

Concurrent serum sickness–like reactions in fraternal twins following amoxicillin exposure

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ABSTRACT

Serum sickness–like reaction (SSLR) is an immunologic process most often triggered by β -lactam antibiotics or viral infections, typically presenting with urticarial rash, arthralgias, and low-grade fever. This report describes concurrent SSLR in 5-year-old fraternal twin girls after amoxicillin exposure for presumed viral pharyngitis. Twin A developed diffuse urticaria, facial and extremity swelling, arthralgias, and mucosal discomfort. Laboratory studies showed leukocytosis, elevated inflammatory markers, and detection of rhinovirus/enterovirus by PCR. She required hospitalization, systemic corticosteroids, and multimodal analgesia, with gradual improvement over several days. Twin B developed similar symptoms three days later, including rash, edema, and joint pain, but had a milder course managed with antihistamines and supportive care. The simultaneous occurrence of SSLR in siblings is rarely reported, and concurrent presentation in fraternal twins has not been described in the literature. This case highlights the interplay of shared environmental exposures, potential infectious triggers, and host susceptibility in SSLR, as well as the variability of disease expression even among related children. Awareness of SSLR in the differential diagnosis of rash and arthralgia following antibiotic exposure can prevent unnecessary investigations, guide supportive treatment, and reduce morbidity.

Keywords: serum sickness-like reaction, twins, amoxicillin, drug hypersensitivity, pediatrics

INTRODUCTION

Serum sickness–like reaction (SSLR) is an uncommon condition most often associated with β -lactam antibiotics, particularly amoxicillin.¹ It is clinically distinguished by the triad of urticarial or erythematous rash, joint involvement, and systemic symptoms such as fever or malaise.² Unlike classic serum sickness, hypocomplementemia is not typical. While classic serum sickness has been reported in twins following equine rabies immunoglobulin,³ concurrent SSLR has not been previously described in siblings. To date, concurrent serum sickness-like reactions occurring in fraternal twins following amoxicillin exposure have not been reported. This presentation highlights the potential interplay between shared environmental exposures,

infectious triggers, and individual host susceptibility in the pathogenesis of SSLR.

CASE PRESENTATION

Written informed consent was obtained from the patients' mother for publication. Both children were up to date on routine childhood immunizations, with no recent vaccinations administered prior to symptom onset.

A comparison of clinical features is shown in Table 1.

Twin A: A 5-year-old girl developed urticarial rash, facial, lip, and extremity edema, and severe arthralgias near the end of a 10-day course of amoxicillin prescribed empirically despite a negative rapid streptococcal antigen



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test. Laboratory evaluation showed leukocytosis with marked neutrophilia, mildly elevated CRP, unremarkable complement levels, and a positive rhinovirus/enterovirus PCR. Intramuscular epinephrine was administered in the emergency department due to initial concern for anaphylaxis in the setting of diffuse urticaria and angioedema. However, the absence of hypotension or respiratory compromise, lack of sustained response to epinephrine, and subsequent progression of severe arthralgias supported a diagnosis of SSLR rather than IgE-mediated hypersensitivity. Symptoms progressed despite scheduled cetirizine with adjunctive diphenhydramine and hydroxyzine, as well as nonsteroidal anti-inflammatory therapy with ketorolac and naproxen. She had worsening pain and limited mobility, which prompted escalation to systemic corticosteroids (intravenous methylprednisolone followed by oral prednisolone) and analgesia with oxycodone and hydrocodone-acetaminophen. She was hospitalized for five days with gradual improvement.

Twin B: Three days later, her fraternal twin developed diffuse urticaria, extremity edema, and arthralgias after completing approximately eight days of empiric amoxicillin for pharyngitis. Laboratory studies revealed mild neutrophilia without leukocytosis, normal inflammatory markers, and complement levels not decreased. She improved rapidly with cetirizine and hydroxyzine, along with acetaminophen and ibuprofen. A single dose of dexamethasone was given in the emergency department, but further steroids were avoided as symptoms resolved. Her hospitalization lasted two days.

DISCUSSION

Both patients developed characteristic findings of SSLR, including urticarial rash, edema, and arthralgias, approximately 8 days into amoxicillin therapy, consistent with the typical 7 to 10-day latency described in recent systematic reviews of pediatric SSLR.^{1,2} The overall presentation was more compatible with SSLR than with other causes of rash and arthralgia, such as anaphylaxis, viral exanthem, erythema multiforme, IgA vasculitis, urticarial vasculitis, or classic serum sickness, which typically demonstrates hypocomplementemia and immune-complex-mediated vasculitis.¹ IgE-mediated anaphylaxis was considered less likely due to the absence of cardiorespiratory compromise and poor response to epinephrine, while normal complement levels excluded classic serum sickness and urticarial vasculitis. Viral exanthem, erythema multiforme, and IgA vasculitis were considered less consistent with the clinical course and absence of purpura or mucosal involvement.

