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NEUROCYSTICERCOSIS - A REVIEW WITH TWO CASE REPORTS

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Abstract : Neurocysticercosis is an endemic disease in India. It is the most common helminthic infection of the CNS and the most common cause of adult onset seizures worldwide. Rightly designated among 'neglected infections of poverty' by the CDC, this devastating disease has few case-control studies for management, less practical diagnostic criteria and lesser clear treatment guidelines. In this article we present 2 unusual presentations of neurocysticercosis. The first is a case of parenchymal neurocysticercosis with all stages simultaneously found in a single patient. The second is the rare subarachnoid variety with fatal outcome. We also review the pathogenesis, types and stages with radiologic-pathologic correlation, dilemmas in diagnosis and treatment and current trends in management of neurocysticercosis.

Keyword :neurocysticercosis, parenchymal, subarachnoid, taeniasis, cysticercosis, racemose

Introduction:

Neurocysticercosis(NCC) was first described by Rumler in 1558 when he found liquid filled vesicles adhering to the dura during the autopsy of a patient who died of seizures. In India it was first found by Armstrong in 1888 in Madras in a coolie who died of seizures. NCC is caused by the larva of Taenia solium(pork tapeworm). It is prevalent in unsanitary environment where there is contamination of food with human faeces. It is common in vegetarians also as against the common misconception that cysticercosis occurs only in pork consumers. Hence cysticercosis is a “biological marker of social and economic development” of a community (Carpio et al). 26.3% to 56.8% of adult onset seizures in developing countries is attributed to NCC (Del Brutto et al 2005). Rajaseker et al(2006) has reported a seizure prevalence of 3.83 per 1000 in a population based door-to-door community survey of 50,617 people from Vellore district in Tamilnadu. NCC was found in 28.4% of them by CT scan. The disease burden of NCC in India surpasses many other developing countries (Kashinath et al).

A 42 years female from from a poor socio-economic background from Arakkonam was brought with 5 episodes of new onset recurrent seizures over 12 hours. She did not regain consciousness after the 3 rd episode. Her daughter gave a history of holocranial dull aching headache in the patient for 2 months with occasional vomiting but without vertigo or tinnitus or blurring of vision. No weakness of limbs or sensory disturbances were reported. She had no significant past history and consumed mixed diet. Family history was significant in that her mother had recurrent seizures of adult onset for several years for which she had not taken treatment and had died of seizures 4 years ago. On examination the patient was drowsy and disoriented with GCS of 11/15 and stable vitals.

She had hypotonia of all 4 limbs with depressed deep tendon reflexes and bilateral extensor plantar. Pupils were normal in size and reaction and fundus showed mild blurring of disc margins bilaterally. The patient was immediately treated as per status epilepticus protocol.

A CT scan taken revealed multiple cysticerci in various stages throughout the brain.

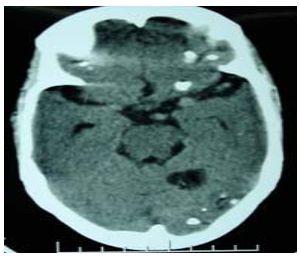

fig.1) NCC vesicular stage

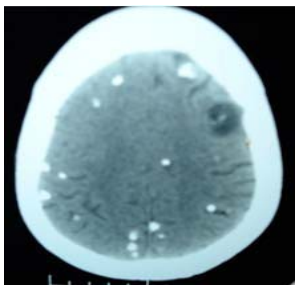

fig.2) NCC colloid stage

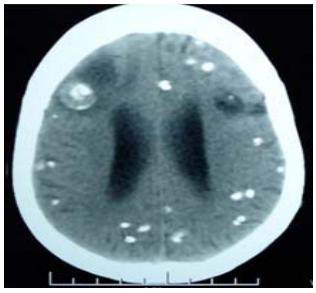

fig.3) NCC granular stage

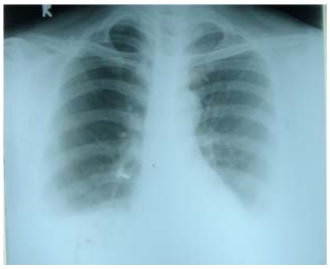

fig.4) Chest X-ray

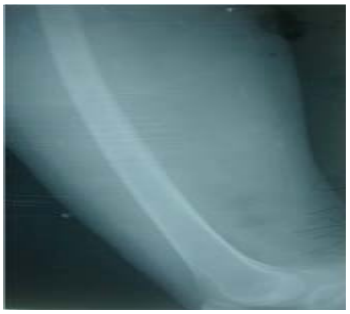

fig.5) X-ray soft tissue of thigh

X-ray of the chest showed a calcified lesion in left lung above aortic knuckle. (fig.4)

