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Rare disease

Central nervous system infection with *Acanthamoeba* in a malnourished child

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Summary

A 3-year-old male child presented with moderate-to-high grade fever and non-projectile vomiting, generalised seizures and altered sensorium for 1 month. CT scan revealed a communicating hydrocephalus with no basal exudates. The microbiological tests were negative for *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitides*, brucellosis, cryptococcosis, HIV and *Mycobacterium tuberculosis*. Intracranial pressure was relieved by ventriculo-peritoneal shunt, and the child was empirically started on ceftriaxone, and antitubercular therapy with isoniazid, rifampicin, ethambutol and streptomycin, along with steroids and supportive treatment for seizures. The symptoms persisted. On further investigation the cerebrospinal fluid showed growth of *Acanthamoeba* spp., following which the initial treatment was stopped and a combination antiamoebic regimen of cotrimoxazole, rifampicin and ketoconazole was started, after which he showed clinical improvement. The treatment was continued for 6 months and on follow-up at 1, 3 and 6 months, there was a remarkable clinical improvement with no residual symptoms.

BACKGROUND

Free-living amoebae belonging to the genus *Acanthamoeba* are the causative agents of a fatal infection of the central nervous system (CNS)—granulomatous amoebic encephalitis (GAE).[1] This form of encephalitis is more commonly encountered in immuno-compromised population and in persons with debilitating conditions. However, there are reports of GAE, caused by *Acanthamoeba* spp. occurring in immuno-competent individuals and in malnourished children with no apparent immunodeficiencies.[2]

The symptoms of CNS infection are headache, confusion, nausea, vomiting, fever, lethargy, stiff neck, focal neurological deficits and signs of increased intracranial pressure.[1] Pathological findings generally include severe haemorrhagic necrosis, fibrin thrombi and signs of chronic inflammation. Numerous trophozoites can be identified within the tissue. Generally, in immuno-competent individuals, well-developed granulomas form around the organisms, while in immuno-compromised individuals, granuloma formation is weak or does not occur at all.[1] However, the exact host–parasite interplay leading to the pathological features is unclear.

The ante-mortem diagnosis of *Acanthamoeba*-induced CNS infection is difficult and is made rarely through ante-mortem brain biopsies and cerebrospinal fluid (CSF) examination.[2] In most of the reported cases the diagnosis is usually established at autopsy. The conventional diagnostic tests like wet mount microscopy, culture and indirect immuno-fluorescence tests are performed ante-mortem on the CSF. However, the sensitivity of these tests for identifying *Acanthamoeba* is low.[1] Consequently, CNS infections by *Acanthamoeba* remain under-diagnosed, under-reported and therefore undertreated.

Various therapeutic modalities (mono and combination therapies) reported in literature have shown variable efficacies, but there is no consensus regarding the drugs of choice, dosage, duration of treatment and the diagnostic and prognostic markers during the course of the disease.

We are reporting this case of chronic meningo-encephalitis in a malnourished child. The child did not have a typical presentation and was diagnosed to have meningo-encephalitis caused by *Acanthamoeba* spp. detected on a CSF culture. The child was successfully treated with a combination regimen of three drugs.

CASE PRESENTATION

A 3-year-old male child presented to the paediatric emergency department of the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, with moderate-to-high grade fever and vomiting for almost 1 month. The fever was gradual in onset and associated with chills and rigours. There was no rash. There were 10–12 episodes of non-projectile vomiting per day. He also had an episode of generalised seizures 8 days back which was followed by alteration of sensorium. There was no history of contact with a patient of tuberculosis or any other relevant history. The birth history of the child was not significant, although one of the siblings died at 3 days of age, possibly due to hypothermia. The patient was immunised with BCG and diphtheria, pertussis and tetanus; however, record of other vaccinations was not known. He was poorly built with low body weight (10 kg), and height (82 cm) at the age of 3 years and had features suggestive of acute-on-chronic malnutrition.

INVESTIGATIONS

The patient received symptomatic treatment from a local hospital, where a CT scan examination of the head revealed a communicating hydrocephalus, after which the patient was referred to PGIMER. The patient was

admitted in the paediatric emergency with a Glasgow Coma Scale of 10 (eyes—3, movement—5 and voice—2); he was afebrile, with normal haemodynamic parameters (pulse rate of 128/min, respiration rate of 30/min and blood pressure of 110/70 mm Hg). There was no icterus, no cyanosis, no lymphadenopathy and jugular venous pressure was normal. On neurological examination, the child was conscious but not interacting with parents, there was neck rigidity, generalised hypertonia, brisk deep tendon reflexes and extensor plantar response bilaterally. His cranial nerve examination was normal. The examination of other systems was normal.

On CT scan examination of the head, there were bilateral dilated lateral, third and fourth ventricles suggestive of hydrocepahalus under pressure, with no basal exudates. A right-sided ventriculo-peritoneal (VP) shunt was inserted to relieve the intracranial pressure, and the shunt CSF showed proteins 129 mg%, sugar 55 mg%, and no white blood cells. The child was empirically started on ceftriaxone, and antitubercular therapy (ATT) with isoniazid, rifampicin, ethambutol and streptomycin, along with steroids and supportive treatment for seizures. However, his symptoms persisted which led us to think of other causes of chronic meningitis. A lumbar puncture was repeated after 3 days for CSF examination and sent for chronic meningitis workup. It showed proteins 265 mg%, sugar 37 mg% and 240 cells/mm^3 (all polymorphs). Haematological examination showed haemoglobin of 7.3 gm/dl, thin layer chromatography 12 600/mm^3, with polymorphs 56%, lymphocytes 35%, monocytes 06% and eosinophils 01%; C reactive protein was 92.18 g/dl. The bacterial cultures for blood and CSF were sterile, and serology was negative for *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitides* by latex agglutination test (LAT), for brucellosis by standard agglutination test (SAT), for *Cryptococcosis* by LAT, and also negative for HIV. Ziehl-Neelsen's stain and PCR test performed on CSF were negative for acid-fast bacilli (AFB) and *Mycobacterium tuberculosis* complex DNA, respectively; Montoux test, chest x-ray and gastric aspirate for AFB was also not suggestive of tuberculosis. The CSF showed growth of *Acanthamoeba* spp. on the second day of culture on non-nutrient agar overlaid with *Escherichia coli*.

