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Extraparenchymal Neurocysticercosis in the United States

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Abstract

Neurocysticercosis (NCC) is endemic in the developing world but is becoming more common in the United States because of immigration. Although NCC is pleomorphic in its presentation, extraparenchymal NCC may be challenging to diagnose and treat. Extraparenchymal NCC is probably more frequent than previously thought. Neurologists and neuroradiologists in the United States are often unaware of the pretreatment/post-treatment radiographic patterns of extraparenchymal NCC and the potentially poor prognosis if not correctly diagnosed and managed. The review of this condition is important given increasing incidence in the United States.

Key Indexing Terms:

Neurocysticercosis; Extraparenchymal; Hydrocephalus; Meningitis; Intraventricular; Subarachnoid

Neurocysticercosis (NCC) is the most common disease causing cystic lesions in the central nervous system, especially in developing and tropical countries.[1] Although NCC is pleomorphic in its presentation, extraparenchymal NCC may be challenging to diagnose and treat. With increasing immigration from endemic areas, there will be an increasing frequency of extraparenchymal NCC in the United States. Neurologists and neuroradiologists in the United States are often unaware of the pretreatment/post-treatment radiographic patterns of extraparenchymal NCC and the potentially poor prognosis if not correctly diagnosed and managed. Herein, we review the literature on extraparenchymal NCC as a cause of meningitis and hydrochephalus and discuss the challenges in diagnosis and management of these cases.

DEFINITION

Extraparenchymal NCC is defined as neurocysticercosis involving the subarachnoid, meningeal and intraventricular space.[1–3] Thus, the clinical manifestations of extraparenchymal NCC range from asymptomatic lesions to meningitis and hydrocephalus.[1–3]

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EPIDEMIOLOGY OF EXTRAPARENCHYMAL NCC

NCC is the most common parasitic infestation of the central nervous system worldwide.[1–4] It is quite prevalent in India and Latin America but is also of emerging importance in the United States, especially in the Southwest United States with high volumes of immigration from endemic regions of Latin America.[4,5] This increase likely includes extraparenchymal cases, and a recent study reported an overall frequency of subarachnoid cysts in 2%, ventricular cysts in 6% and hydrocephalus in 16% of NCC cases.[4] Intraventricular NCC, the presence of *Taenia solium* cysts in the cerebral ventricular system, occurs in 7% to 30% of patients with NCC.[6–9] Cysticercal meningitis (CM), although reported to constitute 42% to 48% of cases in Latin American case-series of NC, is somewhat uncommon with <8% of cases having meningitis among adult patients.[2,3,10–12] However, extraparenchymal NCC is probably more frequent than previously thought and these cases represented almost one-third of NCC in a medical center in New Mexico.[6]

PATHOGENESIS OF EXTRAPARENCHYMAL NCC

The disease occurs when humans ingest eggs of *Taenia solium* from contaminated food.[1] Brain parenchyma is most likely seeded through hematogenous dissemination and the ventricular system, subarachnoid space and basal cisterns are then seeded via the choroid plexus.[1] Subarachnoid cysts can also grow abnormally as a membranous and/or cystic mass called racemose cysticercosis.[3] Cysticercus racemosus is a form multilobular grape-like cluster without scolex, most frequently located in the basal cisterns, Sylvian fissure or ventricles.[6–9] These cysts continually grow and commonly result in basilar arachnoiditis[3] with inflammation and fibrosis in and around critical structures, causing meningeal inflammation, hydrocephalus due to cerebrospinal fluid (CSF) outflow obstruction or cerebrovascular complications.[6–9] Although neurocysticerci undergo 4 stages of involution: vesicular, colloidal, granulovacuvolar and calcific, this evolution does not occur in the intraventricular or the subarachnoid forms (or racemose type) of NCC.[13] The cyst often tends to migrate to the fourth ventricle because of gravity and CSF flow patterns.[6–9]

