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Case Report

A rare case eumycetoma: Successful treatment with itraconazole

Rusmawardiana, Fifa Argentina, Raden Pamudji, Putri Laksmi Karim

Department of Dermatology and Venereology Medical Faculty of Sriwijaya University/ Dr. Mohammad Hoesin General Hospital Palembang, South Sumatra, Indonesia.

Abstract Eumysetoma is a chronic infectious disease characterized by an enlarged subcutaneous mass, often caused by the fungus Madurella mycetomatis. Eumycetoma can affect all age groups, but often occurs in young people between 20 and 40 years, in children rarely 3-4.5% but can be up to 30% of cases, dominant in males with a ratio of 4:1, mainly working agricultural activities. Treatment of eumycetoma with medication antifungal group Triazola (Itraconazole) and surgery are the therapy of choice. We report a case of eumycetoma treated with itraconazole. A 57-year-old man with complaints of progressive chronic wounds. Dermatological status showed multiple nodules, there were sinuses with discharge and grain on the feet. Histopathological examination revealed suppurative granuloma and Splendore-Hoeppli phenomenon in the dermis layer. The patient was diagnosed with eumycetoma and treated with itraconazole 2x200mg. Administration of itraconazole 2x400 therapy in eumycetoma patients is effective and provides clinical improvement.

Key words
Eumycetoma; Itraconazole; Madurella mycetomatis.

Introduction

Eumycetoma is a chronic infectious disease characterized by an enlarged subcutaneous mass, often caused by the fungus Madurella mycetomatis.[1,2] Eumycetoma is included in mycetoma disease, mycetoma can be caused by fungi (eumycetoma) such as Eumycetes or filamentous fungi and bacteria (actinomycetoma) such as Actinomyces and Nocardia bacteria, which includes Schizomycetes.[3-6]

Eumycetoma is widely found in tropical and subtropical countries known as the mycetoma belt (15^{o} south latitude and 30^{o} north latitude).[2,5,7] Eumycetoma can affect all age groups but often occurs in young people between 20 and 40 years, in children, it is rarely 3-4.5% but can be up to 30% of cases.[2,4,7] The incidence of mycetoma both eumycetoma and actinomycetoma in Indonesia are not known for certain, in the study of Sammy *et al.* found four cases of eumycetoma and four cases of actinomycetoma during 1989-2013 at Dr. Cipto Mangunkusumo Hospital.[8]

The manifestation is a triad mycetoma: swelling, draining sinuses, and grains or also called granules or sclerotia.[7,9] In early infection, the lesions are tender, painless, slowly spreading nodules with papules and draining sinuses on the surface of the nodules. The sinuses exudate and grains are aggregates of causative organisms so that they can be used to determine the etiology

Address for correspondence
Dr. Putri Laksmi Karim
Department of Dermatology and Venereology Medical Faculty of Sriwijaya University/ Dr. Mohammad Hoesin General Hospital Palembang, South Sumatra, Indonesia.
Email: putrilaksmikrim92@yahoo.com

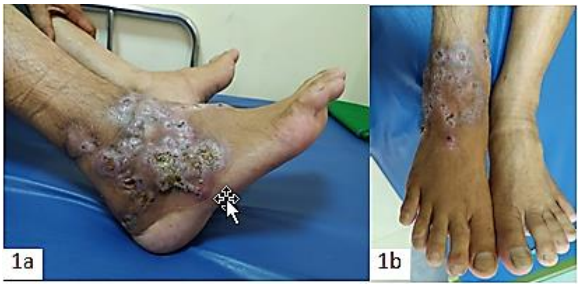

Figure 1 Region dorsum pedis et malleolus dextra: erythematous papules, multiple, lenticular to nummular, discrete, partially confluent, and partially erosion until ulcer, covered with yellow to brown crusts. The surface has sinuses with discharge accompanied by brown to black grains.

of mycetoma. The grain that comes out of the sinuses varies in size, color, and consistency.[2,7,9]

Eumycetoma can be treated with medication and surgery. Chronic eumycetoma usually has a low response to drug therapy, so combination therapy with surgery is needed. Triazola antifungal (Itraconazole) is the therapy of choice given for a long period of 1-2 years and must pay attention to the response and side effects of the drug.[10] We report a rare case of chronic eumycetoma treated with itraconazole without surgery

Case report

A 57-year-old man, a coffee farmer, came with a complaint of nodule with wound on his right ankle which had been increasing since 1 year ago. About 5 years ago, a nodule appeared on the inside of the right foot sometimes itchy and painful. The patient treated was given topical medication but it did not improve. About 3 years ago, nodule papules increase appeared around the right ankle, there was a wound in the middle. About 1 year ago the preexisting papules and nodules increased in number, softened, partially ruptured, produced brownish-white granules, and the patient's feet began to swell and become painful. Nodule papules appear on the sole of the right foot more and more spread and multiply patients to the hospital. On the dermatological status of the medial, lateral malleolus, dorsum pedis dextra there were plaques, multiple lenticular erythema nodules to discrete, partially confluent in the middle, excoriations were partially covered with yellow-black crusts that were difficult to remove, ulcers were 0.4x 0.2 x 0.2 cm, base of necrotic tissue, there is pus, tenderness, edges are not raised **(Figure 1)**.

