

## INTRODUCTION

*Balamuthia mandrillaris* is an opportunistic free-living amoeba that has been found in soil, dust and water and is pathogenic in humans. Cutaneous, respiratory tract and central nervous system (CNS) infection occurs in all age groups, in both immunocompromised and immunocompetent individuals, especially in children and older adults. Males are affected more than females. Around 200 cases have been reported from various regions throughout the world, mostly in case reports and a few small case series. Cases reported are predominantly from areas with warmer climates. One case from Africa was reported in 2022. More than 95% of cases are fatal.

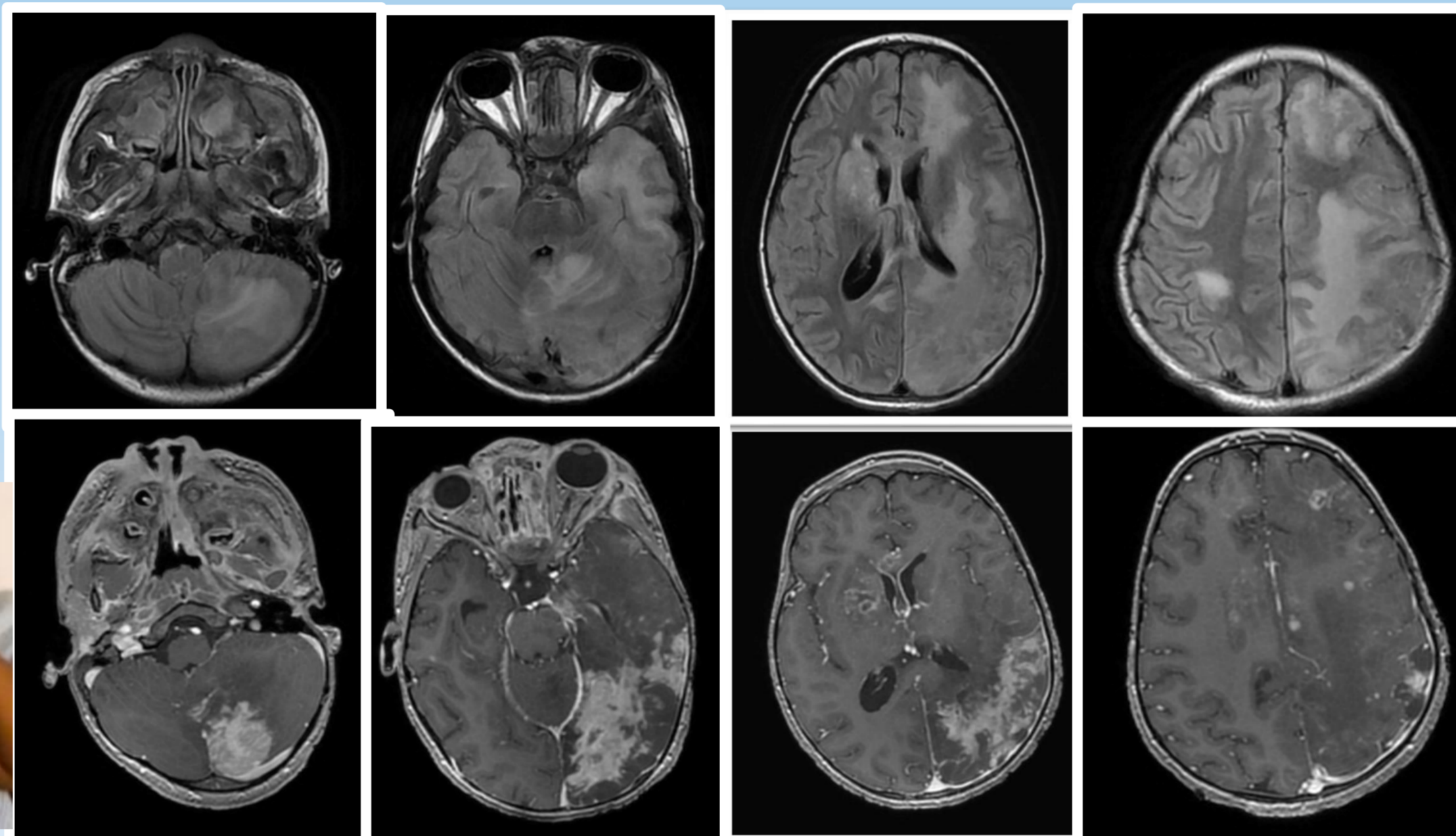
Cutaneous infection precedes CNS involvement by months to years in some patients. Clinical presentation of *Balamuthia* amoebic encephalitis (BAE) is non-specific with fever, headache, confusion, seizures, changes in gait and speech. With disease progression symptoms of increased intracranial pressure and worsening encephalopathy develop. Neuroimaging reveals single or multiple ring-enhancing, space-occupying lesions, with perilesional edema and at times necrosis and haemorrhage, involving the cortex, basal ganglia, thalamus, brainstem and cerebellum. No cases of spinal cord involvement have been reported. Diagnosis is usually made on biopsy with PCR testing for *Balamuthia mandrillaris* now available. There are case reports of next generation sequencing of cell free CSF or plasma being used as well.

