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Azithromycin-Related Bicytopenia: An Exceptional Adverse Effect

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ABSTRACT

Macrolide antibiotics are commonly prescribed and are usually well tolerated. Azithromycin-related anemia and thrombocytopenia has not been reported previously. Here, we present the case of a 63-year-old man with bicytopenia following azithromycin treatment for ocular toxoplasmosis. He developed both thrombocytopenia and anemia after less than 7 days of treatment. Pyrimethamine, known for its hematologic side effects, was stopped on admission. However, the platelets drop continued to worsen. Then, azithromycin has been incriminated. All his symptoms and laboratory abnormalities were recovered within 7 days after the discontinuation of azithromycin treatment. Physicians must be aware of azithromycin-induced bicytopenia because its early detection can decrease the severity of these side effects.

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Introduction

Macrolide antibiotics are commonly prescribed worldwide and used in the treatment of a wide range of infections. They are usually well tolerated and have a low incidence of allergic side effects (0.4–3%) (1). Macrolides' spectrum of activity includes most gram-positive and only selected gram-negative organisms, as well as, several intracellular bacteria. Compared to erythromycin, azithromycin has more potent antibacterial activity against gram-negative organisms and has a favourable profile against intracellular bacteria (2). The most commonly reported side effects of azithromycin were gastrointestinal adverse reactions, represented by abdominal pain (53.1%), nausea (21.7%), vomiting (12.8%), and diarrhea (12.5%) (3).

Other side effects were less commonly reported, such as taste disturbances, headache, ototoxicity, hepatotoxicity and even cardiac toxicity. In fact, azithromycin were associated with a significantly increased risk of cardiovascular death (2). Hematologic toxicity such as leukopenia, thrombocytopenia, agranulocytosis, neutropenia, and neutrophilia were also reported (2). Here, we report an exceptional case of azithromycin-related bicytopenia in a 63-year-old man with ocular toxoplasmosis.

Case Report

A 63-year-old man was hospitalized for floaters and blurred vision, which started few days before consultation. His medical history included ocular toxoplasmosis and chronic bronchitis treated with formoterol (oral inhalation 12mcg/day), tiotropium bromide (oral inhalation 18mcg/day) and budesonide (oral inhalation 400 mcg per day). Considering the patient's medical history, the diagnosis of a recurrence of toxoplasma chorioretinitis was suspected and promptly confirmed based on a retinal angiogram. His laboratory tests at admission showed elevated inflammatory markers such as elevated erythrocyte sedimentation rate (70 mm/h) and C-reactive protein levels (32 mg/l). His white blood cells count was 5130/mm^3, his hemoglobin rate was 13g/dl and his platelets rate was 356000/mm^3. He was treated with pyrimethamine (100 mg on the first day followed by a daily dose of 50 mg), azithromycin (500 mg the first day, followed by 250 mg daily), oral corticosteroid (prednisolone at a dose of 1 mg/kg/day) and was discharge from the hospital.

One week later, the patient consulted us for an exacerbation of his chronic bronchitis with fever (38.2°C).

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He reported also recurrent episodes of epistaxis that is why he was readmitted. Abnormal laboratory investigations revealed bicytopenia including normochromic normocytic anemia (Hb=9.3g/dl) and thrombocytopenia (platelets=45000/mm^3). A peripheral blood smear confirmed the result of the blood count. Others laboratory tests showed an increased C-reactive protein levels (256mg/L), hepatic cytolysis (aspartate aminotransferase=78U/L and alanine aminotransferase=200U/L) and cholestasis. Pyrimethamine, known for its hematologic side effects, was stopped on admission. However, 8 days later, the platelets drop continued to 22000/mm^3. Then, azithromycin has been incriminated. Seven days after discontinuation of azithromycin, the platelets increased to 75000/mm^3 and a week later, to 685000/mm^3. Hemoglobin rate reached 13.3g/dl. Neither similar signs nor symptoms were observed after the reintroduction of pyrimethamine, which confirmed our hypothesis that bicytopenia was azithromycin-induced. The patient was discharged after improvement of his blood test. He was treated with pyrimethamine and sulfadiazine. No recurrence of thrombocytopenia nor anemia was noted during the follow-up.

Discussion

Ocular toxoplasmosis is the most frequent cause of posterior uveitis, leading to visual impairment in a high proportion of patients (4). Antibiotics used for its treatment include trimethoprim-sulfamethoxazole, pyrimethamine, sulfadoxine, sulfadiazine, clindamycin, tetracyclines, clarithromycin, azithromycin and others used alone or in combination. They act primarily against tachyzoites and do not affect encysted forms (5). Previous studies reported that the frequency and severity of adverse effects was significantly lower with a regimen containing azithromycin rather than sulfadiazine in the treatment of toxoplasmic chorioretinits along with pyrimethamine (6). Another study reported that azithromycin may be an effective alternative for patients with ocular toxoplasmosis who cannot tolerate standard therapies since it has fewer side effects (7).

A review of the literature shows that azithromycin-induced bicytopenia has not been reported previously and that azithromycin has no major or consistent adverse effects. However, the incidence of treatment-related abnormalities in blood cell count, particularly leukocyte/neutrophil rate, has been mentioned (8-10) as well as a case reporting agranulocytosis following azithromycin-treatment (11). Besides, a severe thrombocytopenia caused by azithromycin in an 81-year-old female who presented hematuria, epistaxis and ecchymosis was reported (12).

Azithromycin is well absorbed. It reaches high and sustained tissue concentrations and penetrates the blood-brain (13, 14) and blood-ocular barriers (14) when they are inflamed. The recommended dose is 500 mg as a loading dose followed by 250 mg daily. Its efficiency against Toxoplasma gondii has been reported with an effect on the cystic form if administered for longer than 4 weeks (15).

In conclusion, we presented a documented case of azithromycin-related anemia and thrombocytopenia. Physician should be aware of its rare side effects in order to closely monitored patients. An early detection of any side effect can decrease the severity of possible complications and prevent mortality.

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