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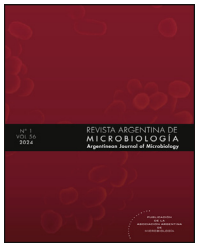

BRIEF REPORT

Atypical human cystic Echinococcosis with multiple cerebral cysts caused by *Echinococcus canadensis*

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Abstract Cystic echinococcosis is a zoonotic parasitic infection and a recognized neglected disease primarily caused by species within the *Echinococcus granulosus sensu lato* (*s.l.*) complex. Its cerebral clinical presentation is uncommon and usually manifests as a solitary hydatid cyst. We report an atypical case of cystic echinococcosis with multiple cerebral cysts in a 16-year-old boy from Córdoba Province, Argentina. Microscopic examination of the cyst contents revealed the presence of protoscolices characteristic of *Echinococcus* spp., confirming the parasitic nature of the lesions. PCR and DNA sequencing identified the parasite as *Echinococcus canadensis* genotype G6, one of the five species within *E. granulosus s.l.* complex known for its zoonotic potential and prevalence in certain geographic regions. This case underscores the importance of considering hydatid disease in the differential diagnosis of intracranial cystic lesions, particularly in endemic areas. Moreover, the identification of *E. canadensis* G6 adds to the growing evidence of its significant role as an etiological agent of cystic echinococcosis in our region.

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PALABRAS CLAVE
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Quistes cerebrales múltiples;
Diagnóstico de equinococosis

Equinococosis quística humana atípica con múltiples quistes cerebrales ocasionada por *Echinococcus canadensis*

Resumen La equinococosis quística es una infección parasitaria zoonótica y una enfermedad desatendida reconocida, causada principalmente por especies del complejo *Echinococcus granulosus sensu lato (s.l.)*. Su presentación clínica cerebral es infrecuente y, por lo general, se manifiesta como un quiste hidatídico solitario. En este trabajo se describe un caso atípico de equinococosis quística con múltiples quistes cerebrales en un adolescente de 16 años procedente de Córdoba, Argentina. El examen microscópico del contenido quístico reveló la presencia de protoescólices característicos de *Echinococcus* sp., confirmando la naturaleza parasitaria de las lesiones. El análisis por PCR y secuenciación de ADN identificó al parásito como *Echinococcus canadensis* genotipo G6, una de las cinco especies del complejo *E. granulosus s.l.* reconocida por su potencial zoonótico y prevalencia en determinadas regiones geográficas. Este caso destaca la importancia de considerar la hidatidosis en el diagnóstico diferencial de las lesiones quísticas intracraneales, especialmente en zonas endémicas. Además, la identificación de *E. canadensis* G6 refuerza la evidencia creciente de su papel relevante como agente etiológico de la equinococosis quística en nuestra región.

Cystic echinococcosis (CE) is a zoonotic parasitosis mainly caused by *Echinococcus granulosus sensu lato* (*s.l.*)[1]. The World Health Organization has classified echinococcosis as a neglected disease, posing a significant health challenge in endemic regions. In this regard, Western China, Central Asia, South America, certain countries in the Mediterranean region, and Eastern Africa are considered areas of high endemicity for this parasite infection. Moreover, approximately 5000 new cases of CE are reported annually in countries such as Argentina, Brazil, Chile, Peru, and Uruguay[2–4].

The life cycle of the parasite involves definitive hosts (dogs and other canids), and intermediate hosts (such as sheep, goats, pigs, cattle, and camelids) that harbor hydatid cysts containing parasite larvae in different tissues. Humans are accidental intermediate hosts, with the liver (67–89%) and lungs (10–15%) being the most frequently affected organs[5]. Cerebral hydatidosis is a rare clinical presentation of CE, usually manifesting as a single hydatid cyst. Its diagnosis remains a major challenge, especially in endemic rural areas[6].