## OBJECTIVE

Description of two cases of BAE in immunocompetent children.

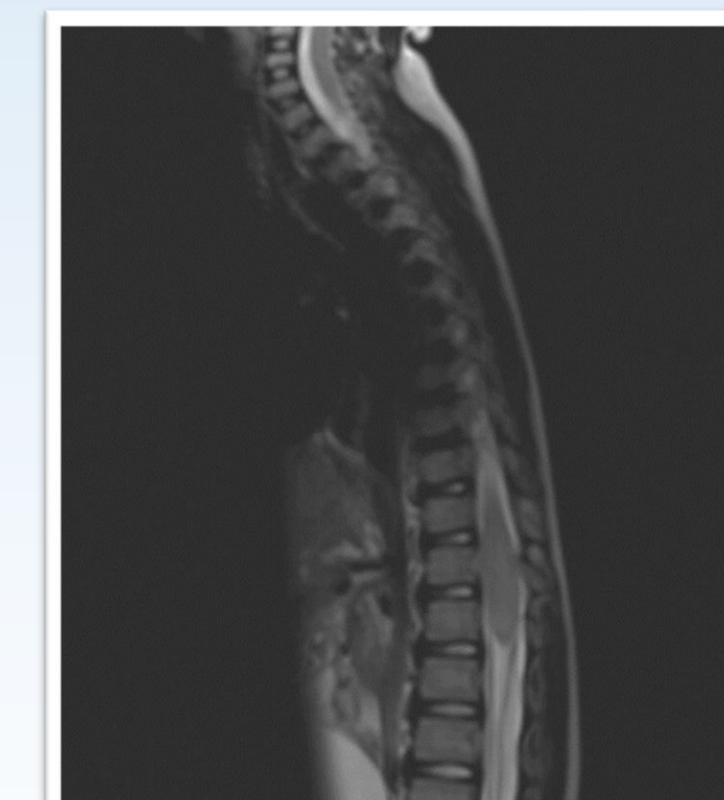
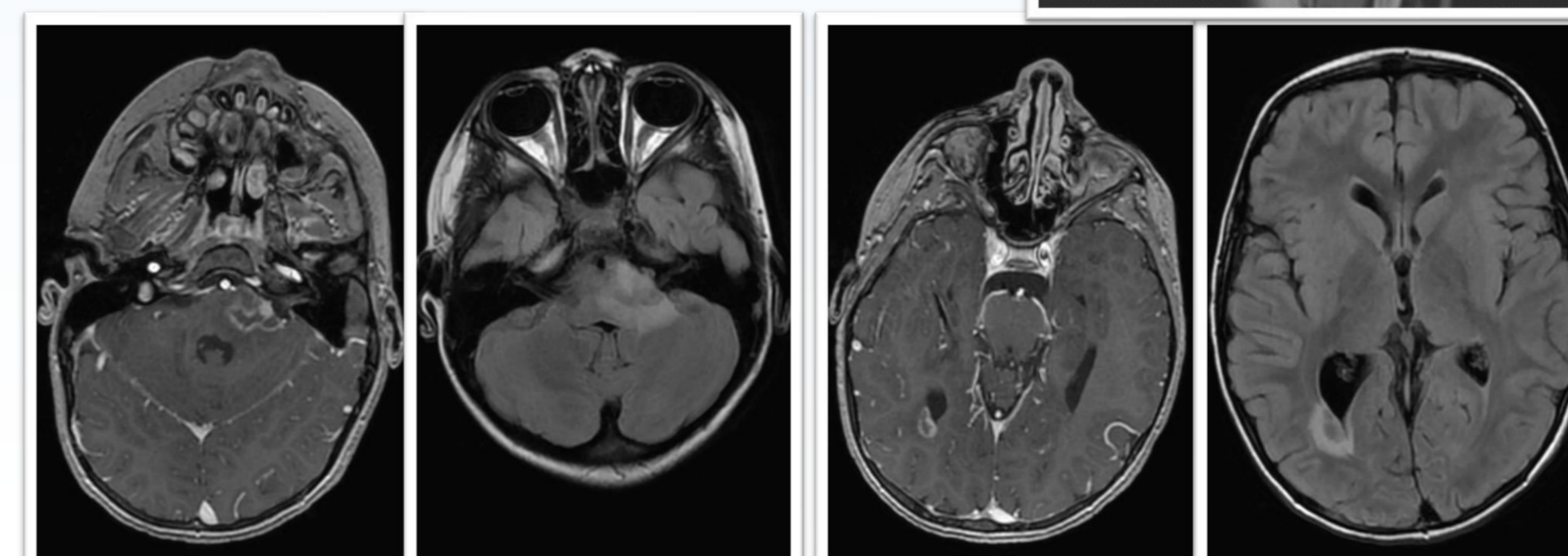
## CASE 1