X-rays of the deltoid and thigh muscles revealed multiple rice grain calcifications.(fig.5) An ocular examination did not reveal any ocular cysticercus. Stool exam was negative for ova and parasites and occult blood. A detailed environmental and diet history was undertaken which revealed pig rearing in home for sacrificial slaughter and pork consumption during festivals.

A diagnosis of disseminated cysticercosis was made and patient was started on dexamethasone 8mg iv BD, albendazole 400mg PO BD, phenytoin 100mg iv TDS, ranitidine 50mg iv BD and calcium and vitamin supplements. The patient improved rapidly with steroids and regained full function in 24 hours.

Interesting aspects of this case:

- Clear history of adult onset seizures presenting as status epilepticus.
- Probable familial clustering from history of seizures in mother
- Environmental factor of pig rearing
- All stages of parenchymal NCC found in her brain Calcified cystcicerci in muscles and lung

Case 2:

A 32 years old male was diagnosed to have subarachnoid NCC at our centre after his first episode of seizure 3 years ago. MRI showed racemose NCC with cluster of grapes appearance. HIV serology was negative. He was treated with prolonged courses of albendazole 4 times over the 3 years. He was also given continuous anti-epileptic and steroid therapy and was on follow up in epilepsy clinic for recurrent seizures. But the patient stopped taking medications for the last 1 month. He developed headache with altered sensorium 1 week prior to admission at our centre for which he was admitted at a private hospital. He also developed paucity of movements in his left upper and lower limbs 3 days later which progressed to complete paralysis and he gradually lapsed into coma. He was referred in a comatose state after he developed status epilepticus. On examination patient was unconscious and hypotensive with GCS 5/15, absent movements in left side, bilateral papilledema and sluggish pupillary response and prominent neck stiffness. A CT was done which revealed persistent racemose subarachnoid NCC and a right MCA territory infarct in the corona radiata.

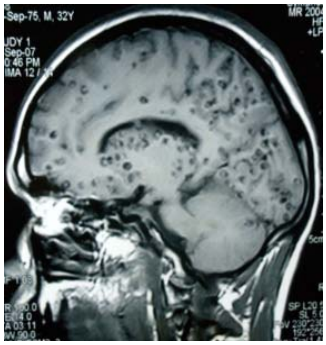

fig.6) Saggital view MRI showing subarachnoid NCC

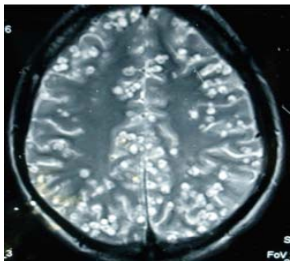

fig.7) T-2 MRI axial view showing Racemose NCC

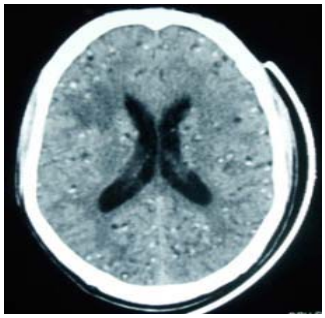

fig.8) Axial CT of racemose NCC with right corona radiata infarct

A diagnosis of subarachnoid meningoencephalitic NCC with vasculitic infarct was made and patient treated with dexamethasone 10mg iv and mannitol 1g/kg iv infusion. A ventriculo-peritoneal shunt was also planned. But we lost the patient before the procedure when he developed refractory seizures.