Intraventricular neurocysticercal cysts occur singly or in multiples and frequently coexist with parenchymal and subarachnoid cysts.[6–9] However, a cyst in the fourth ventricle tends to be solitary, without accompanying parenchymal cysts.[6–9] Intracranial hypertension is a common manifestation of extraparenhymal NCC and the increased intracranial pressure can be from the mass effect of a giant subarachnoid cyst,[14] or from obstructive hydrocephalus produced by direct obstruction of the ventricular system by a cyst,[15] distortion of ventricular CSF pathways[16] or blockage of CSF pathways within the subarachnoid space from the inflammatory reaction.[15]

There is lack of understanding of the pathophysiology of extraparenchymal NCC. Whether chronic inflammation in extraparenchymal NCC is due to continuous cyst degeneration or continuous antigen release from dead parasitic tissues is unknown.[17] Circulating antigen detection assays could help establish whether living parasites are still present after apparent radiographic cyst regression, providing an indication to continue or reuse antiparasitic treatment.[18]

CLINICAL MANIFESTATIONS OF EXTRAPARENCHYMAL NCC

The clinical and radiologic manifestations of NCC are pleomorphic. Several varieties of NCC have been recognized depending upon the number, location and evolutionary stage of the cysticerci in the human brain.[19] Epilepsy, focal neurological signs and intracranial hypertension are the most common clinical manifestations of the disease.[1]

In a recent study in the United States, it was found that extraparenchymal NCC occurs mainly in young adult male Hispanic immigrants who typically present with (1) subacute or chronic intracranial hypertension from mass effect or hydrocephalus; (2) chronic meningitis characterized by lack of meningeal signs of examination, a mild-to-moderate CSF lymphocytic pleocytosis and increase in protein; (3) radiographic hydrocephalus with or without obvious cysts; (4) radiographic presence of cysts in the ventricles or subarachnoid space and (5) protracted clinical or radiographic course after antiparasitic treatment.[6]

Hydrocephalus develops in approximately 30% of all patients with NCC because of obstruction by intraventricular or subarachnoid lesions.[6–9] Intraventricular NCC can cause non-communicating hydrocephalus by obstructing the CSF pathway and communicating hydrocephalus by development of ependymitis.[6–9] Abrupt permanent obstruction can cause sudden death due to brain herniation.[6–9] Life-threatening acute intermittent hydrocephalus (Brunn syndrome) can occur due to cystinducing intermittent CSF obstruction from a ball-valve mechanism.[7,8] Overall, extraparenchymal NCC has a more aggressive behavior and a higher morbidity and mortality rate than parenchymal form.[6–9]

The presence of subarachnoid cysts can cause chronic cysticercal meningitis. CM is characterized by inflammatory CSF and negative bacterial and fungal cultures.[10] There have been no systematic studies of CM. In a recent study of patients with CM, these patients often had intracranial hypertension, meningeal signs, CSF hypoglycorrachia, positive CSF results in an enzyme-linked immunosorbent assay for cysticercal antigens, negative CSF cultures for bacteria, fungi and mycobacteria and longer clinical course of NCC.[10] The management of the chronic inflammation and the complications caused by this meningitis are usually very difficult, and the mortality rate can be up to 33%.[6–9] It is likely that CM is often not identified and its correct identification may reduce morbidity and risks of unnecessary surgery in patients with chronic NCC and CSF shunts.[6–9]

DIAGNOSIS OF EXTRAPARENCHYMAL NCC

Extraparenchymal NCC is associated with a local inflammatory response with high protein concentration and cell counts in the CSF.[10] Clinical manifestations and CSF findings are similar to the more common tuberculous and fungal meningitis,[9,10] as the CSF findings consist of pleocytosis (usually lymphocytic but frequently polymorphonuclear), reduced glucose and elevated protein.[10] In 1 series of cysticercal meningoencephalitis, confusion with tubercular meningitis was present in 61.5% cases.[3,10] An important differentiating feature is the presence of eosinophils in the CSF.[3,10] This eosinophilia is usually seen only in the initial phases of the illness, and Wright-Giemsa staining of the CSF is required for visualizing eosinophils (which can be mistaken for polymorphonuclear cells) in the CSF.[6,10]