Laboratory examination was normal, microscopic examination of 10% KOH found spores, bacterial culture and mycobacterium tuberculosis was negative, fungal culture are not growing. Biopsy from the nodule on the lateral side of the right pedis. Histopathological results with hematoxylin-eosin (HE) staining were epidermal rate ridge flat. The dermis showed a predominant neutrophil inflammatory infiltrate surrounding an eosinophilic amorphous granular mass, 1-2 multinucleated giant cells, and edematous fibrocollagenous stroma. No signs of malignancy were found. On periodic acid schiff staining (PAS), Splendore-Hoeppli phenomenon and immunohistochemistry (IHK) were found following the description of chronic granulomatous suppurative inflammation ec eumycetoma **(Figure 2)**.

Based on the clinical course and examination as well as the results of histopathological examination, the diagnosis of the patient was eumycetoma. The patient was treated with itraconazole 2x200mg for 6 months and give clinical improvement **(Figure 3)**.

Discussion

Eumycetoma is a chronic infection caused by fungi that affect the cutis, subcutis, bone, and viscera tissue although very rarely, it is characterized by sinuses containing masses of causative organisms which are often called

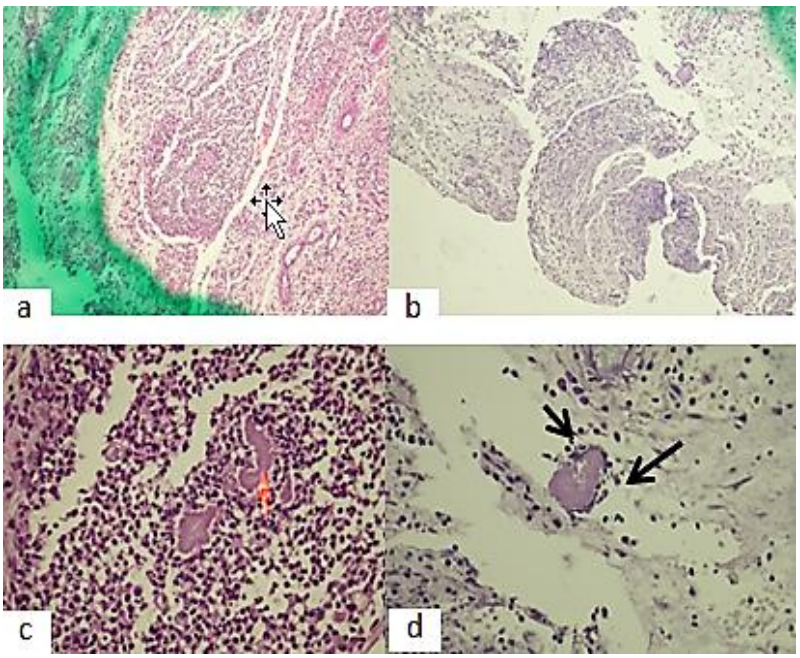

Figure 2 Histopathological examination with HE staining 100x (a) and 400x (c) of the dermis showed predominantly neutrophils surrounding an eosinophilic amorphous granular mass, multinucleated giant cells, edematous fibrocollagenous stroma (red arrows); PASS 100x (b) and 400x (d) the Splendore-Hoeppli phenomenon (black arrow) is found.

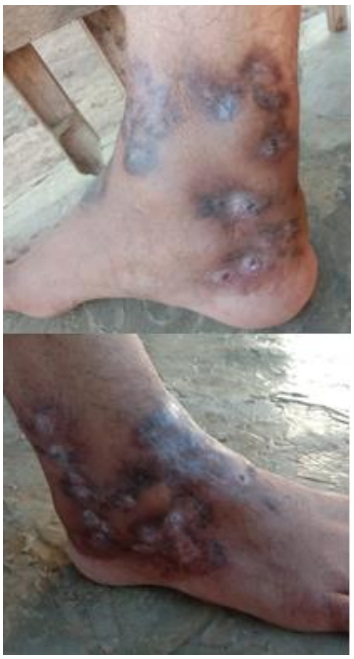

Figure 3 Evaluation of the clinical picture 6 months of treatment: some nodules are shrinking, new lesions are not present and old lesions improve.

