

Case Report

Long-lasting undetected neurocysticercosis

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Abstract

Neurocysticercosis is the most common parasitic disease of the nervous system, nevertheless, it can remain undetected for a long period of time, especially if it occurs in non endemic areas and regions with low-endemicity. Inadequate diagnostic procedures and lack of clinician's dedication towards this health issue can lead to a missed diagnosis.

Herein, we present a case of a 51-year-old male, with a missed diagnosis of neurocysticercosis for more than two decades. A history of epilepsy had started twenty-one years earlier and was of unclear etiology. Recently, after neurological worsening and headaches, brain computed tomography and magnet resonance imaging was performed as well as Western blot immunoassay of serum and cerebrospinal fluid, surgery, and pathohistological examination of the extracted cysts. Neurocysticercosis was confirmed. Combined therapy that consisted of albendazole and prednisolone was administered for a period of four weeks. Also, antiepileptic therapy was continued. Both clinical status and brain imaging showed the apparent improvement in the patient's condition.

Review of the literature was implemented in the discussion that deals with proper and adequate therapy option and outcome factors in neurocysticercosis patients. Over a long period of time, the majority of patients develop seizures as the most common symptom, which requires the administration of medications. Proper diagnostic procedures and adequate combination of surgery and conservative treatment are essential.

Key words: anticonvulsants; albendazole; immunoassay; magnetic resonance imaging; neurocysticercosis.

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Introduction

Cysticercosis is a parasitic tissue infection caused by ingestion of eggs from the adult pork tapeworm, *Taenia solium* [1]. Cysticercosis usually invades the skin, muscles, eyeballs or the central nervous system (CNS). Neurocysticercosis is a form of cysticercosis and it refers to the involvement of the central nervous system. It can affect brain parenchyma, cerebrospinal fluid (CSF) space or even the content of the spinal canal [2]. Neurocysticercosis is the most common parasitic disease of the nervous system. It is a human-to-human infection, the most often exhibited in areas with deficient sanitation [3].

Similar to the classic histological staging of parenchymal cysticercosis into four stages (vesicular, colloidal, granular nodular, and calcification stage), brain magnetic resonance imaging (MRI) reveals the five grades in the development of parenchymal cysticercus. This is important for the treatment of this disease, as stage 1 lesion responds best to the therapy, while in stage 5 antihelminthic treatment is useless [4].

Encysted larvae can remain asymptomatic for years, but when the larvae provoke a host immune response, patients usually develop brain edema and/or seizures [5]. MRI is expectedly superior method compared to the computed tomography scans (CT), as the brain lesion could remain unrecognized for years or even decades if the second method is used only, especially in the early stage of the disease. Clinical and microbiological features of neurocysticercosis must be taken into account, in order to get the right diagnosis.

Therapy of neurocysticercosis remains the matter of debate and controversies, even after many published papers dealing with this issue. The type of adequate antiparasitic therapy, the role of corticosteroid therapy, timing and effectiveness of antiepileptic therapy were so differently viewed by different authors that an evidence-based guideline had to be established [5].

Case Report

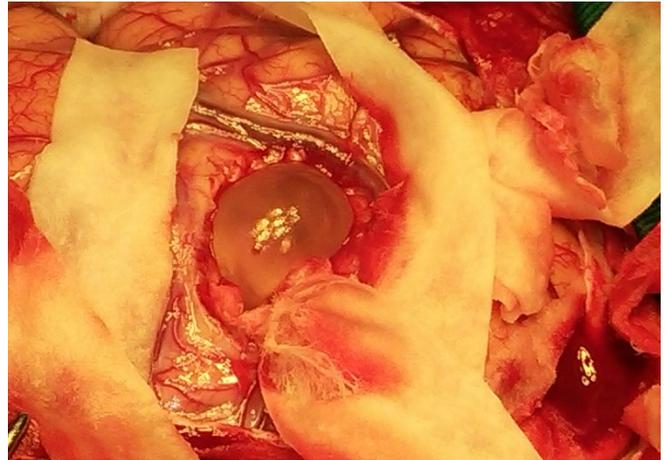
Herein, we present a case of a 51-year-old male. A history of epilepsy had started 21 years earlier when the