However, this staining of the CSF is not routinely done in most places.[9,10]Although the suspicion of NCC as the cause of chronic meningitis is increased when CSF eosinophils are found, CSF eosinophils (above 5%) occur in only 15% of patients.[6] It is often a common practice to attribute chronic meningitis and hydrocephalus to tubercular meningitis in the presence of appropriate epidemiologic history and treat empirically by shunting and antitubercular therapy. Thus, an astute clinical acumen is required to make the diagnosis of CM.

Neuroimaging findings of extraparenchymal cysticerci are subtle and are usually not seen by computed tomography (CT). Common neuroimaging findings to suspect the diagnosis include hydrocephalus (with or without obvious cysts), cysts obstructing CSF pathways or freely floating inside ventricles, cysts in the basal subarachnoid cisterns, migrating cysts across the cerebral aqueduct and ependymitis or arachnoiditis.[6] The most common CT finding in subarachnoid NCC is hydrocephalus.[1,11] Because the cyst membrane is thin and the fluid is isodense with the CSF, uninflamed extraparenchymal cysticerci are usually not visible on CT scanning and may only reveal subtle, indirect findings on magnetic resonance imaging.[11] Therefore, neuroimaging may reveal hydrocephalus without noticeable cysts.[1,11]

Neuroimaging findings are variable depending on the stage of the infection. During the vesicular stage, cysts and scolex are both imaged without enhancement.[1,20] In the colloidal vesicular stage, ring enhancement and edema are appreciated by both CT and MR imagings.[1,20] The granular nodular phase is characterized by decreased ring enhancement and edema, along with the calcification of cysts.[20] During the final involution stage, calcification is observed on CT and MR imaging as small areas of hypointensity.[1]

The diagnosis of NCC is often made based on presence of lesion highly suggestive of NCC on neuroimaging study, positive serum immunoassay for the detection of anticysticercal antibodies, positive CSF immunoassay for detection of anticysticercal antibodies and epidemiologic criteria including individual coming from an area where cysticercosis is endemic.[1] These diagnostic criteria have been stratified in 4 categories—absolute, major, minor and epidemiological—on the basis of their individual diagnostic strength.[1] Based on a previous consensus, the absolute criterion for the diagnosis of NCC that is being considered as pathognomonic of this disease is the detection of a scolex inside a cyst by CT or MRI.[1] However, *C racemosus* does not have a scolex and patients with this form of the disease tend to be excluded, although this is a more severe form of NCC.[4,8,10,11,21] *Taenia* antibodies are considered as a major criterion, whereas the positive serologic test in the CSF is listed as a minor criterion.[12] Polymerase chain reaction in CSF has also been used for the diagnosis of NCC but is not widely available.[12] However, extensive and comprehensive revision of the diagnostic criteria of NCC, especially of extraparenchymal NCC is mandatory according to many recent publications.[4,8,10,11,21]

TREATMENT

There is still no consensus regarding optimal treatment strategies in patients with extraparenchymal NCC.[6–9] Various therapeutic modalities include antihelminthic

medication, microneurosurgical removal, ventriculoperitoneal shunting and endoscopic management.[10]

