

A Rare But Fatal Case of Granulomatous Amebic Encephalitis with Brain Abscess: The First Case Reported from Turkey

Nadir Gözlenen Ölümcül Seyirli Beyin Absesinin Eşlik Ettiği Granülomatöz Amebik Ensefalit Olgusu: Türkiye'den Bildirilen İlk Olgu Sunumu

ABSTRACT

The incidence of protozoal and helminthic infestations of the central nervous system (CNS) is less than 1%, but these infestations tend to follow a fatal course. They are more common among children, the elderly and immunocompromised individuals. CNS infections due to *Entamoeba histolytica* have been known for a long time. In recent years, especially in developing countries, there has been an increase in CNS infections due to free-living amebas (FLAs). Acute CNS infection due to *Naegleria fowleri*, which ends in death within 2-7 days, is termed primary amebic meningoencephalitis (PAM); subacute or chronic CNS infections due to *Acanthamoeba* spp, *Balamuthia mandrillaris*, and *Sappinia diploidea*, which occasionally cause cerebral abscess, are termed granulomatous amebic encephalitis (GAE). This paper presents a case of GAE with abscess formation in a 75-year-old male patient.

KEY WORDS: Brain abscess, Granulomatous amebic encephalitis, Treatment

ÖZ

Protozoa ve helmintlerin sebep olduğu santral sinir sistemi (SSS) infeksiyonları <%1 oranında gözlenir ve oldukça fatal seyirlidirler. Çoğunlukla çocuk, yaşlı ve immün sistemi baskılanmış bireylerde gözlenir. *Entamoeba histolytica*'nin sebep olduğu SSS infeksiyonu tablosu uzun yıllardır bilinmektedir. Son yıllarda ise, özellikle gelişmekte olan ülkelerde özgür yaşayan amiplerin sebep olduğu SSS infeksiyonu olgularında artış gözlenmektedir. *Naegleria fowleri*'nin sebep olduğu akut seyirli, 2-7 gün içinde ölümle sonuçlanan SSS infeksiyonu; primer amibik meningoensefalit (PAM) olarak adlandırılırken, *Acanthamoeba* spp, *Balamuthia mandrillaris* ve *Sappinia diploidea*'nın sebep olduğu subakut ya da kronik seyirli yer yer serebral abse formasyonu gösterebilen SSS infeksiyonu ise; granülomatöz amebik ensefalit (GAE) olarak adlandırılmıştır. Bu bildiride, 75 yaşında erkek hastada saptanan, abse formasyonu gösteren GAE olgusu sunulmuştur.

ANAHTAR SOZCÜKLER: Beyin absesi, Granülomatöz amebik ensefalit, Tedavi

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INTRODUCTION

Amebic meningoencephalitis and cerebral amebic abscess due to *Entamoeba histolytica* occurs in less than 10% of such infestations as a part of systemic amebiasis (7). The existence of free-living ameba in soil and fresh water that caused fatal CNS infections was first reported in Australia in 1965 by Fowler and Carter (3). At the present time, approximately 500 human cases of CNS infection due to FLA have been reported worldwide. Here, we present a case of GAE with abscess formation that was identified in a 75-year-old male patient.

CASE REPORT

A 75-year-old male patient presented to the emergency room with headache, speech problems, and nervousness. On neurological examination, the patient was found to be agitated and had motor dysphasia. Laboratory tests showed an elevation in the erythrocyte sedimentation rate, reaching 50 mm/hour, and monocytosis (8.84%). Cranial MRI demonstrated a cystic mass with a diameter of 5.4x4 cm in the left temporal region with peripheral contrast enhancement (Figure 1A,B,C). Purulent fluid consistent with an abscess was drained through a left pterion craniotomy (Figure 1D). Histopathological examination of the specimen showed marked endothelial proliferation of the glial tissue and areas of focal necrosis. Serial sections demonstrated multiple amebic trophozoites within the liquefaction necrosis (Figure 2). Immunohistochemical staining with GFAP showed areas of gliosis. *E. histolytica* was ruled out after failure to demonstrate it in stool (3 times), negative indirect hemagglutination and anti-amebic antibody titer <1/32 in blood. The pathogen was defined by the Department of Parasitology as free-living ameba, though its subtype could not be determined since it did not grow on the culture medium. Postoperative CSF analysis was notable for containing 1.6 g/L of protein, 3.0 mmol/L of glucose, and a pronounced lymphocytic pleocytosis of 92%. In light of these clinical and laboratory findings, the case was considered to be an instance of GAE and was treated with Amphotericin-B 1.5 mg/kg/d i.v. in 2 divided doses and Miconazole 350 mg/m² daily i.v. in 3 divided doses for 8 days. The patient's agitation and dysphasia improved significantly. On the control CT scan, the cystic lesion in the left temporal region was absent and the herniation was markedly improved. The patient was discharged but readmitted to the

