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CASE REPORT

Successful treatment of primary amebic meningoencephalitis: A case report

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Abstract

This is the case report of a 34 year-old man with primary amebic meningoencephalitis due to infection of free-living amebas which were isolated from the cerebrospinal fluid and nasal swabs. The clinical pictures were similar to that of acute bacterial meningitis except for the presence of eosinophilia. The patient responded to a combination of metronidazole, tinidazole and amphotericin B. He further improved after ventriculo-peritoneal shunt was inserted for the complication of hydrocephalus. A review of the literature showed that there were five previous cases of primary amebic meningoencephalitis who were successfully treated. Most cases who responded were given amphotericin B, in some cases with metronidazole.

Key words: Primary amebic meningoencephalitis, Free-living ameba, CNS infection.

INTRODUCTION

Pathogenic free-living amebas may infect the central nervous system causing a primary amebic meningoencephalitis (PAM) by Naegleria fowleri[1], and granulomatous amebic encephalitis by either Acanthamoeba spp[2], or Balamuthia mandrillaris, previously known as leptomyxid ameba.[3] There has been increasing reports of free-living amebic infection of the central nervous system in the recent years[4,5]; with more than 200 cases of amebic central nervous system infection reported worldwide.[6,7] Majority of these infections were PAM and the remaining were granulomatous amebic encephalitis. Most cases of PAM died within 7-10 days with few being successfully treated. This is the case report of a patient who survived a PAM.

CASE REPORT

A 34 year-old man was sent to the emergency room of the Hospital by police as he was found to be in stupor. There was no past history available. On examination, he had poor personal hygiene with poor nutritional status. There was fever of 39.6°C, profuse yellowish nasal discharges, and a wound over the left lower leg. Neurological examinations showed neck stiffness, positive Kernig's sign and Babinski's sign but no other focal neurological sign. Three days later, the patient's condition deteriorated and was in deep coma with decerebrate posture over both sides.

The peripheral blood examination revealed leukocytosis of 11,260/mm^3 with 16% eosinophilia. The liver and renal function tests were normal. Cerebrospinal fluid (CSF) examination showed xanthochromia with raised leukocyte count of 630/mm^3, predominantly neutrophils. The CSF sugar level was low at 33 mg/dL with concomitant blood glucose of 100 mg/dL. The protein level was normal at 44 mg/dL. Electroencephalograms demonstrated diffuse slowing. Brain computed tomography (CT) with contrast, abdominal ultrasound and colonoscopic examination were normal. Cultures from blood, urine and CSF for bacteria, tuberculosis and fungi were all negative as well as antigen test for cryptococcus and antibody tests for herpes simplex virus type I and II, HIV and syphilis. Provisional diagnosis of acute bacterial meningitis was made and the patient was treated with latamoxef 1.5 gm twice per day for 10 days. As there was poor response to the cephalosporin, anti-tuberculous treatment with isoniazid 300mg, rifampicin 600mg and ethambutal 1200mg daily were given.

The cerebrospinal fluid examination was repeated after two weeks. It continued to show leukocytosis predominantly neutrophils with low

