SVOA Neurology

ISSN: 2753-9180

ScienceVolks Open Access

Case Report

Bacterial Brain Abscess in a Patient with Granulomatous Amebic Encephalitis. A Misdiagnosis or Free-Living Amoeba Acting as Trojan Horse?

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***Received:** July 13, 2021* ***Published:** July 24, 2021*

DOI: https://doi.org/10.58624/SVOANE.2022.02.026

Abstract

Amebic encephalitis is a rare and devastating disease. Mortality rate is almost 90% of cases. Here is described a very rare case of bacterial brain abscess in a patient with recent diagnosis of granulomatous amebic encephalitis. Case Description: A 29-year-old woman presented with headache, right hemiparesis and tonic-clonic seizure. Patient was diagnosed with granulomatous amebic encephalitis due to Acanthamoeba spp.; although, there was no improvement of symptoms in spite of stablished treatment. Three months after initial diagnosis, a brain MRI showed a ring-enhancing lesion in the left frontal lobe compatible with brain abscess. Patient was scheduled for surgical evacuation and brain abscess was confirmed intraoperatively. However, Gram staining of the purulent content showed gram-positive cocci. Patient improved headache and focal deficit after surgery. Conclusion: It is the first reported case of a patient with central nervous system infection secondary to Acanthamoeba spp. who presented a bacterial brain abscess in a short time.

***Keywords:** amebic encephalitis; Acanthamoeba spp; bacterial brain abscess*

Introduction

Free–living amoebae cause potentially fatal infection of central nervous system. Two clinical entities have been described for amebic encephalitis: primary amebic meningoencephalitis (PAM), and granulomatous amebic encephalitis (GAE). Naegleria fowleri and Paravahkampfia francinae cause PAM, while Acanthamoeba spp., Balamuthia mandrillaris and Sappinia pedata are the etiologic agents of GAE [1]. Amebic encephalitis is an uncommon disease, the incidence of PAM ranges from 0 to 8 cases each summer in United States [2]. Published reports of GAE due to Acanthamoeba in the period from 1990 to 2018 were 69 cases [3].

Here the authors describe a very rare case of bacterial brain abscess in a patient with recent diagnosis of central nervous system infection secondary to Acanthamoeba spp.

Case Description

A 29-year-old woman presented in August 2019 with headache and fever. By the day 10 after symptoms started, patient had memory and speech disturbances. Around the day 14, patient presented right hemiparesis and generalized tonic-clonic seizure.

Patient, originally from Venezuela, had been in Dominican Republic in 2018 and was living in Venezuela before arriving to Peru in April 2019. Patient underwent liposuction of buttocks in Venezuela in January 2019.

Patient was admitted in Hospital Nacional Arzobispo Loayza (Lima-Peru), in September 2019 for right hemiparesis, tonic -clonic seizure and constant headache. According to available data from this hospital, a cerebrospinal fluid sample was taken and contained 22 cells/uL,20% polynuclear cells, 80% mononuclear cells, glucose 63 md/dl, protein 44.3 mg/dl. Cerebrospinal fluid culture was positive for Acanthamoeba spp.; this culture was performed in Instituto Nacional de Salud (Lima-Peru), public institution that has one of the most important laboratories for the diagnosis of free-living amoebae in Peru. No information about neuroimaging before lumbar puncture.

Patient received for almost three months a treatment with intravenous fluconazole 600 mg per day, oral azithromycin 500 mg per day, oral albendazole 800 mg per day, oral miltefosine 150 mg per day and oral trimethoprim/ sulfamethoxazole 160mg/800mg three times per day. Patient did not have improvement on her clinical condition in spite of stablished treatment, being transferred to Hospital Nacional Cayetano Heredia (Lima-Peru), in December 2019. Physical examination in this latter institution showed patient disoriented, right hemiparesis (2/5), reactive pupils, no anisocoric, positive right Babinski sign. Lung and heart exam within normal limits. No skin lesion was observed. A brain MRI with contrast and laboratory exams were ordered.

Brain MRI depicted a ring-enhancing lesion in the left frontal lobe of 3.8 cm x 4.5 cm x 4 cm in size, with mass effect compatible with brain abscess (Figure 1).

