

Free-living amoebae (*Balamuthia Mandrillaris*) in Peru

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Abstract

Free-living amoebas are eukaryotic microorganisms that inhabit many environments naturally. These amoebas are aerobic microorganisms, consuming bacteria, yeasts and other eukaryotes. There are three species frequently reported in humans, the first two are: *Acanthamoeba sp.* (T-4) and *Balamuthia mandrillaris*. The third amoeba is: *Naegleria fowleri*, known as the "brain-eating amoeba". *Naegleria fowleri* does not produce a skin lesion and directly infects the brain of the host killing in 5-7 days. These amoebas are responsible for meningoencephalitis with a case fatality >98%. Peru is the second country with the highest number of cases for free-living amoebas (*Balamuthia mandrillaris*). In this update we present the events that led to the opening of a research line little investigated in Peru. Currently, we are working on the cultivation and sequencing of strains of *Balamuthia mandrillaris* isolated from deceased patients and environmental samples.

Background

In the 70s, reports of amoebic meningoencephalitis cases began, some with skin lesions and others not. These patients came from the north coast of the country, specifically from Piura and Trujillo [1,2]. Some doctors described the few reports, but in some cases, the real identity of these amoebas never be established, because in those years there were no molecular biology techniques. In this sense, there is no molecular evidence to support the claim that these infections have been by *Acanthamoeba* or *Balamuthia mandrillaris* are morphologically indistinguishable in paraffin tissue.

Beginning in the mid-1980s, at the Institute of Tropical Medicine Alexander von Humboldt of the Universidad Peruana Cayetano Heredia (IMT-AvH), a group of doctors began to identify some cases that presented with cutaneous lesions and within a few weeks or months developed abscesses brain tumors with fatal results [3,4]. On the other hand, Drs. Visvesvara, Julio Martínez and Frederick Schuster in the northern hemisphere, who re-described a clinical presentation for a new species of free-living amoebas, calling it "*Leptomyxa sp.*" They describe for the first time a new pathogen called *Balamuthia mandrillaris*.

In 1986, a mandrill died at the San Diego Zoo with a meningoencephalitis, the results of their findings are published by Visvesvara., et al. 1993 [5]. This clinical picture was very similar to that observed in a group of patients from Peru and USA. Some years later, tissue samples from some deceased patients from Peru were sent to the Control Disease Center (CDC) where this group had been working and confirmed the presence of *B. mandrillaris* as a causative agent in human tissues in Peru [6].

In 1997, Claudia Velarde MD of the Universidad Peruana Cayetano Heredia (UPCH) develops as subject of the Bachelor Thesis "**Free living amoeba in Peru: A Anatomic-Pathological Study, a descriptive study of the anatomic-pathological findings of the necropsies performed at affected patients with this entity in IMT.**" During this time 100% of patients died with or without treatment [7].

10 years later, the epidemiological data are updated, including more cases in the capital and provinces. This time, Patricia Álvarez MD (from UPCH) develops her specialty thesis titled: "**Histopathological Findings of cutaneous infection by *Balamuthia mandrillaris* in the**

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Hospital Nacional Cayetano Heredia (HNCH) 2000-2007. Where cases were described from 2000 to 2007, there were 18 cases of infections with free-living amoebas with cutaneous involvement. Only 10 cases have been analyzed, unfortunately 8 biopsies were not found. The range of the ages of the patients was from 7 - 57 years. 70% of the patients were male, 50% were younger than 15 years, 7 of them with facial and 3 extra facial injuries [8-11].

Update in Peru

In 2010, our group published the first report of a survivor with the use of Miltefosina, Albendazol and Fluconazol [12]. This was the first time the drug was used in a human patient with an advanced encephalitis course. A medical staff raised the idea from the work of F. Schuster in 2006, resulting in the patient surviving the infection. Peru is one of the two countries that reports the largest number of cases worldwide, this being a little known entity with a high mortality rate >98%. However, In Peru, six surviving patients have been treated with a combination of fluconazole or itraconazole, in addition to albendazole and miltefosine. Three patients had CNS involvement at the time of presentation, and three more had cutaneous involvement only [13]. One of them had facial center lesion, this patient did not develop cerebral lesion after 3 months of treatment [13].

