Nasal cartilage destruction associated to cutaneous histoplasmosis in AIDS

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Abstract

Background: Systemic histoplasmosis is a disease of high morbidity and mortality in immunocompromised patients. Patients with AIDS get the infection through inhalation of spores, triggering a primary lung infection with a subsequent hematogenous spread to multiple organs, including the skin. Tissue necrosis have been documented in cutaneous histoplasmosis with multiple clinical manifestations that mimic other diseases.

Case presentation: We report the case of nasal cartilage destruction associated to cutaneous histoplasmosis in AIDS. A 24-year-old man, resident in Ecuadorian coast, with a history of HIV for 7 years without any treatment. In the last 3 months, he has been presenting a molluscum-like lesions on his nasal bridge with subsequent dissemination to the trunk and extremities. He was admitted to the emergency department for dyspnoea, cough, and malaise. Due to his respiratory failure, he was admitted to the intensive care unit (ICU) with mechanical ventilation. Physical examination reveals a crusted surface ulcer that involves the nose and cheeks, associated with erythematous papules, some with a crusted surface which are spread to the face, trunk, and upper limbs. The patient has a specific skin involvement with a butterfly-like ulcer appearance and destruction of the upper and lower lateral cartilage of the nose. At admission CD4 cell count was 11/mm3 with a HIV viral load of 322,908 copies. Mycological cultures identified Histoplasma capsulatum. A treatment with highly active antiretroviral therapy (HAART) was established, associated with liposomal amphotericin B at a dose of 3 mg/kg/day and itraconazole 200 mg twice a day for 12 months.

Conclusions: Cutaneous histoplasmosis is a rare manifestation of pulmonary histoplasmosis in patients with AIDS. The cutaneous manifestations included papules, nodules, plaques, and ulcers. A histology examination is required to rule out other fungal or parasitic infections. Treatment includes highly active antiretroviral therapy (HAART), amphotericin B liposomal and itraconazole, the latest for at least 12 months.

Keywords: Case report, Histoplasmosis, HIV, AIDS, Nasal cartilage destruction

Background

Histoplasmosis is an endemic deep fungal infection caused by a dimorphic fungus Histoplasma capsulatum [1]. The disease is acquired through inhalation of the spores in endemic areas with large amount of spores [2]. In immunodeficient individuals, the clinical manifestations are variable. Patients with AIDS triggering a primary lung infection with a subsequent hematogenous spread to multiple organs, including the skin. Lower ratio of T:CD4 lymphocyte has been associated with cutaneous-systemic manifestations. In HIV patients, histoplasmosis induce atypical dysfunction of the tissue macrophages in the dermis with infiltration of inflammatory cells and cytokines with consequent tissue necrosis [3]. We report a young-male-patient with AIDS and systemic histoplasmosis with a complete destruction of the dorsal and lateral cartilage of the nose and a consequent flattening of the nose tip to the maxillary bone.

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Case presentation
A 24-year-old man seeking medical attention for slow growing molluscum-like lesions on his nasal bridge that spread to the trunk and extremities in the last 3 months. He has a history of HIV for 7 years without any treatment.

He was admitted to the emergency department for dyspnoea, cough, and malaise and due to his respiratory failure, he received mechanical ventilation.

Physical examination reveals a butterfly-like crusted ulcer appearance over the nose with a slow expanding surface until reach 5 cm on each side of the cheeks, associated with many erythematous papules some with a crusted surface which are spread to the face, trunk, and upper limbs (Fig. 1a–d). The cutaneous biopsy showed an ulcerated epidermis that alternates with areas of hyperkeratosis, papillomatosis, acanthosis, irregular and pseudoepitheliomatous hyperplasia. Oedema and vascular congestion were noted in the papillary dermis surrounded by a diffuse lymphohistocytic infiltrate with multinucleated giant cells that contain a large number of small spores of histoplasma-like fungi positive to with Periodic Acid-Schiff (PAS) staining. Necrosis, cellular debris, and neutrophil aggregates was abundant (Fig. 2a–c). Nasal CT scan showed a destruction of the dorsal, lateral, and alar cartilage of the nose. Lung CT scan showed bilateral pulmonary consolidations associated with reticular thickening and scattered pulmonary micronodules in more than 60% of the field (Fig. 3a, b). A final diagnosis of systemic histoplasmosis and nasal cartilage destruction was established with histoplasma PCR positive, and leishmania and tuberculosis PCR negative. A treatment with highly active antiretroviral therapy (HAART) was established, associated with liposomal amphotericin B at a dose of 3 mg/kg/day and itraconazole 200 mg twice a day for 12 months.

Discussion and conclusion
Cutaneous-systemic histoplasmosis is an infection caused by a dimorphic fungus Histoplasma capsulatum, highly prevalent in Central and South America [4]. The infection is an indicator of AIDS with CD4 cell count less than 150 cells × mm³ [2, 5]. In accordance with that, our patient has 11 × mm³ with a viral load of 322,908 copies. The fungus can spread to many organs as liver, spleen,

Fig. 1 Clinical presentation of the case. a Localized central-facial ulcer-crusted plaque that involves the nose and cheeks with perilesional brownish erythema, compromising the nasal mucosa with a consequent reduction in the volume of the nasal pyramid. b Notice the flattening of the nasal tip due to the weakening of the nasal cartilage. c, d Result posttreatment with a complete destruction of the cartilage of the nose and consequent crushing on the nose tip. Source: Hospitalization
bone marrow, lymph nodes, gastrointestinal tract and central nervous system [6].