A 5-year-old female presented with new onset focal seizures, left-sided hemiplegia, choreoathetoid movements and encephalopathy. She had developed facial and nasal swelling, 18 months prior to presentation. An MRI brain scan revealed T2/FLAIR hyperintensities in the left cerebral hemisphere, left midbrain, left cerebellum, corpus callosum and right basal ganglia with irregular lesional and rim enhancement and oedema. A stereotactic brain biopsy demonstrated extensive, multifocal granulomatous inflammation. Multiple amoeboid trophozoites were present in the foci of granulomatous inflammation. Real-time polymerase chain reaction assay confirmed *Balamuthia mandrillaris*. Despite receiving combination therapy including miltefosine, fluconazole, azithromycin, amphotericin B, flucytosine co-trimoxazole, rifampicin and albendazole, the child deteriorated rapidly and demised within a month. Autopsy confirmed extensive cortical destruction resulting from amoebic encephalitis.



## CASE 2

A 6-year-old male presented with a 1 month history of progressive leg weakness, paraesthesias, and urinary retention. A non-contrasted MRI scan of the brain and spine demonstrated an intra-medullary spinal cord lesion from T11 to the conus medullaris with no brain lesions. A well-delineated intramedullary mass was resected. Histology demonstrated features of an infective lesion with trophozoites and non-caseating granulomas. Real-time polymerase chain reaction assay confirmed *Balamuthia mandrillaris*. Postoperatively the child developed progressive right sided limb and facial weakness. Repeat imaging revealed new rim enhancing lesions in the pons on the left and in the right peritrigonal periventricular white matter. Combination therapy was initiated, initially with miltefosine, fluconazole, albendazole, co-trimoxazole, azithromycin and flucytosine. Later, nitroline was added. Despite this, he developed new lesions and eventually deteriorated and demised 6 months after initial presentation.