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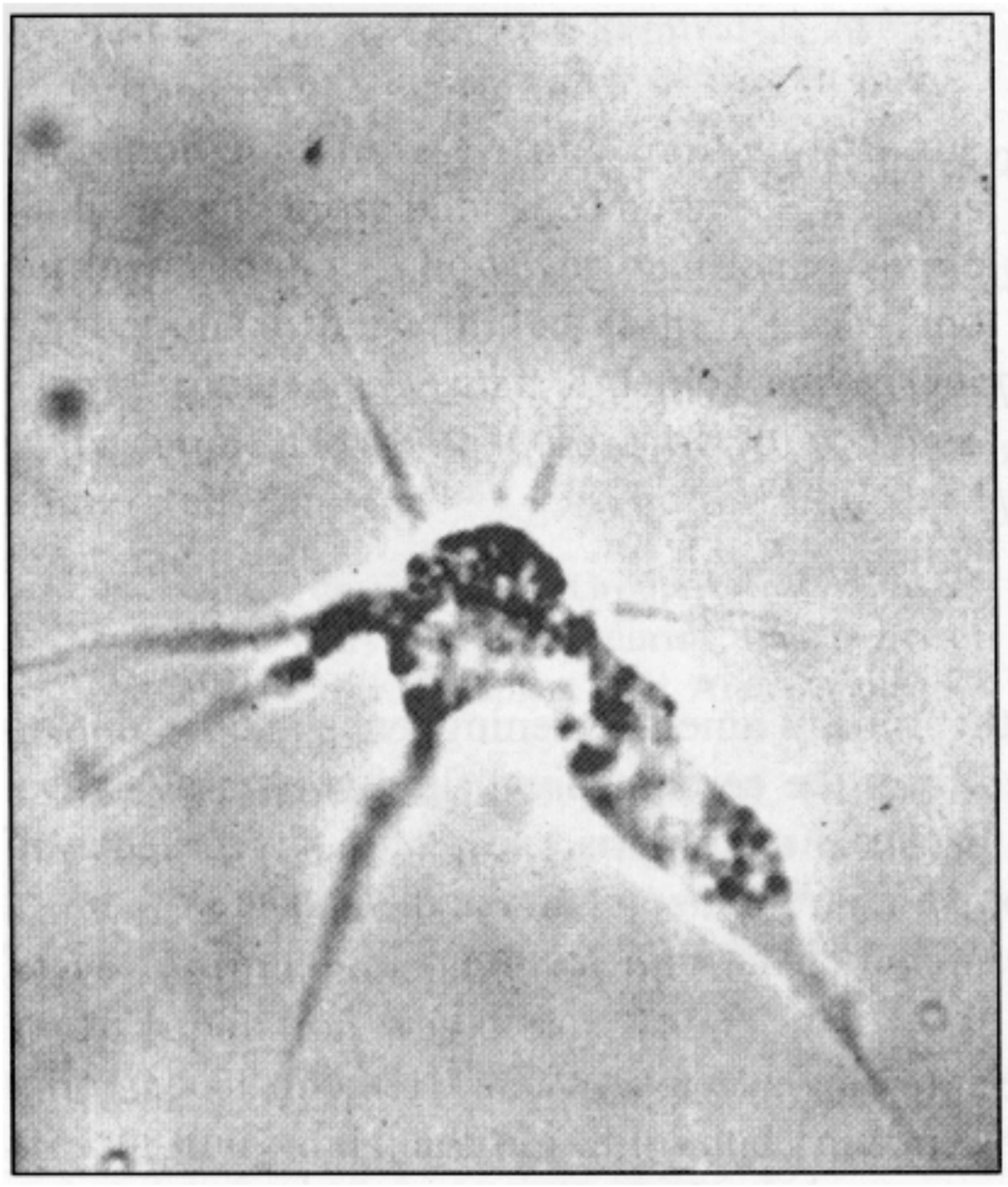

FIG. 1: The trophozoite of the free-living amoebae was about 8-12 um in size with a centrally located nucleus and multiple filopodias.

glucose level of 36 mg/dL. The concomitant blood glucose was 106 mg/dL. As there was eosinophilia, special efforts were made to look for parasite in the cerebrospinal fluid. Free-living amebas were found microscopically with sedimentation method in cerebrospinal fluid, as well as in the nasal swabs and stool at different times between day 18 and day 42. The trophozoites were about 8-12 µm in size with a centrally localized nucleus. Most of the amoeba possessed 4-8 filopodias in spindle shape (Figure 1). Attempts to culture the parasites using E-coli plated non-nutrient agars were unsuccessful. Immunohaemagglutination test for Entamoeba histolytica was negative in both serum and cerebrospinal fluid. The patient was treated with oral metronidazole 750 mg daily and tinidazole 2 g daily for six weeks, and amphotericin B at 1 mg/kg/day iv for two weeks. The patient improved over months and no amebas were found in two subsequent cerebrospinal fluid samples. A repeat CT brain 10 months later showed communicating hydrocephalus with no granuloma. A ventriculo-peritoneal shunt was done with substantial clinical improvement. The patient could follow instruction and communicate in simple phrases, eat by himself at two years. However, his limbs remained spastic. The patient did not develop other diseases during the follow-up.