Medical Therapy

Although parenchymal cysts have historically been treated quite effectively with antihelminthics such as praziquantel and albendazole, medical therapy alone is not favored for extraparenchymal NCC because of the limited efficacy in such cases, and a risk of developing acute hydrocephalus during the clinical treatment period.[6–9] Good results for antiparasitic treatment with different albendazole and praziquantel regiments for intraventricular and subarachnoid cysticercosis have been reported.[17,22–24] However, although treatment with antihelminthic medication such as albendazole has been shown to improve outcome in live, cystic parenchymal cysticercosis, the benefits of antihelminthic treatment in patients with solitary cystic lesion remain uncertain.[25] Antihelminthic agents hasten the evolution of intraventricular viable cysts, which may trigger an inflammatory response similar to that seen with the natural history of the parasite.[13] This may result in long-term sequelae.[1,2,11,26] Extraparenchymal cysts may regress only after long-term and multiple antiparasitic courses.[1,2,11,26] The optimal treatment to prevent chronic inflammation is unknown due the lack of understanding of its pathophysiology and lack of controlled trials to help guide management. Similarly, controversy exists regarding the use of corticosteroids, alone or in combination with antihelminthic drugs.[1,2,25,26]At a previous consensus meeting, experts agreed that no single-treatment approach could be advocated and that management options varied according to the type of clinical presentation.[11] However, intraventricular NCC has a risk of ependymitis in those treated with antihelminthics, thus necessitating surgical evaluation before medical treatment.[10]

Surgical Therapy

In patients presenting with acute hydrocephalus, surgery is the only option.[6–9] Neurosurgical procedures for NCC are still part of the armamentarium when treating this disease and good results for open craniotomy and rigid endoscopic surgery in patients with intraventricular and subarachnoid NCC have been reported.[27,28] Infratentorial intraventricular cysts have been treated with open surgery for excision, whereas it is generally suggested that supratentorial cysts, because of not only location but also the need to often treat hydrocephalus in these patients, be removed endoscopically.[29] Ependymitis is a relative contraindication for surgical removal of the cysts.[6–9]

Ventriculoperitoneal CSF shunting is burdened by a high shunt dysfunction rate, risk of infection and high mortality rates, whereas microneurosurgical approaches can be technically demanding and associated with various complications.[6–9] For these reasons, endoscopic approaches for intraventricular NCC have been described in recent years and often allow for cyst removal and hydrocephalus treatment, freeing the patient from shunt procedures.[30,31]

Although the literature regarding the use of endoscopic management of intraventricular NCC is scarce, this modality has shown encouraging results in the treatment of intraventricular NCC.[6–9] In a recent comparative study of 140 patients from Mexico with intraventricular

NCC, traditional treatment with albendazole and steroid had similar outcome versus neuroendoscopic surgery in terms of survival, hospitalization.[9] However, almost all patients with traditional treatment remained with at least 1 shunt, whereas most of the patients from the neuroendoscopic surgery series did not have any shunts.[9] Thus, the neuroendoscopic approach to intraventricular neurocysticercal cysts is safe and effective and offers the additional benefit of avoiding shunt placement.[6–9] At centers having the required expertise, this should be the treatment of choice. Traditional treatment is a second option where the endoscopic procedure is not available. However, endoscopic cyst excision can be difficult and hazardous in patients with severe ependymitis and dense adhesions and intraventricular bleeding could also report.[6–9] Thus, despite its many advantages, neuroendoscopy has some limitations even when performed by experienced hands.

Regarding subarachnoid NCC, there are no controlled trials on the management of this form of extraparenchymal NCC.[1,2,26] In a series of patients treated with only CSF diversion, 50% died at a median follow-up of 8 years and 11 months.[21] More recently, case series using antiparasitic drugs, corticosteroids and shunting for hydrocephalus have been associated with an improved prognosis compared with older studies.[1,2,21,26] Thus, most experts consider subarachnoid NCC a clear indication for antiparasitic therapy.[21] However, the optimal dose and duration of antiparasitic therapy for subarachnoid cysticercosis has not been established.[21] In the largest case series, Proano et al[9] treated 33 patients with giant cysticerci with albendazole (15 mg/kg/day) for 4 weeks and most patients required several courses of antiparasitic therapy. However, with controversy in the literature in the optimal management of this condition and without further evidence-based guidelines to help management of extraparenchymal NCC, the decision of the total dose and duration of antiparasitic and steroid therapy must be made on a case-by-case basis.