## CONCLUSION

BAE is a rare with devastating disease with a very high mortality rate. Many treatment combinations have been used based on treatment regimes used in cases that survived and on in-vitro studies. The CDC has a recommended regime available on their website including pentamidine, sulfadiazine, flucytosine, fluconazole, azithromycin or clarithromycin and miltefosine. Nitroline has also been used recently in a case that survived, based on previous in-vitro studies. Unfortunately, despite surgical resection and pharmacological treatment most patients progress rapidly and ultimately demise. It is possible, that with earlier recognition of this condition and earlier initiation of therapy outcomes may improve.

## REFERENCES

- Bhosale NK, Parija SC. Balamuthia mandrillaris: An opportunistic, free-living ameoba - An updated review. Trop Parasitol. 2021 Jul-Dec;11(2):78-88. doi: 10.4103/tp.tp\_36\_21.
- Kofman A, Guarner J. Infections Caused by Free-Living Amoebae. J Clin Microbiol. 2022 Jan 19;60(1):e0022821. doi: 10.1128/JCM.00228-21.
- Berger JR. Amebic infections of the central nervous system. J Neurovirol. 2022 Dec;28(4-6):467-472. doi: 10.1007/s13365-022-01096-x.
- Haston JC, Cope JR. Amebic encephalitis and meningoencephalitis: an update on epidemiology, diagnostic methods, and treatment. Curr Opin Infect Dis. 2023 Jun 1;36(3):186-191. doi: 10.1097/QCO.0000000000000923.
- Cope JR, Landa J. The Epidemiology and Clinical Features of Balamuthia mandrillaris Disease in the United States, 1974-2016. Clin Infect Dis. 2019 May 17;68(11):1815-1822. doi: 10.1093/cid/ciy813.
- Hara T, Yagita K. Pathogenic free-living amoebic encephalitis in Japan. Neuropathology. 2019 Aug;39(4):251-258. doi: 10.1111/neup.12582.
- Wang L, Cheng W. Balamuthia mandrillaris infection in China: a retrospective report of 28 cases. Emerg Microbes Infect. 2020 Dec;9(1):2348-2357. doi: 10.1080/22221751.2020.1835447.
- Tootla HD, Eley BS. Balamuthia mandrillaris Granulomatous Amoebic Encephalitis: The First African Experience. J Pediatric Infect Dis Soc. 2022 Dec 28;11(12):578-581. doi: 10.1093/jpids/piac096.
- Chen XT, Zhang Q. Pathogenic free-living amoebic encephalitis from 48 cases in China: A systematic review. Front Neurol. 2023 Feb 9;14:1100785. doi: 10.3389/fneur.2023.1100785.
- Yang Y, Hu X, Min L, Dong X, Guan Y. Balamuthia mandrillaris-Related Primary Amoebic Encephalitis in China Diagnosed by Next Generation Sequencing and a Review of the Literature. Lab Med. 2020 Mar 10;51(2):e20-e26. doi: 10.1093/labmed/lmz079.
- Kalyatanda G, Rand K. Rapid, Noninvasive Diagnosis of Balamuthia mandrillaris Encephalitis by a Plasma-Based Next-Generation Sequencing Test. Open Forum Infect Dis. 2020 Jun 1;7(7):ofaa189. doi: 10.1093/ofid/ofaa189.
- Laurie MT, White CV. Functional Assessment of 2,177 U.S. and International Drugs Identifies the Quinoline Nitroline as a Potent Amoebicidal Agent against the Pathogen Balamuthia mandrillaris. mBio. 2018 Oct 30;9(5):e02051-18. doi: 10.1128/mBio.02051-18.
- Spottiswoode N, Pet D. Successful Treatment of Balamuthia mandrillaris Granulomatous Amoebic Encephalitis with Nitroline. Emerg Infect Dis. 2023 Jan;29(1):197-201. doi: 10.3201/eid2901.221531.

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