Acute, persistent quinine-induced blindness

A case report

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Summary

Quinine-induced blindness arising during empirical treatment for malaria in a young man is reported. The condition was noteworthy because it was total and permanent, which is at variance with other published reports. The condition usually disappears within minutes to weeks, but persistent deficits tend to be mild and are rare. Although quinine is an essential anti-malarial agent, physicians should be fully aware of possible side-effects.

Case report

A 22-year-old man presented to a peripheral hospital with a 2-day history of rigors, abdominal cramps, lumbar pain, nausea, vomiting, dysuria and dizziness. He was given oral quinine sulphate 600 mg and tetracycline 250 mg because malaria was suspected clinically. The patient vomited and both drugs were re-administered. He then became confused and disorientated for time and place. Drowsiness, bitemporal headache, persistent abdominal cramps, malaise, tinnitus and perception of yellow spots in the visual field occurred. During the next 12 hours, 3 additional doses of quinine and tetracycline were administered. On awakening next morning, the patient was totally blind. No other drugs were prescribed, and the patient denied having ingested Datura stramonium seeds (Jackson weed).

On admission to 1 Military Hospital, physical examination revealed a young, seemingly healthy, adult male with a regular pulse rate of 60/min, blood pressure of 140/98 mmHg and oral temperature of 37°C. Peri-orbital swelling and conjunctival injection were observed. The pupils were widely dilated and responded poorly to light. Both retinas were pale and oedematous on fundoscopy. The patient's visual acuity was severely impaired, but he could still perceive movement. The quinine was discontinued and pyrimethamine 75 mg plus sulphadoxine 1 500 mg (3 Fansidar tablets) was administered as a stat dose, since the diagnosis of malaria could not be dismissed.

Fundoscopic examination at this stage revealed severe arteriolar spasm. Nifedipine (10 mg 3 times a day) and oral prednisone (60 mg/d) were administered. On the second hospital day the visual acuity appeared to be 6 and 7,5 in the right and left eyes, respectively. Poor accommodation and light reflexes were present and the pupillary diameter had decreased. Gonioscopy revealed pale retinas, severe arteriolar spasm and areas of haemorrhage.

The serum urea, creatinine and electrolyte values were normal while a full blood count was notable only for a white cell count of $15,6 \times 10^9$/ml; liver function tests and urinalysis were within normal limits. Two sets of slides, taken on different occasions, for testing for malaria, and repeated blood culture and viral serological tests (including for Rift Valley fever) were all non-contributory.

Visual evoked potential (VEP) tests and electroretinography (ERG) were performed on three occasions at approximately monthly intervals. The first ERG was performed 9 days after admission and was consistent with retinal (particularly cone) and optic nerve dysfunction secondary to macular damage. The second ERG showed progression of rod and cone deterioration, while the third ERG remained unchanged from the second.

Fluorescein angiography was performed 20 days after admission and showed slight disc illumination and persistent arteriolar spasm.

One week after admission to 1 Military Hospital, nimodipine (a centrally acting calcium antagonist that dilates cerebral vessels; not registered for use in this country at the time) 1 mg/h was infused for 2 hours, followed by 2 mg/h for 40 hours. Oral nimodipine 60 mg 4-hourly was administered for a further 72 hours. At this stage arteriolar vasospasm had decreased, but no objective evidence of visual improvement was demonstrable. Severe, virtually total, visual impairment of vision has persisted.

Discussion

This case demonstrated many of the features of quinine-associated blindness, but differed from other reported cases of ocular quinine toxicity in that severe, persistent total bilateral blindness is considered to be extremely rare.[1]

Systemic toxicity occurs in approximately 1% of patients to whom quinine is given. Ocular quinine toxicity is a well-known problem, but is not dose-related. It is, however, more common where doses in excess of 4 g have been administered,[2] but has occurred with as little as 0,13 g.[3] The fatal oral dose for adults is somewhere between 3 g and 8 g.[2,3] Toxicity usually occurs when plasma concentrations exceed 5 - 8 mg/l[4] and manifests as skin, visual, inner ear, central nervous system and gastro-intestinal disturbances.[5] The skin disturbances consist of flushing and diaphoresis. Cases of mild-to-moderate toxicity are characterised by epigastric pain, nausea, vomiting, clouded vision, tinnitus, weakness, drowsiness, confusion, seizures, and occasionally blindness.[6] In severe cases, a deep coma and respiratory and circulatory arrest may occur.[2,5,6] Renal failure and haemolysis (with anaemia) may also occur. Death is usually due to depressed myocardial contractility and cardiac dysrhythmia.

