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Rare disease

Unexpected postmortem diagnosis of acanthamoeba meningoencephalitis in an immunocompetent child

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Summary

Meningoencephalitis caused by *Acanthamoeba* spp. is a rare opportunistic infection, difficult to diagnose and treat, which causes death in almost all cases. Here, the authors report a 5-year-old Iranian immunocompetent girl who died of fulminant acanthamoeba meningoencephalitis. To the authors' knowledge, this is the first case of acanthamoeba meningoencephalitis in Iran.

BACKGROUND

Amebae of the genera *Naegleria*, *Acanthamoeba* and *Balamuthia* are inhabitants of soil, water and other environmental substrates, when they feed on other microscopic organisms, especially bacteria and yeasts. All three genera have been associated with opportunistic infection of the central nervous system (CNS) and *Acanthamoeba* cause keratitis. Primary amebic meningoencephalitis caused by ameboflagellate *Naegleria fowleri*, typically affect children and young adult who have been swimming or diving in warm, freshwater lakes or pools. The parasite enters the brain and produces an acute haemorrhagic meningoencephalitis, that is usually fatal within 1 week of onset of symptoms. Diagnosis is usually established at autopsy examination by finding trophozoites (cysts are rarely seen) in tissue sections. Acanthamoeba meningoencephalitis may be caused by several species of *Acanthamoeba* that include *A castellani*, *A cullbertsoni*, *A polyphaga* and *A astronyxis*. It is usually a subacute or chronic opportunistic infection of chronically ill debilitated and immunocompromised individual, leading to death, weeks to months following onset of symptom.[1] In addition, less commonly it may be the cause of an acute suppurative meningoencephalitis similar to that cause by *N fowleri*.[2] Infection is thought to spread haematogenously from primary foci in skin, pharynx or the respiratory tract. Exposure to fresh water is not necessary because cysts of *Acanthamoeba* readily become airborne and may be recovered from throat and nasal passage.[1] The present case highlights the importance of including amebic encephalitis when cerebrospinal fluid (CSF) examination is negative for routine organisms and treatment with conventional antimeningitis drugs has failed.

CASE PRESENTATION

A 5-year-old Iranian girl from a rural area was admitted to emergency department on December 2010 with a 8-day history of nasal discharge, productive cough and low-grade fever that had received cotrimoxazole (40 mg of sulphametoxazole/kg and 8 mg trimethoprim/kg/day), erythromycin (40 mg/kg/day), which had improved partially. Several days later, on the early morning, she waked up suddenly with severe headache, ophthalmia and projectile vomiting. Several weeks ago, her parents had noticed a wound on her arm which had healed completely. In the emergency ward, clinical examination revealed febrile (T=38c) sick looking but conscious child oriented in time, person and place. Vitals were stable. CNS examination was remarkable for the presence of meningeal signs. Rest of the systemic examination was non-contributory.

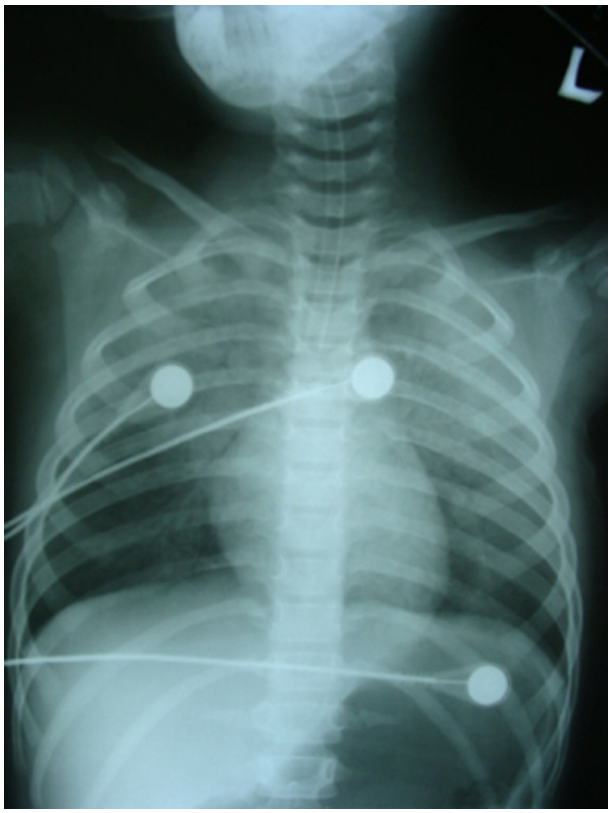

Figure 1 CXR shows no abnormality.