Oral histoplasmosis is a rare manifestation of systemic histoplasmosis and is hardly reported around the world. The spores of the fungus are present in areas with high humidity and abundant rainfall, especially in soils containing bird and bat faeces. In an immunocompetent patient, the infection usually is asymptomatic. Primary infection is acquired through the inhalation of microconidia that once, in the tissues grow as dimorphic yeasts, reaching a morbidity and mortality of up to 39% in immunocompetent patients [7].
Despite the existence of defensive innate immunity mechanisms such as leukocytes, macrophages, NK cells, antigen-presenting cells and complement, this first line of defence is incapable by itself to control the fungus. The infection affects the lungs, and then by hematogenous spread it can reach other organs. Cutaneous manifestations were developed in up to 25% in men with HIV. The skin and mucosal involvement is highly frequent [8, 9].

Cutaneous histoplasmosis include papules, nodules, plaques, pustules, aceneiform eruptions, umbilicated papules resembling molluscum contagiosum lesions and ulcers, the latter mimic other fungal or parasitic infections [10].

Nasomaxillar histoplasmosis is extremely rare; and palate, gingiva, and tongue are the most frequently locations reported of disseminated histoplasmosis that compromise central facial area. We present a patient with complete destruction of the nasal cartilage due to histoplasmosis with a butterfly shape. Compromise of the nasal and oral mucosa has been reported, although with a lower prevalence. The diagnosis is made by histology and periodic acid Schiff (PAS) stain, which is considered the gold standard. Although the culture is highly specific, it has several limitations including a variable sensitivity in HIV patients between 75% and 85–95% [1, 3, 11–13].

The destruction of nasal cartilage is the result of hematogenous dissemination of the fungus spores, triggering a cascade of pro-inflammatory cytokines and the cytogenetic effects generated by tissue macrophages, lymphocytes and neutrophiles that progressively destroy the fine and delicate nasal cartilage [14].

Differential diagnosis include drug rash, eosinophilic folliculitis, prurigo secondary to HIV, scabies, psoriasis, penicilliosis, and other bacterial and fungal infections. Due to its necrotic appearance mucormycosis must be considered first, however the prevalence is low in Ecuador. In our endemic area, cutaneous ulcer and nasal destruction could be a misleading Leishmaniasis, especially due to the similar clinical and histologic manifestations between the intracell amastigotes and histoplasma. Also, primary cutaneous tuberculosis should be considered in endemic areas due to his pulmonary and verrucous cutaneous compromission. In the context of central facial ulcer-necrotic disease, clinician should rule out, NK/T cell-lymphoma, squamous-cell carcinoma, Wegener’s granulomatosis, and sarcoidosis [15–18].

In literature, only 19 cases of central facial involvement due to Histoplasma have been reported, 13 of them had AIDS with CD4 cell counts < 150/mm³, and 3 died because of delay or non-adherence to treatment [12]. Treatment include with liposomal amphotericin B, itraconazole and HAART in HIV positive patients [12, 19–28].

Our patient received liposomal amphotericin B 3 mg/kg/day for two weeks, followed by itraconazole 200 mg orally twice a day for one year. Antifungal therapy has been determined to continue until serum and urine antigens were < 2.0 ng/mL [17, 18]. After 1 year of treatment, Itraconazole 200 mg/day should be continued until blood cultures negative for Histoplasma, antigenuria or antigenemia < 2 ng/mL in patients with more than 150 CD4/mL on antiretroviral therapy for more than 6 months (29).

There are many clinical presentations of this infection which usually start as primary lung histoplasmosis and can compromise central facial area.

There are previous reports of nasal septum perforation that does not include the entire nasal pyramid and butterfly-like appearance. To the best of our knowledge, this is the first reported case of a complete destruction of the nasal cartilage by histoplasma in a butterfly shape.

A prompt response to treatment is expected to prevent fatal outcomes, especially when clinician has to considerer many other etiologies that mimic this presentation.

Abbreviations
AIDS: Acquired immune deficiency syndrome; HIV: Human immunodeficiency virus; PAS: Periodic Acid-Schiff; HAART: Highly active antiretroviral therapy; ICU: Intensive care unit.

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Author contributions
LE: Wrote the paper and performed the analysis. JGR: Wrote the paper and preformed the analysis. VPL: Collected the data and performed the analysis. AM: Collected the data and performed the analysis. ST: Histopathology and analysis tools. AM: Collected the data and performed the analysis. LE: Wrote the paper and performed the analysis. JGR: Wrote the paper and performed the analysis. ICO: Wrote the paper and performed the analysis. All authors have read and approved the manuscript.

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The author's institutions does not require ethical approval letter for publication of a single case. The patient has given written informed consent for publication of the case.

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A written consent to publish this information was obtained from study participant.

Competing interests
The authors declare that they have no competing interests.

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