CONCLUSION

Extraparenchymal NCC may be a more common form of NCC in the United States than previously thought and is often difficult to diagnose, more complex to treat and carries a graver prognosis because it is frequently associated with intracranial hypertension, progressive course and significant mortality. The clinical course is protracted and difficult to cure. Different medical (anthelmintics, steroids), surgical (cyst excision, CSF diversion) or medical-surgical approaches have been reported but not adequately studied. Because clinicians in the United States outside the Southwest United States are often unfamiliar with NCC as a cause of chronic meningitis, chronic ventriculitis or hydrocephalus without obvious cysts, the diagnosis of extraparenchymal NCC often depends on the correct interpretation of neuroimaging which may miss the diagnosis. Thus, meningeal and intraventricular NCC should always be considered by clinicians and radiologists in the differential diagnosis of chronic meningitis and hydrocephalus, particularly in patients from Latin America.

REFERENCES

1. Del Brutto OH. Neurocysticercosis. Semin Neurol 2005;25:243–51. [PubMed: 16170737]
2. Cardenas G, Carrillo-Mezo R, Jung H, et al. Subarachnoidal neurocysticercosis non-responsive to cysticidal drugs: a case series. BMC Neurol 2010;10:16. [PubMed: 20202200]

3. Del Brutto OH. Meningeal cysticercosis. In: Singh G, Prabhakar S, editors. *Taenia solium* cysticercosis: from Basic to clinical science. Oxford, United Kingdom: CABI Publishing; 2002. p. 177–88.
4. Wallin MT, Kurtzke JF. Neurocysticercosis in the United States: review of an important emerging infection. Neurology 2004;63:1559–64. [PubMed: 15534236]
5. Ong S, Talan DA, Moran GJ, et al. Neurocysticercosis in radiographically imaged seizure patients in U.S. emergency departments. Emerg Infect Dis 2002;8:608–613. [PubMed: 12023918]
6. Figueroa JJ, Davis LE, Magalhaes A. Extraparenchymal neurocysticercosis in Albuquerque, New Mexico. J Neuroimaging 2011; 21:38–43. [PubMed: 20002970]
7. Goel RK, Ahmad FU, Vellimana AK, et al. Endoscopic management of intraventricular neurocysticercosis. J Clin Neurosci 2008;15: 1096–101. [PubMed: 18653345]
8. Kalra V, Mishra D, Suri A, et al. Intraventricular neurocysticercosis. Indian J Pediatr 2009;76:420–3. [PubMed: 19205637]
9. Proano JV, Torres-Corzo J, Rodriguez-Della VR, et al. Intraventricular and subarachnoid basal cisterns neurocysticercosis: a comparative study between traditional treatment versus neuroendoscopic surgery. Childs Nerv Syst 2009;25:1467–75. [PubMed: 19557421]
10. Cardenas G, Jung H, Rios C, et al. Severe cysticercal meningitis: clinical and imaging characteristics. Am J Trop Med Hyg 2010;82: 121–5. [PubMed: 20065006]
11. Garcia HH, Evans CA, Nash TE, et al. Current consensus guidelines for treatment of neurocysticercosis. Clin Microbiol Rev 2002;15: 747–56. [PubMed: 12364377]
12. Michelet L, Fleury A, Sciutto E, et al. Human neurocysticercosis: comparison of different diagnostic tests in cerebrospinal fluid. J Clin Microbiol. 2011;49:195–200. [PubMed: 21068283]
13. Suri A, Goel RK, Ahmad FU, et al. Transventricular, transaqueductal scope-in-scope endoscopic excision of fourth ventricular neurocysticercosis: a series of 13 cases and a review. J Neurosurg Pediatr 2008;1:35–9. [PubMed: 18352801]
