ACTA RADIOLÓGICA PORTUGUESA
Setembro-Dezembro 2016 | nº 109 Volume XXVIII | 51-54

Caso Clínico / Radiological Case Report

AFRICAN HISTOPLASMOSIS

HISTOPLASMOSE AFRICANA

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Recebido a 15/09/2016
Aceite a 07/11/2016

Abstract

African histoplasmosis (AH) is a fungal infection due to Histoplasma capsulatum var. duboisii. Unlike classic histoplasmosis, infections caused by H. duboisii most commonly affects the skin, subcutaneous tissues, lymph nodes and bones. Till present, in Europe, all published cases have been from natives from Africa who moved to Europe. There are few reports in the literature describing the radiologic features of AH.
The authors report a case of a 7-year-old girl, from Guine-Bissau, who had multiple skin and subcutaneous lesions and left lower limb deformity. The presence of H. duboisii was confirmed by culture and histologic examination. Imaging studies were performed and showed multiple calcified and non-calcified subcutaneous lesions compatible with granulomas/abscesses; axillary and thoracic lymphadenopathies; and signs of chronic osteomyelitis. Although these imaging features are not pathognomic they should raise awareness for the diagnosis of AH in patients that are African or people who have travelled from this continent. Imaging plays a crucial role not only in the diagnosis of this disease but also in monitoring the response to therapy and detecting recurrence.

Key-words

African histoplasmosis; Child; Disseminated histoplasmosis.

Resumo

A histoplasmose africana (HA) é uma infecção fúngica provocada por Histoplasma capsulatum var. duboisii. Contrariamente à forma clássica, infeções causadas pelo H. duboisii afetam mais comummente a pele, tecido celular subcutâneo, gânglios linfáticos e osso. Na Europa, todos os casos publicados até à data foram de nativos de África que migraram para a Europa. Existem poucos relatos, na literatura, que descrevam as características radiológicas da HA.
Os autores descrevem o caso de uma paciente de 7 anos de idade, oriunda da Guiné-Bissau, que se apresentou com múltiplas lesões cutâneas e do tecido celular subcutâneo, e deformidade do membro inferior esquerdo. A presença de H duboisii foi confirmada através de exame cultural e histológico. Os estudos imagiológicos realizados demonstraram: múltiplas lesões subcutâneas calcificadas e não calcificadas compatíveis com granulomas/abcessos; adenopatias axilares e torácicas; e sequelas de osteomielite crónica. Apesar destas características de imagem não serem patognomónicas, a hipótese de diagnóstico de HA deve ser equacionada em pacientes oriundos de África ou que viajaram para este continente. A imagiologia desempenha um papel essencial não só no diagnóstico, mas também na monitorização da resposta ao tratamento e na detecção de recorrência.

Palavras-chave

Histoplasmose Africana; Criança; Histoplasmose disseminada.

Introduction

Histoplasmosis is a granulomatous disease caused by the fungus Histoplasma capsulatum. There are two recognized pathogenic subspecies for humans, namely: 1) classic form caused by Histoplasma capsulatum var. capsulatum (Hcc) endemic in North and Latin America; 2) African form caused by Histoplasma capsulatum var. duboisii, endemic in Central and West Africa and Madagascar[1-7].
African Histoplasmosis (AH) is characterized by the presence of granulomatous and suppurative lesions involving the skin, subcutaneous tissues, lymph nodes and bones. It rarely affects lungs and visceral organs, unlike the classical form caused by H. var. capsulatum. In most of the exposed individuals H. duboisii results in a subclinical infection which is limited to the skin and to the subcutaneous tissue, but disseminated disease can also occur particularly in immunodeficient individuals[1-7]. We present a case of a girl with disseminated AH.

