

PSEUDOCYSTIC FORM OF NEUROCRYPTOCOCCOSIS IN PREGNANCY

CASE REPORT

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ABSTRACT - We report a case of neurocryptococcosis which is unique in the literature because the patient had a pseudocystic form of the disease during pregnancy and without any evidence of AIDS. The clinical picture was that of intracranial hypertension and the epidemiological background was highly suggestive of cysticercosis. CT showed multiple round hypodense lesions in the basal ganglia and cerebellum, without contrast enhancement. Since a scolex was not visible, the diagnosis of neurocysticercosis was considered probable. CSF examination was not performed in view of its high risk. The patient had progressive downhill course. Autopsy disclosed multiple gelatinous pseudocysts in the cerebral and cerebellar gray matter, containing abundant *Cryptococcus neoformans*. Meningeal involvement was minimal. The child was delivered by caesarean section and was free of infection, but died later of hyaline membrane disease. The neuroimaging appearances of this rare instance of the pseudocystic form of neurocryptococcosis mimicked closely neurocysticercosis and only postmortem examination allowed correct diagnosis. The pseudocystic form has so far only been reported in AIDS.

KEY WORDS: neurocryptococcosis, neurocysticercosis, pregnancy, pseudocysts.

Neurocriptocose na gravidez: forma pseudocística. Relato de Caso

RESUMO - Relatamos o primeiro caso da forma pseudocística da neurocriptocose na gravidez, em paciente sem evidência de AIDS. O quadro clínico era de hipertensão intracraniana que se manifestou no segundo trimestre da gravidez. A tomografia computadorizada do crânio evidenciava múltiplas lesões hipodensas, císticas, não impregnadas por contraste, localizadas na substância cinzenta cerebral e cerebelar. Dados epidemiológicos, clínicos e tomográficos apontavam para o diagnóstico provável de neurocisticercose. A autópsia, porém, revelou múltiplos pseudocistos de material gelatinoso com *Cryptococcus neoformans* em abundância. Havia mínimo comprometimento meníngeo. A revisão da literatura mostrou que a forma pseudocística da neurocriptocose só foi até o momento relatada em pacientes com AIDS. Os casos de neurocriptocose na gravidez até hoje publicados foram todos da forma meningítica.

PALAVRAS - CHAVE: neurocriptocose, neurocisticercose, gravidez, pseudocistos.

Neurocryptococcosis is rare in pregnancy. Since the first report in 1936, 23 further cases not associated with acquired immunodeficiency syndrome (AIDS) have been recorded, all of which had the meningitic form¹⁻⁴. The following case is unique in that the main feature was voluminous intraparenchymatous pseudocysts filled with parasites and leading to severe intracranial hypertension.

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CASE REPORT

A 29-year-old woman was admitted because of progressive sleepiness with a duration of four months. She had been previously in good health and was in the 24th week of a first pregnancy. She was born and dwelt in a rural area where cysticercosis is prevalent and had further predisposing factors for teniasis (pig raising, poor sanitary conditions). On the fourth day after admission she had an episode of vomiting. There was no fever or sweating. Neurological examination disclosed nuchal rigidity, bilateral paresis of the sixth nerve and papilledema. There was universal muscular reaction to painful stimuli, myotactic reflexes were normal and cutaneous-plantar reflex was bilaterally in flexion. The CT scan showed diffuse cerebral edema and multiple hypodense lesions in the basal ganglia (Fig 1), which were not enhanced by contrast. There was also an image suggestive of a cyst in the right lateral ventricle. She received dexamethasone with slight improvement in the level of consciousness but no substantial changes in the neurological evaluation. On the 8th day of treatment she had respiratory arrest, after which she was kept under mechanical ventilation. Pupils became fixed and mydriatic; corneo-palpebral and oculocephalic reflexes were abolished and there was no response to painful stimuli. CT scan showed worsening of cerebral edema and tonsillar herniation. No CSF examination was performed. Dexamethasone was maintained, with mannitol and dopamine added. After a recovered cardiac arrest she was submitted to caesarian delivery of a living male child weighing 750 g. After 24 hours brain death was diagnosed.

Laboratory tests - Erythrocyte sedimentation rate: 45 mm (1st hour); cell counts, glycemia, electrolytes, bilirubin, renal and thyroid function tests normal. ALT, 260 U/l; AST, 152 U/l. Serum immunological tests for human immunodeficiency virus (HIV), syphilis and toxoplasmosis, negative. Antinuclear factor and anti DNA, non-reagent. Plain chest radiographs normal.