patient was admitted, diagnosed and treated in one of the major health facilities in Serbia. At that time antiepileptic therapy was introduced - Phenobarbitone 100mg a day. Besides epilepsy, no other clinical sign was present. A brain CT was performed and a radiologist described “a small tumor” in the right temporal region, deeply located near the *capsulaexterna* and thalamus. Unfortunately, only the radiologist’s report remained, without the brain CT scan. The nature of this lesion in the brain remained unclear, as no other diagnostic method was used, for an unknown reason. From the preserved medical records, an explicit recommendation for conservative treatment was found due to the high risk of the neurological deficit if operated. Except for occasional seizures that presented once in three or four years, he was without any other clinical presentation. The patient stopped seeing his neurosurgeon or neurologist and continued to take medication as mentioned above, antiepileptic therapy only.

The patient was admitted to the Clinic of Neurosurgery in Nis, for the first time, twenty-one years after the first seizure and initial brain CT. On admission, he had moderate left hemiparesis and intense headaches. Brain CT and MRI were done (Figure 1). A multicystic tumor-like formation was found. It resembled stage 3 neurocysticercosis, as it showed a thick capsule with an impure liquid content signal and surrounding edema, in the cystic phase;

Biochemical analysis of the serum was done in order to establish the degree of the cerebral and meningeal inflammation (Er: $3.78 \cdot 10^{12}$, Hct 35 L/L, Hg 119 g/L, neutrophilia 80.5%, lymphocytopenia 15.9%, and monocytopenia 0.13 19^9). The number of eosinophils was normal. Biochemical and cytological

Figure 2. Intraoperative finding. Extraction of the cyst through a small brain incision of the right parietal lobe.

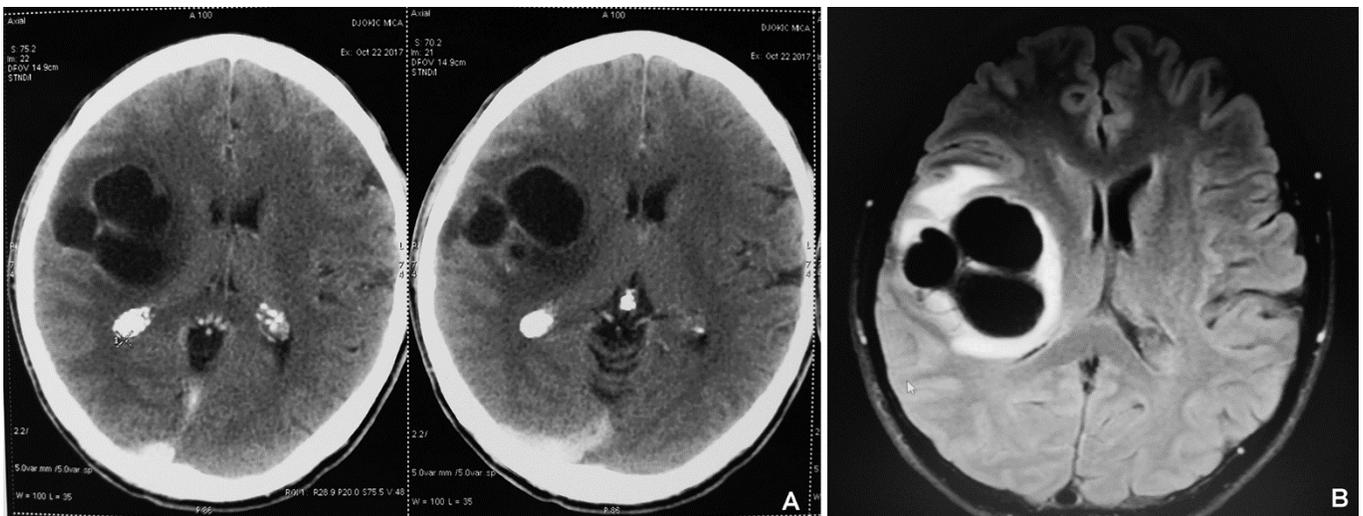


examination of the CSF showed normal cell number, and the slight increase of proteins 380 mg/L, normal glucose (3.4 mmol/L), and electrolytes.