TREATMENT

Subsequent to the growth of *Acanthamoeba* spp., the initial antibacterial and antitubercular treatment was stopped and the child was put on a combination antiamoebic regimen of cotrimoxazole (20 mg/kg/day), rifampicin (10 mg/kg/day) and ketoconazole (5 mg/kg/day), to which he showed clinical improvement from day 2 of starting the regimen.

OUTCOME AND FOLLOW-UP

He became afebrile, his sensorium and cognition dramatically improved, he started responding to commands and became ambulatory. The child was discharged from the hospital after 10 days with an advice for follow-up and continuation of prolonged combination therapy for 6 months with the three-drug regimen. On follow-up at 1, 3 and 6 months, there was remarkable clinical improvement and there were no residual symptoms.

DISCUSSION

Our case presented with some unusual and not-well-known features in comparison with other reported cases of chronic amoebic meningitis. There was no apparent history of any associated immuno-compromised condition, although there was acute-on-chronic malnutrition which could have contributed to the disease onset and progression. Some workers have also reported cases of amoebic meningitis in immunocompetent individuals from India,[2 3] and malnutrition has been suspected as a risk factor.[2] No apparent portal of entry could be identified in this case as there was no visible skin ulcer/lesion, and the respiratory system was apparently normal. Olfactory nerve route is known as a portal of entry for GAE and could have been the initial site of infection.[1] There was no history of exposure to any natural water bodies and the child used to be bathed in municipal tap water. His presentation was not typical for he had only CNS features and granulomatous lesions were absent in the brain. There was presence of a communicating hydrocephalus which is again atypical for CNS infections with *Acanthamoeba* spp. In another case reported from India where there was a communicating hydrocepahalus, the child was found to have a dual infection with *M tuberculosis*.[2] The workup for tuberculosis in our case, was negative, and the patient dramatically responded to antiamoebic regimen.

Combination regimens have proven to be more successful than single-drug therapies in human infections because many drugs exhibit amoebostatic but not amoebicidal activity. No single drug has yet been shown to be effective against both the trophozoite and cystic stages of *Acanthamoeba*.[1] In vitro sensitivity studies of virulent *Acanthamoeba* have shown ketoconazole, pentamidine, hydroxystilbadimine, paramomycin, polymyxin, colistin, trimethoprim-sulphamethoxazole, sulfadiazine, flucytosine, amphotericin B, clotrimazole and phenothiazines to be of variable efficacy.[2] A few regimes have reported successful clinical and parasitological cure, of which the combination of cotrimoxazole (20 mg/kg/day), rifampicin (10 mg/kg/day) and ketoconazole (5 mg/kg/day) has been used by some workers.[2 3] However, there is very variable opinion regarding the appropriate duration of therapy which may range from 2 to 9 months. An 8-year-old previously asymptomatic girl, who developed CNS infection with *Acanthamoeba* was treated with this combination drugs for 5 months and she achieved complete resolution of all symptoms, although CSF remained positive for *Acanthamoeba*. Her drug therapy was discontinued, and on follow-up at 6 months, the clinical examination was normal and CSF became sterile.[2] Another 3-year-old boy was treated for 2 months with the regime with which the symptoms resolved, and on follow-up at 1 year the child was normal.[2] One 15-year-old female child was treated with the same regimen for 9 months, although there was clinical improvement at 3 months. The authors mentioned that although CSF examination demonstrated no evidence of *Acanthamoeba* after 3 months of therapy, they decided to continue the therapy for a total of 9 months as most drugs are amebostatic and not amebocidal; and *Acanthameba* is notorious to lie dormant as cysts for prolonged periods.[3]

A course of therapy of 3–5 months duration may be sufficient as evident in the above reports, depending on the clinical response and parasitological clearance which can be

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followed up with monthly CSF examinations. A prolonged therapy (more than 5 months) may seem unnecessary and will need to be justified. Most of the patients in whom successful therapeutic outcome was achieved were immunocompetent individuals and immune restoration may have augmented drug therapy in remission of the infection, as has been suggested previously.[2]

Learning points

- *Acanthamoeba* meningitis can present with atypical signs and symptoms in immuno-competent hosts.
- A high index of suspicion can lead to a timely diagnosis of this rare cause of chronic meningitis, and *Acanthamoeba* should be included in the workup of chronic meningitis.
- Appropriate targeted treatment, if started timely, may lead to good outcomes in this otherwise highly fatal condition, especially in immune-competent individuals.
- A combination therapy of 3–5 months may be appropriate for treating *Acanthamoeba* meningitis.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Marciano-Cabral F,** Cabral G. *Acanthamoeba* spp. as agents of disease in humans. *Clin Microbiol Rev* 2003;**16**:273–307.
2. **Singhal T,** Bajpai A, Kalra V, *et al*. Successful treatment of *Acanthamoeba* meningitis with combination oral antimicrobials. *Pediatr Infect Dis J* 2001;**20**:623–7.
3. **Saxena A,** Mittal S, Burman P, *et al*. *Acanthameba* meningitis with successful outcome. *Indian J Pediatr* 2009;**76**:1063–4.