"grains".[1,2] The predisposing factor for the emergence of eumycetoma in the presence of several minor trauma injuries due to stones, splinters, and thorns resulting in skin abrasion, this can occur if the patient walks barefoot. Dominant in males with a ratio of 4:1, mainly working agricultural activities.[4,7] The agen causative fungal enters the subcutaneous tissue (usually the feet, hands, or back) through trauma, forming abscesses that can extend to the muscles and even bones, eventually draining through the chronic sinuses.[5] In this case there is a history of trauma to the legs. The patient is a farmer who rarely uses footwear when working. Trauma to the foot causes a chronic, progressive skin infection. The clinical picture of the patient was multiple nodules and found several sinuses with discharge and grain. The history and clinical picture support the diagnosis of eumycetoma.

The causative agent of eumycetoma is divided based on the type of grain, which produces black and white or grayish grains.[4] Investigations to establish the diagnosis of eumycetoma are direct examination with calcium hydroxide (KOH), skin tissue culture/culture, histopathology, radiology, molecular examination, and physical examination. immunology.[4,6] Examination of potassium hydroxide (KOH) can be performed to differentiate eumycetoma and actinomycetoma. The difference between the causative organisms lies in the size of the filaments. Eumycetoma has wider filaments with a diameter of 2-4 μm while actinomycetoma has finer filaments with a diameter of 1 μm or less. Direct microscopic examination of grain specimens reveals the difference between these two filaments. A positive gram stain indicates actinomycetoma and a negative gram stain indicates eumycetoma. Examination of grains with the addition of KOH did not allow to see the fine filaments of actinomycetoma.[3,7] In this case, minimal discharge was found in the lesion and there were blackish grains. On KOH

examination the patient found spores and on gram examination, no bacteria were found.

Histopathological is one of examination for eumycetoma. The grain is seen in the center of the suppurative granuloma zone of the subcutis. Neutrophil invasion is sometimes seen in the grain. Rows of histiocytes can be seen around the area of suppuration, above the inflammatory infiltrate and progressive fibrosis and several multinucleated giant cells may be seen. Splendore-Hoeppli phenomenon can be found around the grain.[4,9] The histopathological picture of the lesion is chronic granulomatous inflammation with a central abscess surrounded by neutrophils. Fibrosis and granulomatous inflammation composed of macrophages, epithelioid cells, and multinucleated giant cells are seen surrounding the abscess. The central zone contains abundant polymorphonuclear cells surrounded by lymphocytes, plasma cells, histiocytes, and fibroblasts. Granules (50-250 m) were found in the center of inflammation surrounded by an eosinophilic matrix which is an immune complex.[3] On histopathological examination the patient found chronic granulomatous suppurative inflammation, a predominant neutrophil inflammatory infiltrate surrounding an eosinophilic amorphous granular mass, multinucleated giant cells, edematous fibrocollagenous stroma in the dermis. On periodic acid Schiff staining (PAS), Splendore-Hoeppli phenomenon and immunohistochemistry (IHK) were found according to the picture of chronic suppurative granulomatous inflammation ec eumycetoma.

Triazole antifungal (Itraconazole) is choiced treatment for a long period of 1-2 years, must pay attention to the response and side effects of the drug.[10] Ketoconazole at a dose of 400-800 mg/day for 9-12 months has been the main therapy for decades. In 2013 the Food and Drug Administration in the United States restricted the use of ketoconazole because of side effects on the liver, drug interactions, and problems with the adrenal glands, therefore itraconazole is recommended.[7] In chronic cases a combination of antifungal treatment and surgery may be successful. Surgical excision combined with itraconazole 200 mg twice daily until clinically good may be effective in cases of eumycetoma caused by P. boydii. Lim *et al.* reported the combination of medication and long-term treatment required for this infection with a success rate of 30%.[1] Treatment of eumycetoma takes a long time and difficult, the duration of treatment is months to years and successful treatment depending of the caused agent. Therapy combination of surgery and antifungal drugs are the main choice. Treatment duration with antifungals are varied, from several months to years with a median of 12 months depending on the severity of the disease. In this case, Itraconazole 2x200 mg without surgical combination was given lesions improvement and the patient's subjective complaints were reduced.

Conclusion

The diagnosis of eumycetoma is obtained from anamnesis, physical examination, and supporting examinations. The itraconazole in patients gave good results and effectiveness in cases, itraconazole 2x200 mg was continued and further evaluation would be carried out. Education is important in the success of treatment, in patients with eumycetoma it is necessary to provide education about the disease, maintaining hygiene, using personal protective equipment when in contact with potential sources of infection such as thorns and animals, as well as need long duration and regular treatment.

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