The etiology in these cases remains uncertain. Although streptococcal infection cannot be definitively excluded, negative rapid tests make this less likely. Importantly, recent reports highlight how positive streptococcal testing can confound the diagnosis of SSLR by directing clinicians toward rheumatic or post-infectious syndromes.⁴ Such diagnostic pitfalls underscore the need for careful interpretation of test results when clinical features better align with SSLR. Rhinovirus/enterovirus was detected in Twin A, supporting a possible infectious contribution. Viral testing was negative in Twin B, but this does not exclude infection. The respiratory viral panel evaluates a limited set

Table 1. Comparison of clinical features in Twin A and Twin B

Feature	Twin A (Patient A)	Twin B (Patient B)
Age/Sex	5-year female	5-year female
Clinical severity	Severe; prolonged course with impaired mobility	Mild-to-moderate; self-limited
Antibiotic exposure and timing	Onset near the end of a 10-day amoxicillin course	Onset three days after completing ~8 days of amoxicillin
Initial symptoms	Urticarial rash; facial/lip and extremity edema; arthralgias; severe pain; no response to epinephrine	Urticarial rash; extremity edema; arthralgias; milder pain
Key laboratory findings	Leukocytosis; CRP mildly elevated; C3 91 mg/dL, C4 24 mg/dL; rhinovirus/enterovirus positive	Mild neutrophilia; CRP normal; C3 121 mg/dL, C4 41 mg/dL
Hospital course	5 days; systemic corticosteroids, antihistamines, multimodal analgesia including opioids	2 days; antihistamines and analgesia; brief steroids then discontinued per allergy consultation
Outcome	Gradual resolution with tapering antihistamines	Rapid resolution

CRP: C-reactive protein.

of 18 pathogens and may also yield false-negative results for included targets depending on the timing of sampling and viral burden. Serum sickness-like reactions occurring during antibiotic treatment have been described as infection-associated urticarial syndromes with unpredictable recurrence, rather than reproducible drug hypersensitivity.⁵ The simultaneous development of SSLR in fraternal twins raises the possibility of shared host susceptibility. Because these were dizygotic twins and no genetic analyses were performed, these observations support a role for shared environmental exposures and host susceptibility rather than a definitive genetic predisposition. Although classic serum sickness has been reported in identical twins following rabies immunoglobulin,³ concurrent SSLR in siblings have not been previously described. The combination of shared environmental exposures, parallel viral illness, and similar timing of antibiotic exposure aligns with emerging models suggesting a multifactorial interplay among infection, drug exposure, and individual predisposition in SSLR pathogenesis.⁵

The differences in clinical severity between the twins also highlight the heterogeneity of SSLR and its implications for clinical management. Twin A experienced a more severe, protracted course requiring systemic corticosteroids and multimodal analgesia, whereas Twin B improved rapidly with supportive care alone, with a shorter hospital stay. This variability is consistent with a 10-year cohort study demonstrating that SSLR can range from mild, self-limited cases to more severe episodes necessitating inpatient management for pain control or impaired mobility.⁶ Recent pediatric emergency department data similarly report that SSLR and SSLR-like illnesses are significant drivers of acute care utilization, with systemic symptoms such as joint pain and swelling associated with more prolonged or complicated courses.⁷ A large acute-care cohort found that children with amoxicillin-associated reactions re-utilized emergency or urgent care services in approximately 10% of cases, with urticaria, angioedema, and systemic symptoms predicting repeat visits.⁸

Evidence supporting corticosteroid therapy remains limited. Steroids are frequently prescribed in moderate to severe cases, but studies show wide variability in practice and no clear evidence of accelerated recovery. Current recommendations, therefore, reserve corticosteroids for substantial discomfort, decreased mobility, or refractory symptoms.^{1,6}

Management also includes planning for future antibiotic use. SSLR rarely represents a fixed β -lactam allergy, and lifelong avoidance is not routinely necessary.⁹ Evaluation by an allergy specialist and consideration of supervised oral challenge can safely clarify tolerance in most children.¹⁰ However, families should be counseled that recurrence is possible, as SSLR and SSLR-like reactions may reappear unpredictably even after a previously tolerated re-exposure.⁵

Conclusion: This dual presentation highlights the rare concurrence of SSLR in fraternal twins and the multifactorial pathogenesis involving host susceptibility, viral triggers, and antibiotic exposure. Recognition of SSLR within this broader framework can help clinicians avoid unnecessary investigations, guide appropriate therapy, and provide informed counseling regarding future β -lactam use.

Ethical approval

Written informed consent was obtained from the patients' mother for publication of these cases.

Author contribution

The author declares contribution to the paper as follows: Study conception and design: KD; data collection: KD; analysis and interpretation of results: KD; draft manuscript preparation: KD. The author reviewed the results and approved the final version of the article.

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Conflict of interest

The author declares that there is no conflict of interest.

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