E. granulosus s.l. is a species complex exhibiting considerable genetic diversity[1] and has recently been reclassified into five main species comprising ten genotypes (G1–G10). These species include: *E. granulosus sensu stricto* (covering genotypes G1 to G3, commonly associated with the sheep-dog cycle), *E. equinus* (G4, associated with horses), *Echinococcus ortleppi* (G5, associated with cattle), *Echinococcus canadensis* (G6, camel strain; G7, pig strain; G9, probably a variant of the pig strain; G8 and G10, cervid strains), and *E. felidis* (lion strain)[4]. Among these, genotype G1 is responsible for the majority of human CE cases worldwide, accounting for approximately 88% of infections, while genotypes G6 and G7 contribute an additional 11%[7]. In Argentina, *E. canadensis* G6 has been identified in human CE cases, with goats and cattle serving as the primary intermediate host in the region[8–10]. Particularly, the Neuquén Province is a highly endemic region for CE in Argentina, and *E. canadensis* G6 has been reported in 57.1%[8], 36.5%[9] and 34.7%[11] of human cysts. This proportion of human cysts attributed to *E. canadensis* G6 is much higher than that reported worldwide[7].

In this study, we present a clinical case of CE with multiple cerebral localizations caused by *E. canadensis* G6 in a 16-year-old boy from a rural area of Córdoba province, Argentina. This case contributes to the current knowledge of the genetic diversity of *E. granulosus s.l.* species circulating in Argentina, highlights the importance of molecular typing for epidemiological surveillance and understanding of transmission dynamics, adding to the growing evidence that *E. canadensis* G6 plays a more significant role in human infection than previously recognized.

In January 2024, a 16-year-old boy from a rural area in northern Córdoba province, Argentina, was admitted to Rawson Hospital in the city of Córdoba, presenting with weakness in the lower limbs and an unsteady gait, experiencing frequent falls over the past four months, as well as generalized, involuntary, uncoordinated movements during the preceding month. The patient had no known medical history, and worked as a rural laborer involving husbandry and slaughter of cattle, bovines, and equines. He kept dogs and cats as pets.

Physical examination revealed right hemiparesis (facial, brachial, and crural) with a strength scale of 4/5, mild spasticity in the upper limbs, uncoordinated finger-to-nose test, inexhaustible clonus in the right foot with positive Babinski reflex, right ataxia and hemiplegic gait.

Brain magnetic resonance imaging (MRI) with intravenous contrast revealed multiple cystic lesions with homogeneous content and thin walls, distributed in both cerebral hemispheres (supratentorial), causing midline displacement. An additional cystic lesion was observed in the posterior fossa

