

Probable Aripiprazole Induced Erythema Multiforme in an Elderly Patient: A Case Report

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Dear Editor,

Erythema Multiforme (EM) is an immune mediated dermatological condition involving both mucosal and cutaneous sites. The most commonly involved mucous membranes are lips, tongue and buccal mucosa [1]. The authors report an unusual case of mucosal EM induced by aripiprazole in an elderly patient with very late-onset psychosis, which warrants clinical attention given the increasing use of this agent in older adults.

A 67-year-old married male presented with an 8-month history of illness of insidious onset and progressive course, characterised by delusion of infidelity, along with secondary low mood, disturbed sleep, and reduced appetite. There was history of hypertension, for which he had been on regular treatment with amlodipine 10 mg once daily for the past 15 years. There was no history of drug allergy or past psychiatric illness. Substance use history was non-significant.

General physical examination was within normal limits. On mental status examination, there was delusion of infidelity with secondary low mood along with passive death wishes, and poor insight. Aripiprazole 5 mg was initiated along with clonazepam 0.25 mg HS for sleep disturbance. Patient did not have any prior exposure to any other antipsychotics and the dose of aripiprazole remained constant. After three days of starting medications patient developed swelling of lips, he started to have difficulty in chewing food but continued the medications; three days later, the patient developed bleeding of both lips along with crusted erosions with oral mucosal involvement and had difficulty in speaking.

On dermatological evaluation, patient had swelling and inflammation limited to lips and oral mucosa associated with crusted erosions and bleeding of lips. A provisional impression of mucosal-type EM was made, and the patient was advised to undergo blood investigations including Complete Blood Count (CBC), Liver Function Tests (LFT), and Renal Function Tests (RFT). A skin biopsy was also planned; however, the patient dropped out of the treatment. There was no history suggestive of fever, recent infections, trauma, insect bites or allergies and diagnosis of mucosal-type EM was made based on the clinical expertise of the dermatologist; this does not establish a definitive conclusion. The reported side effect may also be attributable to clonazepam. Rechallenge could not be performed as the patient was lost to follow-up.

All medications were immediately discontinued, topical corticosteroids (triamcinolone acetonide 0.1% and mometasone furoate 0.1%) and liquid paraffin application were advised. The cutaneous manifestations gradually resolved within 4-5 days after stopping medications without any further complications, obtained through telephonic follow-up.

While cutaneous adverse reactions to antipsychotics occur in approximately 5% of patients, most are benign and readily reversible upon drug discontinuation [1]. EM is an immune-mediated condition characterised by the appearance of discrete target lesions that typically erupt over a period of approximately 72

hours. It is commonly preceded by viral infections and may also be triggered by medications such as Non-Steroidal Anti-inflammatory Drugs (NSAIDs), antiepileptics, and antibiotics. EM represents a more serious immune-mediated reaction with mucocutaneous involvement that can significantly impact treatment adherence and compliance—a critical concern in elderly psychiatric patients who already face higher morbidity risks [2].

Aripiprazole is a partial agonist at dopamine D2 and serotonin 5-HT1A receptors, and antagonist at 5-HT2A receptors. It is absorbed from gastrointestinal tract and reaches peak plasma concentration in 3-5 hours of ingestion. It has mean half-life of 75 hours and some known side effects are insomnia, orthostatic hypotension during initial dosing, nausea, akathisia and lower incidence of weight gain [3]. Incidence of development of cutaneous eruptions such as EM due to aripiprazole is rare; which may be due to slower onset of development of lesions, usually 1-3 weeks after the initiation. The mechanism of development of EM as in this case is not known [3]. This case highlights the importance of early recognition and rapid intervention when mucocutaneous lesions develop during antipsychotic therapy. Parker CA reported a 61-year-old male developing lichenoid drug eruptions after being started on aripiprazole, and on immediate stopping the offensive agent, the symptoms had improved [3].

According to the Naranjo Adverse Drug Reaction Probability Scale, the reaction occurred after initiation of aripiprazole and improved upon its discontinuation. No similar reaction was attributable to amlodipine or clonazepam. The case was thus classified as 'probable,' with a score of 7 for aripiprazole [4]. Yang HW et al., highlights that clonazepam, a benzodiazepine, can cause lichenoid type of cutaneous eruptions in few patients in dose range of 0.5 to 2 mg/day. The lesions reported were scaly patches, covering the entire body, which does not match the description of current case [5].

The clinicians should remain vigilant for cutaneous adverse reactions when initiating atypical antipsychotics in elderly patients, particularly those with late-onset psychosis. Prompt medication withdrawal and dermatological consultation can prevent progression and ensure optimal psychiatric management.

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