We have recently been able to demonstrate five more cases of *Balamuthia mandrillaris* by genomic analysis. This will allow us to analyze in greater depth the different strains that infect patients (Figure 1 and 2). Currently focused on the cultivation of all strains of *Balamuthia mandrillaris*, isolated from humans, the environment and the study of chemotherapy against *Balamuthia mandrillaris* [14-16].

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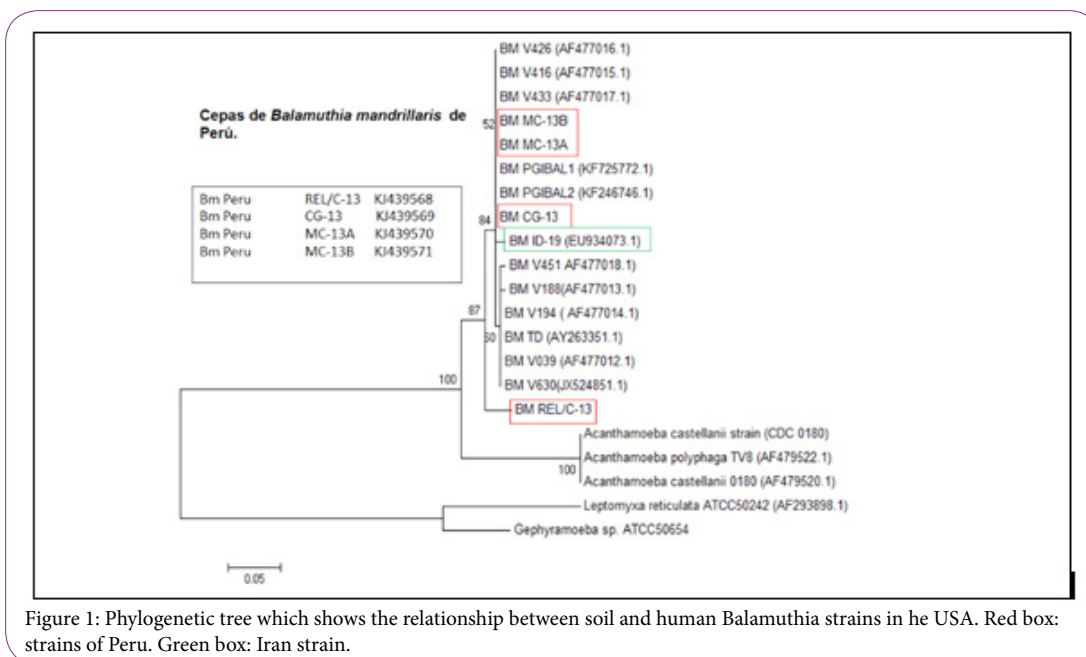


Figure 1: Phylogenetic tree which shows the relationship between soil and human *Balamuthia* strains in he USA. Red box: strains of Peru. Green box: Iran strain.