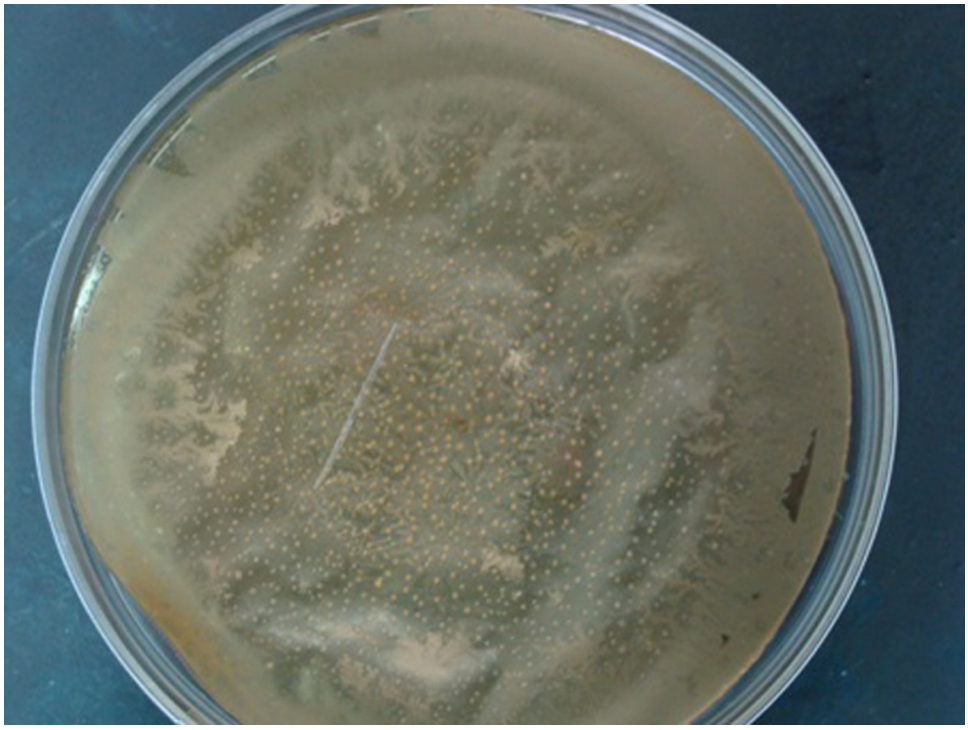

Figure 2 Acanthomoeba had left tracks on the *E coli* lawn.

INVESTIGATIONS

Laboratory data showed leucocyte count 13 800/mm^3, C reactive protein level of 1.2 mg/l and lumbar puncture showed increased intracranial pressure, bloody fluid with total cell count of 50 cell/mm^3 (98% lymphocyte), protein of 150 mg/dl and CSF/plasma glucose ratio of 0.16. Gram stained cerebrospinal fluid smears showed no bacteria or fungi. Repeat CSF count showed an increase in mononuclear count (150 mononuclear cells/mm^3). CT scan showed diffuse cerebral oedema (patient's CT scan is not available, we send her chest x-ray that shows no abnormality (figure 1)).

DIFFERENTIAL DIAGNOSIS

Common human CNS pathogen, such as bacteria, mycobacteria and fungal agents should be considered in the differential diagnosis, so Gram staining, Ziehl-Neelsen staining for acid and alcohol-fast bacilli and Indian ink preparation for cryptococci, should be done. In addition, *Acanthomoeba* in the lesions may be misinterpreted as macrophage. Differentiation of *Acanthomoeba* from macrophage requires experience in recognising the characteristic nuclear morphology of these parasites, particularly in areas of intense inflammation and necrosis. It is necessary to be aware of the clinical and epidemiologic features that distinguish primary from secondary CNS amebic infection and of the various organisms that are associated with these forms of disease. This is not only true for patients with the more classical presentation of these infectious syndromes, but also for those who are culture negative for common human CNS pathogens. So, acanthamoeba meningoencephalitis should be considered in the differential diagnosis when CSF examination is negative for routine organisms and treatment with conventional antimeningitis drugs has failed.