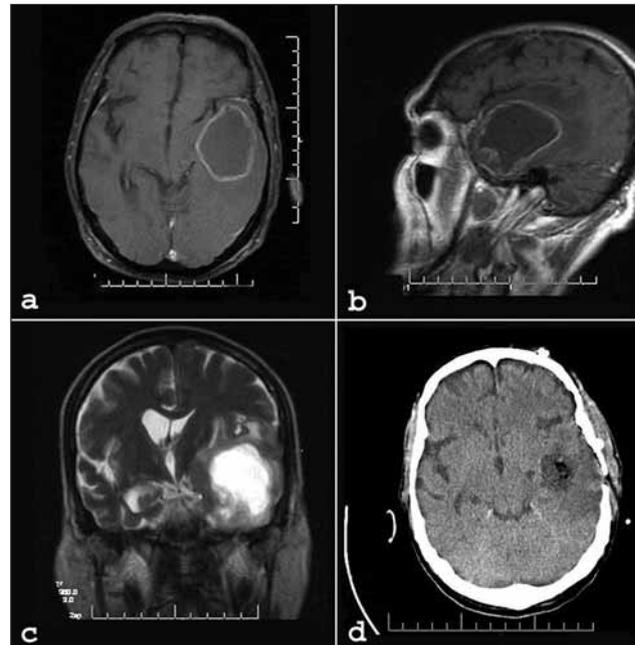


Figure 1: T1-weighted, contrast-enhanced cranial MR images of the patient before the first operation. A 5.4x4 cm cystic mass located in the left temporal region, isointense with CSF, showing peripheral contrast enhancement, consistent with abscess, and causing 5 mm of rightward subfalcine herniation was visible on axial (A) and sagittal (B) images. On the coronal non-contrast enhanced T2-weighted MR image, the cystic mass appears more hyperintense than CSF and causes uncal herniation (C). The CT image without contrast following the first operation shows that the cystic lesion in the left temporal region has disappeared (D).

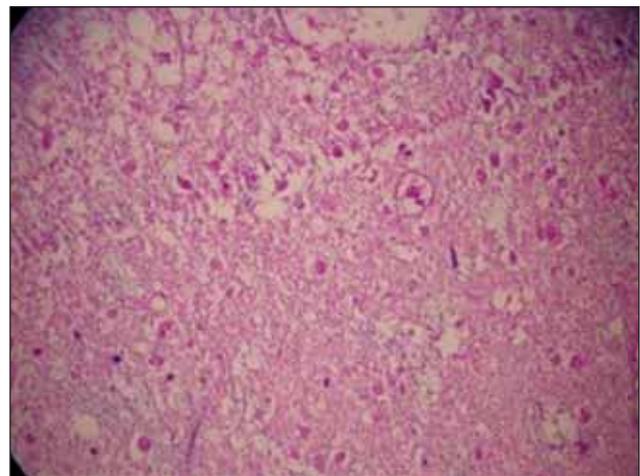


Figure 2: Histological sections of the cyst's capsule obtained intraoperatively showed marked endothelial proliferation in the glial tissue and areas of focal necrosis. Serial sections from different levels depict liquefaction necrosis and multiple amebic trophozoites within the necrosis (Hematoxylin-Eosin; x400).

emergency room in 3 months with motor dysphasia, agitation, and headache. The CT scan displayed an abscess measuring 5.6x4 cm and subfalcine herniation; hence, an urgent re-operation was

performed on the patient. The abscess was drained and its capsule was resected using microsurgery. Liposomal Amphotericin-B (AmbizomR) 200 mg/d i.v. and Miconazole 350 mg/m²/d i.v. in 3 divided doses were given for 8 days, when allergic reactions to Amphotericin-B developed in the postoperative period. Control CT demonstrated midline shift due to mass effect and edema. Thus, re-operation was required on postoperative day 7 to remove the craniotomy bone flap, and antimicrobial therapy was continued. The general condition of the patient was poor and he died due to cardiopulmonary arrest 115 days after first admittance to the hospital.

