

Extreme Positive Patch Test Reaction to Ampicillin 30 Years After Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis



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A 50-year-old woman was referred to our allergy department (London, UK) to investigate a historic adverse reaction to ampicillin, which occurred over 30 years ago in her home country of Romania. Five days after commencing oral ampicillin, she developed a prodromal febrile illness, followed by multiple painful erosions and fluid-filled blistering lesions over the face, hands, and torso. She had an estimated 10% to 30% body surface area (BSA) involvement (skin detachment), in addition to associated oral mucosal involvement. She was diagnosed with Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and was advised to avoid all penicillin-class antibiotics. Because of the historic nature of the reaction in a different country, skin biopsy report and laboratory studies were not obtainable. Drug allergy testing was not conducted at the time. Informed consent was obtained from the patient for publication.

At our drug allergy clinic, 30 years later, patch testing was performed on the upper right back using IQ Ultra chambers (Chemotechnique Diagnostics, Vellinge, Sweden) with ampicillin (10% dilution in white petrolatum, using extracted commercial powder from an injection vial). Patch test readings at both day 2 (Figure 1, A) and day 4 (Figure 1, B) revealed extreme positive (++++) vesicular reactions, with notable large 90 × 70 mm extension beyond the initial chamber application site (10 × 10 mm). We treated the patch test reaction with topical clobetasol ointment, and no systemic flare eruptions were observed. We diagnosed SJS/TEN due to ampicillin and advised ongoing avoidance of all penicillin-class antibiotics.

SJS/TEN is a life-threatening severe cutaneous adverse reaction (SCAR), classified as a type IVc delayed hypersensitivity, with inflammation predominately mediated by CD8+ cytotoxic T-lymphocytes. Commonly implicated drug causes include sulfonamides, β -lactams, anticonvulsants, and allopurinol. It is characterized by an initial prodromal illness, followed by diffuse painful progressive erythema, mucocutaneous blistering, and skin detachment.¹ SJS and TEN exist on a spectrum based on the maximum extent of BSA detachment, whereby SJS affects less than 10% of the BSA, whereas TEN affects more than 30% of the

BSA. SJS/TEN overlap describes cases in which 10% to 30% of the BSA is detached. Skin biopsy may help support the diagnosis.¹

A recent systemic review suggests that patch testing in SJS/TEN is useful and safe, but also drug dependent.¹ Only 5 other cases of ampicillin-induced TEN confirmed via patch testing have been reported internationally (Italy, Germany, and Japan, between 1975 and 1993),¹ and ours is notably the first from the United Kingdom.

T-cell-mediated drug hypersensitivity to antibiotics is purported to be lifelong, in contrast to IgE-mediated allergy, whereby sensitization can be significantly lost over time (ie, approximately 80% lose penicillin type 1 allergy at 10 years).² There is limited literature regarding the value of long interval patch testing in evaluating historic cases of delayed-type hypersensitivity reactions. In one recent study evaluating the long-term reproducibility of patch testing in antibiotic reactions, 17 of 20 patients showed persistent reactivity on repeated patch testing after a mean interval of 6 years, with the longest reported interval of 14.7 years.² Of these patients, 18 had originally experienced maculopapular exanthema, 1 had DRESS (drug reaction with eosinophilia and systemic symptoms) syndrome, and 1 had acute generalized exanthematous pustulosis (none with SJS/TEN).²

Here we describe a case of SJS/TEN due to ampicillin confirmed by patch testing 30 years after the original event, which is particularly notable for an extreme positive patch test reaction, implying strong persistent T-cell activation and memory. We highlight that patch testing in SCARs (including SJS/TEN) should still be considered of value in the diagnostic workup, even if there is a long interval (decades) between an index drug reaction and the time of clinical evaluation.

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FIGURE 1. Extreme positive (+++) patch test reaction to ampicillin (10% pet) at day 2 (**A**) and day 4 (**B**) readings, with large 90 × 70 mm extension beyond the initial IQ Ultra patch test chamber application site (10 × 10 mm). The black arrow (**A**) indicates the bottom edge margin of the applied patch test chamber.