DISCUSSION

This patient was initially thought to have acute bacterial meningoencephalitis. However, he had eosinophilia and attempts to isolate the conventional infective agents failed. The microscopic examination of the cerebrospinal fluid and nasal swab then demonstrated the presence of ameba. Based on the morphology of the ameba, the negative immunohaemagglutination test for Entamoeba histolytica, the clinical course and the brain CT finding, the patient was diagnosed to have PAM from free-living ameba. Appreciation of central nervous system disease due to free-living ameba occurred when Fowler and Carter in 1965[1] reported the first case of PAM due to Naegleria fowleri, which was initially reported as Acanthamoeba. Since then more than 144 cases of PAM have been reported mostly due to N. fowleri.[6,7] The morphology of the parasite of our patient was more suggestive of Acanthamoeba, although PAM was more commonly due to N. fowleri. The exact characterization of the free-living ameba in our patient was thus uncertain. PAM usually present acutely with the initial symptoms of headache, fever, nasal discharge and obstruction and occasional smell and taste abnormalities.[1-7] The patients usually progress rapidly within days with nausea, vomiting, fever, neck stiffness, seizures and impairment of consciousness with drowsiness, confusion, delirium and deep coma. Most patients usually die within one to two weeks.[1,4,6,7]

Our patient is thus unusual as he survived with amphotericin, metronidazole and tinidazole. He further improved when ventriculo-peritoneal shunt was done for hydrocephalus. A review of the literature showed that survival of patients in PAM is very rare.[8-11] Table 1 is a summary of the previous five survivors with the present case report as the sixth. The first two survivors were reported by Apley et al [8] in 1970 from Britain. These two patients had played in a muddy puddle with another boy who died 15 days after the onset of meningeal symptoms from PAM. These two patients were treated with intravenous amphotericin B for 10 days. However, amebas were only found in one of the two survivors (Case 1). The 9 year-old girl reported by Seidel et al[10] (Case 4) was treated with intravenous and intrathecal amphotericin B, oral miconazole and rifampin. Case 5 reported by Brown[11] was a 32 year-old man treated with amphotericin B 75 mg/day for 10 days and oral rifampin 600 mg daily. Our patient was also treated with

TABLE 1. Summary of survivors in patients with PAM

No.	Age (yrs)	Gender	Clinical manifestations	Location of amoebas found	Source of exposure	Therapy	Authors
1	6	M	Headache, anorexia, sorethroat, neck stiffness, Kernig's sign, skin rash	CSF	Warm muddy puddle	amphotericin B, sulphadiazine	Aplcy et al[8]
2	4.5	M	Sorethroat, headache, abd pain, irritable	No amoeba was noted	Warm muddy puddle	amphotericin B, sulphadiazine	Apley et al[8]
3	?	?	?	CSF	Pool	amphotericin B	Anderson & Jamieson[9]
4	9	F	Headache, vomiting, lethargy, neck stiffness, papilloedema	CSF	Hot spring	amphotericin B, miconazole, rifampin	Seidel et al[10]
5	32	M	Fever, headache, lethargy, meningeal sign	CSF	Stagnant fresh water lake	amphotericin B, rifampin	Brown[11]
6	34	M	Fever, nasal discharge, conscious disturbance, neck stiffness	CSF, nasal discharge	?	amphotericin B, metronidazole, tinidazole	Lee et al

PAM = Primary amebic meningoencephalitis; ? = Data unavailable.

amphotericin B, metronidazole and tinidazole. From the reported cases in the literature and our patient, amphotericin B may be effective in PAM. Rifampin and metronidazole may also be beneficial. Both drugs have good penetration of blood-brain barrier.[12,13]

Most patients with PAM had history of water activities such as swimming in fresh water pools or lakes. The route of entry to the brain is thought to be via olfactory bulb to the frontal base of brain.[4-7] A high ambient temperature of the water may also be an important factor. Our patient did not give a history of swimming. There was however, profuse nasal discharges with amebas similar to that in cerebrospinal fluid seen in the nasal swab. There was thus evidence of nasal inflammation supporting olfactory nerves as route of entry to the brain. The reason that free-living amebas were found in the stool in our patient remained obscure and might come from swallowing of the profuse nasal discharges. PAM among patients who have not been swimming has been seen. It was hypothesized that dust harboring amebic cysts may be inhaled and cause human infection.[14] PAM is not infrequently seen in Australia, Eastern Europe and the USA.[4-7] Free-living ameba was reported to be found in the environment in Japan, South Korea and India.[15-17] However only about 15 patients with PAM or granulomatous amebic encephalitis had been reported in India, Thailand, Japan, South Korea and China.[6,7] In Taiwan, there were only few reported cases of Acanthamoeba keratitis and PAM.[18,19,20] Rare reports of PAM in the developing countries may thus be due to lack of awareness.[5]

