immunosuppressive agents in cardiac transplantation, their nephrotoxicity has limited their unrestrained use in patients.[9] By delaying the need for calcineurin inhibitors, thymoglobulin preserves greater renal function without increasing the risk for acute rejection.[9,10] Akin to its use in the patient presented in this case report, thymoglobulin also is used in the treatment of acute cellular rejection in heart transplant recipients with signs of heart failure.[11]

Case Report

A 35-year-old man with a history of familial cardiomyopathy who underwent orthotopic heart transplantation presented with grade 3R acute cellular rejection. The patient's immunosuppressive regimen consisted of thymoglobulin 150 mg once daily, tacrolimus 2.5 mg twice daily, hydrocortisone 100 mg once daily, and mycophenolate mofetil 1000 mg twice daily. On day 7 of thymoglobulin treatment, the dermatology department was consulted to evaluate a pruritic eruption. The patient reported that he noticed redness of the palms and soles, as well as redness accentuated in the axilla, groin, and other skin creases 2 days prior. The patient also reported symmetric bilateral hand pain that had started 1 day following rash onset. He denied fever and remained afebrile throughout his hospitalization.

On physical examination, the patient displayed a blanching, erythematous, edematous, evanescent macular rash with some areas of wheal formation symmetrically distributed in the bilateral axillae, inframammary folds, and groin (Figure, A and B). The palms and soles were tender with diffuse blanching erythema. The eruption was accentuated at the lateral and medial borders of both feet (Figure, C). There was concern that the patient may have a form of serum sickness with a blunted incomplete response due to his concomitant use of immunosuppressive agents. Shortly after evaluation, the patient left the hospital against medical advice before the recommended evaluation and systemic workup could be implemented.

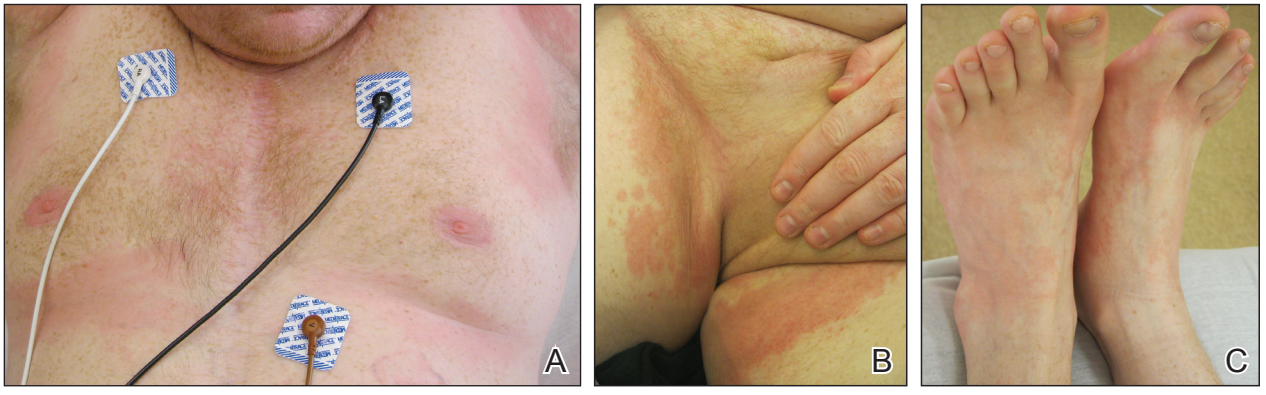
The patient returned for an outpatient appointment approximately 1 week later. Medical records indicated that the patient's skin eruption had resolved. Tests for antithymoglobulin antibodies at this visit were negative. The antithymoglobulin antibody enzyme-linked immunosorbent assay has a diagnostic sensitivity of 86%[12] and large interlaboratory variability.[13] Given the presence of other features of serum sickness, a false-negative result was considered by dermatology. Nonetheless, one must consider other differential diagnoses, including a simple cutaneous adverse drug eruption or viral exanthem that might have in fact been causative.

Comment

We present an atypical case of possible serum sickness in a heart transplant recipient following thymoglobulin treatment of acute cellular rejection of the cardiac allograft. Serum sickness is a clinical diagnosis supported by laboratory data. Some authors have suggested major and minor diagnostic criteria to aid with the diagnosis.[7] Major diagnostic criteria include onset more than 7 days after the initial thymoglobulin administration, persistent high fevers (temperature, >38.4°C), persistent arthritis/arthralgia, and positive heterologous antibodies on enzyme-linked immunosorbent assay. Minor diagnostic criteria include rash, acute renal failure, trismus, and low serum complement (C3 and C4).

The variable cutaneous presentations of serum sickness are important to recognize in the process of making the correct diagnosis. Rash is frequently reported in serum sickness, with some studies displaying rates of up to 93%.[4,14] The skin findings are most frequently described as urticarial or serpiginous macular lesions.[3] Other variations of the eruption exist, and morbilliform eruptions or a combination of morbilliform and urticarial eruptions have been reported.[3] It is important to judge cutaneous eruptions of serum sickness within the context of the potential cytopenia in a patient being treated with ATG. As such, purpuric eruptions have been attributed to serum sickness in thrombocytopenic patients receiving ATG for bone marrow failure.[14]

Usually, cutaneous eruptions of serum sickness initially are identified in the groin, axilla, and periumbilical region, and then they proceed to include the trunk and extremities.



Serum sickness with blanching erythematous, edematous, evanescent macules, as well as patches and thin plaques with some areas of wheal formation symmetrically distributed in the axillae and inframammary folds (A), groin (B), and lateral and medial borders of both feet (C).

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