Calcified Mass on Brain CT in a Teenager with Refractory Seizures

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SUMMARY – *Cerebral echinococcosis is very rare, representing 2% of all cystic echinococcosis (CE) cases. Primary echinococcal cysts of the brain are extremely rare in pediatric patients. We report on a 16-year-old boy referred to our tertiary center with intractable epilepsy for the previous three years despite receiving full doses of three antiepileptic medications. Brain computed tomography (CT) showed a left frontal calcified mass. Magnetic resonance imaging (MRI) of the brain revealed a well-defined spherical mass in the left frontal lobe, slightly hypointense on T1-weighted and heterogeneous hyperintense on T2-weighted images with no contrast enhancement. With a broad differential list in mind, a surgical intervention was planned. During surgery, a primary calcified cerebral echinococcal cyst with severe adhesion to the adjacent dura of the frontal region was discovered and removed intact. Histopathology examination confirmed the diagnosis. Only phenobarbital was continued and no medical therapy for CE was administered. Two years after surgery, the patient remained free of seizures. In areas endemic for CE, cerebral echinococcal cyst should be included in the differential list of patients with intractable seizures. Though rare, this entity can present itself as a calcified mass on neuroimaging. Surgical removal of the calcified cyst is necessary for control and treatment of the epilepsy.*

Introduction

Human cystic echinococcosis (CE) occurs when a person becomes an intermediate host of the dog tapeworm, *Echinococcus granulosus*¹⁻⁴. The disease is endemic in Iran, the Middle East, and Mediterranean countries^{1-3,5}. It occurs most commonly in the liver and lungs^{2-4,6}. Cerebral echinococcal cyst is very rare and represents only 2% of all CE cases^{1-3,5}. Cerebral echinococcal cysts are more common in children and young adults. They are mostly located in the supratentorial region and tend to occur in the distribution of the middle cerebral artery, most frequently in the parietal lobe¹⁻⁶.

Primary CE5 is very rare and represents less than 1% of all cerebral hydatid cysts^{1,2,7,8}. A review of the English language literature disclosed only eight cases of primary echinococcal cyst of the brain in the post-CT scan era

to date^{2,5-10}. All of the reported cases occurred in adult patients. We report on a 16-year-old boy with primary calcified cerebral echinococcal cyst who presented with a long-term history of intractable epilepsy. To the best of our knowledge, this is the first pediatric case with primary CE5 cyst in the English language literature.

Case Report

A 16-year-old boy was admitted to our hospital with a six-year history of grand mal epilepsy that had gradually become refractory to full doses of phenytoin, phenobarbital, and carbamazepine for the previous three years. Except for grand mal seizures, his medical history was unremarkable. He lived in a rural area of western Iran with a history of contact

Figure 1 A) Plain skull x-ray showing a focus of calcification in the left frontal area (arrow). B) Axial non-contrast brain CT scan showing a well-defined calcified mass in the left frontal region.

Figure 2 A) Axial T1-weighted MRI of the brain showing a well-defined slightly hypointense spherical mass in the left frontal area. B) Axial T2-weighted MRI of the brain showing a well-defined inhomogeneous hyperintense spherical mass with calcified dark signal rim in the left frontal area.

Figure 3 A) Gross pathology showing a well-encapsulated grayish white mass with adherent dura. B) Caseous material seen inside the lesion.

Figure 4 Post-operative axial brain CT scan showing no residual mass lesion (taken one month after surgery).

with sheep and dogs. He had never undergone neuroimaging studies earlier; his epilepsy was evaluated only with electroencephalography (EEG).

Upon admission, neurological examination was normal. Plain radiography of the skull showed a round inhomogeneous calcified mass in the left frontal region (Figure 1A). CT scan

of the brain showed a round calcified mass in the left frontal region accompanied by atrophy of the adjacent frontal lobe and dilatation of the frontal horn of the left lateral ventricle (Figure 1B). Magnetic resonance imaging (MRI) of the brain revealed a well-defined spherical mass in the left frontal lobe, slightly hypointense on T1-weighted and heterogeneous hyperintense

on T2-weighted images with no contrast enhancement (Figure 2A,B). In the center of the lesion, there was a collapsed membrane with scalloped outlines. With regard to the calcified lesion in the cerebral parenchyma and differential list for this condition, surgical intervention was planned for the patient.

A left frontal craniotomy was performed. During the operation, a well-defined grayish white mass was removed, completely intact, with adherent dura (Figure 3A). In addition, there was a thick gliosis around the mass lesion. On opening the mass, it was found to be filled with a caseous material (Figure 3B). Histological study revealed calcified cerebral hydatid cyst.

The post-operative course was uneventful. The patient received phenobarbital 100 mg daily and two years after surgery, he remained free of seizures. Due to the calcific nature of the lesion, no medical therapy for CE was administered following surgery. Post-operative CT scans taken one month and one year after surgery showed no residual mass lesion (Figure 4). The evaluation for echinococcal cysts in other organs was negative.

Discussion

The echinococcal cyst is the larval form of *Echinococcus granulosus*^{1,5,6,11,12}. After ingestion, the eggs lose their enveloping layer, thereby releasing the hexacanth embryos, which penetrate the small intestine wall, and are carried to the liver via the bloodstream; from the liver they can reach other organs, among which the central nervous system^{1,4,12}. When an embryo of *Echinococcus granulosus* is lodged in the brain substance, a slow-growing, thin-walled cyst is formed, inside which the further larval stage of the parasite develops^{1,4,12}. The hydatid cyst wall is made up of three layers: 1) the outer layer or host-derived adventitia, which is thin, 2) the intermediate layer (laminated layer), which is made up of acellular material, and 3) the inner layer, which is the germinal layer from which broad capsules and protoscolices bud^{1,3,6}. The outer layer (pericyst) contains blood vessels and provides nutrients for the parasite³. The wall of the cyst is whitish, smooth and soft to touch and has a certain amount of elasticity. The fluid in the cyst is watery and colorless, but occasionally may be whitish or yellow^{1,6,12}. The growth rate of cerebral hydatid cysts has been estimated at about 1-10 cm per year⁴.