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REFERENCES

1. Fowler M, Carter RF. Primary amoebic meningitis probably due to Acanthamoeba sp. BMJ 1965;2:740-2.
2. Martinez AJ. Is Acanthamoeba encephalitis an opportunistic infection? Neurology 1980;30:567-74.
3. Visvesvara GS, Schuster FL, Martinez AJ. Balamuthia mandrillaris, N.G.,N.Sp., agent of amebic meningoencephalitis in human and other animals. J Euk Microbiol 1993;40:504-14.
4. Visvesvara GS, Stehr-Green JK. Epidemiology of free-living ameba infections. J Protozool 1990;37:S2533.
5. Martinez AJ, Guerra AE, Garcia-Tamayo J, Cespedes G, Gonzalez-Alfonzo J, Visvesvara GS. Granulomatous amebic encephalitis: a review and report of a spontaneous case from Venezuela. Acta Neuropathol 1994;87:430-4.
6. Ma P, Visvesvara GS, Martinez AJ, Theodore FH, Daggett P-M, Sawyer TK. Naegleria and Acanthamoeba infections: review. Rev Infect Dis 1990;12:490-513.
7. Martinez AJ. Free-living amebas: infection of the central nervous system. Mt Sinai J Med 1993;60:271-8.
8. Apley J, Clarke SKR, Roome APCH, et al. Primary amoebic meningoencephalitis in Britain. BMJ 1970;1:596-9.
9. Anderson K, Jamieson A. Primary amoebic meningoencephalitis. Lancet 1972;1:902-3.
10. Seidel JS, Harmatz P, Visvesvara GS, Cohen A, Edwards J, Turner J. Successful treatment of primary amebic menigoencephalitis. N Engl J Med 1982;306:346-8.
11. Brown RL. Successfult reatment of primary amebic meningoencephalitis. Arch Intern Med 1991;151:1201-2.
12. Thea D, Barza M. Use of antibacterial agents in infections of the central nervous system. Infect Dis Clin North Am 1989;3:553-70.
13. Nau R, Sorgel F, Prange HW. Pharmacokinetic optimisation of the treatment of bacterial central nervous system infections. Clin Pharmacokinet 1998;35:223-46.
14. Lawande RV, Abraham SN, John I, Egler LJ. Recovery of soil amebas from the nasal passages of children during the dusty harmatten period in Zaria. Am J Clin Pathol 1979;71:201-3.
15. Kuroki T, Yagita K, Yabuuchi E, Agata K, Ishima T, Katsub Y, Endo T. Isolatin of Legionella and free-living amoebae at hot spring spas in Kanazawa, Japan. [In Japanese] Kansenshogaku Zasshi 1998;72:1050-5.
16. Shin HJ, Kim CH, I KI. Immunological approach for classification of free-living amoeba in Korea. [In Korean] Kisaengchunghak Chapchi 1992;30:289-98.
17. Bose K, Ghosh DK, Ghosh KN, Bhattacharya A, Das SR. Characterization of potentially pathogenic free-living amoebae in sewage samples of Calcutta, India. Braz J Med Biol Res 1990;23:1271-8.
18. Tseng SH, Hu For, Lee GS, Chang SC, Chen CL, Luh KT. Acanthamoeba keratitis: report of a case. J Formosan Med Assoc 1989;88:512-6.
19. Chan MY, Chan YC. Acanthamoeba keratitis: report of the first two cases in Taiwan. Trans Ophthalmol Soc ROC 1988;27:692-8.
20. Chen ER, Hsieh HC, Shih CC, Yang RF, Chen SS, Chen YT. Detection of amoebae in the cerebrospinal fluid from a patient with an acute meningo-encephalitis. Chinese J Microbiol Immunol [In Chinese] 1975;8:298.