Postmortem examination. The body weighed 75 kg and measured 160 cm, in good state of nutrition and preservation. The lungs were slightly increased in volume and consistency (right 580 g.; left 520 g) and showed diffuse congestion. Other organs were macroscopically normal. The brain weighed 1245 g and showed flattening of gyri and herniation of the cerebellar tonsils. The leptomeninges were slightly hyperemic, but thin and transparent in the convexity and base. Major arteries were unremarkable. Frontal sections of the cerebral hemispheres showed confluent cystic lesions with gelatinous translucent contents of yellowish to tan color. These were situated bilaterally in the basal ganglia and the dentate nuclei of the cerebellum (Fig 2). At these sites, the nervous parenchyma was

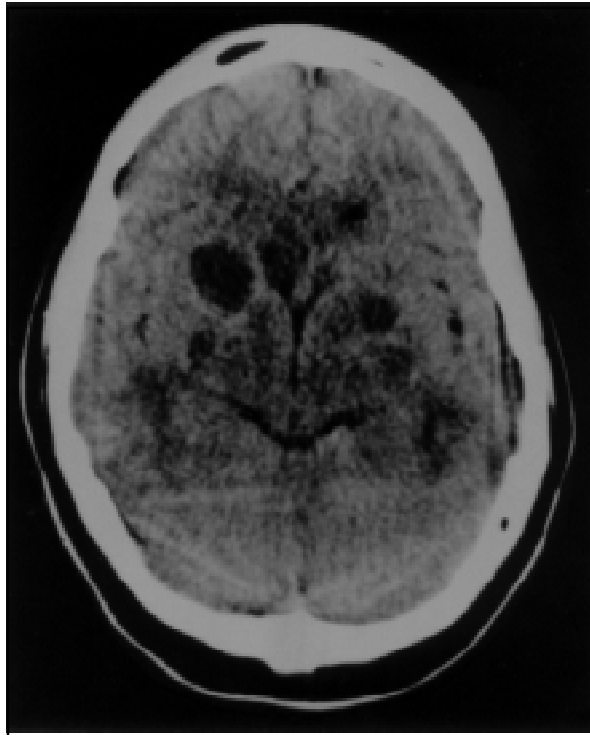


Fig 1. CT scan revealing cyst-like lesions in the basal ganglia.



Fig 2 (Above). Coronal section through the cerebral hemispheres showing various cavities filled with gelatinous material replacing most of the basal ganglia and compressing the lateral ventricles. Note absence of lesions in the meninges, cerebral cortex and white matter. (Below) Similar appearance in the dentate nuclei of the cerebellum.

completely replaced by the gelatinous substance. The lateral ventricles were collapsed and no intraventricular cyst was found. In the cerebral cortex and in the white matter of the cerebral or cerebellar hemispheres there were no microcystic lesions, though some were found in the midbrain. Microscopical examination showed that the cystic lesions were filled by an abundance of fungi highly suggestive of *Cryptococcus neoformans*. The yeasts were surrounded by a thick amorphous capsule with copious basophilic material between them and some showed sprouting (Fig 3). The microorganisms were found in much smaller numbers in the cerebral and cerebellar leptomeninges and penetrated along Virchow-Robin spaces unhindered by inflammatory reaction. Examination of other organs disclosed isolated fungi only in lung capillaries but not in alveoli, which were devoid of exudate.

The newborn survived one week. At autopsy hyaline membrane disease was the main finding. There was no evidence of fungal infection in the child or placenta.

