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Recognition and Management of Serum Sickness-Like Reaction to Amoxicillin: A Case Report

Prepoznavanje in obvladovanje serumski bolezni podobne reakcije na amoksicilin: predstavitev kliničnega primera

Irena Deželak, Igor Potparić, Mihaela Zidarn

Abstract

This case report discusses a rare adverse reaction to amoxicillin, presenting as a serum sickness-like reaction (SSLR) in a 44-year-old male. The patient developed acute generalized urticaria, oedema, and polyarthralgia seven days after starting amoxicillin for a suspected lower respiratory infection. Initial treatment with systemic glucocorticoids and antihistamines provided partial relief. However, the patient's symptoms worsened, leading to hospital admission. Elevated inflammatory markers, including tryptase, were observed, although there were no signs of anaphylaxis. The patient's condition improved significantly following the discontinuation of amoxicillin and continued supportive care. This case highlights the importance of recognizing and appropriately managing SSLRs, emphasizing the critical need for careful evaluation of antibiotic necessity to prevent unnecessary patient risks.

Izvleček

Ta predstavitev kliničnega primera obravnava redek neželeni učinek na amoksicilin, ki se kaže kot serumski bolezni podobna reakcija (SSLR) pri 44-letnem moškem. Pri bolniku se je 7 dni po začetku jemanja amoksicilina, zaradi predpisanega suma na okužbo spodnjih dihal, razvila akutna urtikarija, edem in poliartralgija. Začetno zdravljenje s sistemskimi glukokortikoidi in antihistaminiki je zagotovilo delno olajšanje. Zaradi nadaljnjega poslabšanja simptomov je bil bolnik hospitaliziran. Pri bolniku smo opazili povišane označevalce vnetja, vključno s triptazo, čeprav znakov anafilaksije ni bilo. Bolnikovo stanje se je bistveno izboljšalo po prekinitvi jemanja amoksicilina in ob nadaljevanju podporne oskrbe. Ta klinični primer poudarja pomen prepoznavanja in ustreznega obvladovanja SSLR, pri čemer opozarja tudi na pomen premišljene uporabe antibiotikov, da bi preprečili nepotrebna tveganja za bolnika.

University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia;

Correspondence / Korespondenca: Irena Deželak, e: dezelak.irena@gmail.com

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Ključne besede: neželeni učinek zdravila; zapoznela preobčutljivost; penicilini; premišljena uporaba antibiotikov

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1 Introduction

Amoxicillin is one of the most commonly prescribed antibiotics. It is also one of the more common drugs related to a rare adverse reaction called serum sickness-like reaction (SSLR). The median duration of therapy before symptoms appear is six to nine days, and the median age of affected individuals is 4 years (1), indicating that this rare reaction predominantly occurs in the paediatric population. In addition to antibiotics, NSAIDs, bupropion, phenytoin, and propranolol are associated with SSLRs (2).

Historically, true serum sickness has been linked with murine or chimeric monoclonal antibodies (3). However, various antibiotics can mimic this condition, resulting in SSLR. These reactions present with similar but milder symptoms compared to classic serum sickness and do not involve the formation of immune complexes or complement activation. Commonly implicated antibiotics include cephalosporins, penicillins (particularly amoxicillin), sulphonamides, ciprofloxacin, and minocycline (1,2,4). The mechanism behind these reactions remains unclear, though it is hypothesized that the medications either function as haptens or generate metabolites toxic to cells. Discontinuation of the offending antibiotic usually suffices to resolve the symptoms (5).

Clinical features include fever, rash, and polyarthralgia. Additional symptoms may include polymyalgia, lymphadenopathy, malaise, proteinuria, and oedema (6). Unlike in true serum sickness, circulating antigen-antibody complexes are absent, and renal and hepatic involvement is rare. It is a diagnosis of exclusion, requiring a detailed history and laboratory workup (2,6,7). The differential diagnosis for SSLRs includes severe conditions such as erythema multiforme, Kawasaki's disease, and disseminated gonococcal or meningococcal infections. SSLRs are distinguished by the patient's history and nontoxic appearance. These reactions are self-limited and generally have a favourable prognosis (8).

Management of SSLRs involves discontinuing the causative medication. Symptomatic relief can be achieved with antihistamines and nonsteroidal anti-inflammatory drugs. For severe cases, a short course of corticosteroids may be prescribed. It is also recommended to avoid the offending drug and related agents in the future (8).