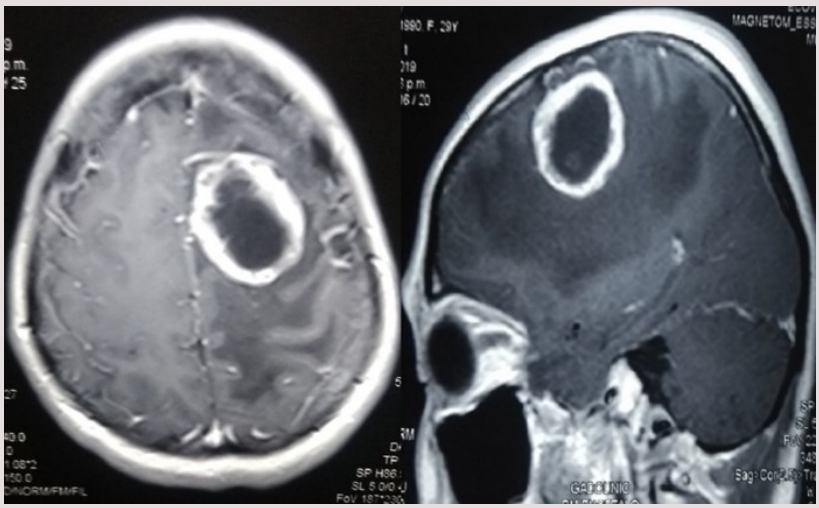

Figure 1. *Brain MRI shows a single rim-enhanced lesion in the left frontal lobe.*

Blood cell count was 5100 leukocytes/ul with lymphopenia (Table 1). Serology was: HIV on ELISA test negative, anti-HTLV-I/HTLV-II negative, VDRL/RPR negative, HBsAg negative, anti-HBs 184.58 mlU/ml, Toxoplasma IgG 0.1 IU/ml. Urine culture was negative.

Table 1. Laboratory values

Parameter	One day before surgery	One day after surgery	Eight days after surgery	Three months after	Reference range*
Hematocrit (%)	35	28	27	36	33-45
Hemoglobin (g/dL)	11.2	8.6	8.2	11.4	11-15
Red blood cells (10^6 cells/ uL)	4.02	3.08	2.92	4.48	4-5.5
Platelets (10^3cells/uL)	479	499	487	359	150-400
White blood cells (10^3cells/uL)	5.1	5.41	5.89	3.19	5-10
Neutrophils (%)	76.7	72	52.5	42.7	40-75
Eosinophils (%)	2.5	0	1.2	0.6	0-5
Basophils (%)	0.2	0	0.8	0.6	0-1.7
Monocytes (%)	2.4	4	6.3	8.5	0-10
Lymphocytes (%)	17.6	24	37	47.3	15-35
Neutrophils (10^3cells/uL)	3.91	3.9	3.09	1.36	2-7.5
Eosinophils (10^3cells/uL)	0.13	0	0.07	0.02	0-0.5

Basophils (10^3cells/uL)	0.01	0	0.05	0.02	0-0.1
Monocytes (10^3cells/uL)	0.12	0.22	0.37	0.27	0-0.8
Lymphocytes (10^3cells/uL)	0.9	1.3	2.18	1.51	1.5-3.5
Sedimentation rate (mm/h)	36			11	0-15
Total proteins (g/dL)	6.9				6.3-8.2
Serum glucose (mg/dL)	81		76	74	75-110
Creatinine (mg/dL)	0.9	0.3	0.4	0.53	0.7-1.2
Sodium (mmol/L)	139	142	138		135-148
Potassium (mmol/ L)	4.02	3.8	3.43		3.5-5.3
Chloride (mmol/L)	105	109	102		98-107
C-reactive protein (mg/L)	7.37				0-0.7

* Reference range of the Laboratory from Hospital Nacional Cayetano Heredia

Patient was scheduled for surgery consisting of left frontal craniotomy and evacuation of abscess. In order to prevent further dissemination of amoebae, surgical planning included to remove the abscess avoiding any leak of its content on the surrounding tissue. The capsule was thick and the content purulent. Several samples were taken for culture and Gram staining. Figure 2 shows images from surgery.

