

Chronic urticaria on woman with toxoplasmosis post spiramycin treatment: A rare case

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Abstract

Spiramycin is a macrolide antibiotic with a bacteriostatic action and is used as a toxoplasmosis treatment since the FDA considers it safe and can be taken throughout early pregnancy. As the therapeutic use of spiramycin increases, reports of hypersensitivity responses, characterized as urticaria, are also on the rise. A 27-year-old woman presented to the hospital with chief complaints of recurrent rash with redness and severe itch on her entire body for one week. The rash appeared after the patient was diagnosed with toxoplasmosis and instructed to take spiramycin regularly. Two months ago, the patient experienced the same complaints. The patient was diagnosed with spiramycin-induced chronic urticaria and administered dexamethasone, diphenhydramine, and fexofenadine orally. Clinical improvement is evident after three days of treatment, as evidenced by a weekly decrease in the UAS-7 score. Urticaria is a hypersensitivity reaction that can be triggered by antibiotic consumption. A comprehensive diagnosis is needed to determine the etiology of urticaria, including the history of drug consumption. Treatment of urticaria includes education and the administration of antihistamines and corticosteroids. Chronic urticaria requires special treatment from a dermato-venerologist.

Key words

Chronic urticaria; Toxoplasmosis; Spiramycin; Macrolide.

Introduction

Urticaria is a common occurrence in primary care. Urticaria is said to affect 20% of Indonesians, with a prevalence of 0.27–2.1%, or at the very least, every individual has experienced urticaria once in their lifetime. The prevalence of women who suffer from chronic urticaria in the United States was 310 cases per 100.000 adults, more than twice that of men (146 cases per 100.000 adults). Chronic urticaria

prevalence was highest in patients aged 40–49 years (256 cases/100.000 adults) and 50–59 years (246 cases/100.000 adults).¹

However, in the last decade, an increasing understanding of pathogenesis has shown the different urticaria subtypes.² The difference between the urticaria subtypes is essential not only for diagnosis and in deciding treatment but also for research purposes. Urticaria is characterized by a rash that appears rapidly with or without angioedema. A welt has three distinct characteristics: erythema and swelling in the center of varying size, itching and burning sensation at times, and can heal itself in 1-24 hours. While angioedema is characterized by sudden swelling of the lower dermis and

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subcutis, which can be more painful than itching, it can also involve the mucous membrane and recover up to 72 hours slower than heel.^{3,4}

Most common patients suffer acute urticaria that can resolve within six weeks. Patients with chronic urticaria will experience wheals or angioedema almost daily, with recurrence lasting at least six weeks.⁵ Patients with chronic urticaria experienced a health-related degradation in the quality of life. An explicit warning may lead to emotional upset, making patients retire from social activities.⁶ Patients will have trouble sleeping, feel tired, and be sensitive because of the itching. They may have anxiety, depression, somatization, and obsessive-compulsive disorder as well. Urticaria has become the second most common skin eruption after exanthema drug eruptions, and the frequency appears to increase. Urticaria can be aggravated by drug consumption and is called drug-induced urticaria (DIU). Antibiotics are the second cause of DIU; one is a macrolide. While allergic sensitization is either a developed condition or not immunologically mediated, DIU may be immunologically mediated (allergic) (pseudo-allergic). Allergic DIU is mainly a type I hypersensitivity (IgE-mediated), while pseudo-allergic DIU is a complex immune reaction. The majority of DIU cases are non-immunological. Only about 10% of DIU cases have type I hypersensitivity.⁷ After NSAIDs, antibiotics also contribute to causing urticaria.

Spiramycin, an antibiotic discovered in 1952, is a product of *Streptomyces ambofaciens*. Spiramycin works by inhibiting peptide synthesis in bacteria when translocated.⁸ Spiramycin is a member of the macrolide drug class and is currently used in many infection cases, for example, as toxoplasmosis infection prophylaxis for early pregnancy that the Food and Drug Administration and the Centers for

Disease Control and Prevention approve.^{9,10} Macrolide is an antibiotic class that can cause hypersensitivity other than beta-lactams, sulfonamides, and fluoroquinolones. Anaphylaxis and urticaria are immediate hypersensitivity reactions. There are few publications that explain how to diagnose a logarithm and hypersensitivity due to macrolide. The incidence of hypersensitivity reactions due to medications without specific allergy histories is estimated to be 0.3-0.4%. The DPT (Drugs Provocation Test) confirmed the allergy to macrolide in 8 of 107 patients suspected of having it in 2004. Another study published in 2011 found that allergy to macrolide was confirmed by DPT in 4 of 114 patients (or approximately 3.5%).¹¹

Case report

A 27-year-old woman presented to the hospital with a chief complaint and a history of urticaria. The first symptoms appeared twice in the last two months after being diagnosed with toxoplasmosis due to miscarriage and advised to take spiramycin (3×500 mg) regularly as therapy. She mentioned wheals and an itch that went away after a day. Her hives were transient, did not burn, and did not leave bruising as they resolved. The recurrent attack is characterized by wheals, erythema, and an itchy rash on the entire body, starting from the head and spreading to the chest, stomach, arms, and legs (**Figure 1**).

The recurrent rash lasted one week, with no signs of improvement and a severe itch that disrupted the patient's sleep and daily activities in general. Shortly after that, in addition to the above symptoms, she began to have episodes of angioedema on the eyes and lips (**Figure 2**).

All these episodes resulted in emergency room visits where an antihistamine from a general



Figure 1 Dermatological lesion of urticaria and angioedema on the body and arms of the patient.



