Cysticercosis and cerebrovascular disease: a review

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Abstract
Ischaemic cerebrovascular disease is a relatively common but under-recognised complication of neurocysticercosis. It is usually caused by inflammatory occlusion of the arteries at the base of the brain secondary to cysticercotic arachnoiditis. In most cases, the involved vessels are of small diameter and the neurological picture is limited to a lacunar syndrome secondary to a small cerebral infarct. However, large infarcts related to the occlusion of the middle cerebral artery or even the internal carotid artery have also been reported in this setting. CT and CSF examination usually support the cause-and-effect relationship between neurocysticercosis and the cerebral infarct by showing abnormalities compatible with cysticercotic arachnoiditis. An accurate diagnosis of this condition is important since early treatment with steroids is advised to ameliorate the subarachnoid inflammatory reaction which may cause recurrent cerebral infarcts.

Cysticercosis is the most frequent parasitic disease of the CNS, and one of the most pleomorphic of neurological disorders. Clinical manifestations of neurocysticercosis (NCC) are nonspecific and largely depend on the number and topography of lesions and the host immune response to the parasite. NCC is usually manifested by seizures, progressive intellectual deterioration, and signs and symptoms of increased intracranial pressure. In addition, a variety of focal neurological signs occur in many patients. While such deficits are usually related to parenchymal brain cysticerci, in an important number of patients they occur as the result of a cerebrovascular event.

Cerebrovascular complications of NCC were first described in the nineteenth century in a patient with cysticercotic meningitis who had angiitis of small intracranial vessels. Since then, several authors have recognised the association between NCC and cerebrovascular disease. Most of these reports have focused on the histopathological and angiographic aspects of cysticercotic angiitis, but little emphasis has been placed on the clinical manifestations of this condition or in the therapeutic approach. In recent years, several patients with brain infarcts due to NCC have been reported, nevertheless, stroke is an under-recognised complication of NCC, and authoritative textbooks of neurology do not consider this parasitic disease in the differential diagnosis of cerebral infarcts. This paper presents a review of the literature on this subject, and discusses the pathophysiology of cysticercosis induced cerebrovascular disease.

Lacunar infarction
This is the most common cerebrovascular complication of NCC. Cysticercosis-induced lacunar infarcts are usually located in the territory of the lenticulostriate branches of the anterior or middle cerebral artery, and result from occlusive endarteritis secondary to the intense inflammatory reaction within the subarachnoid space that is triggered by meningeal cysticerci. Such inflammatory reaction is composed of hyalinised parasitic membranes, collagen fibres, lymphocytes, plasma cells, eosinophils, and multinucleated giant cells. These changes cause abnormal thickening of the leptomeninges at the base of the skull with subsequent entrapment and occlusion of blood vessels around the circle of Willis.

Small cerebral infarcts due to NCC have been associated with lacunar syndromes which are indistinguishable from those caused by atherosclerosis. These patients may present with an ataxic hemiparesis, pure motor hemiparesis, or sensorimotor stroke, due to a lacune that is usually located in the posterior limb of the internal capsule or the corona radiata. CT provides clues to the aetiology of the infarct as it shows associated abnormalities in most cases. In a series of seven patients with a lacunar syndrome due to NCC, we found CT evidence of NCC in six cases: four patients had a suprasellar cysticercus ipsilateral to the infarct, one had a large meningeal cyst in the vicinity of the infarct, and the other patient had hydrocephalus due to diffuse arachnoiditis. CSF analysis is of paramount importance in the evaluation of patients with suspected cysticercotic angiitis, as it shows a mild pleocytosis and elevated protein contents in most cases. In addition, immunological reactions (ELISA and complement fixation test) for the detection of anticysticercal antibodies are almost always positive in CSF due to active meningeal disease. Cerebral angiography may be completely normal because the involved vessels are too small to be imaged, or may show segmental narrowing of major intracranial vessels when the process of angiitis is more extensive.

Large infarctions
Cerebral infarcts involving the deep and superficial territory of a major intracranial artery have occasionally been reported in patients...
Cysticercosis disease: a review

Cysticercosis
disease:
cysticercotic
profound
cases.26
literature reveals
cerebral
cortex,
or both. They had a protracted
course and most of them died as the result of
either the cerebral infarct or the associated
arachnoiditis. CT was available in three of
these patients and showed a large meningeal
cysticercus adjacent to the brain infarct in
every case. Angiography showed occlusion of
the supraclinoid segment of the internal car-
ottid artery in two patients, and occlusion of the
middle cerebral artery in the remaining three.
Postmortem examination of the brain of
patients dying with this disorder showed inter-
esting findings. Besides occlusive endarteritis,
some blood vessels of large diameter showed
occlusion of their lumens by atheroma-like
deposits that resulted from disruption of the
endothelium secondary to the invasion of the
vessel wall by a severe inflammatory reaction
induced by meningeal cysticerci.24