Anamnestic, the patient remembered that three decades ago he had eaten the meat of a pig whose liver was covered with bubbles. Allegedly, the meat was properly cooked, as always. After a while, the patient’s younger brother was treated for “intestinal worms” of unknown species. He denies that any of the members of his present family had any indication of parasite infestation. Epidemiological survey revealed no relevant data of any other teniasis/cysticercosis risk factors.

The patient was operated, and during the surgery, three thin-walled cysts were extracted through the small topectomy not wider than 2 cm in diameter (Figure 2). We decided to perform gyrectomy rather than section through the cortical sulcus. Small dimensions of

Figure 1. A: Brain CT, B: MRI - a right temporal multicystic lesion.



cortical topectomy were essential due to adjacency of the motor cortex. Postoperatively, headaches and hemiparesis disappeared. Postoperative brain CT was done (Figure 3).

Surgery was delicate concerning the nearby location of the motor cortex and basal ganglia. Nevertheless, the neurological finding improved and satisfactory postoperative CT brain showed a good start of the treatment. The next step was a consultative examination by an infectious disease specialist who administered a proper antiparasitic therapy -

Figure 3. Postoperative CT. The finding after the removal of the cysts.

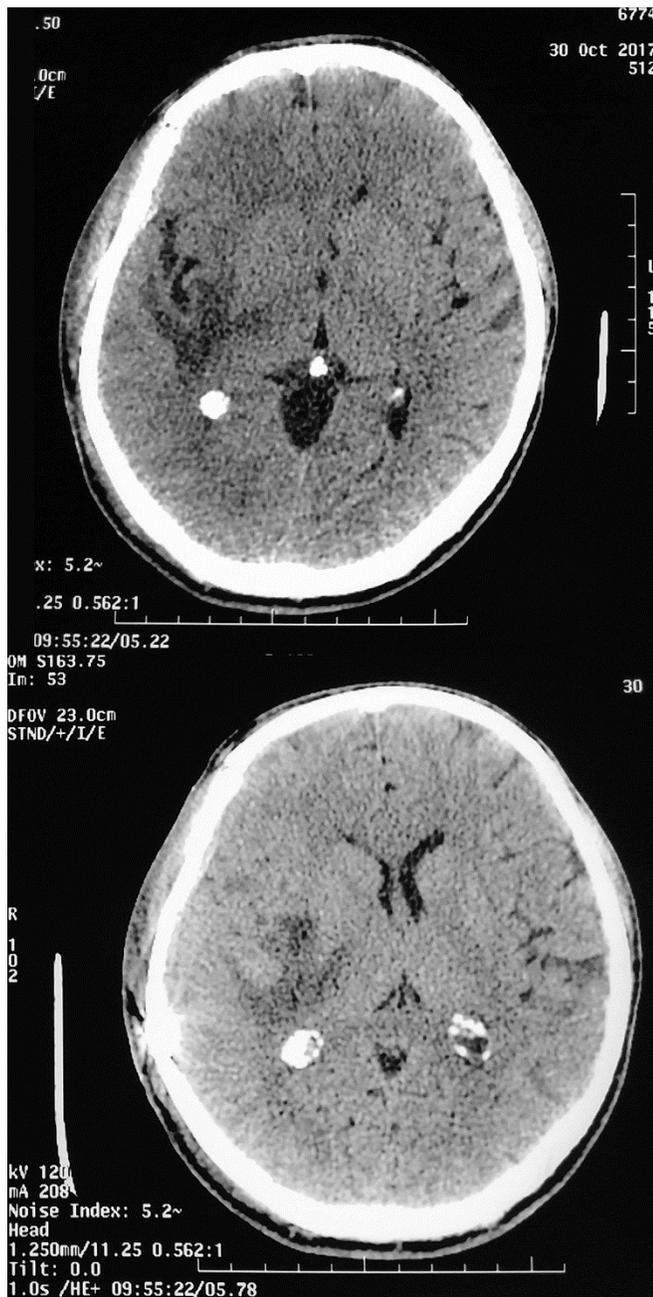


Figure 4. HE staining. Magnification 4 X. Cysticercus tissue (*Cysticercus cellulosae*). Cuticle, subcuticular cellular layer and innermost mesenchyme with numerous calcerous corpuscles (micro calcifications).