2 Case presentation

A 44-year-old male, previously healthy and not on any regular medication, presented to the emergency department of the University Clinic for Pulmonary Diseases and Allergy Golnik with acute generalized urticaria, seven days after initiating treatment with oral amoxicillin for a suspected lower respiratory infection. The patient was prescribed amoxicillin (1000 mg, two tablets a day for eight days) empirically by the primary care physician due to a three-week persistent productive cough without prior investigations such as chest X-ray or inflammatory markers. On clinical examination, he appeared generally well with no signs of distress. Skin examination revealed widespread urticarial plaques (Figure 1). No mucosal involvement or lymphadenopathy was noted. Pulmonary and cardiac examinations were unremarkable, and the patient was afebrile. The patient had noticeable swelling of the hands and face. Laboratory investigations revealed a normal complete blood count, liver enzymes, and renal function tests, with one elevated inflammatory parameter (white blood cell count of 13.82 × 10^9/L). Chest X-ray and ECG findings were unremarkable. Based on the clinical manifestation, the diagnosis of a delayed hypersensitivity reaction

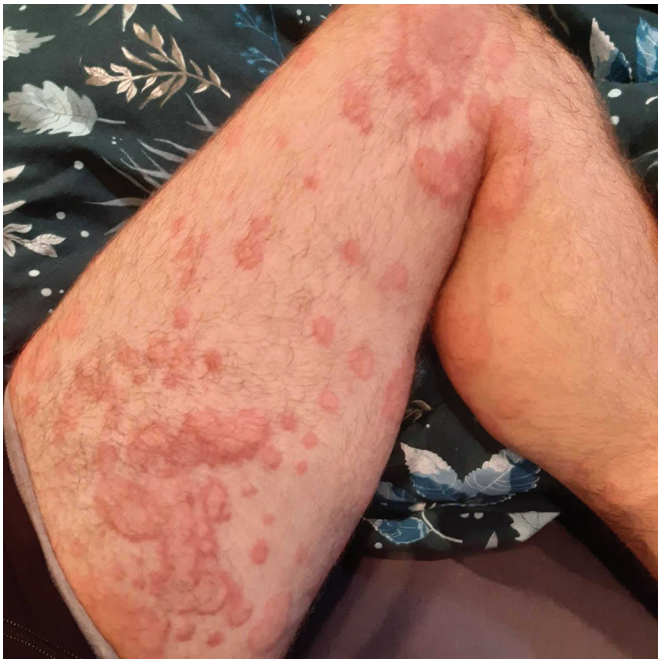

Figure 1: Skin presentation on lower extremity.
Used with permission of the patient.
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was made, with amoxicillin suspected as the most likely trigger. The patient received a systemic glucocorticoid (methylprednisolone 125 mg i.v.) and an antihistamine (clemastine 2 mg i.v.). An antihistamine (desloratadine 5 mg, 2x1 per day) was prescribed for home use.

Two days later, the patient returned to the emergency room due to worsening fatigue, loss of appetite, and cutaneous symptoms. During the interim, he had received two additional doses of systemic glucocorticoid (methylprednisolone 125 mg i.v.) from his primary doctor. At this time, his pulse was elevated (120/min), respiratory rate was 20/min, subfebrile (37.7°C), blood pressure was 135/80 mmHg, and oxygen saturation was 96%. Laboratory investigations revealed noticeably elevated inflammatory parameters (white blood cell count of 11.19 × 10^9/L, C-reactive protein 171.8 mg/L, erythrocyte sedimentation rate 17 mm/h), elevated tryptase (17.40 µg/L), as well as a pathological urine sample (proteins 0.18 g/L, glucose 28 mmol/L) with normal serum renal function. Due to the worsening of his condition, the patient was admitted to the hospital. Alongside an oral antihistamine (desloratadine 5 mg, 2x2 per day), an oral antibiotic (moxifloxacin 400 mg) was initiated due to the elevated inflammatory markers. No clear infection source was identified, as urine and respiratory cultures were negative, and the chest X-ray showed no infiltrates.

Follow-up lab results after one day showed CRP 195 mg/L, normal electrolytes, renal function, and liver enzymes. By the third day of hospitalization, CRP had decreased to 74.1 mg/L, with WBC 7.70 × 10^9/L. During the four-day hospitalization, the oedema resolved, and the patient generally felt better. The patient was discharged with instructions to continue antihistamines and complete a course of moxifloxacin. Post-discharge, the urticarial rash persisted for another 10 days, and some skin peeling was present at the end. A few days after discharge, the patient noticed arthralgia, particularly in the hands, elbows, shoulders, and knees, which lasted for about a week. The patient was advised to avoid penicillin antibiotics until further testing could be performed.