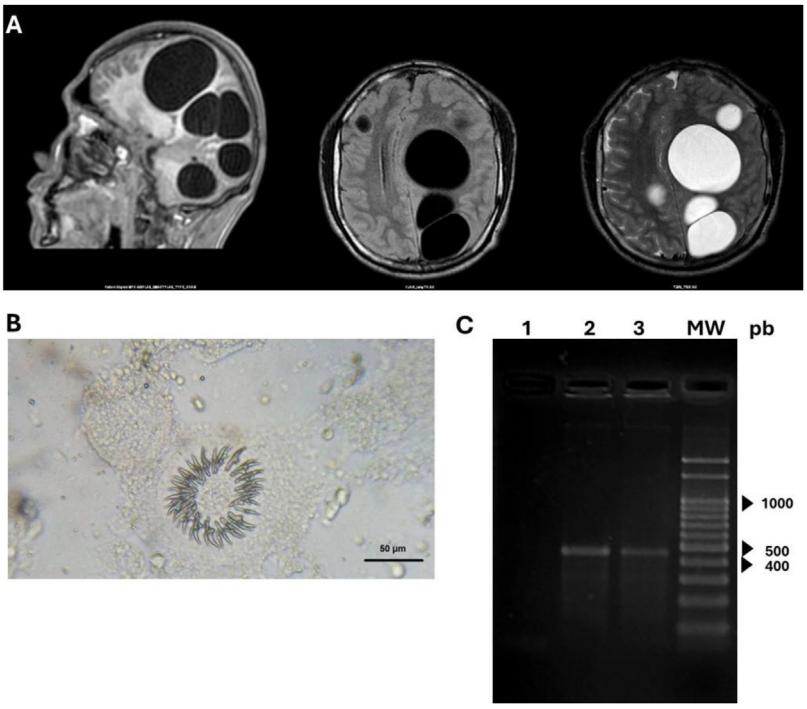

Figure 1 Cystic Echinococcosis with multiple brain localizations. (A) Brain MRI without contrast (left and middle images): sagittal and axial views, FLAIR sequence. Brain MRI with contrast (right image): supratentorial axial view, T2 sequence. (B) Light microscopy of a cyst material sample from the brain showing a characteristic hook crown (400× magnification). (C) Agarose gel electrophoresis (2%) showing amplification products (∼466 bp) from PCR from a cyst material sample from the brain. Lane MW: molecular weight ladder; lane 1: negative control (water); lanes 2 and 3: cyst samples from patient; bp: base pairs. MRI: magnetic resonance imaging; FLAIR: fluid attenuated inversion recovery; T2: T2-weighted imaging; PCR: polymerase chain reaction.

(cerebellum), with the largest measuring 60 mm. No peripheral edema or contrast enhancement was noted (Fig. 1, panel A). A panoramic tomography with intravenous contrast revealed hypodense cysts in both renal parenchyma, the neck of the pancreas, and various striated muscles, including the right gluteal region, right subscapular area, external oblique of the abdomen, and the vastus intermedius of the left quadriceps. Additionally, cysts were observed in the heart. No cysts were detected in the pulmonary or hepatic parenchyma. A Doppler echocardiogram confirmed three cysts in the septum and a right lateroapical cyst.

Serologies for HIV, HBV, HCV, syphilis, toxoplasmosis, and Chagas disease were negative. ELISA and an immunochromatographic rapid test for hydatidosis were positive. Due to the suspicion of multiple hydatidosis, the patient was started on albendazole 400 mg orally every 12 h, initiated one month prior to the surgical intervention[12,13].

The patient underwent surgical intervention, including guided frontal corticotomy, craniectomy, and cyst evacuation. Microscopic examination of the cyst material revealed the presence of characteristic *Echinococcus* spp. hooks (Fig. 1, panel B), and molecular analysis by PCR and amplicon sequencing (Cox1 F, Cox1 R)[14] identified *E. canadensis* G6 (Fig. 1, panel C, Supplementary Figure).

For PCR and amplicon sequencing, DNA was extracted from cyst material using the DNeasy Blood & Tissue Kit® (Qiagen, USA) following the manufacturer's instructions. PCR assay was performed using a set of primers specific for *E. granulosus s.l.* 5′-TTTTTTGGGCATCCTGAGGTT-3′ (Cox1 F) and 5′-TAAAGAAAGAACATAATGAAAATG-3′ (Cox1 R) that amplify a fragment of 466 bp including the cytochrome c oxidase subunit I (cox1) gene. Amplification was conducted according to Bowles et al.[14] with minor modifications. Briefly 30 ng of DNA template, 0.2 µl dNTP (2 mM), 5 pmol of each primer, 0.6 µl $MgCl_2$ (50 mM), 1 U Taq Pegasus DNA polymerase (Productos Bio-Lógicos, Argentina), 20 mM Tris−HCl (pH 8.4), 50 mM KCl in a total volume of 20 µl. Negative control with no DNA was included. PCR amplification was performed in a TC1000-G thermal cycler (DLAB®) using a touchdown annealing strategy[1], starting at 55 °C and decreasing by 1 °C every two cycles for the first 20 cycles, followed by 15 cycles at 45 °C. Denaturation was carried out at 95 °C for 5 min initially and 30 s thereafter, with extension at 72 °C for 60 s per cycle and 5 min in the final cycle. PCR products were subjected to electrophoresis in 2% agarose gel and visualized by ethidium bromide staining (Fig. 1, panel C). To confirm this finding, the PCR amplification product was subjected to a direct nucleotide sequencing reaction in both directions by using the PCR primers (Cox1F and Cox1R) on an Applied Biosystems SeqStudio Genetic Analyzer (ThermoFisher) at the Departamento de Diagnóstico Molecular, LACE Laboratorios, Córdoba, Argentina. Sequences obtained were aligned using MEGA version 11 and manually edited with BioEdit. The resulting nucleotide sequence was subjected to BLAST searches using the data available on GenBank (http://www.ncbinlm.nih.gov/genbank/). To determine the similarity and difference rates between the sequence and

those described for *E. granulosus s.l.* genotypes, we downloaded all 366 bp Cox1 sequences of genotypes described by Avila et al.[1] and a BLAST 2 sequences alignment (https://blast.ncbi.nlm.nih.gov/Blast.cgi) was performed. This *E. granulosus s.l.* isolate was identical to *E. canadiensis* G6 sequence (Supplementary Figure).

