Dapsone Maculopathy

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After the injection of about 10 gm of dapsone, a 38-year-old male showed a whitish-yellow patch in the macular region of both eyes, with decreased visual acuity of the counting finger in the right and 0.04 in the left eye. Two weeks after the start of systemic steroid therapy the patch disappeared, and on follow-up at 11 months, visual acuity was 0.02 in the right and 0.08 in the left eye, with macular degeneration and foveal nonperfusion. This retinal damage seems to be ischemic in origin and to be caused by a combination of acute severe peripheral hypoxemia and the vascular obstructive effect of red cell fragmentation resulting from massive hemolysis.

Key words: dapsone, hemolysis, ischemia, systemic steroid

INTRODUCTION

Dapsone (4,4-diaminodiphenylsulphone) has been used for the treatment of leprosy, dermatitis herpetiformis, and pneumocystis carinii pneumonitis, and ocular side effects have rarely been reported.1,2 We report a case of macular ischemia due to an overdose of dapsone.

CASE REPORT

In April 1996, a 38-year-old man, who since 1990 had been treated for chronic hepatitis, was referred to Chonnam University Hospital after the ingestion of 10gm of dapsone in a suicide attempt. His appearance was cyanotic and he had undergone gastric lavage at a local clinic. The results of blood analysis were as follows: total hemoglobin content was 6.9 gm/dl (normal range: 13 to 18 gm/dl); methemoglobinemia, 34% (normal range: below 3%); alkaline phosphatase, 153 unit/l; aspartate aminotransferase, 765 unit/l; alanine aminotransferase 171 unit/l; total bilirubin, 12.7 mg/dl; indirect bilirubin, 7.2 mg/dl, and lactate dehydrogenase, 1,980 unit/l. Glucose-6-phosphate dehydrogenase was not deficient. Due to massive intravascular hemolysis, five units of packed red blood cells were transfused, and severe methemoglobinemia was treated with methylene blue and ascorbic acid.

Because of gradually decreasing visual acuity of counting finger in the right and 0.04 in the left eye, an ophthalmologic examination was performed three weeks after ingestion of this massive overdose. The anterior segment and vitreous of both eyes were normal. On biomicroscopic examination with dilated pupil, a symmetrical whitish-yellow patch with a geographic border and the fovea at its center was seen in the macular region of both eyes (Figs. 1A & B). There was no retinal edema, hemorrhage or exudate and the optic disc was normal. Fluorescein angiography showed abrupt termination of the arterioles and minute late staining of fluorescein dye in the foveal capillary wall (Figs. 1C & D).
Methylprednisolone (250mg) was intravenously injected four times a day for three days. This was followed by oral prednisolone (60mg) daily for eleven days, and a reduced dosage was then administered for one month. Five weeks after admission to our hospital, the whitish-yellow patch disappeared and visual acuity slightly improved to 0.02 in the right and 0.08 in the left eye. This patient’s general condition also improved and except for an alkaline phosphatase level of 94 unit/L, laboratory findings were normal. Four weeks after the start of methylprednisolone therapy, however, a non-severe similarly-shaped macular lesion reappeared and then disappeared within two weeks. On follow-up at 11 months, visual acuity was unchanged, but the retinal pigment epithelium of the macula had degenerated (Figs. 2A & B). Fluorescein angiography showed fewer perfused foveal capillaries (Figs. 2C & D). Visual evoked potential was measured; there was no response in the right eye and in the left, this was delayed.

DISCUSSION

Dapsone usually acts bacteriostatically, but the mechanism involved has never been fully elucidated; it probably involves the inhibition of folic acid synthesis in susceptible organisms, and there are serious side effects. The drug’s therapeutic dosage is usually 100 to 200 mg/day, and the most
frequent adverse effects are dose-related hemolytic anemia and tissue hypoxia induced by methemoglobinemia. In most patients whose daily dose of dapsone is 200 mg or more, hemolysis occurs. Symptomatic anemia occurs only occasionally, and this may be 7-14 days after the ingestion of an overdose.\(^2\) In the elimination process, monoacetyl and diacetyl derivatives, as well as hydroxylamine dapsone form in the liver.\(^3\) Accordingly, patients with hepatic dysfunction who are deficient in glucose-6-phosphatase may be susceptible to dapsone toxicity.\(^4\)

Fragmented red cells are regularly seen in patients on dapsone, particularly at dosage levels of 100mg or more, but the cause is unclear.\(^5\) It has been suggested that red cell fragments resulting from massive hemolysis may obstruct blood vessels of small caliber and considerable length, such as macular capillaries.\(^2\) In a patient who had ingested excessive dapsone, Kenner et al\(^2\) observed that the macular and paramacular retina was yellow-white, with no macular edema or serous retinal detachment. The patient complained of blurred vision two weeks after ingestion, and fluorescein angiography revealed nonperfusion in the region of the discolored retina, with abrupt termination of the vessels. After systemic prednisolone therapy for five weeks, visual acuity improved to 6/18 in each eye. In the present case, the findings were similar to those of Kenner et al; fluorescein angiography revealed abrupt termination of the arterioles, dye staining of the foveal capillary wall in the late stage.

Fig. 2. (A-B) Change was seen in the retinal pigment epithelium in the macular region of both eyes. (C-D) Fluorescein angiography showing a reduced number of perfused capillaries.
and a decrease in the number of perfused foveal capillaries. This appears to suggest that there was vascular obstruction caused by red cell fragments.

This retinal damage seems to be ischemic in origin, and to be caused by a combination of acute severe peripheral hypoxemia and the vascular obstructive effect of red cell fragmentation resulting from massive hemolysis. A massive overdosage of dapsone thus causes ischemic retinopathy and optic neuropathy, and leads to permanent visual loss. We therefore believe that before dapsone therapy, all patients should be screened for the presence of glucose-6-phosphate dehydrogenase deficiency and hepatic dysfunction; if the administration of dapsone leads to blurred vision, macular function tests and fluorescein angiography should be performed. In addition, patients should be warned of the danger of accidental ingestion.

REFERENCES