Interesting aspects of this case:

Rare variety of racemose NCC

Refractory to medical therapy with recurring lesions

Meningoencephalitic presentation

Rare complication of vasculitic infarct

Fatal nature of the disease

Discussion on Neurocysticercosis: The parasite:

Taenia solium is an intestinal cestode with complex life cycle with 2 hosts. Pigs are intermediate hosts. Porcine cysticercosis is endemic in areas where human faeces are accessible to pigs. Humans are the only definitive hosts and can develop two forms of disease – taeniasis and cysticercosis. · Humans acquire infection by eating undercooked pork meat infested with cysticerci and develop taeniasis. Humans harbour adult worms in the gut and release proglottids containing fertilised ova in faeces. · Human cysticercosis occurs from ingestion of ova with food contaminated with faeces or from auto-inoculation. The former is important in India as sewage irrigation is common in our country. Following consumption, the oncospheres penetrate the mucosa and the larvae disseminate in the body and form cysticerci. In humans cysticerci have been identified in the skeletal muscle, brain, eye, subcutaneous tissue and even lung. In most locations cysticerci spontaneously degenerate. The minority that invade the CNS develop into NCC. Incidental calcified granulomas are found in 10-20% of population. Hence symptomatic NCC patients represent only the tip of the iceberg of disease burden in the population.

Types of NCC:

Parenchymal
Extra-parenchymal
a. Sub-arachnoid
b. Ventricular
c. Spinal
d. Ocular

3. Mixed

Parenchymal NCC:

These are usually small, 1-2 cm lesions found in the cerebral cortex or cortex-subcortex junction areas. Some argue that "parenchymal" location of NCC is the cross-sectional view of subarachnoid NCC located deep in sulci or perforating branches in perivascular spaces (Uribe and Rabiela et al). Active parenchymal NCC is the most common form of NCC found in symptomatic patients. They may have radiologic evidence of parasite degeneration and inflammation. It has 5 patho-radiologic stages (Eric.T.Kimura et al). These stages are not found in subarachnoid and ventricular forms of the disease.

Non-cystic stage – The larva has not yet developed into a cyst. It is asymptomatic with no radiologic findings.

Vesicular stage – The stage of viable larval cyst without host response. They appear on CT as small and round well demarcated low density areas without peri-lesional edema and do not enhance. They have the pathognomonic 'hole-with-dot' or 'pea-in-pod' appearance. When found extensively , the brain can have a 'swiss cheese' pattern. The scolex may appear as a small 2-3mm isoattenuatting structure inside the lesion. The patient is asympto-matic. Fig.1 shows a cysticercus in vesicular stage in the left occipital lobe.

Colloid stage – It is the first stage of involution where the transparent fluid is replaced by viscous colloid. It represents the 'acute encephalitic phase' of NCC. CT shows ill-defined hypo or isodense lesion with perilesional edema which enhances on contrast administration. Symptoms start developing in patient in this stage. Fig.2 shows a colloid stage cysticercus in the left frontal lobe.

Granular stage – The scolex is no longer viable. The cyst wall thickens and becomes fibrotic and collapses. The lesion becomes thicker, has more edema and has thicker contrast enhancement. Also some specks of calcification appear. Fig.3 shows a granular stage cysticercus with calcified scolex and spotty calcifications in cyst wall with perilesional edema in the right frontal lobe

Inactive or calcified stage – Hyperattenuating calcific nodules represent burnt out end stage lesions without edema.

Figs 2 and 3 show multiple calcified cysticerci scattered throughout the brain giving a starry sky pattern.

Subarachnoid NCC:

In this devastating variety NCC are found in the fissures and basal cisterns. Cysts can enlarge to several centimetres forming giant cysticerci which can have mass effect. Multiple, grape like, clustered non-viable unencapsulated bladders which lack scolices form the racemose NCC. Hydrocephalus is the most common CT finding in this form. Ischemic cerebrovascular complications can occur. In a study of 28 patients with subarachnoid form of NCC 53% had angiographic evidence of middle or posterior cerebral artery occlusion (Barinagareementeria et al). Figs 6,7 and 8 show racemose NCC with fig.8 showing a complication of right corona radiata infarct.

Ventricular NCC:

They appear as lesions causing distortion of ventricular cavity which are isodense to CSF. They can be identified easier in MRI. Intermittent or persistent hydrocephalus features predominate. The cysts move with changes in patient's head position – ventricular migration sign in MRI.