Ophthalmic quinine toxicity consists of disturbed colour perception, photophobia, diplopia, night blindness, scotomata, mydriasis with poorly reactive pupils, iris atrophy, total blindness and clouded or flickering vision.[1,6] Total blindness may be delayed by several hours.[1,2] Amblyopia is often first noted the morning after the ingestion of quinine[6] and usually lasts for minutes to weeks, but virtually total recovery usually occurs. Pupillary dilation (often with absent light reflexes) is proportional to the degree of visual impairment. Severe to

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total impairment of light perception,[3] hippus[3] and loss of accommodation[6] may occur. Fundoscopic findings may vary from normal[3] to those compatible with pronounced retinal artery constriction and optic disc and retinal oedema.[1,5,7] Optic atrophy and vasospasm may be demonstrable only days to weeks later.[3,6] Brownish, macular specks may be present but usually disappear.[8] In a study of 165 patients with acute ophthalmic quinine toxicity, plasma quinine levels were usually higher than 15 mg/l during and 10 mg/l 10 hours after ingestion[1] but did not accurately predict retinal toxicity.

ERG studies at the onset of amblyopia are normal according to some authors[9] and abnormal according to others.[3,7] The paucity of ERG changes in some studies is probably due to the late stage at which studies were performed, since the ERG tends to return to normal as vision improves. Electro-oculo-graphic (EOG) changes tend to parallel the decline of visual acuity[9] and suggest associated retinal pigment epithelium involvement.[9] VEP studies[6] demonstrate bilateral wave-form and latency abnormalities suggesting nerve fibre layer and optic nerve conduction abnormalities.

Serial visual field examinations demonstrate progressive, central, concentric return of vision — occasionally with persis-tent tunnel vision or central scotomata.[1,5] Of 165 reported patients with acute quinine poisoning, 19 had persistent visual defects of which 11 were peripheral field defects, 5 central scotomata, 1 defective colour vision and 2 monocular blind-ness.[1]

The pathogenesis of the amblyopia is unknown, but may be due to ischaemic neuroretinal damage secondary to retinal vasospasm,[4] as is supported by the initially normal ERG. Alternatively direct retinal and neural quinine toxicity may occur,[3,4,8] as is suggested by the initially normal fundus in patients with early ERG abnormalities. EOG and VEP studies (in both patients and experimental animals) have demonstrated retinal ganglion, nerve fibre and rod and cone atrophy. The relative importance of these mechanisms is uncertain.

Discontinuation of quinine therapy when amblyopia occurs is imperative.[8] Various therapies have been advocated. Many cases of quinine-induced amblyopia resolve spontaneously ren-dering evaluation of therapeutic options impossible. Thera-peutic modalities that have been suggested include stellate ganglion blockade,[10] intravenous administration of ACTH, use of vasodilators,[5] and enhancement of quinine elimination. Quinine elimination is putatively increased by forced acid diuresis,[11] haemodialysis, peritoneal dialysis and plasma exchange.[2] Charcoal haemoperfusion[7] decreases serum levels but does not significantly decrease total body quinine after tissue distribution has been completed.[5] Nevertheless dramatic, albeit transient, clinical improvement has occurred in haemo-perfused patients. However, symptoms may return within hours due to quinine redistribution and release.[7] Haemo-perfusion may be repeated until the patient is stable and is of potential use early in the course of events while high serum levels are present,[5] since there is a correlation between high serum levels and quinine-induced blindness.[1] Since no evidence of significant influence by any of these options has been demonstrated, it may well be true that only supportive therapy may be necessary.[1]

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