14. Proano JV, Madrazo I, Avelar F, et al. Medical treatment for neurocysticercosis characterized by giant subarachnoid cysts. N Engl J Med 2001;345:879–85. [PubMed: 11565520]
15. Estanol B, Kleriga E, Loyo M, et al. Mechanisms of hydrocephalus in cerebral cysticercosis: implications for therapy. Neurosurgery 1983;13: 119–23. [PubMed: 6888689]
16. Lobato RD, Lamas E, Portillo JM, et al. Hydrocephalus in cerebral cysticercosis. Pathogenic and therapeutic considerations. J Neurosurg 1981;55:786–93. [PubMed: 7310501]
17. Nash TE, Singh G, White AC, et al. Treatment of neurocysticercosis: current status and future research needs. Neurology 2006;67:1120–7. [PubMed: 17030744]
18. Fleury A, Hernandez M, Avila M, et al. Detection of HP10 antigen in serum for diagnosis and follow-up of subarachnoidal and intraventricular human neurocysticercosis. J Neurol Neurosurg Psychiatry 2007;78: 970–4. [PubMed: 17337467]
19. Del Brutto OH. Single parenchymal brain cysticercus in the acute encephalitic phase: definition of a distinct form of neurocysticercosis with a benign prognosis. J Neurol Neurosurg Psychiatry 1995;58: 247–9. [PubMed: 7876864]
20. do Amaral LL, Ferreira RM, da Rocha AJ, et al. Neurocysticercosis: evaluation with advanced magnetic resonance techniques and atypical forms. Top Magn Reson Imaging 2005;16:127–44. [PubMed: 16340333]
21. Garcia HH, Del Brutto OH, Nash TE, et al. New concepts in the diagnosis and management of neurocysticercosis (*Taenia solium*). Am J Trop Med Hyg 2005;72:3–9. [PubMed: 15728858]
22. Agapejev S, Da Silva MD, Ueda AK. Severe forms of neurocysticercosis: treatment with albendazole. Arq Neuropsiquiatr 1996;54:82–93. [PubMed: 8736150]
23. Proano JV, Madrazo I, Garcia L, et al. Albendazole and praziquantel treatment in neurocysticercosis of the fourth ventricle. J Neurosurg 1997;87:29–33. [PubMed: 9202261]
24. Del Brutto OH, Sotelo J, Aguirre R, et al. Albendazole therapy for giant subarachnoid cysticerci. Arch Neurol 1992;49:535–8. [PubMed: 1580817]
25. Singh G, Rajshekhar V, Murthy JM, et al. A diagnostic and therapeutic scheme for a solitary cysticercus granuloma. Neurology 2010;75: 2236–45. [PubMed: 21172847]

26. Del Brutto OH, Roos KL, Coffey CS, et al. Meta-analysis: cysticidal drugs for neurocysticercosis: albendazole and praziquantel. Ann Intern Med 2006;145:43–51. [PubMed: 16818928]

27. Colli BO, Martelli N, Assirati JA Jr, et al. Results of surgical treatment of neurocysticercosis in 69 cases. J Neurosurg 1986;65:309–15. [PubMed: 3734881]

28. Madrazo I, Garcia-Renteria JA, Sandoval M, et al. Intraventricular cysticercosis. Neurosurgery 1983;12:148–52. [PubMed: 6601248]

29. Psarros TG, Krumerman J, Coimbra C. Endoscopic management of supratentorial ventricular neurocysticercosis: case series and review of the literature. Minim Invasive Neurosurg 2003;46:331–4. [PubMed: 14968398]

30. Bergsneider M Endoscopic removal of cysticercal cysts within the fourth ventricle. Technical note. J Neurosurg 1999;91:340–5. [PubMed: 10433327]

31. Rangel-Castilla L, Serpa JA, Gopinath SP, et al. Contemporary neurosurgical approaches to neurocysticercosis. Am J Trop Med Hyg 2009; 80:373–8. [PubMed: 19270284]