Clinical Reports

A case of ocular toxicity to ethambutol – an idiosyncratic reaction?

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Summary: Optic neuritis, a well known adverse effect of ethambutol, is related to the dose and duration of the therapy. The patient described here developed rapidly progressive deterioration of vision after only 3 days of treatment with ethambutol. Such a case has not been reported before and it is suspected that this was an idiosyncratic reaction.

Introduction

Optic neuritis is reported to occur in 5% of patients receiving 25 mg/kg of ethambutol per day and in less than 1% of patients receiving a daily dose of 15 mg/kg (Mandell & Sande, 1975). The shortest duration of therapy after which the visual disturbance has been reported was 26 d in the series of Kass (1965). The patient described here was most unusual in that the onset of visual disturbance occurred only 3 d after starting treatment with ethambutol and the vision continued to worsen despite discontinuation of the drug.

Case report

A 26 year old male Jordanian was admitted in December 1983 with clinical, radiological and bacteriological features of pulmonary tuberculosis. He had had no significant illnesses in the past and in particular had not suffered from any eye troubles. He was non-diabetic and his renal and liver function tests were normal. He had smoked 40 cigarettes a day for about 10 y. He weighed 52 kg.

He was put on rifampicin 450 mg/d, isoniazid 300 mg/d, ethambutol 800 mg/d and pyridoxine 50 mg/d. After only 3 d, he started experiencing blurring of vision and narrowing of his visual field as if looking through a pipe. There was no pain or redness

of the eyes. When he contacted his physician after 6 d of therapy with ethambutol, he was found to have bitemporal hemianopia, which was confirmed by perimetry (Figure 1). His pupils reacted sluggishly and vision was 6/60 on both sides but the colour vision was intact. Ethambutol was stopped immediately. A computed tomographic scan of the brain was normal and fluorescein angiogram showed no abnormality. Considering the possibility of an allergic reaction, 40 mg of prednisolone daily was given for 15 d without improvement. His vision continued to deteriorate and 2 weeks after the onset there was no pupillary reaction, light perception or visual evoked response.

About 1 month after the beginning of the visual problem, he was started on 1000 µg of hydroxocobalamin intramuscularly. Four days later he reported perception of light in both eyes and a definite pupillary reaction was noted. His vision continued to improve and after 2 weeks of therapy, he could read large print and walk about without difficulty.

The patient was discharged home with the advice to continue isoniazid, rifampicin, pyridoxine and hydroxocobalamin. Inadvertently, in the local clinic his therapy was changed from hydroxocobalamin to cyanocobalamin and the vision started deteriorating again. In one month's time he once more became completely blind. A reassessment at this stage did not reveal any neurological symptoms and signs and a computed tomographic scan was again normal. He had not taken any other drugs apart from cyanocobalamin and antituberculous drugs. A repeat course of hydroxocobalamin injections failed to produce any improvement.

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Figure 1 Perimetry: the shaded areas show loss of vision.

More than 1 y later he remains completely blind with no perception of light. The pupils are dilated with no reaction. The discs show optic atrophy on both sides.

Discussion

The patient described here developed rapidly progressive deterioration of vision only 3 d after the beginning of standard antituberculous drugs in the usual doses. The presence of the bilateral symmetrical field defects, the absence of other neurological signs and normal scan rule out the possibilities of multiple sclerosis, tuberculous meningitis, brain tumour or hydrocephalus.

Optic neuritis which can occur with isoniazid, can be prevented by as little as 6 mg of pyridoxine per day (Mandell & Sande, 1975). Our patient had received 50 mg/d of pyridoxine from the start of his antituberculous therapy. Although exudative conjunctivitis secondary to rifampicin has been described (Cayley & Majumdar, 1976), optic neuritis has never been reported. It is, therefore, most probable that ethambutol was the drug responsible for the visual problem in our patient.

The onset of the visual disturbance has ranged from 26 d to 317 d (average 151 d) after the commencement of the therapy in one series (Kass, 1965). Our patient, who was started on a daily dose 15 mg/kg of ethambutol, was most unusual in that the symptom of visual disturbance was noted only 3 d after the beginning of the therapy. Pre-existing renal disease, liver damage or diabetes pre-dispose to visual disturbance (Spiteri & James, 1983) – none of which were present in our patient.

The rapid onset of the visual disturbance soon after the institution of the therapy and progressive deterioration of vision after discontinuation of the drug are suggestive of an idiosyncratic reaction. Hypersens-

sitivity to ethambutol, manifesting as a systemic reaction, has been reported by Kerremans & Majoor (1981) but ocular manifestation as part of an allergic reaction has not, as far as we know, been described previously.

Most of the authors who describe the ocular toxicity of ethambutol advise no active treatment except discontinuation of the drug (Mandell & Sande, 1975; Girling, 1982). In one series (Harada *et al.*, 1979) however, 9 cases of ethambutol toxicity were treated by stopping the drug and administration of vitamin B₁₂. This measure brought about cure in 61% of the eyes involved. In our patient, a most interesting sequence of events occurred. For about a month after stopping ethambutol, there was no change in the vision. Improvement began on the fourth day of starting treatment with hydroxocobalamin but deteriorated again when the therapy was changed to cyanocobalamin.

The sequence of events such as described in our patient has not been reported previously. It is difficult to say whether the partial and temporary improvement that occurred was related to the natural history of the disease or the therapy. Nevertheless, the rapid onset of recovery seemed to have been related to the institution of therapy with hydroxocobalamin and the equally fast deterioration of vision again seemed to have coincided with changeover of the therapy from hydroxo- to cyanocobalamin. It has been reported by Chisholm *et al.* (1967) that in tobacco-induced optic neuritis hydroxocobalamin is more useful than cyanocobalamin and one wonders whether such was the case here.

It seems that ocular toxicity of ethambutol can occur within days and not necessarily after months of treatment. It is also, perhaps, justified to treat such patients with hydroxocobalamin. Although most of the patients recover their vision with no active treatment, it is possible that hydroxocobalamin might initiate and hasten the process of recovery.

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