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Case Report

Voriconazole induced lupus. A case report and brief review

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Abstract A 50-year old male developed lupus erythematosus after taking voriconazole for the treatment of mycetoma.

Key words
Variconazole, lupus, mycetoma.

Introduction

Voriconazole is commonly used for the treatment and prophylaxis of invasive fungal infections in both immunocompetent and immunocompromised patients. Established adverse events include visual disturbances, hepatic toxicity and photosensitivity.[1]

Drug induced lupus erythematosus (DILE) is a clinical entity that closely mimicks systemic lupus erythematosus. A variety of pharmaceutical agents can cause it after their continuous dosage. Mostly the manifestations disappear after discontinuation of the responsible drug.[2] This disorder has been described for the first time in 1945 by Hoffman.[3]

Case report

A 50 years male labourer had discharging nodular lesions on his left foot for the last 9 years. The lesions were initially small, later progressed and enlarged associated with yellowish discharge. He was diagnosed as a case of mycetoma and took multiple systemic treatments for his disease including dapsone for one and a half year that gave him partial relief. He also had multiple incisions and drainage for it. He presented to Mayo Hospital, Dermatology Department, and was prescribed voriconazole. After six weeks of continuous exposure to the drug he developed an erythematous rash on the cheeks and nose sparing the nasolabial folds along with history of arthralgias involving the large joints including elbows, knees but there

Figure 1 Malar rash after continuous use of voriconazole

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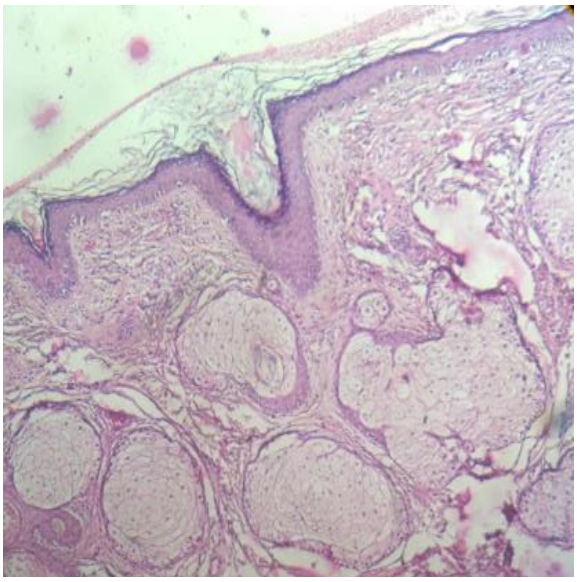

Figure 2 Variable epidermal atrophy basal vacuolar degeneration lymphocytic interphase dermatitis

was no history of arthritis. History of photosensitivity was positive. There was no history of muscle weakness, Raynaud's phenomenon, dryness of eyes or ears. No history of diabetes mellitus, hypertension and tuberculosis. Clinically, drug induced lupus was kept in his diagnosis and relevant investigations were sent that showed lupus eythematosus on histopathology. ANA, anti smith antibody and anti dsDNA were negative. Voriconazole was stopped in the patient. Gradually myalgias and arthralgias were settled and his rash disappeared over a period of months.

Discussion

Voriconazole, a broad spectrum triazole fungal agent, is indicated for refractory candida and other emerging invasive fungal infections. Similar to other azole agents, the mechanism of action of voriconazole is inhibition of cytochrome P450 dependent 14-α lanosterol demethylation, a vital step in cell membrane ergosterol synthesis by fungi.[4] The most common adverse effects of voriconazle is photophopia,[4] the second most common adverse reaction occurring in fewer than 10% treated patients are dermatologic, mostly rashes.[5,6] Severe reactions have been reported as well like toxic epidermal necrolysis, photosensitivity reactions, lupus erythematosus and pseudo porphyrias.[7,8]

Drug induced lupus refers to a condition whose clinical, histological, and immunological features are similar to those seen in idiopathic lupus erythematosus after exposure to certain drugs and resolve after their withdrawal.[9] The diagnostic criteria is not well established for DILE, it is usually diagnosed by a process of elimination to rule out SLE.[9,10] Resolution of symptoms when treatment with the culprit drug is discontinued, assist in establishing the correct diagnosis. Our patient was male, 59 year old. Women outnumber men in idiopathic SLE whereas DILE affects both genders in similar proportion. Patients with DILE also tends to be older.[11]

The clinical features of DILE are different from SLE. Most patients have one or more clinical symptoms of SLE such as arthralgias, lymphadenopathy, rash and fever with no prior history of autoimmune disease. 50% patients present with constitutional symptoms. As many as 90% patients of DILE present with arthralgia which is often the only clinical manifestation of DILE. Our patient had arthralgias that were bilateral symmetrical and settled after withdrawal of drug. 25% patients with DILE present with cutaneous findings. Absence of central nervous system and renal involvement is more suggestive of DILE than of SLE.[6,12]

DILE differs from drug hypersensitivity. No evidence of drug specific T-cells or antibodies has been found. The proposed hypotheses are genetic susceptibility, an individual's acetylator status, and drug's susceptibility to

myeloperoxidase-mediated oxidative transformation.

Most patients are positive for ANA antibody, but this is not always the case. Failure to detect ANA does not rule out DILE.

Anti dsDNA antibodies are a rare finding in systemic DILE. Therefore, positivity should lead to suspicion of idiopathic lupus. Abnormal findings in blood are more common in DILE. Anti-Ro positivity can occur in DILE.[13]

In our patient, the drug was discontinued and he was given hydroxychloroquine. He got completely cured in a period of two months.

As newer therapies are developed for a number of diseases, the incidence of autoimmune disorders is on rise. Clinical and serological manifestations resolve after withdrawal. This case highlights the importance of recognizing adverse dermatological reactions noted with voriconazole whose clinical use continues to expand.

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