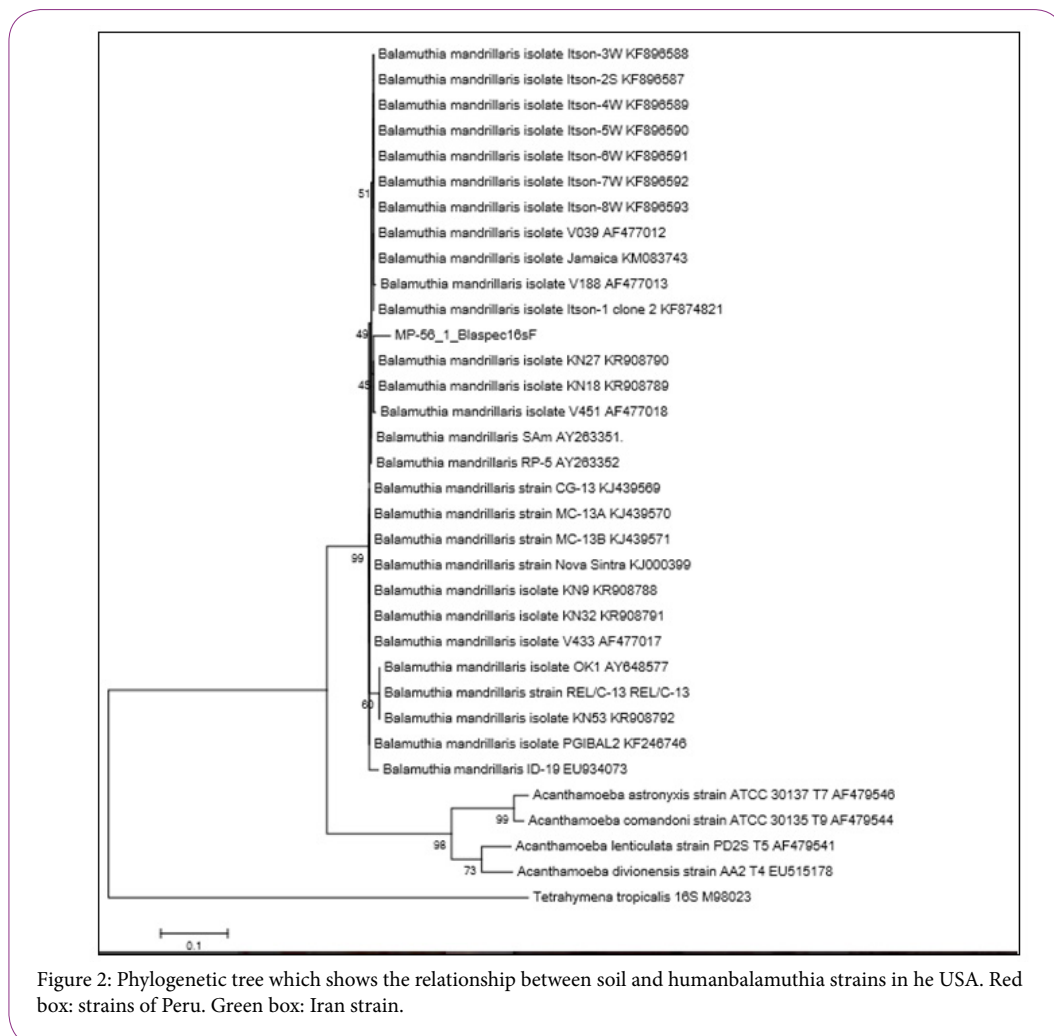


Figure 2: Phylogenetic tree which shows the relationship between soil and human *Balamuthia* strains in he USA. Red box: strains of Peru. Green box: Iran strain.

Discussion

B. mandrillaris can be found in soil, dust and fresh water [17,14]. *Balamuthia mandrillaris* is an emerging pathogen capable of inducing a characteristic skin lesion and the potential for progressing to commonly fatal encephalitis.

Balamuthia mandrillaris is a free-living amoeba that has been reported more 200 cases around the world. In our country, the vast majority of cases have been for *Balamuthia mandrillaris* with a total of 55 cases reported from 1974 to 2012 [18]. The number of cases presented to date makes Peru in the second place of incidence of Meningoencephalitis by *Balamuthia*, while the first place is occupied by the United States. Recently in the USA the complete series of cases by *Balamuthia* has been published, the number of patients borders on 109 cases [19].

Our studies have shown that patients infected environment. Overexposure, the load of microorganisms in the environment and possibly a state of immunosuppression are predisposing factors to infection free-living amoeba. Recently, Cabello-Vilchez et al. [14] reported the environmental isolation of four *B. mandrillaris* strains from soil sources in the coast of Perú. So, it is possible to isolate *Balamuthia mandrillaris*. In the phylogenetic tree (Figure 1), *B. mandrillaris* is a close relative of the monophyletic genus *Acanthamoeba*. The relationship between strains isolated from humans who died of *B. mandrillaris* and the strains of Peru from the soil of the north coast can be observed.

Conclusion

Balamuthia mandrillaris is a free-living amoeba found in soil that can cause fatal granulomatous amoebic encephalitis in both healthy and immunocompromised patients. The diagnosis to free-living amoeba infections is challenging and should be considered in the evaluation of all patients with unexplained encephalitis and the appropriate exposure risks within the past 3 years. Brain, skin lesion biopsy is crucial for arriving at the correct diagnosis. Many cases have been reported in the north coast of Peru, in the provinces Piura, Lambayeque, Trujillo, Lima, and in the south coast in Ica and very recently Arequipa.

The research of *Balamuthia mandrillaris* on environmental samples, such as soil and water, is very important. The culture and isolation in environments close to the populations, could establish some relation with the strains isolated and identified in humans.

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Competing Interests

The author declares that there is no competing interests regarding the publication of this article.

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