The patient demonstrated a favorable postoperative recovery under oral albendazole therapy. A second surgery for posterior fossa cyst evacuation was proposed but later declined. After six months of continued treatment, follow-up CT revealed resolution of cardiac, pancreatic, and striated muscle cysts, with partial regression of posterior fossa lesions. Clinically, right brachiocrural hemiparesis, gait, and upper limb spasticity improved. The patient remains under outpatient follow-up with ongoing albendazole therapy.

In March 2025, the patient was admitted to the emergency department with progressive gait disturbance, limitations in daily activities, ataxia, and an increase in both focal and generalized seizure episodes over the preceding month. Brain imaging revealed new cysts and enlargement of pre-existing cerebellar lesions. The findings, consistent with disease reactivation, are likely due to the patient having discontinued antiparasitic treatment two months prior to the relapse.

This case underscores the importance of considering hydatid disease in the differential diagnosis of intracranial cystic lesions, especially in endemic areas. The identification of *E. canadensis* G6 in this atypical case of CE highlights important aspects relevant to the epidemiology of this parasite.

Traditionally, within the *E. granulosus s.l.* complex, *E. granulosus s.s.* G1, has been recognized as the predominant etiological agent responsible for the majority of human hydatidosis cases worldwide often associated with transmission via sheep as intermediate hosts. In contrast, the closely related *E. canadiensis* G6, was found to be responsible for 7.34% of infections worldwide. This genotype is known from Africa and Asia, where it is transmitted mainly by camels and goats, and South America, where it appears to be mainly transmitted by goats[7]. In this regard, Soriano et al.[10] reported that in the Neuquén Province of Argentina, goats are infected with *E. canadiensis* G6. More recently, a molecular epidemiology study conducted by Ávila et al.[1] reported the presence of *E. ortleppi* G5 and *E. canadensis* G6 in human cases from the Provinces of San Juan and Catamarca, as well as *E. canadensis* G7 in pigs from Córdoba Province, Argentina. Notably, *E. canadensis* G6 and *E. ortleppi* G5 were identified as causative agents of CE in young patients, suggesting that these species are actively involved in human transmission cycles in Argentina.

Although treatment strategies do not differ among species within the *E. granulosus s.l. complex*, species-specific biological and clinical differences have been reported. Debiaggi et al.[11] analyzed a large series of human CE cases (n = 90) from the Province of Neuquén, Argentina, and found significant differences between *E. granulosus s.s.* and *E. canadensis* G6. Specifically, *E. granulosus s.s.* cysts were more frequently located in the liver, whereas *E. canadensis* G6 cysts showed a predominance of pulmonary and extrahepatic localizations. Moreover, the diameter of lung cysts caused by *E. granulosus s.s.* was significantly larger than those attributed to *E. canadensis* G6, and the proportion of inactive cysts was notably higher in G6 (55.6%) compared with *E. granulosus s.s.* (15.3%). In line with these findings, Sadjjadi et al.[15] and Örsten et.a.l.[16] also reported that *E. canadensis* genotypes, G6 and G7, are more frequently associated with extrahepatic sites (including lung, spleen, and occasionally brain) than *E. granulosus s.s.* Nevertheless, although several studies have addressed the genetic characterization of *E. granulosus s.l.*, data on the relationship between clinical features and genetic diversity remain limited[16].

Further studies in endemic regions are needed to better understand the clinical implications of infections caused by distinct *E. granulosus s.l.* species. Additionally, the prevalence of specific genotypes in livestock populations could impact the efficacy of vaccination strategies aimed at interrupting parasite transmission and reducing the incidence of human infection[4].

In conclusion, the identification of *E. canadensis* G6 in a human case of cerebral hydatidosis in Córdoba province in Argentina highlights the growing recognition of genetic diversity within the *E. granulosus s.l.* complex as a causal agent of CE in our region.

Ethical approval statement

This study was approved by the Research and Ethics Committee of Rawson Hospital.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

The data presented in this study are available in the article and Supplementary Material.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.1016/j.ram.2026.100708.

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