Clinical History

A 7-year-old African girl from Guinea-Bissau was referred to our hospital for therapeutic optimization. Upon review, her history started at least 6-year before with multiple cutaneous and nodular subcutaneous lesions scattered throughout the body, which increased over time. At presentation she had persistent scattered cutaneous lesions and subcutaneous abscesses associated with cutaneous fistulas, and left lower limb deformity. Laboratory studies showed anemia and high erythrocyte sedimentation rate (ESR); she was HIV negative. Radiographs were performed and showed numerous calcified and non-calcified soft-tissue

lesions, more prominent in the lower limbs and pelvic region (Figure 1). Multiple osteolytic lesions with a sclerotic rim and endosteal scalloping were also detected in the tubular bones, especially in both tibia and in the small bones of hands and feet. No aggressive periosteal reaction or cortical destruction were detected. These lesions were located in the epiphysis or metaphyses adjacent to the growth plate and in the diaphyses. Diaphysial bowing on the left tibia was also noted (Figure 1 B, C, E). Computed Tomography (CT) of the thorax demonstrated hilar and axillary lymphadenopathy, without pulmonary lesions (Figure 2). Magnetic Resonance Imaging (MRI) of the lower limbs showed multiple subcutaneous lesions hyperintense on T2-weighted images and peripheral rim enhancement compatible with abscesses (Figure 3A-C). MRI also demonstrated multiple bone lesions hypointense on T1-weighted images and hyperintense on T2-weighted images, without enhancement after contrast administration (Figure 3 D-F). Bone scintigraphy was negative. These lesions were compatible with sequelae of chronic osteomyelitis. The presence of Histoplasma capsulatum var duboisii in ulcerations and lymph node was confirmed by direct microscopic examination (Figure 4) and by culture. The patient was treated with amphotericin B and posaconazol. During the follow-up an inability to produce INF-gama was detected, and adequate replacement treatment was initiated. After 22 months of follow-up in our hospital she remains under treatment and stable.

Discussion

AH is a systemic fungal infection, which occurs most commonly in the tropical areas of Africa[1-7]. All reported cases in Europe were imported from endemic areas because the fungus can remain viable for many years within tissues without clinical evidence of disease[3,5,7]. It affects most commonly adults in their third and fourth decades; childhood histoplasmosis is rare. Males are affected more often than females (2:1); yet, in childhood, they are equally affected[3,5]. H. duboisii is acquired mainly by airborne contamination from the acidic soil containing excrements of bats and, rarely, by direct inoculation[1-7].

There are two main clinical presentations: 1) localized: lesions are scanty and there is no systemic involvement; 2) disseminate: multiple lesions through the body; usually there is systemic involvement with anaemia, loss of weight, fever and other constitutional disturbances; liver and/or spleen can be affected[1-7]. Infections of the lungs, urinary bladder and large bowel have been reported and have a poor prognosis[1-4, 6].

Our case report represents a disseminated form of the disease with typical imaging findings in the skin, subcutaneous tissue, lymph nodes and bones. Multiple suppurative abscesses and granulomas were detected in our patient. As previously described in the literature these lesions can arise from foci in the superficial flat bones or develop independently[1].

