Paliperidone Injection–Associated Delayed-Onset Rash

To the Editor: Paliperidone, a benzisoxazole second-generation antipsychotic drug, is the primary active metabolite of risperidone.[1] Paliperidone is indicated for the treatment of patients with schizophrenia and related disorders as a monotherapy and as an adjunct to other pharmacotherapies. Paliperidone exhibits affinity for α_1, α_2, D_2, H_1, and 5-HT_{2A} receptors and is thought to improve symptoms by mixed central serotonergic and dopaminergic antagonism.[2] Paliperidone may be administered orally or as a long-acting injectable (LAI) formulation (paliperidone palmitate); however, it is recommended to prescribe oral paliperidone or risperidone to determine tolerability prior to initiating the LAI injection.[1] A literature review in PubMed found no reports of patients experiencing delayed allergic reaction to LAI paliperidone, if no reaction developed while administering oral paliperidone, in a test-dosing regimen.

Case report. A 64-year-old man with a history of a schizoaffective disorder and cannabis use was hospitalized following a suicide attempt by ingestion of 12 mg of clonazepam. He reported compliance with his prior-to-admission medications, lamotrigine and venlafaxine, which were given on hospital days 1 and 2. On day 3, these medications were discontinued in preference for antipsychotic pharmacotherapy with oral paliperidone and a plan to transition to LAI paliperidone. The patient received oral paliperidone for 6 days with no adverse reaction. Subsequently, on hospital day 10, he was administered the first loading dose of LAI paliperidone. Two days later, he developed a cutaneous eruption on his abdomen. The rash was initially managed with topical steroids and oral antihistamines. The rash continued to worsen by hospital day 14 and spread to his bilateral lower and upper extremities, thus oral paliperidone was discontinued. The patient became hypotensive, tachycardic, diaphoretic, and dyspneic. He was prescribed a 2-week course of prednisone along with topical triamcinolone, oral hydroxyzine, and famotidine. A skin biopsy showed superficial perivascular and interstitial infiltrates of lymphocytes, eosinophils, and neutrophils and leukocytoclasis. Hemorrhage and fibrin deposition were not noted, confirming urticaria and erythema multiforme and ruling out Stevens-Johnson syndrome and toxic epidermal necrolysis. The rash diminished dramatically following treatment with prednisone, hydroxyzine, and famotidine and resolved completely by hospital day 23. Paliperidone was considered to be the cause of the allergic reaction and was not rechallenged. Close follow-up was recommended because of the long half-life of LAIs.

On the basis of the Naranjo Adverse Drug Reaction Probability Scale,[3] the patient met criteria for a probable allergic reaction with a score of 6. Paliperidone was deemed to be the cause of this cutaneous eruption because of the timing of onset, the skin biopsy results, and absence of recent medication changes. This vignette reports a delayed reaction to LAI paliperidone that resulted in an edematous erythematous rash with urticarial and erythema multiforme. The number of days to establish medication tolerability is not noted by the paliperidone palmitate manufacturer, and it remains unknown as to whether this condition would have appeared following a longer oral tolerability trial. Such a test-dose practice was utilized frequently in the early days of LAI neuroleptic drugs. Clinicians should be aware of the potential for a delayed rash onset following LAI administration even in patients for whom oral tolerability has been demonstrated.

References

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