DISCUSSION

Meningoencephalitis resulting from systemic *Entamoeba histolytica* infection has been known for many years (7). The concept of PAM was described by Fowler and Carter in 1965 (3). A review of the literature revealed less than 300 human cases of PAM and 200 cases of GAE up to the present time. A case with the clinical features of PAM that was not supported by the growth of the pathogen on cultures was presented in a medical meeting in 1976 in Turkey (9). This was the first case to be reported in Turkey with the clinical features of GAE.

GAE resulting from *Acanthamoeba* species (*A. castellanii*, *A. culbertsoni*, *A. rhyssoides*, and *A. polyphaga*) is generally observed in individuals who suffer from a chronic disease, have had an organ transplant, are undergoing immunosuppressant treatment, or have a compromised immune system, as in patients having AIDS. Furthermore, GAE has also been reported during outbreaks of bacterial infections such as *Legionella* and *Mycobacteria* (5,14). GAEs caused by *Balamuthia mandrillaris* and *Sappinia diploidea*, which are rarer than *Acanthamoeba*, can be seen in immune-competent individuals and children as well. Patients who are healthy until the onset of the symptoms tend to have recently gone swimming in fresh water (2,4,14).

The onset of the clinical features of GAE caused by FLA, for which the incubation periods are not exactly known, is usually insidious and can take between a few weeks to a few months to become manifest. Temporal lobe involvement is common in GAE, and caused by all three types of FLA. Other regions of the CNS where lesions may be observed are the midbrain, occipital lobe, and posterior fossa. Coma generally develops 7-9 days after the onset of

the clinical symptoms; the outcome of the disease is usually the death of the patient (8,11,14).

Granulomas and abscess formations are more frequent during *Balamuthia mandrillaris* and *Sappinia diploidea* infections causing GAE in individuals with normal immunity, as occurred in the present case. Appearances of lesions in CT with focal and/or multifocal contrast enhancement are frequently mistaken for brain tumors, hemorrhagic infarctions, and radiation necrosis. When the abscess is formed, the center of the lesion and the capsule appear hypointense and slightly hyperintense, respectively, on T1-weighted images, while the center appears isointense or hyperintense and the boundaries of the capsule become more prominent on T2-weighted images (10).

The diagnosis of GAE can be established by demonstrating the pathogen in the cerebrospinal fluid (CSF) and/or infected tissues, by the growth of the pathogen in the culture or by serologic tests (6,11). Cerebrospinal fluid examination reveals an increased number of white blood cells, elevated protein, and decreased glucose levels (2,8,14). In recent years, it has been argued that it is difficult to see the *Acanthamoeba* spp in the CSF. Our case supported this argument. *Balamuthia mandrillaris* and *Sappinia diploidea* have never been seen. Trophozoites and cyst forms of all three types of FLA can be depicted by electron microscope in the lesion and in the walls of the infected vessels. In cases where it is difficult to establish the diagnosis, immunohistochemical tests using the FLA amebic antigen can be performed and ultrastructural analyses can be carried out (4,11,14).

There is no ideal standard therapeutic method that can be recommended for the treatment of GAE. Antimicrobial therapy for these infections is generally empirical, and patient recovery is often problematic. GAEs caused by *Acanthamoeba*, *Balamuthia* and *Sappinia* have been treated, more or less successfully, with antimicrobial combinations, including sterol-targeting azoles (clotrimazole, miconazole, ketoconazole, fluconazole, itraconazole), pentamidine isethionate, 5-fluorocytosine and sulfadiazine (12,13). Patients who were diagnosed and given an anti-amebic treatment for cerebritis (or encephalitis) should be followed up by repeated CT or MRI scans.

The primary objectives of the surgical treatment of GAE are to remove the lesion, which causes a mass effect such as hematoma, cyst, or abscess, and to establish a definite diagnosis. In cases with abscess formation, surgeons should wait for the late capsulation stage while planning the surgical treatment, as the central necrotic area does not contain any brain tissue (15). More recently, percutaneous, minimally invasive methods (stereotaxic surgery, CT-guided, ultrasound-guided aspiration and drainage in patients with craniotomy, etc.) are preferred for patients with poor general health. These methods can also be used for multiple and small lesions that are located deep in the brain, in critical regions and in the presence of concomitant encephalitis (1).

CONCLUSION

In conclusion, although GAE is encountered rarely and has a poor prognosis, it should be considered as a diagnosis for any patient with subacute and/or chronic meningoencephalitis without evidence of bacteria by staining, antigen detection tests, or culture. More effective antimicrobial drugs can be chosen for post-surgical treatment; furthermore, better survival may be achieved by diagnosing the disease in the early stages by immunohistochemical tests using FLA amebic antigens and determining the subtype of FLA (2,5,7,13,15).

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