Figure 2 Recovery of lesions in one month.

practitioner was administered with no improvement in symptoms. Her family history revealed a father with irritant dermatitis and her mother with Addison's disease. Vital signs and the general examination are within the normal range. Dermatological status showed urticaria lesions characterized by erythema macules, raised plaques of multivariate shape and size, and apparent border lesions that spread from the face to the chest, arms, legs, and stomach. A negative workup has been shown for autoimmune diseases, food allergies, and environmental allergies through specific investigations. A positive workup has been shown for IgG and IgM toxoplasma serology. A diagnosis of chronic urticaria was established.

Initial treatment consisted of H1 antihistamines (AHs) (desloratadine). Despite this treatment, the response was poor; the patient was forced to stay home, had already stopped the drug consumption, and still experienced intermittent hives. At the second attempt of treatment, we decided to start on steroid injections (2×5 mg), antihistamine injections (3×1 cc), and fexofenadine (1×80 mg) orally for three days. Her urticaria activity score for the preceding seven days (UAS7) was 42 (**Figure 3**).

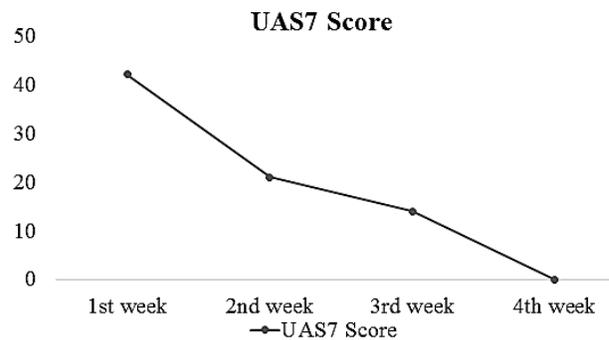


Figure 3 The progression of case 1's urticaria activity score over seven days (UAS7) as evaluated at each weekly visit.

The benefit came very fast from the first dose. Within seven days of starting this medication, her hives were controlled. The UAS7 fell to 7 (at the first month's evaluation), with a progressive decrease after each course. No side effects were noted during her treatment. She was free of severe itch and urticaria lesions at the time of this case study, two months after the recurrent urticaria.

Discussion

Urticaria describes various conditions in which bumps (or wheals) or itchy white or red lumps on the skin.¹² These features result from mast

cell degranulation releasing granule contents, primarily histamine.¹³ A detailed medical history is intended to identify potential triggers and aggravating factors of drug-induced urticaria and to rule out a differential diagnosis.¹⁴ The most common causes include certain foods, drugs, infections, insect bites, and internal diseases. Medications reported to be associated with urticaria include antibiotics, NSAIDs, opiates, antihypertensives, and antidepressants.¹²

These allergic reactions range from immediate to non-immediate hypersensitivity reactions. Immediate reactions are often IgE-mediated and may result in urticaria, angioedema, and anaphylaxis.¹⁴ Macrolide antibiotics are widely used to treat acute and chronic respiratory infections and are common alternatives to penicillin in penicillin-allergic patients. Macrolides are classified according to the number of carbon atoms in their lactone ring: 14 membered (erythromycin, clarithromycin), 15 membered (azithromycin), and 16 membered (spiramycin, midecamycin). Due to their metabolic and immunological features, macrolide antibiotics are regarded as low-allergy risk medicines. Hypersensitivity reactions resulting from macrolide use infrequently occur (0.4–3%).¹⁵

The presented case history demonstrates the close relationship between spiramycin therapy and urticaria. The patient developed wheals and itch after starting spiramycin at 3500 mg regularly, which went away after one day. The recurrent attack presented with wheals, erythema, and an itchy rash on the entire body and lasted for one week with no sign of recovery. Through specific investigations, a negative workup has been shown for autoimmune diseases, food allergies, and environmental allergies; thus, these causes can be excluded. Inflammatory markers were not monitored in this case but may have been elevated.¹³

According to the literature, there is no standard and reliable approach for diagnosing macrolide hypersensitivity reactions. Skin testing is considered an unreliable tool and has not yet been validated. In vitro diagnostic tools such as basophil histamine release and lymphocyte transformation tests have also not been validated. However, the drug provocation test (DPT) appears useful in confirming macrolide allergy and finding safe alternatives.¹¹ DPT is widely considered to be the “gold standard” for diagnosing or ruling out hypersensitivity to a particular substance.¹⁵ Based on the relationship between medication initiation, the onset of symptoms, and the negative results of the specific investigation to exclude other causes, the patient was diagnosed with chronic urticaria.

The patient had failed first-line treatments for chronic urticaria with persistent and troublesome symptoms. Initial treatment consisted of H1 antihistamines (AHs) (desloratadine). The patient is given steroid injections of 25 mg, antihistamine injections of 31 ccs, and fexofenadine, 180 mg, orally for three days. The rational use of steroids can help stabilize mast cell membranes, further inhibit histamine release, and reduce the inflammatory effects of histamine and other mediators.¹² Within seven days of starting this medication, her hives were controlled. The UAS7 fell from 42 to 7. The limitation of this case report is that the inflammatory test was not carried out to see an increase in IgE levels or the DPTs test, which are essential to either confirm or rule out a macrolide allergy. Although the case is rare, it is necessary to watch out for allergic reactions in patients taking spiramycin.

Conclusion

Urticaria caused by spiramycin is a rare occurrence that is expected due to immunological mediation. As a result, a doctor must raise awareness and improve patients'

quality of life by carefully prescribing with caution, along with an allergy, check test, or patch test when used for the first time, mainly when used to treat other infections promptly. Weekly scoring by the UAS7 method to monitor the symptoms must be done to prevent further complications. Comprehensive therapy and education to avoid medication in cases of previously reported proven spiramycin allergy and to avoid triggers such as stress are critical. Chronic urticaria requires consultation with a dermatovenerologist. Safe alternatives for toxoplasmosis may be a great solution to this problem.

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