

An Unusual Case of Lobomycosis in a Nonendemic Area and its Response to Therapy with Itraconazole and Clofazimine

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Abstract: *Lobomycosis is an endemic chronic deep fungal infection caused by Lacazia loboi an uncultivable fungus, occurring mostly in Amazon regions. Total 550 cases reported worldwide, 58.5% cases are from Brazil. 160 cases of lobomycosis have been reported among the Kaiabi Indians, an ethnic population that lives in central Brazil. This disease is characterised by skin nodules and plaques resembling keloid. We report a case of 35 old female who presented with multiple skin coloured to pinkish nodular infiltrative lesion coalescing to form a large painless plaque, measuring 15 * 18cm*3cm over left thigh with left inguinal lymphadenopathy. The lesions started after a trauma to left thigh and progressed slowly since 2018 august. The initial lesions were pruritic papular in nature. A provisional diagnosis of Lobomycosis was made after clinical examination. Chromoblastomycosis, keloidal lepromatous leprosy, dermatofibrosarcoma pirtuberans, verrucous cutaneous leishmaniasis were kept as differential diagnoses. To confirm the diagnosis routine investigations were sent which were within normal limit. X - ray and MRI showed no bony involvement. A 5mm punch biopsy was taken from an active lesion. H&E examination and calcofluor white stain showed granulomatous inflammation and fungal structures connected to each other by ill - defined tubule formation and diagnosis was suggestive of lobomycosis. Fungal Culture was negative. Following Treatment with oral itraconazole 200mg twice daily and clofazimine 100mg once daily visible clinical improvement seen after 3months and 70% improvement in the lesion seen after 6months of therapy. Timely treatment of lobomycosis with oral itraconazole and clofazimine lead to profound shrinkage in disease and diminished disease complication and minimise the requirement of surgical intervention. We report a case of lobomycosis because of its rarity and typical clinical presentation in our area and showing dramatic improvement with our treatment.*

Keywords: Lobomycosis, thigh, itraconazole, clofazimine

1. Introduction

Lobomycosis is an endemic deep fungal infection caused by lacazia loboi an uncultivable fungus, occurring mostly in Amazon regions. It is a chronic granulomatous fungal infection of the skin and subcutaneous tissues characterized by nodular or keloid like lesions, first described by Jorge Lobo in 1930.² Lobomycosis has been given many different names, like lobomycosis, Jorge Lobo's disease, keloidal blastomycosis, and lacaziosis. The cutaneous lesion associated with the infection are polymorphic. Few are papule, plaque, ulcers, atrophy, tumours, macules, gummata, scleroderma, infiltrations, or scars. The pathogenesis of lobomycosis is poorly understood due to its long incubation period and slow progression. Due to long incubation period it is difficult to know the exact time and location of exposure. However The main mode of transmission is mostly traumatic contact with certain tree trunks of tropical rainforests. Animal to human transmission has not been confirmed.³

2. Case Report

A 35 year old female presented with multiple skin colored to pinkish nodular infiltrative lesion coalescing to form a large painless plaque measuring 15*18**3cm over left thigh with left inguinal lymphadenopathy.

The lesions started after a trauma to left thigh and progressed slowly since 2018 august. The initial lesions were pruritic papules which progress to form a asymptomatic nodular and plaque like lesion with woody band like structures. A provisional diagnosis of Lobomycosis was made after clinical examination. Medicine

and orthopedics consultation ruled out systemic and bone involvement respectively. There was no similar history in sibling, parents, family members. X - ray and MRI showed no bony involvement. The initial differential diagnosis should include keloids, lepromatous leprosy, and verrucous cutaneous leishmaniasis, besides other, more common subcutaneous mycoses such as blastomycosis, sporotrichosis, chromoblastomycosis, paraccocidiomycosis, and African histoplasmosis caused by H. capsulatum var. duboisii even if in this case the travel history could exclude this last etiology.⁴ A punch of 5mm was taken from the lesion. H& E examination and calcofluor white stain was done. On staining with haematoxylin and eosin there is stratified squamous Epithelium over fibro collagenous dermal stroma with sweat glands, lymphocytes, epithelioid cells, giant cells, and hemosiderin - laden histiocytes with eosinophilic splendore Hoeffli material. Calcofluor white stain showed fungal structures connected to each other by ill - defined tubule formation and diagnosis was suggestive of lobomycosis. Fungal Culture was negative. Treatment with oral itraconazole 200mg twice daily and clofazimine 100mg once daily visible clinical improvement seen after 3months and 70% improvement in the lesion seen after 6months of therapy. Routine investigations like LFT, CBC, RBS were done every month and found to be normal.

3. Discussion

Lobomycosis is a neglected disease with rising number of cases in different part of the world with unknown prevalence. A large hidden prevalence amongst forest people dwelling in remote areas has been suggested as the probable cause of this rise in cases. A effective drug therapy for the treatment of lobomycosis is lacking, and surgical resection

of keloidal skin lesions is often followed by disease recurrence. The pathogenesis of lobomycosis is poorly understood due to its long incubation period and slow progressive nature. It difficult to find the exact time and location and cause of the disease. However The main mode of transmission is mostly traumatic contact with certain tree trunks of tropical rainforests. The diagnosis of lobomycosis is difficult because the lesions are mistaken for cutaneous leishmaniasis, nontuberculous mycobacterial infections including leprosy, sporotrichosis, or other dermatological mycoses.

The clinical features of lobomycosis are slowly progressing keloidal nodules, which may ulcerate or develop a verrucous appearance over time.

Lesions may be pruritic or cause a burning sensation in isolated or disseminated form. Cases are usually localized to the lower limbs, followed by the ears, upper limbs, and head.^{6, 7}In the disseminated form is associated with body deformities, an intense pruritus.

Molecular testing has also successfully employed for the diagnosis of lobomycosis ^{8, 9, 10}. Amplification and direct sequencing of fungal ribosomal RNA genes yielded the diagnosis of lobomycosis in a European man who had travelled to the Amazon region of Venezuela.⁸ Another

approach has been to amplify the gp43 like gene.⁹Molecular testing may not always be available in endemic regions, clinical and microscopic diagnosis remain gold standard for the diagnosis. It is accepted that characteristics of the fungus *L. loboi* itself and the fibrosis that develops in long standing cases make it difficult to treat. For many years multiple antifungal and antibiotic regimens have been attempted with unsatisfactory outcomes. One studies used sulfadimethoxine 1000 mg/day for an 80 - year - old patient in Venezuela in 1961.¹¹ sulfamethoxypryridazine 500 mg/day for two cases of 50 - year - olds in French Guyana in 1962 ¹². The former study showed partial remission of skin infiltrations and nodules¹¹, while the latter showed no clear resolution of skin lesions¹². An experimental approach using ketoconazole 400 mg/day showed a decrease in the number of *Lacazia* fungi and mild to moderate remission of skin lesions ¹³. In another study (1980), ketoconazole 200 mg/day for six months given to a 45 - year - old farmer in Brazil resulted in an unsatisfactory outcome with no cure.¹⁴

In our case timely treatment of lobomycosis with oral itraconazole 200mg twice daily and clofazimine 100mg once daily for 6 months lead to profound reduction in size of the lesion and disease complications. We recommend to include lobomycosis in the list of reportable diseases and early intervention with oral itraconazole and clofazimine to be considered for standard treatment of this disease.



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