

Low-Dose Sertraline-Induced Erythema Multiforme in a Child

Mohammad Amjad Ullah Khan, M.D. and Kate Fitzgerald, M.D.

To the Editor:

Introduction

ADVERSE CUTANEOUS REACTIONS are rare side effects of serotonin-selective reuptake inhibitors (SSRIs) (Lamoreux et al. 2006). The dermatological side effects include rashes, erythema multiforme minor, erythema multiforme major or Steven Johnson syndrome, and toxic epidermal necrolysis (Lamoreux et al. 2006; Mockenhaupt et al. 2008; Levi et al. 2009). Erythema multiforme is a dermatological condition that presents with pinkish red blotches prevalent on the extremities. The lesions are symmetrically placed and are mildly itching, though rare instances of severe itching may occur. Generally, erythema multiforme minor resolves within 7–10 days but can develop to erythema multiforme major and life-threatening Steven Johnson's syndrome. The classical presentation is the target lesions, which are composed of a round shape and three concentric regions; a central reddish area, an edematous pink area, and an outer lying red ring. The lesions may blister and can have only two regions, with an absent edematous pink area. The lesions may appear with varying clinical morphology, several days after the etiological event, which lends to the nomenclature—(multiforme). The dermatological presentation presents on a spectrum varying from only cutaneous involved erythema minor, to mucosal affected erythema multiforme major (or Steven-Johnson Syndrome), to severe reaction of toxic epidermal necrolysis (Lamoreux et al. 2006; Levi et al. 2009). The proposed etiology is a hypersensitivity reaction, and causative factors include mycoplasma pneumoniae, herpes simplex virus infections, autoimmune diseases, and medications (Lamoreux et al. 2006; Mockenhaupt et al. 2008; Levi et al. 2009). SSRIs have rarely been implicated with sertraline, the only drug cited for Steven Johnson syndrome and toxic epidermal necrolysis (Bodokh et al. 1992; Mockenhaupt et al. 2008; Lange-Asschenfeldt et al. 2009; Levi et al. 2009). Sertraline has been reported in six cases, all of whom were adults (Gales and Gales 1994; Beauquier and Fahs 1998; Jan et al. 1999; Thédenat et al. 2001; Lange-Asschenfeldt et al. 2009). We present sertraline-induced erythema multiforme in a 9-year-old boy, which to our knowledge is the only case described in a child.

Case Report

J. is a 9-year-old boy of Caucasian descent who presented to the outpatient psychiatry clinic with complaints of excessive worrying daily about multiple things. He worried about his mother's health, harm befalling her, his own health, catching the flu, or having cancer. He slept well during the night, but in the bed in his mother's

bedroom while his mother slept on the couch. He had occasionally refused going to school by using somatic complaints of stomach ache and headache. He sought reassurance from his mother every day that she would pick him up from school. He ate well though he was selective in his choices. He enjoyed playing with his sister and her friends, but had only a few friends of his own. He had good focus and concentration, organized his tasks, and followed directions at school and at home. He had never seen a psychiatrist. His mental status examination was unremarkable. A review of health systems revealed abdominal migraine and restless leg syndrome for which he had been taking cyproheptadine for 22 months and ferrous sulfate for 11 months, respectively. He had tolerated both the medications well with no adverse effects. He had tried nortriptyline for headache, but discontinued it 11 months earlier due to lack of efficacy. No drug or food allergies were reported. Vital signs were stable. Laboratory tests including lipid panel, comprehensive electrolytes, and complete blood count with differential were essentially within normal limits. Rating scales employed included Multidimensional Anxiety Scale for Children, Child Behavior Checklist, and Social Communications Questionnaire. Results of the rating scales were consistently higher in anxiety domains. A diagnosis of generalized anxiety disorder, separation anxiety disorder with a rule out of obsessive compulsive disorder was established.

A comprehensive treatment plan was discussed with the mother and the patient. We discussed pharmacological treatment and individual psychotherapy. The mother agreed to the choice of sertraline with the patient's assent. The patient was enrolled in individual psychotherapy, and medication treatment was started with sertraline 25 mg every day with a plan to follow up in 10 days. Two days after starting sertraline, the patient's mother noticed a rash on his back and chest. She took the patient to his pediatrician's office where the physical examination revealed more spots on his arms and legs. The rash was mainly in the trunk area and was not itchy, painful, or bothersome to the patient. Diagnostic target lesions of erythema multiforme were observed. These lesions consisted of a dark central papule, with a pale immediate area surrounded by peripheral erythematous area. The mother or child did not report hives, welts, lip swelling, wheezing, or difficulty in breathing. His outpatient psychiatrist (the author) was contacted, and it was decided to discontinue sertraline with an immediate follow up in the outpatient psychiatry clinic for reassessment. On follow up at the child psychiatry outpatient clinic, a few days later, the patient was seen to have resolving rash with very discreet lesions, mainly on the trunk. Treatment choices were discussed with the mother again. We were concerned that sertraline triggered the

erythema multiforme reaction and that it could have progressed to Steven Johnson syndrome or toxic epidermal necrolysis. It has been hypothesized in literature that cross reactivity among different SSRI may be present; however, no conclusive supportive data are available. Bearing in mind that the best evidence-based medication treatment for the patient's diagnoses was an SSRI, we decided not to rechallenge with sertraline and cautiously initiated citalopram. Clinical decision making was also influenced by therapeutic alliance with the patient and his family and which led the prescribing physician to feel that the patient would inform us of any unusual reactions. We provided our contact information and the emergency room information to the patient with explicit instructions to call or show up in case of concerns. The patient tolerated citalopram well and was followed up regularly for medication monitoring every few weeks. He has continued to show improvement in anxiety issues. Dermatological adverse effects are fully resolved with no sequelae.

Discussion

This case raises many important aspects of clinical care. This case provides insight into selection of an SSRI after adverse reaction to initial choice. The patient most likely developed an adverse reaction to sertraline that had just been initiated before the onset of rash, rather than cyproheptadine and ferrous sulfate which were started months earlier with no side effects. The patient tolerated citalopram well without any difficulty even though it is an SSRI in the same class as sertraline. This case demonstrates the potential association of sertraline with erythema multiforme, and suggests that switching to another SSRI may be a safe and effective option if sertraline induced rash occurs. Communication and accessibility to this young patient and his mother enabled early intervention and effective change to a different SSRI to achieve control of the patient's anxiety symptoms. A good therapeutic alliance helped foster treatment decisions and highlights the importance of forming physician-patient relationship with young patients.

This case report points to clinically significant information that will help foster treatment decisions, but more research will be extremely valuable in the subject of SSRI adverse effects.

Disclosures

The authors certify that they have no financial relationships or financial disclosures to declare.

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Address correspondence to:
 Mohammad Amjad Ullah Khan, M.D.
 Department of Psychiatry
 Scott & White
 Texas A&M
 24015 31st St
 Temple, TX 76508
 E-mail: mkhan@swmail.sw.org