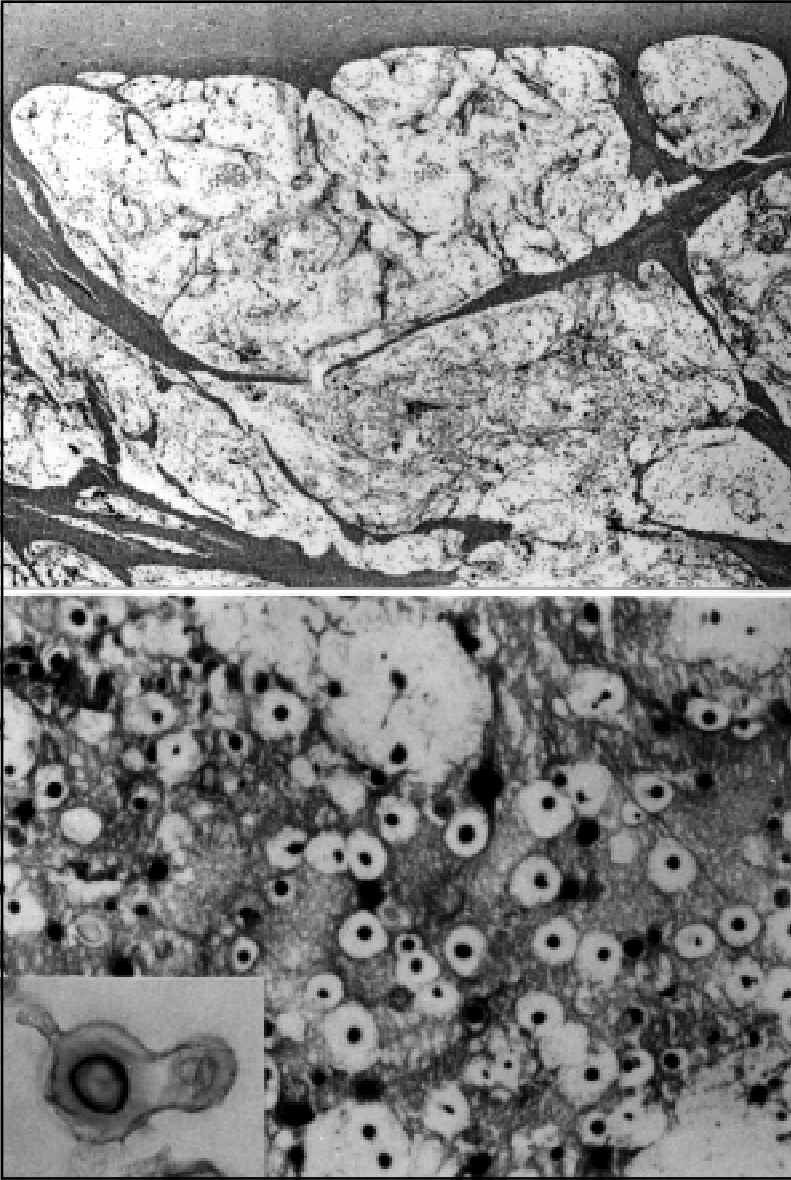


Fig 3 (Above). Photomicrograph of basal ganglia, showing confluent cysts separated by thin septa of remaining nervous tissue. HE x 25. (Below) Abundant PAS positive fungi surrounded by thick capsule amid amorphous material. PAS x 200. Inset. A budding specimen of *Cryptococcus neoformans*. Mucicarmin, x 1000.

DISCUSSION

The main point of interest about the present case was the discrepancy between the expected diagnosis of neurocysticercosis, anticipated from epidemiological, clinical and neuroimaging data and the final diagnosis of neurocryptococcosis revealed by autopsy.

The patient presented with intracranial hypertension and impaired level of consciousness. CT showed multiple cystic lesions in the brain which appeared highly suggestive of cysticerci, though no scolex was demonstrated. These findings and the epidemiological antecedents made the diagnosis of cysticercosis probable⁵. CSF exam was postponed in view of its high risk and dexamethasone was started. As a second CT showed worsening of edema and tonsillar herniation, the CSF examination could not be carried out. Retrospectively, it might have pointed to the presence of fungi and the correct diagnosis.

The neuropathological findings were unexpected. The cysts which appeared radiologically as the vesicular stage of cysticerci turned out to be gelatinous pseudocysts filled with *Cryptococcus*. Such abundance of fungi in the brain parenchyma is unusual, as the parasites tend to grow in the subarachnoid space and penetrate along the Virchow-Robin perivascular spaces. Cysts created in this way are normally small.

Most cases of central nervous system (CNS) infection by *C. neoformans* manifest as meningitis. Rarely, the disease may present as an expanding cerebral mass, formed by gelatinous pseudocysts, granulomas or both⁶. Miszkiel et al.⁷, examining the findings of magnetic resonance imaging (MRI) in patients with AIDS, found nine cases of cryptococcosis in the form of gelatinous pseudocysts larger than 3 mm. in diameter (which they referred to as cryptococcomas), eight in the basal ganglia and one in the cerebral white matter. The presence of parenchymal pseudocysts unassociated with leptomenigeal disease in cryptococcosis has yet to be adequately explained. Edelman et al.⁸ suggest that damage to the microcirculation and the blood brain barrier by HIV-1 may propitiate secondary hematogenous infection of brain tissue by the fungi.

We found no report of pseudocystic gelatinous form of cryptococcosis during pregnancy. Several cases of pregnant women without AIDS¹⁻⁴ or treated by immunosuppressive drugs for lupus⁹ are found in the literature but all had the meningitic form of the disease. Pregnancy may predispose to infections because of adjustments in the immune system in normal women, especially suppression of cell-mediated responses¹⁰. In our patient, autopsy did not favor the possibility of a severely immunocompromised patient. She was well nourished, without cutaneous or mucosal lesions and no organs other than the CNS were affected. Cryptococcal human infections usually occur by inhalation of *C. neoformans*. Although there was no obvious pulmonary lesion, isolated fungi were observed in lung capillaries, which may suggest hematogenous dissemination from an asymptomatic focus.

The CT images of the patient along with clinical and epidemiological data suggested a probable diagnosis of neurocysticercosis⁵. However this proved misleading because it is only when a scolex is seen by CT or MRI that cysticercosis can be considered certain⁵. The present case underlines the importance of pathological examination in establishing a final diagnosis in spite of the current technological progress in neuroimaging.

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