TREATMENT

The child received corticosteroid (dexamethasone sodium phosphate 4 mg/ml intravenously) and ceftriaxone (50 mg/kg/day), after taking appropriate culture specimens. Several minutes later she lost her conscious. She was intubated and mechanically ventilated.

OUTCOME AND FOLLOW-UP

Approximately 1 h later, severe anisocoria (10 mm right and 7 mm left) developed, followed by fixed mydriasis and the patient was pronounced dead 8 days after onset of symptoms. The parents did not agree with autopsy, but postmortem CSF examination showed many red blood cells, mononuclear white blood cells and some cells that morphologically resembled amebic vegetative form, the cells had an irregular shape, vacuolated cytoplasm and a nucleus located centrally or slightly eccentrically, tentatively classified as *Acanthamoeba*. CSF sample was cultured on non-nutrient agar medium seeded with an unspecified strain of *E coli*. After 48 h, the culture plates showed a prolific growth of *Acanthomoeba* trophozoites (*Acanthomoeba* had ingested the bacteria and left tracks on the bacterial lawn, figure 2).

DISCUSSION

Amebic encephalitis is an infrequently encountered mostly fatal, infection of the CNS seen in both normal and immunocompromised individuals. Granulomatous amebic encephalitis (GAE) caused by *Acanthomoeba* spp. and *Balamuthia mandriallis* and primary amebic meningoencephalitis caused by *N fowleri* are the two clinical manifestations of CNS amebic infection. GAE generally occurs in individuals who are immunosuppressed as a result of HIV infection, malignancy or treated with corticosteroid

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and chemotherapic agents.[3–5] Very few cases have been reported in immunocompetent individuals,[6] such as our case. Acanthomoeba presumably enter the CNS through haematogenous spread from a usually transient primary infection in the lung, skin or paranasal sinuses in an immunocompromised host.[7] Our case had a history of skin wound on her arm which had healed, she also had symptoms suggestive of respiratory tract infection. Clinical manifestations of GAE are highly variable, including headache, personality changes, mild fever, seizures, cranial nerve palsies, altered level of consciousness and coma. Alterations in taste and smell may be noted initially, perhaps because of involvement of the olfactory nerve. Patients do not respond to routine antibiotics, and progressive deterioration occurs. Seizures, ataxia, cranial nerve palsies, confusion and coma frequently develop.[8] The presented patient had headache, altered level of consciousness and coma. CSF may reveal decreased glucose and moderately increased protein and pleocytosis with lymphocyte predominance, such as in our case. Microscopically, GAE is characterised by granulomatous reaction but our patient's parents did not agree with autopsy. Diagnosis of amebic meningoencephalitis is typically made by recognition of trophozoites and cysts on examination of brain tissue.[9] We found trophozoites in CSF smear. In our patient, the look and size of the trophozoites were consisted with *Acanthomoeba* spp. However, ancillary techniques including indirect immunofluorescence technique is recommended to confirm the diagnosis. Culture of *Acanthomoeba* is useful for speciation and determination of antimicrobial susceptibility. Some investigators have used serological and molecular diagnostic methods[10] that are non-invasive but are time-consuming, expensive and need further evaluation.[10]

Learning points

- *Acanthomoeba* infection can cause severe and rapidly fatal infection in immunocompromised children. A high index of suspicious is needed for early diagnosis, especially in immunocompetent patients.
- Acanthamoeba meningoencephalitis should be considered in the differential diagnosis when CSF examination is negative for routine organisms and treatment with conventional antimeningitis drugs has failed.
- Differentiation of *Acanthomoeba* from macrophage requires experience in recognising the characteristic nuclear morphology of these parasites, particularly in areas of intense inflammation and necrosis.
- Increasing familarity of the clinician, clinical microbiologists and pathologists with infections due to free living amebae will certainly help in early diagnosis and treatment.
- This case highlights that the first lead to diagnosis of acanthamoeba meningoencephalitis is awareness of the occurrence of this disease.

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Competing interests None.

Patient consent Obtained.

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