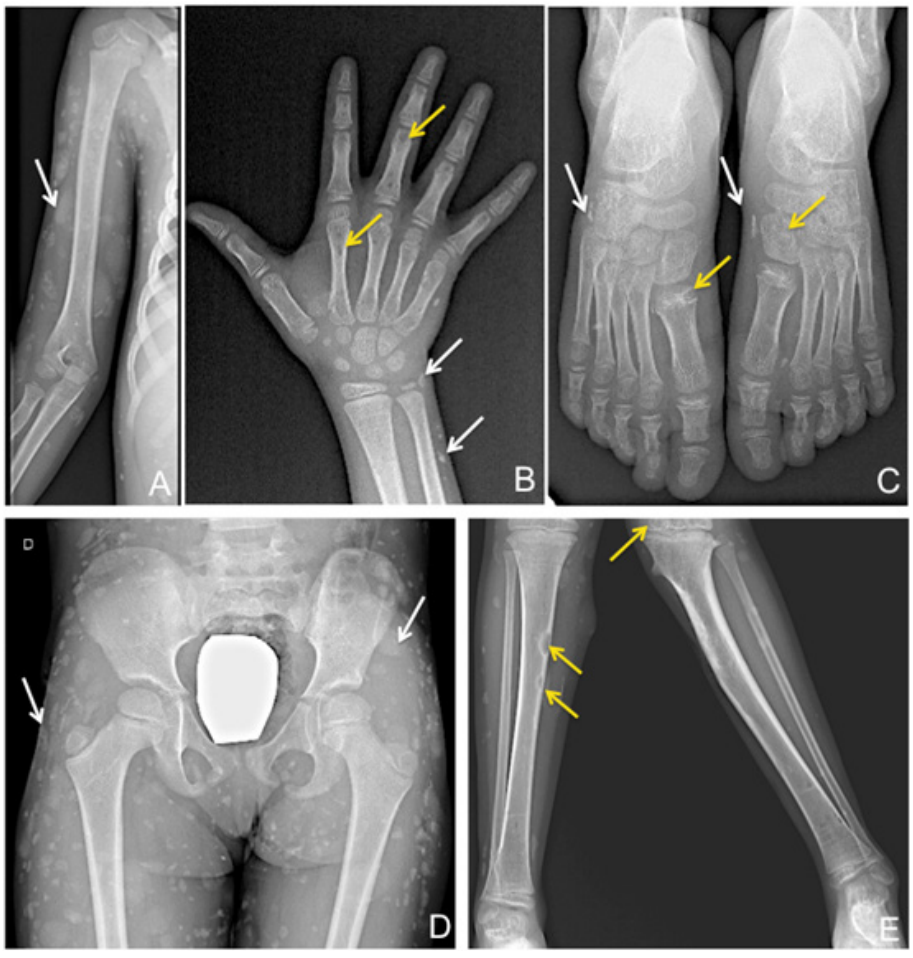

Figure 1 - Frontal X-rays of the right limb (A), left hand (B), feet (C), hip (D) and tibias (E) were performed and showed multiple calcified and non-calcified soft-tissue lesions scattered through the body (white arrows), more prominent in the lower limbs and pelvic region (D and E). Multiple osteolytic lesions with a sclerotic rim were also detected in the tubular bones (yellow arrows), especially in both tibia and in the small bones of hands and feet.

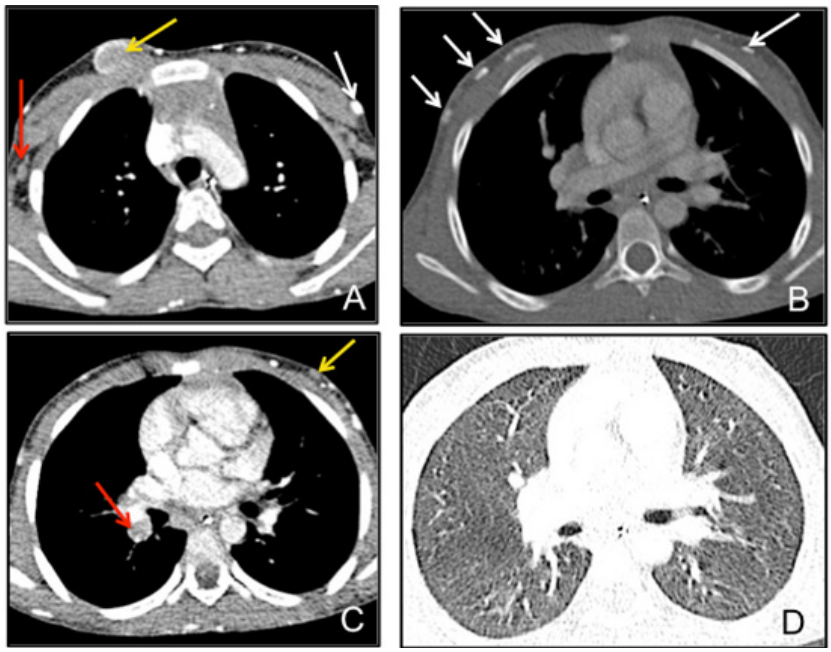

Figure 2 - Axial contrast enhanced CT scans of the thorax on soft-tissue window (A-C) and lung window (D), demonstrated hilar and axillary lymphadenopathy (red arrows in A and C), without pulmonary lesions (D). There are also multiple calcified (white arrows in A-C) and non-calcified (yellow arrows in A and C) subcutaneous lesions scattered through the thorax.