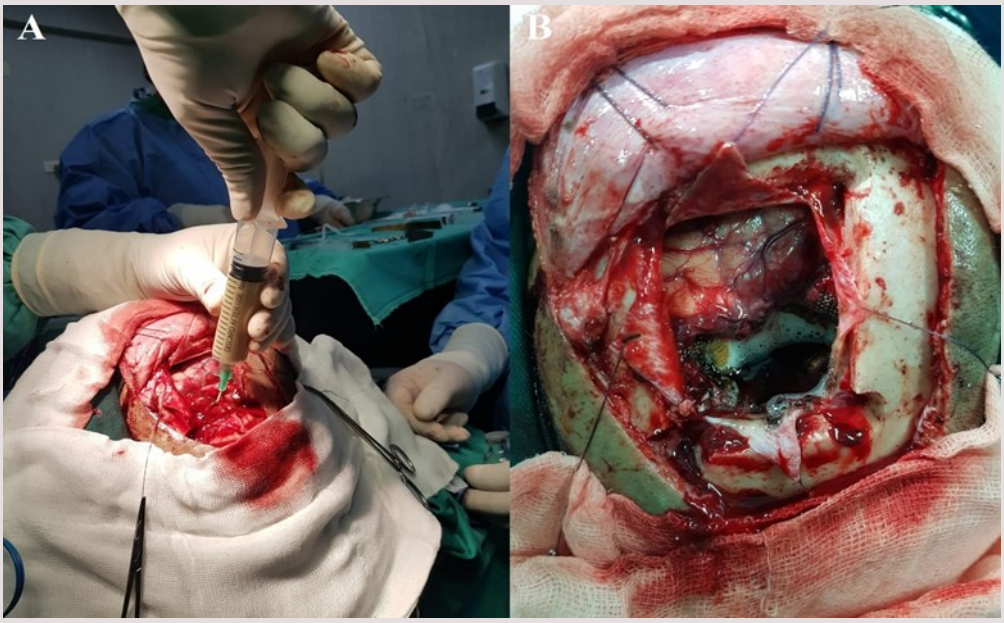

Figure 2. *A: Aspiration of purulent content. B: Cavity after surgical evacuation*

Right hemiparesis and headache improved after surgery. Postoperative head CT scan showed total removal of abscess (Figure 3).

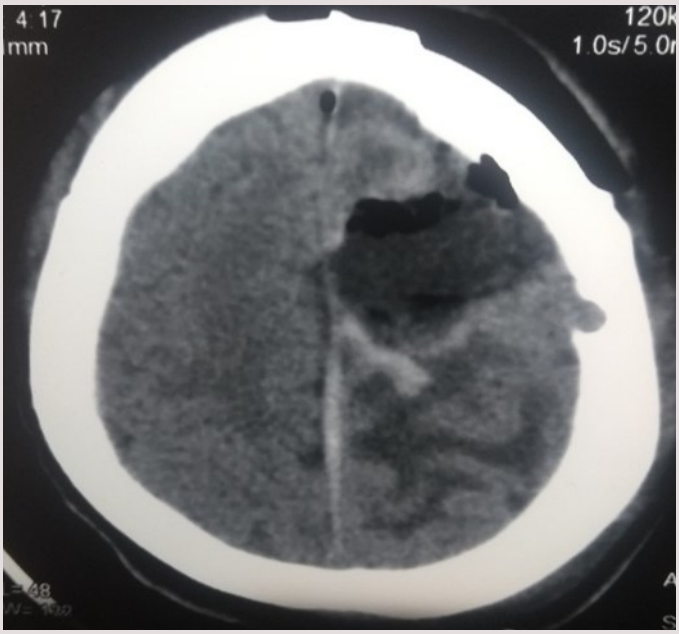

Figure 3. *Postoperative Head CT scan*

Gram staining showed gram-positive cocci, culture was negative and histologic examination was unable to visualize amoebae. With these results, patient was treated as bacterial brain abscess, receiving intravenous ceftriaxone 2 gr twice per day and intravenous metronidazole 500 mg three times per day, both for three weeks. As Table 1 shows, patient had postoperative anemia, without need of blood transfusion. Patient remained stable without any other complication and was discharged to home with oral metronidazole 500 mg three times per day and oral levofloxacin 750 mg per day, both for 14 days. Three months after surgery, patients had no significant symptoms. The last blood cell count showed leukopenia with neutropenia (table 1).

Discussion

The first Acanthamoeba species was isolated from dust and named Amoeba polyphagus in 1913, which was redescribed as Acanthamoeba polyphaga in 1967 [4,5]. Culbertson et al described the first experimental model of central nervous system infection by Acanthamoeba through intracerebral inoculation in monkeys and mice [6]. The first case report was published in 1972 and mortality of GAE due to Acanthamoeba accounts over 85% of cases [7,8].

Acanthamoeba spp. has two stages in its life cycle: trophozoite and cyst, depending on environmental conditions and food availability. Acanthamoeba spp. is widely distributed in the environment including dust, air, soil, river, sea water, sewages, pharmaceutical factory drains and any moist environment that facilitates bacteria growth, since Acanthamoeba feeds on organic particles as well as other microbes such as bacteria [9-11]. This ubiquitous distribution allows many modes of contact with Acanthamoeba [12]. The route of infection can be through skin with posterior hematogenous dissemination to the lungs and brain or by inhalation of amoebic cysts. Likewise, Acanthamoeba has been isolated from nasal mucosa in healthy carriers [13,14]. An in vitro study illustrated how Acanthamoeba kill host cells through cytolysis and phagocytosis [15]. Acanthamoeba infection seems to be more common than previously reported due to the presence of asymptomatic or mild infections [16].