Range of Clinical Presentations in NCC:

Factors influencing the presentation in NCC
Number of lesions
Location of lesions

Stage of development or involution

Intensity of host inflammatory response

Recently host genetic factors have been found to play a role. Polymorphisms in Toll like
receptors (TLR-4) were found to have influence over host inflammatory response (Verma et al). The clinical presentation ranges from asymptomatic to life threatening. Seizures are the most common presentation in parenchymal form. They are usually generalised tonic-clonic or simple partial seizures. Focal neurologic deficits can also occur. In children and young women acute inflammatory response to massive cysticercal infection can cause acute diffuse cerebral edema presenting as a syndrome of confusion, clouding of consciousness, headache, vomiting and papilledema which is termed cysticercotic encephalitis. Psychiatric manifestations like depression and psychosis have been described in parenchymal form. Subarachnoid form can present with mass effect, or

produce basal arachnoiditis resulting inmultiple cranial nerve entrapment or hydrocephalus. Lacunar infarcts in posterior limb of internal capsule and corona radiata are common due to occlusion of lenticulostriate branches from intense inflammatory response. Large cerebral infarctions secondary to occlusion of internal carotid, anterior or middle cerebral vessels can also occur. Ventricular NCC can present with acute hydrocephalus and sudden death due to occlusion of third or fourth ventricle. Brunn's syndrome is constellation of episodic headache, papilledema, neck stiffness, vertigo induced by rotatory movements of head, nausea, vomiting, drop attacks, loss of consciousness with rapid recovery and long asymptomatic periods. It is caused by NCC in the fourth ventricle.

Calcified stage of NCC has been presumed to be inert. But recent findings have proved that recurrent transient perilesional edema can occur around calcified NCC and cause refractory seizures. (Antonuik SA et al). MRI shows evidence of perilesional edema in calcified lesions in 50% of patients with recurrent seizures. (Nash TE, Pretel EJ et al). Histopathologically calcified lesions are surrounded by marked astrocytosis, microgliosis, and inflammatory infiltrates. (Winnie W. Ooi et al). Both single and multiple small punctuate cerebral calcifications are common in NCC in endemic areas and this pattern is uncommon in other infectious diseases. There are 3 evidences to suggest calcified NCC lesions provoke seizures. 1) High prevalence of calcifications in patients with seizures of undetermined etiology. 2) High prevalence of seizures in people with brain calcifications in endemic areas. 3) Increased risk of continued seizures in NCC granulomas that calcify. (TE Nash, Del Bruto et al).

Ocular NCC can present as scotomas, iridocyclitis, panophthalmitis or insidious progressive loss of vision.

Diagnosis of NCC:

The diagnostic criteria which was proposed for NCC in 1996 has been revised and Del Brutto et al have proposed a more accurate and stringent modified criteria devoted exclusively for diagnosis of human cysticercosis in 2001.

Absolute criteria:

Histological demonstration of parasite
CT or MRI showing cystic lesion with scolex
Visualisation of parasite by fundoscopy

Major criteria:

CT or MRI showing lesions suggestive of NCC
Positive electro-immuno transfer blot assay (EITB)
Resolution of cystic lesion spontaneously or with therapy Minor criteria:

Lesions compatible with NCC in CT or MRI

Clinical manifestations suggestive of NCC
Positive CSF ELISA

Cysticercosis outside the CNS Epidemiologic criteria:

Residence in endemic area
Travel to an endemic area
Household contact with an individual infected with T.solium

Unfortunately, most of our patients do not meet the diagnostic criteria. Visualisation of the parasite by fundoscopy and the scolex by imaging and identification of extra-neuronal cysticercosis is rare in our population. Histological demonstration of parasite in NCC is virtually not done. Epidemiologic criteria is useless as ours is an endemic nation. EITB and CSF ELISA for NCC are not widely available in India. Majority of our patients present with a single enhancing lesion in which EITB assay is often false negative. EITB has a specificity approaching 100% and sensitivity from 94-98% only in patients with two or more lesions. EITB is also false negative in patients with calcified lesions.

