

Chloroquine induced urticaria: A newer adverse effect

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ABSTRACT

Malaria an endemic disease of India caused by plasmodium species. Chloroquine, a member of quinolone group of drugs is used to treat malaria. Although it has a very safety profile as it is used during pregnancy, many adverse effects have also been reported. Here we report a case of 30-year-old male admitted with fever diagnosed to be having malaria, who developed urticaria immediately after being treated with first dose of chloroquine which was treated successfully. This is the first case reported ever in an adult having chloroquine induced urticaria.

Keywords: Adverse effect, antihistamines, chloroquine, Malaria

Introduction

Urticaria is a vascular disorder of the skin characterised by recurrent, smooth slightly elevated, pruritic (itchy), pink-to-red edematous lesions. The size of the lesion varies from few millimetres to few centimetres, often with a pale centre.^[1] Urticaria is a common disorder with a lifetime incidence of 15% and more commonly seen among female than male.^[2] Urticaria can also occur as the adverse effects of various drugs. Chloroquine is 7-chloro-4-(4-diethylamino-1-methylbutylamino) quinoline. It is a very effective and common antimalarial drug. It is effective against all erythrocytic forms of plasmodium species.^[3] Though there are many adverse effects have been reported due to chloroquine, the urticaria is the rarest adverse effect of chloroquine which has never been reported till now. Therefore, we report a case of chloroquine induced urticaria following the treatment of Plasmodium falciparum infection.

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Case History

A 35-year-old male presented with chief complaint of Fever with chills and rigors of 5 days duration. Fever is of high-grade with the evening rise of temperature. Patient also had a history of headache associated with fever for 3 days. There is no history of cough with expectoration, wheezing, throat pain, abdominal pain, dysuria, diarrhea, vomiting, retroorbital pain, joint pain. Bowel and bladder habits were normal. He was not a known case of diabetes, hypertension and any other chronic illness. No past history of tuberculosis, asthma, and allergy.

Physical examination of the patient revealed temperature of 101 F, pulse rate of 100/min regular and a blood pressure of 130/80 mm of hg with no anaemia, icterus, cyanosis, clubbing, lymphadenopathy and pedal edema. On abdominal examination the patient had a mild splenomegaly. Other systemic examinations were found to be unremarkable.

The laboratory findings revealed that hemoglobin, red blood cell count, total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate, random blood glucose, liver

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function test, renal profile were in normal limits. The peripheral smear shows *Plasmodium falciparum*. Quantitative buffy coat test was also positive for malaria.

A clinical diagnosis of malaria due to *Plasmodium falciparum* was made and the patient was planned for Chloroquine 10 mg/kg on Day-1, another 10 mg/Kg on Day -2 and 5 mg/Kg on Day 3 as a standard dose. Since Puducherry is not a drug resistant area for the chloroquine, the patient was started on chloroquine. Immediately after consuming the first dose of chloroquine the patient developed skin rashes which was diagnosed to be urticaria as shown in the Figures 1-3. The patient was started immediately on antihistamines and hydrocortisone and the patient improved symptomatically. However, the patient didn't develop any other skin manifestations subsequently.

Discussion

Malaria is an endemic disease in India. India is still facing a major health threat due to the malaria. In 2015, 1.13 million positive cases have been reported in India.^[4] For the treatment of malaria, Chloroquine is in use since 1940s. Till now it is very effective, cheap and reliable drug for the treatment of malaria.^[5] In India except some states which shows resistance to chloroquine, all other states are using chloroquine as the first line drug for the treatment of *Plasmodium falciparum*.^[4] The chloroquine is an oral drug and well absorbed from the gastro intestinal tract. Many theories have been proposed for the mechanism of action of the chloroquine. It is proposed that the chloroquine acts by interfering with the breakdown of the heme molecule. The drug enters the cell and concentrate in the food vacuoles, where it binds with the heme molecule. During the breakdown of hemoglobin, the drug is released and disrupts the sequestration of the heme molecule. Thus, due to failure of heme inactivation and due to toxicity of the heme drug complex, the parasites are destroyed by oxidative damage.^[6,7] Chloroquine not only used in the treatment of malaria, it is used to treat various diseases like amoebic liver abscess, systemic lupus erythematosus, rheumatoid disorders like rheumatoid arthritis as a disease modifying antirheumatic drugs, Porphyria cutanea tarda which acts by removing the excess porphyrin from the liver and in the treatment of the Q-fever.^[7-9] The most common adverse drug reactions seen after the intake of chloroquine is gastro intestinal symptoms like nausea, vomiting, abdominal pain and also anorexia. These symptoms can be decreased by consuming the tablets with the food intake. Chloroquine causes central nervous symptoms like headache, blurring of vision, psychosis, and seizures. In the blood, chloroquine may lead to hemolysis in glucose-6-phosphate dehydrogenase deficient patients and agranulocytosis. Cardiovascular adverse effects like QRS widening, T-wave abnormalities and hypotension will occur. On long-term administration, it leads to ototoxicity, retinopathy, myopathy, and peripheral neuropathy. The chloroquine will lead to cardiac and respiratory arrest if it is given as rapid large intramuscular or intravenous injection.^[10]



Figure 1: Urticarial lesions after the intake of chloroquine in the left arm



Figure 2: Urticarial lesions seen in the left anterior shoulder



Figure 3: Urticarial lesions seen in the left posterior shoulder

Chloroquine is contraindicated in patients with psoriasis as it may precipitate an acute event and it should be used very cautiously in patients with liver and renal disorders.^[10] In searching the review of literature, no case has been reported as urticaria induced by chloroquine. There are many treatment

options available for the management of urticaria. The antihistamines are the first line drug in the management. The second line drugs include tricyclic antidepressants like doxepin, montelukast, prednisolone/corticosteroids and sulfasalazine can be used. Methotrexate, cyclosporine, omalizumab, and intravenous immunoglobulin are the third line of drugs in the management. Intravenous immunoglobulin at the rate of 0.4 g/kg for 5 days and plasmapheresis can be used in the treatment of autoimmune urticarial.^[11] So, the clinicians should keep in mind regarding this adverse effect and manage it effectively.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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