CASE REPORT

Bilateral Optic Neuritis due to Isoniazid (INH)

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Optic nerve involvement is a rare side effect of isoniazid (INH) and has not been described in children. We describe this adverse reaction in a 10-year-old boy, who was treated for tuberculous meningitis. The patient showed almost complete resolution following withdrawal of INH and administration of pyridoxine and steroids.

Key words: *Drug toxicity, Isoniazid, Optic neuritis, Tuberculosis.*

Isoniazid (INH) has been rarely implicated in the causation of optic neuritis in adults(1-4). An extensive literature search failed to locate any report of such an association in the pediatric age-group. It is believed that side-effects of INH are less common and less severe in children(5) and hence, pyridoxine is not routinely prescribed to children receiving INH(6). We report a case of acute loss of vision in a child receiving INH as part of treatment for CNS tuberculosis.

CASE REPORT

A 10-year-old boy born of non-consanguineous union was brought to the pediatric emergency department with loss of vision in both eyes for two days. It started as blurring of vision with an inability to recognize faces and progressed to complete blindness. Physical examination revealed no perception of light with a sluggish, ill-sustained pupillary response to light in both eyes. Fundoscopy revealed bilateral hyperemic optic discs and blurred nasal margins, venous engorgement, cup fullness and a single flame-shaped hemorrhage in the right eye. No other abnormalities were noted on physical examination. The child was receiving four drug anti-tuberculous therapy (ATT); consisting of INH 5mg/kg/d, rifampicin10 mg/kg/day, pyrazinamide 25 mg/kg/day daily, all taken once daily per orally; and streptomycin 20 mg/kg/d once daily intramuscular) for tuberculous meningitis and phenytoin (5mg/kg/d div three doses, per oral) for the past one month. The disease was diagnosed on the basis of prolonged fever, seizures, positive tuberculin test, hilar lymphadenopathy, history of tuberculous contact and characterstic CSF picture suggestive of tuberculous meningitis. CT brain was normal.

At presentation, MRI scan showed bilateral retrobulbar neuritis (left > right). EEG showed generalized slow activity with 5-6 Hz baseline frequency. HIV ELISA was negative. The child was managed with discontinuation of INH, administration of vitamin B_1 (500 mg IM), vitamin B_6 (25 mg IM), vitamin B_{12} (0.5 mg IM) and dexamethasone (2 mg once daily IM). The child was also given 100 mg of vitamin B_6 orally since admission. Methylprednisolone (30mg/kg/d once daily for 5d; IV) was given after two days of dexamethasone therapy. Visual perception improved gradually with resolution of disc swelling and papilledema. No tubercles were seen on fundoscopy. At the time of discharge (day 18), he was able to count fingers up to four feet using his right eye though with his left eye he could only perceive hand movements. The papillitis had resolved bilaterally and the fundoscopy was normal. After two months, visual acuity was 6/9 in the right eye and was 6/18 in

the left eye. After 3 months, there was complete restoration of visual acuity to 6/6 in both eyes. In view of withdrawal of INH, an important first-line drug, the child was given ATT consisting of rifampicin, pyrazinamide, ofloxacin, clarithromycin and streptomycin. After completing the intensive phase he continued to receive rifampicin, ofloxacin and clarithromycin. Prednisolone was given at full doses for 6 weeks and then tapered over the next 6 weeks. The Naranjo algorithm for adverse drug reaction causality assessment(7) yielded a score of 6, suggesting that the adverse drug reaction was probably related to INH.

DISCUSSION

Optic neuritis due to isoniazid has been described sporadically among adult patients(2-4). These reports indicate that the neurotoxic effects of isoniazid may be enhanced by co-morbidities like end stage renal disease requiring hemodialysis(8,9) or malnutrition(3). The onset of visual symptoms generally occurs within ten days of starting anti-tubercular therapy(2,4) but may occur even two to three months after initiation of therapy(2,3,8). Detailed ophthalmoscopic examination reveals a bilateral and often an unequal decrease in visual acuity, loss of color vision, bitemporal hemianopsia(2) or centrocentral scotomata on perimetry(3). Fundo-scopy generally shows bilateral disc hyperemia with blurred borders. Rarely, the fundoscopy may be normal(2). Methylprednisolone is considered useful, as was seen by the visual improvement in our patient. However, the recovery is often incomplete without discontinuation of INH(8). Some reports indicate that the use of oral prednisone is not useful(4). Discontinuation of INH is associated with improvement of the visual dysfunction as early as four days after discontinuation(4,9) with complete recovery usually taking four weeks(1,4,9) but rarely may take up to six months(3,8). In some cases a residual bitemporal hemianopsia may persist. Reintroduction of isoniazid is associated with a quicker onset of optic neuritis but is still reversible. Failure to stop INH may eventually lead to optic atrophy(2-4).

The mechanism of optic neuritis due to INH can be considered to be an extension of the etiology of peripheral neuritis, postulated to be due to INH-induced loss of pyridoxine in the urine or isoniazid-blockade of pyridoxal phosphate synthesis which depletes neurotransmitters(3). However, there are reports of neuritis even in patients receiving pyridoxine supplementation(3,9).

It is unlikely that the boy had tuberculous optic neuritis, as this rare condition is usually associated with chorioretinitis, uveitis or military tuberculosis(10). Our case underscores the fact that optic neuritis can occur in children receiving INH. It is necessary that practitioners watch children receiving INH carefully for visual symptoms and take prompt actions that include discontinuation of INH and supplementation of pyridoxine in equimolar doses. It is also vital that such cases are reported through active pharmacovigilance programs and medical journals, so that recommendation of not supplementing ATT with pyridoxine can be reviewed on the basis of fresh evidence.

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