Rajashekar and Chandy proposed the following diagnostic criteria to identify NCC easily in India based on their studies and clinical experience.

Clinical criteria:

Partial or generalised seizures as the initial symptom
Absence of persistent raised intra-cranial pressure
Absence of progressive neurological deficit
No other active systemic disease CT criteria:
Solitary contrast enhancing lesion
Lesion less than 20mm in diameter
Absence of midline shift or severe cerebral edema The validity and accuracy of the above criteria has not been widely evaluated. Further studies are required to arrive at a reliable and feasible diagnostic criterion in endemic developing nations.

Treatment of NCC:General concepts of treatment (Hector.H.Garcia et al)

1 Treatment should be based on the viability, number of lesions and location.

2 A growing cysticercus should always be treated with anti-parasitic drugs.

3. In patients with NCC and increased intracranial tension, the intracranial hypertension should be treated first. Anti-parasitic therapy is never the priority in this setting.

Anti-epileptics are the primary therapy for seizure control in NCC. Anti-parasitic drugs do not substitute for anti-epileptics.

Medical therapy for NCC:

For viable and degenerating cysts albendazole in dose of 15mg/kg PO up to maximum of 800mg in 2 divided doses was recommended for 1 month. The duration of treatment has been reduced to 15 days and lately to 1 week in subsequent studies. Between second to fifth day of therapy there is exacerbation of symptoms. So it is always given along with high dose glucocorticoids (dexamethasone 4.5-12mg/day) and anti-seizure medications. Mannitol at doses of 2g/kg/day can be used for acute reduction of intracranial tension. For calcified cysts no cysticidal therapy is indicated. Albendazole has better CSF penetration than praziquantel and it has no interaction with steroids and it is also cheaper. Hence it is the preferred drug for therapy.

For subarachnoid NCC, trials have shown that prolonged intensive medical treatment can be very effective even with giant cysts and neurosurgery is required only when there is imminent risk of death.(J. Efferson, V.P. Roano et al).

There have been arguments whether anti-parasitic therapy is really necessary in NCC as the cysts follow a benign course and degenerate and heal with natural evolution of the cysts. And also acute brain inflammation with anti-parasitic therapy will exacerbate symptoms transiently. But recent studies have shown a benefit with anti-parasitic therapy with reduction in number of active cysts and better seizure control. There is also complete resolution of lesions with therapy and less frequent residual calcifications. (A. Carpio et al). Patients with multiple lesions benefit more from antiparasitic therapy than patients with solitary lesions. But these reports need confirmation.

Duration of anti-epileptic therapy is also not clear. In a study from Chandigarh, short duration anti-epileptic therapy for 6 months has been found to be adequate in patients with complete resolution of lesions. In patients with residual calcifications longer duration (up to 2 years) of anti-epileptic therapy may be necessary but it does not

alter the chances for seizure recurrence. (Thussu et al)

Surgical therapy for NCC:

Before anti-parasitic drugs were available surgery was the primary therapy, mainly open surgery for large cysts and intra-ventricular cysts. Now the role of surgery is limited to placing ventriculo-peritoneal shunts for emergent management of hydrocep halus. The main problem is frequent shunt blockage in these patients. Prolonged steroid therapy is advocated for avoiding shunt block. Neuroendoscopic resection can be done for intra-ventricular cysts with obstructive hydrocephalus.

Community treatment and prevention:

Clean hygienic practices will go a long way in prevention and control of NCC. Sewage irrigation should be stopped and all fresh vegetables and fruits should be peeled and cleaned before consumption. Regular inspection of slaughter houses for infected pork and chemotherapy for pigs will prevent transmission of taeniasis in humans. But taenicidal eradiaction in humans may have adverse effects in humans with occult NCC. So mass chemotherapy in humans is not advocated.

Conclusion:

Neurocysticercosis is an underestimated menace to our society with poor epidemiologic data for the estimation of its potential threat. Better guidelines, suitable for our country, needs to be developed for its identification and management. Probably, the best way for treatment is to assess each case of NCC individually for its management. Community prevention and eradication depends on the development of better hygiene and waste disposal practices and improvement in the infrastructure of the society.

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