Progressive midbrain syndrome
This is one of the most devastating complica-
tions of NCC and has been associated with a
mortality rate of 85%.26 Those patients usually
have a history of shunted hydrocephalus due to
diffuse cysticercotic arachnoiditis. In a typical
case, the patient is readmitted a few months
after the shunt was placed because of pro-
gressive neurological deterioration character-
ised by somnolence, paraparesis, impaired
vertical gaze, fixed and dilated pupils, and
urinary incontinence. CT shows normal-sized
lateral ventricles and an ill-defined hypodense
zone in the midbrain tegmentum and medial
thalamus. CSF analysis shows marked pleocy-
tosis and increased protein contents, with
positive immunological reactions to cysticercos-
is. With the aid of MRI, it has been possible to
visualise multiple areas of ischaemia in the
midbrain and thalamus which are the result of
the occlusion of paramedian thalamopedun-
cular branches of the mesencephalic artery.
Such branches are prone to develop inflamma-
tory occlusion as the interpeduncular and
prepontine cisterns are where the gelatinous
exudate associated with cysticercotic arachno-
ditis is more intense.26 The prognosis of these
patients is bad, and they usually die after a
protracted course.46

Transient ischaemic attacks
There have been scarce reports of patients with
NCC who complain of brief episodes of
neurological deficit resembling transient
ischaemic attacks. The first description of this
association was made by Bickerstaff27 under
the heading of "Transient loss of function". While
lacking pathological or angiographic correla-
tion, the author considered that such episodes
were vascular in nature. McCormick et al28
reported a patient who experienced transient
episodes of hemiparesis related to the
upright posture which was resolved in the
supine position. This patient had a large
cysticercus around the internal carotid artery
that occluded its lumen and caused positional
cerebral ischaemia. On the other hand, we
have recently described a patient with transient
episodes of hemiparesis due to a large par-
enchymal brain cysticercus.6 Data from these
reports suggest that NCC may cause transient
neurological dysfunction resembling transient
ischaemic attacks. The pathogenesis of this
condition, however, is not uniform. It may be
of vascular origin or may be related to par-
enchymal brain cysts in a similar way to that
described in patients with cerebral tumours.36

Discussion
As shown in this review, several clinical reports
have implied a link between NCC and isch-
aemic cerebrovascular disease. This association
has been confirmed from data of large series
showing that approximately 3% of patients
with NCC develop a cerebral infarct,21 25 26 36 38
and that 2-5% of patients with cerebral infarcts
have NCC.4 The proportion of patients with
cerebral infarcts due to NCC, however, varies
according to the underlying prevalence of
cysticercosis in a given population. In Mexico,
cysticercosis is the second most frequent cause
of non-atherosclerotic cerebral infarct.4 Such
incidence could be representative of several
other developing countries and industrialised
nations with a high immigrant population
from areas where this parasitic disease is
demic.10 18 21 23 31

In endemic areas for cysticercosis, a patient
may have NCC and a cerebral infarct from
unrelated reasons. The diagnosis therefore of
cysticercosis-induced cerebral infarction
should be established only in patients who meet rigid
inclusion criteria. These patients usually are
younger than 40 years of age and have no risk
factors for cerebrovascular disease. The cause-
and-effect relationship between NCC and a
cerebral infarct must be supported by CT
evidence of a meningeal cyst adjacent to the
infarct or by CSF findings compatible with
active arachnoiditis.

Many infectious diseases of the CNS have
been associated with cerebrovascular dis-
ease,22 24 25 37 40 49 such as, the parallelism
between the inflammatory arteriopathy caused
by NCC and that caused by tuberculous
meningitis. In both conditions, the arteries at
the base of the brain are surrounded by a dense
exudate that causes inflammatory changes in
the entire wall of perforating blood vessels.
Neither CT nor cerebral angiography permit
the differential diagnosis between tuberculous
and cysticercotic meningitis as they show
similar changes in both conditions. Even nec-
ropsy examination of the brain may cause
misdiagnosis if an inexpert pathologist does
not recognise the scarce parasitic membranes
that within the leptomeningeal exudate. Corner-
stones for an accurate differential diagnosis
between tuberculous and cysticercotic menin-
gitis are the neurological examination of the
patient and the result from CSF analysis.
Patients with NCC rarely, if ever, have fever or
neck stiffness; likewise, the levels of CSF glucose are almost always normal in such patients.44 In contrast, patients with tuberculous meningitis usually have fever, neck stiffness, and decreased CSF glucose levels.12 The diagnosis of cysticercotic angiitis has important therapeutic implications. Those patients should be started on steroid therapy as soon as the diagnosis is established to ameliorate the subarachnoid inflammatory reaction which may cause recurrent cerebral infarcts. Further follow up with serial CSF analysis will permit, on individual basis, the tapering of steroids if the severity of inflammation has subsided. This approach is in contrast with that used in patients with atherosclerotic ischemic stroke, where steroids have proved to be harmful.13 The diagnosis of NCC should be included in the list of causes of stroke in the young, particularly in endemic areas, and this condition must be ruled out by proper integration of data from the neurological examination, CT findings, and CSF analysis before other therapeutic measures are attempted.

Patients with meningeal NCC may develop a cerebral infarct while receiving anticycsticidal drugs. Praziquantel and albendazole are highly active drugs against parenchymal brain cysticerci.42-44 and there is increasing evidence that they may also be useful in patients with meningeal cysts.17 In the latter, however, the intense inflammatory reaction developed by the host in response to the acute destruction of the parasites within the subarachnoid space, may enhance the process of angiitis in the neighbouring blood vessels favouring their occlusion. Robles18 reported a patient who died from a cerebral infarct shortly after receiving praziquantel, and we have recently described another patient with a suprasellar cysticercus who developed a cerebral infarct during a course of praziquantel.19 When treating patients with meningeal NCC, a short course of steroids seems justified to decrease such inflammatory reaction, avoiding the risk of a cerebral infarct.