O. Onwuasoigwe

Fluconazole in the therapy of multiple osteomyelitis in African histoplasmosis

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Abstract Amphotericin B has been the standard treatment for deep mycoses including African histoplasmosis, but its use is complicated by its toxicity. More recently, Fluconazole, a water-soluble triazole with anti-mycotic activity and little side effects, has become available. A case of African histoplasmosis from Nigeria, manifesting as multiple osteomyelitis and successfully treated with oral Fluconazole, is presented. Fluconazole may be preferred in the therapy of African histoplasmosis.

Résumé L'Amphotéricine B était le traitement habituel des mycoses profondes notamment de l'histoplasmosis africain, mais son utilisation est limitée par sa toxicité. Récemment, le Fluconazole, un triazole hydrosoluble a activité anti-mycotique avec peu d'effet secondaire a été introduit. Un cas d'histoplasmosis africain se manifestant comme une ostéomyélite à foyer multiple et traité avec succès par le Fluconazole per-os, est présenté. Le Fluconazole peut être préféré dans le traitement de l'histoplasmosis africain.

Introduction

African histoplasmosis (histoplasmosis duboisii), caused by *Histoplasma capsulatum* var. *duboisii*, is a common deep mycosis in Central and West Africa and on the island of Madagascar [5, 6, 7, 12, 16]. The mode of infection is by inhalation of contaminated soil dust [12]. The primary pulmonary involvement is transient, and clinical pneumonitis due to the fungus has not been reported.

Haematogenous bone infection represents a common systemic manifestation of the disease [4, 6, 12, 15, 16]. When osteomyelitis is multiple, as in other disseminated forms of the disease, systemic anti-fungal administration

is imperative. As in classical (*H. capsulatum*) histoplasmosis, Amphotericin B is the universally accepted treatment for African histoplasmosis, but its use is usually interrupted due to frequent development of toxicity [2, 4, 8]. In the last two decades, there have been reports of trials, albeit successful, of several antimycotic azoles in the therapy of different forms of African histoplasmosis [1, 2, 4, 8, 10, 13]. More recently, fluconazole, a water-soluble bistriazole with activity in deep mycosis and little side effects became available [3, 9, 14]. This report presents a case of multiple osteomyelitis from African histoplasmosis successfully treated with oral fluconazole.

Case report

A 10-year-old boy from Umuahia in Abia in eastern Nigeria presented with painful swellings at the shoulder, arm, distal thigh, upper leg, and parasternum, all on the right. The lesions were of 6 months duration. He also complained of deep seated low back pain and low-grade fever, and reported that the shoulder swelling had been incised elsewhere by traditional healers.

On examination, he looked chronically ill. There were palpable discrete cervical lymph nodes. The shoulder mass was fungating and filled the lateral angle of the supraclavicular fossa. Other swellings were soft, and multiple cutaneous discharging sinuses were associated with the arm and the parasternal lesions. Flexion and extension movements of the right elbow were tender and grossly limited.

Haematological examination of the patient revealed haemoglobin of 9 gm/100 ml, ESR of 91 mm/1st h (Westergreen), and WBC of 10000 mm³ with relative neutrophilia. The liver and the kidney function studies gave normal results. Plain X-rays revealed: soft tissue opacity with varnished middle third of the clavicle on the right shoulder (Fig. 1), osteolytic destruction of the lower half of the right humerus involving the elbow joint with surrounding soft tissue congestion (Fig. 2), osteolysis of the distal metaphysis right femur (Fig. 3), and multiple roundish lucencies with sclerotic surroundings on the body of the fourth lumbar vertebra (Fig. 4).

A histological examination of a biopsy specimen of the shoulder mass showed numerous giant cells containing doubly contoured yeast cells, 8–15 µm in diameter, a histopathological feature characteristic of infections due to *H. capsulatum* var. *duboisii*. Yeast cells were also seen extracellularly.

O. Onwuasoigwe (✉)

Orthopaedic Unit, Department of Surgery,
University of Nigeria Teaching Hospital, Enugu, Nigeria

Mailing address: P.O. Box 3336, Enugu, Nigeria

Treatment

The patient was started on oral fluconazole (Diflucan), 100 mg daily, and given one unit of blood by transfusion. One week in the course of antimycotic therapy, the arm and the distal thigh were surgically drained. The distal part of the humerus, found to be pathologically fragmented during this operation, was immobilized with a plaster cast for 10 weeks. Fluconazole was administered for 6 months.

Results

The patient's clinical condition improved progressively and there was radiological evidence of healing (Fig. 5) 4 months into the therapy. Throughout the course of treatment, no side effects were observed clinically, and liver and renal function studies gave normal results.

Discussion

Osteomyelitic lesions are frequent in *duboisii* histoplasmosis, and they are often multiple, especially in the disseminated forms of the disease [6, 15, 16]. The clinical features of the presently described case of multiple osteomyelitis were typical and resembled those reported in the literature [4]. However, the fungating mass on the right shoulder which evolved after the mass was incised by a traditional doctor was unusual. Such atypical lesions simulating other diseases including cancers have been described [11].

Solitary bone lesions in African histoplasmosis may heal spontaneously and are amenable to surgical drainage. Reports of fatality have been made concerning with disseminated forms of the disease [4, 16]. The need for prompt systemic antimycotic therapy in such disseminated forms cannot be over-emphasized. Interruptions in the treatment with Amphotericin B as a result of a development of toxicity have led to exacerbations and even mortality in African histoplasmosis [4, 8]. Several antimycotic azoles (such as Miconazole, Econazole, Ketoconazole, and Itraconazole) and Septrin have been tried in the last two decades for different forms of the disease [1, 2, 4, 8, 10, 13]. These reports suggest attempts to find alter-

Fig. 1 Plain postero-anterior X-ray view of the chest with an arrow pointing to the soft tissue swelling and varnished middle third of the clavicle

Fig. 2 Plain antero-posterior X-ray view of the right humerus showing osteolytic destruction of the lower half of the bone

Fig. 3 Plain lateral X-ray view of the right femur showing distal metaphyseal lysis

Fig. 4 Lateral X-ray view of the lumbosacral spine showing multiple roundish lucencies on the body of L4 vertebra

Fig. 5 Lateral X-ray view of the right humerus showing union of the pathological fractures with sclerosis (evidence of healing) at 4 months of Fluconazole therapy

native tolerable drugs for use in this condition. The efficacy and tolerability of fluconazole in classical histoplasmosis as well as other deep mycoses have been well established [3, 9]. The present report suggests that fluconazole may also be the preferred treatment in African histoplasmosis. Both the safety and the ease of oral administration favor its use.

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