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Dapsone agranulocytosis in a leprosy patient

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Summary Dapsone-induced agranulocytosis is a rare adverse effect. There are various reports of agranulocytosis in patients treated with dapsone for malaria prophylaxis and other dermatological diseases. However, this adverse reaction in leprosy is not often encountered. We describe agranulocytosis in a young patient who was taking dapsone (100 mg) for borderline–tuberculoid leprosy in a rural environment.

Introduction

Since the drug was first introduced in 1941, 73 cases of dapsone-induced agranulocytosis have been reported, including our case.[1] Dapsone agranulocytosis has been described in the chemoprophylaxis of malaria,[2,3] dermatitis herpetiformis,[4–6] granuloma annulare,[7] 'dermatitis',[8] and recently in leukocytoclastic vasculitis.[9]

There have not been many studies on agranulocytosis in patients being treated with dapsone for leprosy. Available literature reveals only 3 case reports[10–12] of dapsone associated agranulocytosis in leprosy patients. We report a case of dapsone agranulocytosis in a young female who was taking dapsone (100 mg) unsupervised for borderline–tuberculoid leprosy in a rural environment.

Case history

A 25-year-old female presented with a high grade fever, with chills, vomiting and weakness, which had lasted 2 weeks—a physical examination revealed a toxic, ill looking, febrile (39°C) patient with a pulse rate of 120/min. She was pale, had multiple shallow ulcers over the tongue and the buccal mucosa. There were a few purpuric spots over the body, and she also suffered from hepatosplenomegaly. All other systems were normal.

The patient had hypopigmented anaesthetic macules over the dorsum of the left foot with poorly differentiated margins. The left popliteal nerve was thickened and tender.

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She had been diagnosed as having borderline–tuberculoid leprosy 8 weeks before her admission and was started on dapsone (100 mg daily). She had discontinued the drug when she commenced the fever.

Investigations on admission showed the following values: Hb-7·1 g/dl, leucocyte count $0{\cdot}6\times10^9$/l. A differential count revealed occasional lymphocytes with an absence of polymorphs. Platelets were adequate. The blood smear showed normochromia and poikilocytosis with few macrocytes. Malarial parasites, sickled RBCs, and G_6PD deficiency were not present. Bone marrow tap from manubrium sterni revealed hypocellular marrow with absent myeloid series. Megakaryocytes and erythropoiesis were normal.

Biochemical parameters were blood urea 47·1 mmol/l, serum creatinine 167·7 μmol/l, serum bilirubin 109 μmol/l (conjugated 49·6 μmol/l, unconjugated 59·8 μmol/l), AST 88 μ/l and ALT 80 μ/l. Venous blood cultures grew *Pseudomonas aeruginosa*. A skiagram of the chest was normal. The patient remained critically ill for about 15 days. She was managed with barrier nursing, cephotaxime and gentamicin, metronidiazole and blood transfusion. On the 15th day, she started showing an improvement; the total leucocyte count improved to 2×10^9/l which steadily rose to 33×10^9/l on the 26th day, indicating a leukaemoid reaction during the recovery phase.[8] She was discharged on the 31st day, after a complete recovery. The total leucocyte count was 12×10^9/l; the differential was polymorphs 72%, lymphocytes 21%, and eosinophils 3%. Repeat bone marrow aspiration showed hypercellularity with increased early granulopoiesis, normal erythropoiesis and megakaryocytosis.

Discussion

Dapsone agranulocytosis is a rare complication. In 1970 Ognibe[3] reported agranulocytosis in 16 US soldiers in Vietnam who were on 25 mg dapsone as chemoprophylaxis for malaria. Friman *et al.*[2] reported the incidence as 1 : 10,000 to 1 : 20,000 in US soldiers who were on chemoprophylaxis for malaria with maloprim. In 17 years (1972–1988) only 7 cases of agranulocytosis associated with the use of dapsone for dermatitis herpetiformis were reported by Hornsten *et al.*[5] Recently it has been reported in a patient with granuloma annulare[7] and leukocytoclastic vasculitis.[9] In only 9 of 72 cases of agranulocytosis was dapsone the only medication taken.[5–8,10–12] Our patient was taking dapsone as the sole therapy.

Why is this complication so rare in leprosy? Obviously the dapsone dose has no relation to this adversity. There has been only 3 cases of dapsone-induced agranulocytosis reported in patients treated for leprosy,[10–12] although millions of patients are treated each year. Furthermore, the daily dose (25 mg) given to the US soldiers who developed agranulocytosis is lower than the daily dose (50–100 mg) given to most leprosy patients.[3] The reaction is purely idiosyncratic rather than dose-dependent and is observed in immunologically hyper-responsive conditions. It is possible that the risk is linked to the type of disease treated, rather than the dose. Hornsten *et al.*[5] suggest that there is an interaction between the drug and the patient's immune system. Dermatitis herpetiformis and granuloma annulare are autoimmune diseases characterized by immunologic hyper-responsiveness[13] and there we found agranulocytosis to occur. Leprosy is a disease in which immunologic reactivity[14] in some aspects is compromised

and agranulocytosis is rare. Borderline–tuberculoid leprosy, being more immunologically responsive, is susceptible to have agranulocytosis.

It would seem wise to keep any new leprosy patient under close observation after initiating treatment, since reactions to dapsone commonly occur in the first weeks to months of taking dapsone. Patients should be advised to report immediately if they develop fever, chill and sore throat as these could be due to Leucopenia, which may progress to agranulocytosis. It is wise to monitor haemoglobin or haematocrit levels and obtain white cell counts weekly during the first 2 months of therapy.

In managing patients the drug should be stopped and cultures of blood, sputum and throat should be taken. The common organisms which causes sepsis in these patients are pseudomonas *E. coli*, *Proteus* and *Staphylococcus aureus*. Initial treatment with aminoglycosides, cephalosporins and metronidazole are recommended. Barrier nursing and good oral hygiene are also advised.

Finally, although leprosy can be managed by nonspecialists in a rural environment, a careful and cautious observation on drug toxicity and reaction should be carried out.

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