**CASE REPORT**

**Serum sickness–like reaction associated with mirabegron**

Marcus G. Tan, MD, Bruce F. Burns, MD, FRCPC, and Steven J. Glassman, MD

**Ottawa, Ontario**

**Key words:** adverse drug reaction; mirabegron; serum sickness–like reaction; urticarial.

**INTRODUCTION**

Serum sickness–like reaction (SSLR) is an uncommon adverse cutaneous drug eruption that mimics serum sickness (SS). Both conditions feature urticarial lesions, joint symptoms, and lymphadenopathy, but only SS manifests hypocomplementemia and renal involvement and is an immune complex hypersensitivity that is usually associated with parenteral nonhuman protein drugs. In contrast, SSLR is associated with numerous oral drugs like antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs. Here we report on a 52-year-old man with SSLR attributed to the selective β-3 adrenoceptor agonist, mirabegron, which is used to treat overactive bladder (OAB).

**CASE PRESENTATION**

A 52-year-old Chinese man presented with a 4-day history of generalized, itchy, fixed urticarial plaques as well as headache, malaise, joint pain and swelling. The urticarial lesions mostly lasted longer than 24 hours. His medical history included depression, anxiety, obsessive-compulsive disorder, vascular malformation, and severe psoriasis. His usual chronic medication included lithium, fluoxetine, risperidone, levomilnacipran, lorazepam, and gabapentin. One month before the illness, he started ustekinumab, 45 mg subcutaneously, for plaque psoriasis and received 2 doses, 4 weeks apart. Seven weeks before the presenting illness he had started mirabegron, 50 mg/d orally for OAB. He was allergic to sulphonamides.

On examination, there were widespread, fixed, annular urticoid plaques (Fig 1, A), with symmetric arthritis of the wrists, hands, ankles, and feet (Fig 1, B) and cervical lymphadenopathy. There were admixed psoriatic plaques. Complete blood count found a neutrophil count of $7.2 \times 10^9/L$, which is at the upper range of normal (2.0-7.5 $\times 10^9/L$), an elevated C-reactive protein (161 mg/L; normal, $\leq 10$ mg/L), but normal erythrocyte sedimentation rate, complement 3 and 4, creatinine, and urinalysis.

Skin biopsy found a normal epidermis with a superficial perivascular and interstitial infiltrate dominated by neutrophils with fewer lymphocytes and eosinophils (Fig 2, A). There was a trace of leukocytoclasis (nuclear dust) and some extravasated red blood cells around dermal capillaries (Fig 2, B).

His reaction was assessed as a probable serum sickness–like reaction, either to ustekinumab or to mirabegron, and the mirabegron was discontinued. He was treated with a 1-month tapering course of prednisone and had a quick recovery. Three months later, when due to receive his next dose of ustekinumab, it was noted that the psoriasis was much improved, and he agreed to a challenge of ustekinumab. Fortunately, there was no recurrence of SSLR upon rechallenge, which was further evidence that the culprit was likely to be mirabegron. The patient remains stable 10 months later and has started fesoterodine for OAB.

**DISCUSSION**

Serum sickness is an immune complex mediated type III hypersensitivity reaction to

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*Abbreviations used:*

OAB: overactive bladder  
SS: serum sickness  
SSLR: serum sickness-like reaction

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From the Divisions of Dermatology and Anatomical Pathology, University of Ottawa and The Ottawa Hospital.

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Correspondence to: Steven J. Glassman, MD, The Ottawa Hospital, Division of Dermatology, 737 Parkdale Avenue, 4th Floor, Ottawa, Ontario, K1Y 1J8, Canada. E-mail: sglassman@toh.ca.

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exogenous, nonhuman proteins. It typically occurs 1 to 2 weeks after parenteral exposure to the offending agent. SS is characterized by fever, lymphadenopathy, urticarial or morbilliform rash, and arthralgia/arthritis. Laboratory investigation finds associated hypocomplementemia (C3 and C4) and proteinuria. Skin biopsy often finds neutrophil predominant inflammation or leukocytoclastic vasculitis.

In contrast, serum sickness—like reaction is probably a nonimmune complex-mediated reaction to drugs and does not manifest hypocomplementemia or renal involvement. The pathogenesis of SSLR is not well understood. It usually occurs 1 to 3 weeks after exposure to the offending drug and more commonly occurs in children. Mirabegron, a relatively novel β3-adrenergic receptor agonist, has not been reported to be associated with SSLR. The most commonly reported side effects of mirabegron are constipation, dysuria, and increased residual urine volume. A case of antineutrophil cytoplasmic antibody—positive vasculitis was reported, but this was not felt to be related. The US Food and Drug Administration lists mirabegron as a potential cause of the following skin conditions: pruritus, urticaria, angioedema, leukocytoclastic vasculitis, and purpura. Arthralgia is also mentioned.

This case shows the similarity and overlap between urticaria, urticarial vasculitis, SS, and SSLR and suggests that these conditions might represent a spectrum of the same hypersensitivity response. Mirabegron should be included in the possible causes of SSLR.
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