At his subsequent follow-up approximately a year later, prick testing and intradermal testing with immediate and delayed readings for amoxicillin, penicillin G, and cefuroxime were negative; all laboratory values were normal, and base tryptase was 4.23 (micro)g/L.

3 Discussion

The patient's presentation and course strongly suggest a delayed hypersensitivity reaction to amoxicillin, most likely a serum sickness-like reaction (SSLR). As outlined in the introduction, common clinical symptoms of SSLR include a skin rash, oedema, and polyarthralgia (6), all of which were observed in this patient, albeit with the polyarthralgia presenting slightly later. The onset of symptoms, occurring seven days after initiating amoxicillin, aligns well with the typical time frame for SSLR development (1).

Proteinuria was noted without signs of kidney damage, consistent with SSLR, which generally does not involve renal impairment (6). The patient's condition improved significantly within 4 days and fully resolved in 14 days following discontinuation of amoxicillin and administration of supportive treatments, including antihistamines and systemic glucocorticoids.

Skin tests were performed to exclude IgE-mediated involvement (type I hypersensitivity) using prick testing and immediate-reading intradermal tests, as well as possible T-cell–mediated involvement (type IV hypersensitivity) using delayed-reading intradermal tests. In serum sickness-like reactions, both prick and intradermal skin tests are generally expected to be negative, as these tests are not designed to detect the underlying mechanisms of SSLR. Nevertheless, skin testing is commonly performed, as it carries a low risk when conducted under controlled conditions and allows for the exclusion of immediate and delayed cutaneous hypersensitivity reactions, which were particularly clinically relevant in this patient, given the elevated serum tryptase, and for guiding future antibiotic use (9).

A notable aspect of this case is the elevated tryptase levels observed in the absence of other signs of anaphylaxis. While there are instances where SSLR and anaphylaxis can coexist, as described by Kim et al. (10), our patient did not exhibit classic anaphylactic symptoms. Elevated tryptase is indicative of mast cell activation and may be attributed to the extensive urticarial involvement observed in approximately 12% of patients with urticaria or angioedema without anaphylaxis (11).

From a practical standpoint, recognizing clinical features that may indicate a more severe delayed drug reaction is essential, particularly as SSLRs remain a clinical diagnosis without specific confirmatory tests. While most SSLRs are self-limited, certain findings should prompt a more extensive evaluation. These include pronounced systemic symptoms, persistent or high-grade fever, markedly elevated inflammatory markers, and signs suggestive of organ involvement, such as proteinuria, cytopenias, or abnormal liver enzymes. In such cases, laboratory assessment should include complete blood count with differential, inflammatory markers

(CRP, ESR), renal and liver function tests, and urinalysis, to help differentiate mild reactions from more severe drug-induced conditions. Complement levels may be considered when true serum sickness is suspected, as hypocomplementemia is typically absent in SSLRs. This structured approach is also important to exclude relevant differential diagnoses, including systemic infections, vasculitis, and severe cutaneous adverse drug reactions, thereby guiding appropriate management and follow-up (4,9).

Another critical point is whether the antibiotic treatment was necessary from the outset. The patient's persistent cough likely stemmed from a recent viral infection, as coughs can persist for 4 to 12 weeks following viral respiratory tract infections due to damage of the bronchial mucosa (12). This possibility is supported by the patient's initial normal chest X-ray, CRP, and clinical examination findings, which showed no signs of a bacterial respiratory infection. Thus, the patient was unnecessarily exposed to the risks associated with amoxicillin, including this rare adverse reaction.

This case underscores the importance of judicious antibiotic use. Overprescription not only contributes to antibiotic resistance but also poses direct risks to patients. Even commonly prescribed antibiotics like amoxicillin can lead to significant adverse reactions, as demonstrated in this case.

4 Conclusion

This case presents a rare adverse reaction to amoxicillin, highlighting the importance of recognizing SSLRs and appropriately managing them. The patient's symptoms, progression, and treatment underscore the benefit of prompt identification and adequate supportive care. Additionally, this case emphasizes the significance of appropriate antibiotic use, as overprescription not only contributes to antibiotic resistance but also exposes patients to unnecessary adverse effects. Careful evaluation of the necessity for antibiotic therapy is essential to protect patient health and improve clinical outcomes, demonstrating the broader importance of judicious antibiotic use.

Conflict of interest

The authors declare they have no conflict of interest.

Inform consent of the patient

The patient gave informed consent for the publication of his case.

Founding sources

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