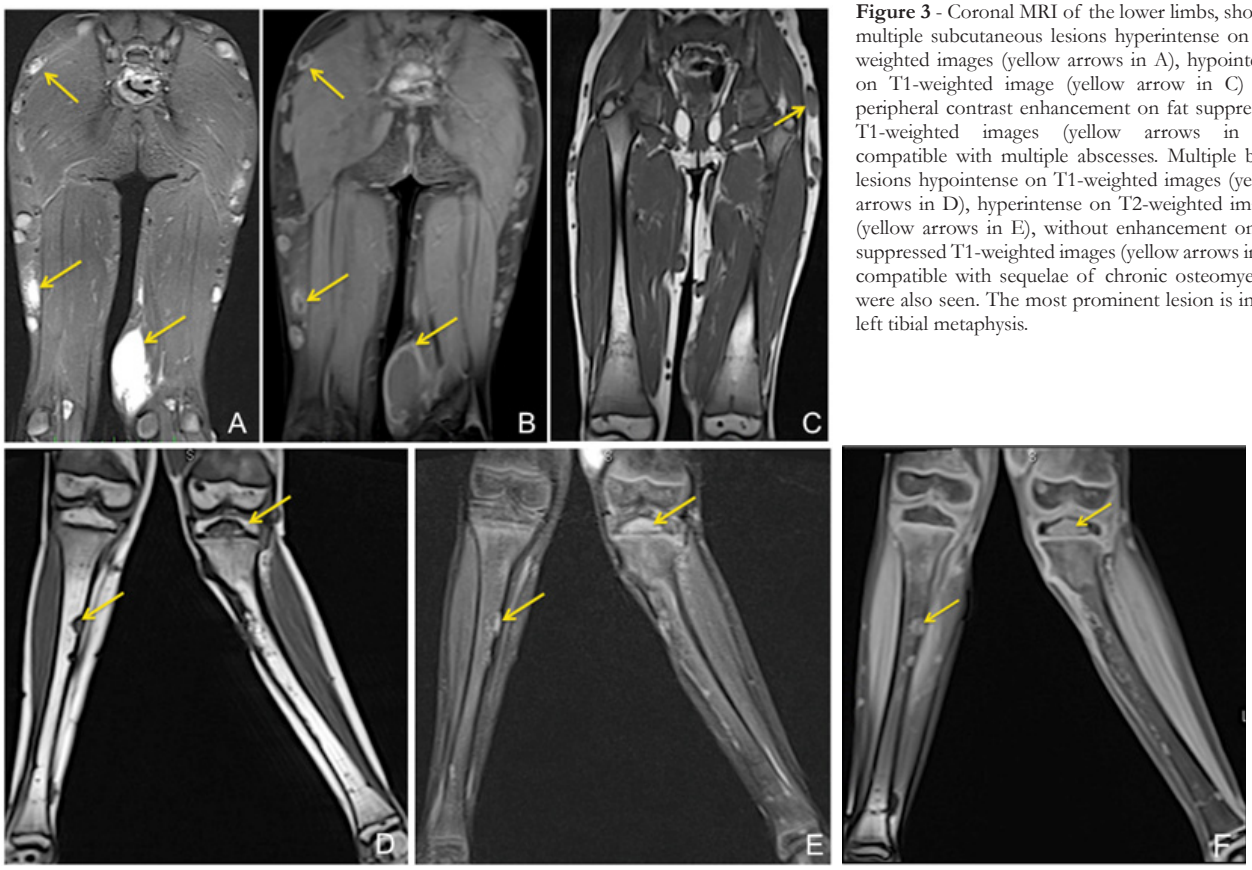

Figure 3 - Coronal MRI of the lower limbs, showed multiple subcutaneous lesions hyperintense on T2-weighted images (yellow arrows in A), hypointense on T1-weighted image (yellow arrow in C) and peripheral contrast enhancement on fat suppressed T1-weighted images (yellow arrows in B), compatible with multiple abscesses. Multiple bone lesions hypointense on T1-weighted images (yellow arrows in D), hyperintense on T2-weighted images (yellow arrows in E), without enhancement on fat suppressed T1-weighted images (yellow arrows in F), compatible with sequelae of chronic osteomyelitis, were also seen. The most prominent lesion is in the left tibial metaphysis.

