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Sir,

Can vitreous haemorrhage indicate non-accidental injury if mild retinopathy of prematurity is present?

Retinal haemorrhage is the most common form of intraocular haemorrhage in infants with non-accidental injury (NAI), while vitreous haemorrhage (VH) is the least common.[1-3] We report a case of NAI with VH as the presenting sign in a baby with mild retinopathy of prematurity (ROP).

Case report

A 755 g, 27 week gestation Chinese female baby was born at home in Hong Kong to an unmarried teenage mother, who did not attend any antenatal visit. This was her first child and the mother was unaccompanied during the whole labour process, the period of which was unknown. The baby arrived at the hospital about 20 minutes after birth. She was intubated and received oxygen of FiO_2 of 21–90% for 35 days. The infant was otherwise well and was screened for ROP at 5 weeks of age.

Posterior zone 2 vascularisation, without ROP, was noted in both eyes. She was examined every 2 weeks. Two months later, stage 2 zone 2 disease was present in the left eye while stage 3 zone 2 disease involving an area of 3 clock-hours was present in the right eye. No plus disease was present. She was discharged but then defaulted follow-up. A month later, she returned and stage 2 zone 2 disease was present in both eyes. The retinal periphery of both eyes was well seen with scleral indentation. Additionally, there was fresh VH in the left eye that originated from the temporal ridge at the 2 and 4 o'clock positions and covered the temporal arcades. The VH covered an area of about 8 disc areas. Apart from the two areas where the VH originated, the other part of the ridge was well seen without any stage 3 disease. No retinal haemorrhage was found. Optic disc and retinal vessels looked normal. Two weeks later, similar VH in the right eye was found. In the left eye, the VH remained the same but two small superficial retinal haemorrhages were found in the nasal retina. The ROP status remained the same. The two retinal haemorrhages resolved 4 weeks later.

In view of the unusual presentation, detailed physical examination, investigations including blood clotting profiles, computed tomography of the brain and a skeletal survey were performed and were all normal. The baby lived with her parental grandparents, both of whom were 52 years old, in a government-subsidised flat. The baby's paternal grandmother, who took care of the baby most of the time, was interviewed. She revealed to us that there were episodes of facial bruising when the baby returned from her parents. However, there was no independent corroboration of these episodes. NAI was strongly suspected. A police investigation was conducted which revealed no other evidence of physical abuse. All the family members claimed that the genetic father of the child was beyond doubt, hence a genetic study was not performed to confirm that. A paediatrician, psychiatrist, social worker and the police were involved in the investigation in this case. A case conference was held and concluded that this was a case of child abuse, although no definite abuser was found.

Comment

Infants with mild ROP rarely develop VH.[4] If conditions such as birth trauma, bleeding tendencies and Terson's syndrome[5] are excluded, one may have to think about the possibility of NAI. VH is the least common form of intraocular haemorrhage in infants with NAI.[3] However, as illustrated in our case, this may not be true in the presence of ROP. In ROP, there are active-growing immature vessels extending towards the peripheral avascular retina. These vessels tend to bleed more easily than the mature ones. In infants, the vitreous body is firmly adherent to the underlying retina, and this adhesion may be even stronger over the ridge in ROP. Any relative movement between them, such as acceleration–deceleration in NAI, may rupture these immature vessels and cause VH. When the severity of violence increases, even the relatively more mature retinal vessel may also bleed and cause retinal haemorrhage. Since no intracranial pathology was found in this child, we further suggest that the level of inflicted trauma in this child is below the threshold for ocular and intracranial haemorrhage in a child with a normal retina, but above the threshold for damage to immature blood vessels associated with ROP.

In summary, the possibility of NAI should be borne in mind in mild ROP cases presenting with VH.

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Sir,

Nightmares with topical beta-blocker

The beta-blockers have been the first line of treatment for glaucoma for many years and the standard against which all other treatments have been compared for their pressure-lowering effects. Timolol, like all beta-blockers, has well-known cardiovascular and respiratory side effects and should be prescribed very carefully, especially in elderly patients with diseases affecting these systems. A small minority of patient get central nervous system (CNS) side effects with topical beta-blockers, which have mainly been reported with oral beta-blockers.[1] These include behavioural changes such as confusion, hallucinations, anxiety, disorientation, nervousness, somnolence and other psychiatric disturbances. Nightmares have been reported commonly with oral beta-blockade but, as far as we know, there has been only one previous case published of nightmares with topical ophthalmic beta-blockers and unlike that case our patient experienced these despite the regular practice of punctal occlusion.

Case report

A 61-year-old man diagnosed to have open angle glaucoma with intraocular pressures of 28 and 26 mmHg in the right and left eye respectively was started on brimonidine 0.2% drops but did not tolerate them very well and had an allergic reaction together with stinging on instillation. His past medical history was unremarkable and he was not on any systemic medications at the time of commencement of the topical treatment. As there were no obvious contraindications to the use of beta-blockers he was commenced on 0.5% timolol maleate drops but returned within 3 weeks as he was feeling very tired and lethargic and was having disturbing nightmares. The drops were being instilled at 0800 hours in the morning and at 2000 hours at night with the patient occluding the lacrimal punctum for 30 s afterwards. The nightmares had begun within a week of the treatment and recurred every night, they were obtrusive in nature and the content was more or less the same with detailed recall of the events. The physical examination and a Mini Mental State Examination were normal, and the results of his recent routine laboratory tests including blood glucose, full blood counts, blood urea and electrolytes were within normal limits. There were no other behavioural or psychiatric disturbances and, at this point, as his nightmares could not be linked to his topical medication it was decided to persist with timolol, but the patient came back within a week and was now very distressed by the nightmares. At this point it was decided to change the eyedrops to pilocarpine 2% three times a day. The nightmares stopped promptly and have not returned over the last 6 months while the intraocular pressure is well controlled at 18 mmHg in both eyes.

Comment

A wide variety of adverse central nervous system (CNS) effects have been reported with beta-blockers including bizarre dreams, nightmares, depression, dizziness, tinnitus, headache, somnolence, inability to concentrate and insomnia.[1–3] They occur either immediately after starting therapy or may be delayed for many years and are mainly seen with oral administration. These side effects are mainly dependent on the plasma concentrations, lipid solubility, protein binding and the volume of distribution of the drug. Topical medications can reach significant concentrations in the systemic circulation mainly by absorption through conjunctival veins, lacrimal passages and the vascular nasal mucosa, and the serum concentrations of timolol have been shown to reach levels of 1.39 ng/ml 1 h after ophthalmic administration,[4] sufficient to cause systemic adverse effects. The various methods described to reduce systemic levels, including closure of the eyelids and lacrimal occlusion, have been shown to reduce the serum levels by up to 65%[5] but may still be inadequate to prevent systemic side effects including CNS effects. The brain primarily contains β1 receptors and, depending on their lipid solubility, the beta-blockers may variably block them, but the exact mechanism for the potential CNS and psychiatric side effects with beta-blockers is still not clear and has been ascribed to depressed melatonin levels in these patients.[6] Only a very small number of individual case reports of ophthalmic medications causing CNS adverse effects have appeared in the literature and only one of nightmares with betaxolol,[7] but unlike our patient, the nightmares were stopped by punctal occlusion. In our patient, the onset of nightmares with timolol, absence of other possible