The clinical presentation of GAE is insidious and takes from several weeks to months before fatal outcome. Symptoms and signs are headache, stiff neck, irritability, nausea, vomiting, fever, lethargy, cranial nerve palsy, hallucinations, cerebellar ataxia, visual disturbances, sleep disturbances, anorexia, seizures, coma, Babinski's sign and Kernig's sign [12].

The diagnosis of GAE includes brain images, microscopic examination, culture, histopathology, serology and molecular techniques. Brain images in Acanthamoeba infection show multiple space-occupying lesions [17,18]. Polymerase chain reaction testing in cerebrospinal fluid has been used as promising tool for diagnosis and identification of multiple genotypes of Acanthamoeba spp [19,20]. CSF examination can show lymphocytic pleocytosis with high protein and low glucose levels. Direct visualization of amoebae in CSF is difficult and could resemble macrophages [21].

Immunosuppression plays a key role in the infection of central nervous system due to free-living amoebae as described in hematopoietic stem cell transplant recipients, cancer and AIDS [7,19,22,23,24].

Patient received miltefosine, drug used in visceral leishmaniasis and Acanthamoeba keratitis, that has showed efficacy in the treatment of amebic encephalitis secondary to Acanthamoeba [25-27]. Miltefosine has in vitro activity against Acanthamoeba spp. with cytotoxicity against trophozoites and cysticidal activity [28,29].

Bacterial brain abscess has an estimated incidence that varies from 0.3 to 1.3 per 100,000 people per year [30,31]. Clinical presentation includes headache (72 %), fever (60%) and focal neurological deficit (57%) [32]. It is originated from contiguous spread of local infection (sinusitis, mastoiditis, middle ear otitis), or through hematogenous dissemination from infective endocarditis, dental infection, pulmonary abscess or in patients with pulmonary circulation shunt [33]. Odontogenic infections become a frequent predisposing condition in the last years, whereas otogenic intracranial abscess is less frequent and commonly due to chronic ear infection with cholesteatoma [34]. Brain imaging provides important information for the diagnosis, head CT scan shows a single rim-enhanced lesion with hypodense centre and perilesional edema located in the frontal and temporal lobes mainly [35]. Brain MRI offers advantages over CT scan, functional sequences such as the measurement of diffusion with apparent diffusion coefficient, proton magnetic resonance spectroscopy and perfusion weighted imaging help to differentiate brain abscesses from necrotic or cystic tumors [36,37].

Antibiotic regimen should cover streptococci, staphylococci, strict anaerobes and Enterobacteriaceae due to the important rate of polymicrobial brain abscesses (>30%) [33].

Stereotactic surgical drainage or open aspiration via craniotomy are usually performed with abscesses larger than 2.5 cm in diameter; however, stereotactic surgery allows aspiration of brain abscess of 1 cm [38,39].

Interestingly, patient had a bacterial brain abscess only three months after being diagnosed and treated for encephalitis secondary to Acanthamoeba spp. There is no case previously reported of very short time between infections of bacteria and free-living amoebae in the central nervous system. Free-living amoebae serve as vectors for other microorganisms such as bacteria, which are able to survive and being isolated from vacuoles [40-42]. Our hypothesis is that the release of bacteria in the central nervous system after antiamoebic drugs might be an explanation of the pathogenesis in this case along with an immunosuppression status that needs further investigation in the patient. Moreover, laboratory diagnosis of free-living amoebae should be included as a part of the work-up in patients with central nervous system infection.

Conclusion

It is the first report of a patient diagnosed with granulomatous amebic encephalitis due to Acanthamoeba spp. who develops within a short period a bacterial brain abscess which was treated with surgery and antibiotics. Free-living amoebae has been previously reported as vectors for bacteria and this case may be the first clinical evidence of the role of amoebae in the pathogenesis of bacterial brain abscess.

Author Contributions

Conceptualization, R.L.; methodology, R.L.; formal analysis, R.L. and W.A.; investigation, R.L.; resources, R.L.; data curation, R.L.; writing—original draft preparation, R.L.; writing—review and editing, R.L. and W.A.; visualization, R.L.; supervision, W.A. All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Acknowledgments

The authors acknowledge the invaluable support of the neurosurgery residents from Hospital Nacional Cayetano Heredia.

Conflicts of Interest

The authors declare no conflict of interest.

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Citation: Lovaton R, Alaba W. "Bacterial Brain Abscess in a Patient with Granulomatous Amebic Encephalitis. A Misdiagnosis or Free-Living Amoeba Acting as Trojan Horse?". SVOA Neurology 2:4 (2021) Pages 117-124.