In the liver and other organs the US appearance of the cyst may change over time, either spontaneously or in response to treatment, and proceeds from an unilocular fluid-filled stage (CE1) through the detachment of the endocyst (CE3a) to either complete solidification (CE4 and CE5) or growth of daughter cysts in its cavity (CE2 and CE3b). CE1 and CE2 are classified as active cysts, and CE4 and CE5 are inactive cysts. CE3 cysts are classified as transitional, although recent studies suggest that CE3b should be reclassified as active. These different stages are seen in the brain as well¹⁴. Our patient had a CE5 inactive cyst, but because of its location the cyst was complicated and this brought the patient to seek medical attention.

Very little is known on the role of different *E. granulosus* strains in causing specific location, but one recent paper reported that of ten patients with cerebral cysts, they all had the G6 genotype in their fluids¹³. Though the authors claim that this indicates a predilection of G6 for the brain, this claim has to be taken cautiously and this finding deserves further studies on larger series.

There are two types of calcification in cerebral hydatid cysts: 1) linear or ring-like peripheral calcification that develops in the pericyst, and 2) round, ball-like calcification, which begins in the center of the cyst and progresses outwards involving all the components of the cyst, making the cyst inactive^{2,5-10,12}.

The differential diagnoses of calcified cerebral hydatid cysts include tuberculoma, cysticercosis, oligodendroglioma, cavernoma, calcified arteriovenous malformation, calcified hematoma, and calcified cerebral abscess^{2,5,7,11,12}.

While calcification may occur in 20-30% of hepatic hydatid cysts⁶, this radiologic finding in cerebral hydatid cyst is very rare and occurs in just about 1% of these patients^{15,16}. Calcification, if present, is usually ring-like, with a curvilinear pattern and starts in the pericyst⁶. With progression of the degeneration process, it develops in all the components of the cyst and leads to dense calcification^{2,5-10}. There is debate in the literature on whether or not calcification (in particular cyst wall calcification) indicates parasite death and subsequently obviates initiating an anti-parasite treatment. Complete calcification of the cerebral hydatid cyst may indicate death of the parasite^{1,7-9,17}, while pericyst calcification *per se* may not necessarily be an indication of the parasite death^{6,18}. Based on this, some experts described calcification as a sign of parasite death^{17,19}, while others have ar-

gued against this²⁰. In one case, for instance, a hepatic hydatid cyst with partial wall calcification was left untreated and after eight years the cyst was removed operatively disclosing live protoscolices²⁰. Cyst calcification is not limited to the inactive WHO cyst types CE4 and CE5. The factor that determines inactivity of the cyst is stability of the cyst consolidation over time²¹. The pathophysiology of cerebral hydatid cyst calcification is unknown, but two hypotheses can be proposed:

1) Spontaneous or traumatic rupture of the cyst leads to leakage of cyst fluid and small hemorrhage in the cyst bed. This causes an intense inflammatory reaction around the cyst in the brain parenchyma and leads to the formation of an adventitial membrane around the cyst. Then, the calcium salt accumulates mainly in the outer layer of the cyst (i.e., adventitia) or sometimes in the wall of mother cysts with consequent partial or total calcification. Calcification of the outer layer of the hydatid cyst disrupts the parasite's nutrient pathway and gradually leads to death of the parasite. This type of calcification is usually peripheral but with progression of the cyst inactivation and death of the parasite it may progress and involve all cyst components.

2) A bacterial infection occurs in hydatid cyst content and leads to inflammation and death of the cyst. Further calcium deposition in the content of the cyst leads to central calcification of the cyst^{1,2,5-8,12}.

During our surgery, there was a thick gliotic layer around the calcified cyst that could have been the result of a prior intense inflammatory process. Histopathological findings of the removed calcified cyst were similar to those seen in a non calcified cyst without any previous infectious reaction. Because of the absence of any infectious reaction in the cyst wall and cyst contents and the presence of a thick ad-

ventitial membrane and intense gliosis around the lesion, we speculate that cyst rupture was the initial cause of the calcification process in our case.

Although impossible to date, it is tempting to speculate that this cyst became clinically appreciable only at a late stage, similarly to what happens in organs like the liver, when complications (e.g., rupture into the biliary tree) lead the patient to seek medical attention. This might explain the rarity of an inactive cyst in late pediatric age, which is in agreement with our hypothesis.

The only treatment of calcified cerebral hydatid cysts that cause neurological symptoms and intractable seizures is surgical removal of the lesion^{2,6-9}. Resection of the calcified cyst leads to improvement of neurological deficits and control of epilepsy^{6,8,9}. Because of inactivity and death of calcified cerebral CE5 cyst, medical treatment of the cyst is not necessary in the postoperative stage.

Conclusion

Primary CE5 cysts are extremely rare in pediatric patients. Epileptic attacks, especially intractable seizures, with presence of an intracranial calcified mass in children and young adults from an endemic area should raise the suspicion of a cerebral cyst. Removal of the calcified cyst is necessary for control and treatment of the epilepsy. This case report contributes to the broadening of our knowledge of the natural history of CE in a relatively rare location and in pediatric patients. This finding suggests that in the brain, as well as in other organs, cysts may change from active to inactive and remain clinically silent. Regardless of biological inactivity, they can still cause complications, as seen in other organs that are more frequently affected than the brain.

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