Rare disease

Recurrent vitreous haemorrhage and epidural haematoma in a child with hypofibrinogenaemia

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Summary

A 14-month-old male infant was brought by parents for redness of the right eye of 18 days duration. Exam and B-scan ultrasonography revealed total hyphema, dense vitreous haemorrhage and lens subluxation in the right eye while CT disclosed right small epidural haematoma. The left eye had neither retinal haemorrhage nor disc oedema. There was no sign of shaken baby syndrome. Fibrinogen level in the blood was very low. The parents are first-degree cousins with two family members having hypofibrinogenaemia. Vitreous haemorrhage recurred after surgical intervention resulting in phthisis and loss of vision. Hypofibrinogenaemia needs to be included in the differential diagnosis of ocular haemorrhage and vision loss.

BACKGROUND

Hypofibrinogenaemia can cause irreversible visual loss from recurrent haemorrhage in children and needs to be included in the differential diagnosis of paediatric ocular haemorrhage, leukocoria and vision loss.

CASE PRESENTATION

This 14-month-old male infant born of first-degree consanguineous marriage was brought by his mother for evaluation of right eye redness of 18 days duration that occurred 2 days after fever and vomiting. There was no history of trauma, child abuse or self-mutilation. Family history was significant for hypofibrinogenaemia in an older brother (and cousin) requiring treatment with fresh frozen plasma at age 1 month at the time of diagnosis during circumcision and at two subsequent hospitalisations for epistaxis and scalp haematoma. Physical exam showed no signs of trauma or bruising. Slit lamp exam revealed total hyphema of the right eye with central

corneal staining. B-scan detected dense vitreous haemorrhage (figure 1). Left eye exam was negative for retinal haemorrhage and optic disc swelling.

INVESTIGATIONS

Coagulation profile showed normal bleeding time, prolonged prothrombin time (7 s; reference 0.85–1.15 s) and activated partial thromboplastin time (120 s; reference 27–39 s) with fibrinogen level decreased to <0.6 g/l (reference 1.8–3.5 g/l). CT of brain showed small right epidural haematoma (figure 2) with minimal midline shift and right vitreous haemorrhage with subluxated lens (figure 3).

Figure 1 B-scan shows severe vitreous haemorrhage in the right eye.

Figure 2 Brain CT shows a right epidural haematoma with mild midline shift.

Figure 3 Orbit CT shows subluxated right lens and diffuse vitreous opacities.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for recurrent hyphema, recurrent vitreous haemorrhage and one episode of mild epidural haemorrhage include child abuse (shaken baby syndrome), Terson's syndrome, self-mutilation and coagulopathies. Child abuse and self-mutilation were absent by history and physical exam. Terson's syndrome includes any intraocular haemorrhage associated with intracranial bleeding (usually subarachnoid) and acutely increased intracranial pressure. Terson's syndrome was ruled out by the absence of signs of rapid rise in intracranial pressure (such as swollen optic nerve head), and the absence of ocular haemorrhage in the left eye.

Diagnosis of inherited hypofibrinogenemia was made and fresh frozen plasma infusions were administered. After maintaining a fibrinogen level of 1 g/l the patient was taken to the operating room. Lavage of anterior chamber successfully cleared both the hyphema and the vitreous haemorrhage, because of lens subluxation (figures 4 and 5). There was dense corneal staining of the central 7 mm. The retina was found attached as viewed through the peripheral cornea.

OUTCOME AND FOLLOW-UP

Despite initial weekly fresh frozen plasma therapy, vitreous haemorrhage recurred as early as 4 weeks postoperatively (figure 6). He received thereafter monthly one unit of fresh frozen plasma therapy (450 mg fibrinogen) for a period of 10 months. He ended up with proliferative vitreoretinopathy (figure 7) and phthisis bulbi (figure 8).

DISCUSSION

Retinal haemorrhages occur frequently in shaken baby syndrome, after self-mutilation, following cardiopulmonary resuscitation,¹ and in various blood dyscrasias² such as

Figure 4 At start of surgery there is total hyphema in the right eye precluding seeing any anterior segment details.

aplastic anaemia,³ coagulopathies and protein C deficiency.⁴ Furthermore, other types of bleeding diathesis should be considered in cases with spontaneous or recurrent retinal haemorrhage. For instance, fibrinogen level is a critical factor for bleeding diathesis. Fibrinogen is a 340-kD plasma protein encoded by three genes (FGA, FGB and FGG) clustered on chromosome 4q and involved in the final steps of coagulation as a precursor of fibrin monomers required for the formation of the haemostatic plug.⁵ Both congenital afibrinogenemia and hypofibrinogenemia are rare disorders with clinical manifestations varying from asymptomatic to life-threatening bleeds or thromboembolic events.