Multiple lymphadenopathy and diffuse bone involvement were also detected; the latter is very common particularly in disseminated infections. The bone lesions are typically lytic, most commonly in the skull, ribs, vertebrae, long bones of arms and legs. Lesions in long bones usually appear in the diaphysis in younger children and in the metaphysis in older patients. When they occur close to the metaphysis these can interfere with maturation of epiphyseal cartilage leading to distortion of a growing bone, which happened in our case. The lesion usually starts in the medulla, and when the periosteum is reached extensive new bone may be formed simulating the involucrum of pyogenic osteomyelitis. In cases of isolated bone lesion the differential diagnosis with neoplasm is essential. When there are multiple lytic lesions, in children, skeletal metastases, langerhans cell histiocytosis (LCH) and tuberculosis should be considered in the differential diagnosis. In older patients multiple myeloma is also a hypothesis. Chronic recurrent multifocal osteomyelitis (CRMO) should also be considered, in children, in the differential diagnosis of osteomyelitis, however this is a

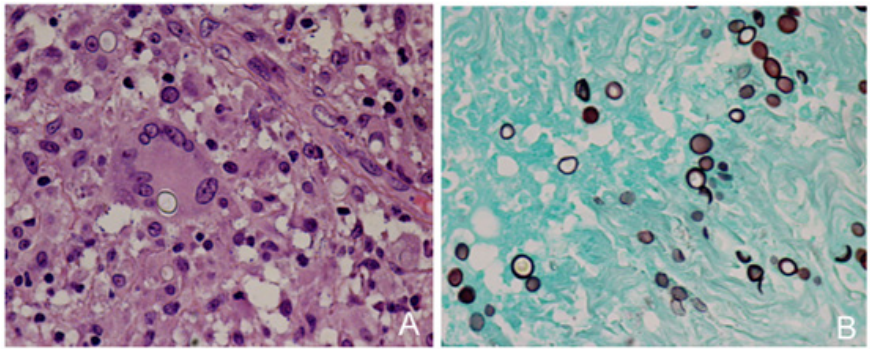

Figure 4 - Lymph node. (A) Round fungi inside multinucleated giant cells (HE, x600). (B) Grocott's stain highlighting the round thickly encapsulated fungi –consistent with Histoplasma duboisii (x600).

diagnosis of exclusion. Besides osseous lesions there were also lymphadenopathy and abscesses, in our patient, which favors an infectious origin. A definite diagnosis requires the culture and isolation of the fungus or its microscopic observation in clinical samples from secretions or biopsy materials, due to the heterogeneity of clinical manifestations. Nevertheless, imaging is essential for diagnosis, to determine the extension of the disease and to monitor response to treatment and/or detecting recurrence.

Treatment includes amphotericin B (2-4 weeks) and azoles[5]. Prognosis of the disease depends on early diagnosis and administration of appropriate and well-conducted therapy. Patients with only skin or isolated bone lesions may have an indolent course and often improve spontaneously. In the disseminated form the course is progressive and can be fatal when there is visceral involvement.

AH often arises in patients who are already suffering from tuberculosis, schistosomiasis, malnutrition, leishmaniasis, or AIDS[6]. Almost all the cases associated to AIDS were disseminated ones rather than localized ones[1-7]. Studies had demonstrated that mutations in the path of gama-INF showed predisposition for many infections, namely for Histoplasma capsulatum infection[8]. So, although disseminated cases have been reported in patients without immunodeficiency they remain uncommon. Our report corroborates the predisposition for disseminated forms of the disease and its association with some kind of immunodeficiency[1-7].

In conclusion, we report a unique case of 7-year-old girl with exuberant imaging findings of typical AH. Despite its rarity, AH should be kept in mind as a possible diagnosis in African-born patients or travellers from this country that have compatible clinical and radiological presentation. Imaging has a crucial role not only in diagnosing this disease but also in monitoring the response to therapy and detecting recurrence.

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