A – cuticle; B – subcuticular cellular layer; C – innermost mesenchyme; D – calcerous corpuscles (micro calcifications).

albendazole tablets in a dose of 400 mg, twice daily for the period of 4 weeks. With respect to the American Academy of Neurology (AAN) recommendation, albendazole therapy was combined with corticosteroid treatment, so prednisolone was administered in a dose of 2 mg/kg/day for 21 days, and then a 1-week taper ensued (4).

After a few days, pathohistological examination revealed the presence of cysticercus tissue (Figure 4).

Immunodiagnostic procedure - Cysticercosis IgG Western Blot (WB, LDBIO Diagnostics, Lyon, France) showed positive results and confirmed the presence of specific IgG antibodies in both samples (serum and CSF). The test was done according to the manufacturer's instructions. The antibodies (anti-cysticercoids) present in the samples are selectively bound to antigens (*Tenia solium* cysticerci extract of porcine origin), and then the phosphatase-anti-human IgG conjugate bonded to immunocomplex (antibody-antigen), and finally, the immune complex reacted with the substrate. Antigens that recognize the specific antibodies present in the samples were detected as purple transversal strips. A positive sample can be presented by numerous bands between 2 and 200 kilodaltons (kDa). A range of 6 to 55 kDa was selected for reading, because of its specificity. Areas 6-26 kDa and 39-55 kDa are the most specific and easily readable and interpretable. The presence of at least 2 clearly defined strains among the 5 described (P6-8, P12, P23-

26, P39, and P50-55) was indicative of serum cysticercosis and neurocysticercosis in CSF.

Seven days after, the patient was discharged from the hospital. He was seen ambulatory in good clinical and neurological condition, a month after. His antiepileptic therapy remained as before because electroencephalogram (EEG) finding required so, but his albendazole and prednisolone therapy had been halted. EEG showed focal spike-wave discharges in the right temporoparietal region, the signs of epileptic discharge. He was complaining of the strange taste of his tears and occasional localized headaches in the operated area. Three months after EEG remains unchanged, but all symptoms have disappeared.

Discussion

Around 50 million people worldwide are estimated to have cysticercosis infection [6]. Cysticercosis is endemic in many regions of Central and South America, sub-Saharan Africa, India, and Asia [7]. The disease is extremely rare in Eastern Europe, particularly in Serbia, while the growing number of migrants in western and south parts EU and USA makes this health issue current. In the USA, fatal cysticercosis affected mainly immigrants from Mexico and other Latin American countries - there were a total of 221 cysticercosis deaths in the period from 1990-2002, mainly in the state of California [8,9]. According to some authors [10], the annual incidence of cysticercosis in Serbia varies between 0 and 0.29 cases per 100,000 population and 0.0002 mortality per 100,000 population in 2013 [11]. In the Clinical Center Niš (in the South East of Serbia), the last case of cysticercosis was detected three decades ago.

Study patient, undoubtedly, ingested ova of *Tenia solium*, more than twenty years ago, as seizures and medical documentation date from that period. Yet, it is unclear why neurological worsening and headache took so long to appear. MRI finding revealed stage 3 lesion with moderate edema alongside to right capsulaexterna, and it could provoke neurological deficit. Nevertheless, cerebrovascular complications of NCC are well known, and they include cerebral infarction, transient ischemic attacks, and subarachnoid hemorrhage [12-14]. These complications are always due to arteritis caused by vessel wall inflammation and cell morphology changes. The reason for the prompt postoperative improvement is likely due to operative decompression which could eliminate the compression effect of the lesion and perilesional edema only but not due to the morphological changes of the arteries. Therefore, the reason for the worsening of the patient is probably the

growth of the lesions, and more important of the perilesional edema. The pathophysiology of perilesional edema is not completely clear, but it seems that it recurs, and repeated episodes tend to be associated with the same lesions in a patient. Neurocysticercosis typically presents either with seizures (70% to 90% of acutely symptomatic patients) or a headache [15-17]. A headache appears usually due to increased intracranial pressure, the presence of hydrocephalus or meningitis. The patient in our study had seizures due to an intracranial process of unknown etiology at the start that was demystified after the surgery. The signs of raised intracranial pressure and focal neurological deficit appeared eventually, so an operation was inevitable and that resulted in establishing an adequate diagnosis.