Hypofibrinogenemia is an inherited fibrinogen disorder defined by a decreased level of normal fibrinogen (activity and antigen between 0.5 g/l and lower limit of normal range for local laboratory).⁵ The normal plasma fibrinogen concentration is ~1.5–3.5 g/l with a half-life of about 4 days. The exact incidence of congenital hypofibrinogenemia is not known, and inheritance through an autosomal-recessive trait and parental consanguinity is

Figure 5 After anterior chamber lavage, there is central dense corneal staining of the right eye with the corneal periphery clear allowing iris details to be seen.

Figure 6 B-scan 4 weeks after surgery shows recurrence of the vitreous haemorrhage after resolution after surgery.

common among affected families. Treatment options include replacement with plasma-derived fibrinogen concentrate, cryoprecipitate infusion or fresh frozen plasma (10–15 mg/kg) to achieve a fibrinogen level of 0.8–1 g/l. Most subjects with hypofibrinogenaemia need no therapy as long as they are asymptomatic and they do not show signs of bleeding.

Peyvandi *et al*⁶ collected 100 patients with inherited afibrinogenaemia or hypofibrinogenaemia and did not report any ocular haemorrhage: the most frequent bleeding sites were the joints, muscle, gastrointestinal tract, nose, uterus and rarely central nervous system and retroperitoneum. The incidence of ocular haemorrhage in hypofibrinogenaemia is uncertain. There are three case reports in the literature describing paediatric patients with intraocular bleeding secondary to hypofibrinogenaemia. Pathengay *et al*⁷ described bilateral visual loss to 6/24 (20/80) right eye and 6/360 (20/1200) left eye from spontaneous subhyaloid haemorrhage in a 14-year-old girl. Clotting profile showed normal activated partial thromboplastin time and normal prothrombin time with fibrinogen decreased to 0.5 g/l. Visual acuity recovered completely 3 months after

Figure 7 B-scan of the right eye shows thickened choroid and vitreous membranes causing proliferative vitreoretinopathy.

Figure 8 Eight months after surgery, the right eye is small (phthisis) with corneal staining.

cryoprecipitate infusion. Marshman *et al*⁸ described progressive bilateral retinal and vitreous haemorrhage in a 36-day-old premature infant with low fibrinogen levels (0.7 g/l). With observation only, haemorrhages resolved and vision was recorded as 6/120 (20/400) using Cardiff cards at age 1 year. Demir *et al*⁹ described a 3-month-old boy who underwent workup for bilateral leukocoria. He was the victim of second-degree cousins previously diagnosed with congenital afibrinogenaemia (plasma fibrinogen level <0.1 g/l). Eye exam revealed shallow anterior chamber, cataractous lens and vitreous haemorrhage bilaterally. Moreover, B-scan ultrasonography revealed tractional retinal detachment in the left eye in addition to bilateral dense vitreous opacities. Brain imaging also showed bilateral intravitreal haemorrhage and subdural haematomas. Bilateral lensectomy and vitrectomy were performed. Proliferative vitreoretinopathy precluded retinal attachment in left eye. Three years later, the right eye achieved finger counting at 2 m with a contact lens with phthisis bulbi in the left eye.

We presented a case of simultaneous epidural and vitreous haemorrhage secondary to congenital hypofibrinogenaemia requiring surgical intervention to clear out the intraocular haemorrhage. Pars plana vitrectomy was not necessary due to the clearing of the vitreous haemorrhage through the anterior hyaloid defect from subluxated lens. Corneal staining precluded any further intervention. The initial episode one-sided epidural and one-sided vitreous haemorrhage seems related to the Valsalva manoeuvre during vomiting. The cause of subsequent recurrent one-sided vitreous haemorrhage is unknown but may relate to the coagulation problem in the absence of retinal tears (by ultrasound) or preretinal new vessel formation. The presence of a subluxated lens may also cause vitreodonesis (pull on the posterior vitreous face) causing fragile vessels that initially bled after vomiting to rupture again view the poor fibrin sealant in hypofibrinogenaemia.

Inherited fibrinogen disorders should be suspected in children presenting with spontaneous intraocular and/or intracranial haemorrhage especially those with positive family history and/or parental consanguinity as in our case. Child abuse and self-mutilation can have similar clinical manifestations and must be ruled out by detailed

history and thorough physical exam. Our patient did not have any of the above findings which, along with the positive family history, made us suspect a coagulation disorder.

Learning points

- ▶ Retinal haemorrhages occur in shaken baby syndrome, self-mutilation, cardiopulmonary resuscitation and blood dyscrasias such as aplastic anaemia, coagulopathies, protein C deficiency and hypofibrinogenaemia.
- ▶ Frequent bleeding sites in hypofibrinogenaemia are the joints, muscle, gastrointestinal tract, nose, uterus, and rarely central nervous system, retroperitoneum and the eye.
- ▶ Congenital hypofibrinogenaemia is inherited through an autosomal-recessive trait and parental consanguinity is common among affected families.
- ▶ Treatment of symptomatic congenital hypofibrinogenaemia includes replacement with plasma-derived fibrinogen concentrate, cryoprecipitate infusion or fresh frozen plasma.

Competing interests None.

Patient consent Obtained.

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