involuntary movements, stroke-like symptoms, extra-pyramidal signs, and dementia.[2] Yet, cysticercotic encephalitis occurs mainly in woman and children.[6]

Our patient presented with the non-specific symptom of a generalized tonic-clonic seizure. In the absence of a history of head trauma, chronic illness, substance abuse and a known epileptic tendency the differential diagnosis of a tuberculoma among other space occupying lesions based on his country of origin was tempting. Using the country of origin as a tool to create a differential diagnosis is one way to approach a patient's complaint, identifying his religion is in our opinion an equally important tool. Our faiths not only convey a set of moral values but also influence how we live and what we consume. Therefore, we are prone to the illnesses of the lifestyles emerging based on our beliefs and an obvious example is the consumption of alcoholic beverages in non-Muslim countries and the consequent higher incidence of alcoholic liver disease as a cause for cirrhosis, while infectious causes prevail in the Middle East.[7,8] Different faiths dictate different forms of behavior, social interactions, and views about how we live and how we die.[9] For this reason, some medical educators have argued that religion is a clinical variable to be considered in every case, and that a "spiritual history" should become a regular part of the patient interview.[9]

In the case of our patient, inquiry into his spiritual history lead to the revelation of pork breeding and consumption and similar cases of seizures in his home village in India. It is known that cysticercosis is the cause of epilepsy in up to 50% of Indian patients presenting with partial seizures, and the most common symptom of NCS occurring in 70-90% of patients.[10] The spiritual history provided the clue to the diagnosis of NCS, only to be verified by the subsequent diagnostic investigations and a diligent physical re-examination to look for sub-cutaneous nodules. His CSF examination revealed a moderate mononuclear pleocytosis, higher than normal protein concentrations, with 0.38 g/l a little lower than the usual range of 0.5-2 g/l, and the expected normal glucose level.[3] The CSF can be tested for the presence of NCS antigens by an enzyme-linked immunosorbent assay (ELISA) and an electroimmunotransfer blot (EITB), so can the serum of patients with the disease.[3] These tests were not available to the treating team. When negative, however, the tests do not exclude the presence of NCS as more than 50% of cases diagnosed by CT scan brain test EITB negative.[2] In a study by a reference laboratory in Mexico it was found that EITB was more sensitive than the ELISA, especially when serum was tested and both were more sensitive in cases with multiple living cysts.[11] The CT scan and MRI brain examinations are proposed as absolute and major criteria and the most effective means in the diagnosis of NCS, un-fortunately, not available to the underprivileged

patient population in need of it.[1] Our patient demonstrated the typical calcifications on CT brain examination as well as nodular-granular stage of the disease in the MRI scan (**Figures 1 & 2**). X-rays of his thighs revealed calcified lesions in the subcutaneous tissues and biopsy of one of the chest lesions confirmed the presence of cysticercosis outside the CNS (**Figure 3**). Patients usually have multiple subcutaneous nodules that are firm, mobile and sometimes painful, occurring mainly on the trunk and extremities.[12]

Based on the proposed diagnostic criteria of del Brutto et al[1] with the neuro-imaging evidence as an absolute criteria and both cysticercosis outside the CNS and epidemiological evidence of residence in an endemic area as minor criteria, we had a case of definite NCS at hand. Treatment of NCS is a controversial issue. It is basically divided into control of complications of the illness with anti-epileptic medications and neurosurgery mainly involving shunt operations and eradication of the parasitic infestation with anti-helminthics, in conjunction with corticosteroids for the prevention of potentially dangerous intracerebral edema formation.[3] The reason for being a controversial issue is that lesions of NCS tend to heal spontaneously with few or no consequences to the host.[3] Arguments against treatment furthermore include the immediate risk from acute inflammation following death of cysts and increased scar tissue formation that might lead to worsened long-term prognosis of the underlying seizure disorder.[3,13] Four years ago one of the eminent experts in the field of NCS, Del Brutto et al pointed out the potential of NCS to cause cancer, stating the loss of regulatory mechanisms from immuno-modulation, transfer of parasitic genetic material to the host, and chronic inflammation leading to loss of tumor suppressor genes as possible mechanisms.[14] This aspect and results of a recent prospective trial indicate a benefit from treatment of this ailment, at least in reducing the number of seizures with generalization, in cases of viable parenchymal parasites.[13] In general treatment needs to be individualized, taking the number, location and viability of the lesions into consideration.[2] Our patient was treated with an anti-epileptic, corticosteroids and the anti-helminthic praziquantel since albendazole is not available to us. A dosage of 50 mg/kg/day for 2 weeks is adopted by most studies and even though it interacts with steroids. the parasiticidal effect is not affected, and single day regimens have been described.[2] With that regimen treatment was uneventful. Epidemiological data helps in the evaluation and diagnosis of suspected cases of NCS and have been included in the revised diagnostic criteria for NCS.[1] Currently they consist of: 1. Evidence of household contact with *Taenia solium* infection. 2. Individuals coming from or living in an area where cysticercosis is endemic. 3. History of travel to disease endemic areas.[1] As in our case the spiritual history gave an important diagnostic clue and in view of the vast numbers of workers of the Indian subcontinent which live in Islamic countries we believe that its addition to the diagnostic criteria proposed by Del Brutto et al might be warranted, to elucidate or consolidate suspicions of NCS based on religious beliefs and practices.

In the absence of the availability of vaccination and the recognition of NCS as a public health problem, education and public awareness of the real source of infection in conjunction with provision of the most basic assets of social development, form the major pillars of prevention of this illness.[3]

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