The guideline issued by the AAN, that is also endorsed by American Epilepsy Society, recommends a combination of albendazole and either prednisolone or dexamethasone in order to diminish the number of active lesions on brain imaging findings and reduce long-term seizure frequency.

There are differences in recommended therapy for patients with a single inflamed cysticercus causing seizures, those who have hydrocephalus caused by obstruction of cysticerci in the ventricles, and those with multiple parenchymal cysticerci [18]. The inflammatory response of the host is a newly recognized important element in the pathogenesis of the disease. After spontaneous resolution of the cystic lesion or even after antiparasitic drug treatment, calcification remains. These rudiments of the disease represent the risk of chronic epilepsy [19]. These facts indicate that symptomatic treatment could be more important than the type of causal treatment. Until recently, there were some doubts about the usefulness of the antiparasitic drugs [20] knowing the fact that only up to 50% of the lesions resolve within 6 months, even after full therapy protocol was administered.

Neurosurgery has a limited role in the treatment of neurocysticercosis. Only when signs of raised intracranial pressure appear or in case of obvious hydrocephalus, surgical treatment is indicated. It seems that minimally invasive techniques are associated with a higher success rate than any other neurosurgical approach in cases that are amenable to endoscopic intervention [21,22].

In the relatively wide study of Colli *et al.*, 160 surgically treated patients with neurocysticercosis were analyzed. The removal of a giant cyst from the parenchyma, cisterns or ventricles for the relief of increased ICP improved most of the symptoms in patients. Patients with a ventricular cyst and

ependymitis/arachnoiditis required the placement of a ventriculoperitoneal shunt after the cyst was removed. The authors concluded that long-term prognosis in patients with cerebral cysticercosis who required surgery was not good. Poor prognostic factors were the location of the cysts in the basal cisterns and patient age under 40 [23].

Our conservative treatment was similar to that of other authors. Some authors [24] demonstrated the effectiveness of short-term antiparasitic therapy in the absence of corticosteroid therapy. Nevertheless, knowing the results of the Singhi *et al.*'s study where single cysts disappeared on 3-month follow-up CT in 53% of patients receiving steroids, in 60% of those receiving albendazole, and in 63% of those receiving both treatments, we decided to apply combined therapy [25]. The effects of the application of corticosteroid therapy without administration of cysticidal therapy in neurocysticercosis have not been properly studied. Based on the results of some studies, there is not enough evidence to recommend corticosteroid treatment alone for patients with solitary intraparenchymal neurocysticercosis granulomata [25-27]. Also, the use of antiepileptic drugs for preventing seizures among patients with neurocysticercosis that had never suffered from it seems to be unjustified. For those presenting with seizures, there is no reliable evidence regarding the duration of treatment required [28].

The treatment effect of albendazole plus symptomatic therapy occurs within the first 30 days after treatment. One month after the application of combined treatment, there is no additional gain concerning disappearance or reduction in the number of active cysts [29].

Some authors make a difference in the outcome depending on the location of the cyst, where patients with intraventricular and parenchymal cysts usually have a good prognosis. For those with hydrocephalus associated with cisternal or racemose cysts and with cysticercotic meningitis, the mortality is high [30]. When taking into account seizure control, symptomatic improvement of non-seizure patients and finely imaging findings, the outcome of treatment was better in the parenchymal than in the extraparenchymal neurocysticercosis. Repeated cysticidal treatment was needed in 26% of parenchymal neurocysticercosis and 39% of extraparenchymal [31].

Conclusion

Therapy of neurocysticercosis remains an untold story, with present doubts concerning both cysticidal drugs and surgical treatment. Sometimes, also,

establishing its diagnosis could be a problem, and can take decades, due to a lack of clinicians' dedication. Over a long period of time, the majority of patients develop seizures as the most common symptom, which requires the administration of medications. Therefore, prevention by health education is emphasized.

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