CASE REPORT

Bilateral large subconjunctival haemorrhages unmasking immune thrombocytopenic purpura during retinopathy of prematurity screening

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SUMMARY

Although thrombocytopenia is known to be associated with pathogenesis of retinopathy of prematurity (ROP), immune thrombocytopenic purpura (ITP) is rare in infancy and not reported to occur with ROP. A preterm infant with aggressive posterior ROP developed bilateral massive subconjunctival haemorrhage after scleral indentation during screening. On evaluation, the infant was found to have severe ITP. Following intravenous transfusion of platelets and immunoglobulin, platelet counts improved and subconjunctival haemorrhage resolved over time. This case highlights the unusual presentation of ITP and also discusses the association of thrombocytopenia with ROP. Ophthalmologists should get prompt haematological work-up of such occurrences.

BACKGROUND

Neonatal thrombocytopenia is commonly associated with retinopathy of prematurity (ROP). Minor subconjunctival haemorrhage may occur during ROP screening with scleral indenter. However, massive haemorrhages are uncommon and not reported in literature. Immune thrombocytopenic purpura (ITP) is rare in infancy. Even in adults, it does not present with subconjunctival haemorrhage. Massive subconjunctival haemorrhage as noted in this case should be promptly worked up to unmask serious but treatable haematological abnormalities like ITP.

CASE PRESENTATION

A 32-week born infant with birth weight of 1250 g presented at 37-week postmenstrual age (PMA) for ROP screening. The infant had a history of respiratory distress requiring mechanical ventilation, *Escherichia coli* sepsis and hyperbilirubinaemia in the neonatal period. Complete blood count during neonatal period revealed increased white cell count ($13.4 \times 10^9/L$) with normal platelet counts ($236.0 \times 10^9/L$).

The infant was diagnosed elsewhere with both eyes zone 1 aggressive posterior ROP and intravitreal injection of bevacizumab was given 5 days earlier. Upon regular follow-up at our centre, regression of ROP was noted with vascularisation reaching zone 3.

At 47 weeks PMA, the infant developed bilateral extensive subconjunctival haemorrhage immediately after indirect ophthalmoscopy examination

with scleral indentation, performed by an experienced examiner. No retinal or vitreous haemorrhage was noted. Note was made of petechial rash over both cheeks and upper limbs as well (figure 1). Paediatric referral was subsequently done to evaluate for haematological disorder.

No hepatosplenomegaly/lymphadenopathy was detected on physical examination. Also, the child was active and feeding well.

INVESTIGATIONS

Haemogram revealed severe thrombocytopenia (platelet counts $5.0 \times 103/\mu L$, haemoglobin 9.3 g/dL, total leucocyte count $7.9 \times 103/\mu L$). Differential leucocyte levels and coagulation profile were unremarkable. Peripheral blood smear showed decreased platelets but morphology of all cell lines was normal. Thyroid function tests were normal. TORCH profile was non-reactive. Maternal haemogram and serology for hepatitis B, hepatitis C and HIV were unremarkable.

DIFFERENTIAL DIAGNOSIS

Subconjunctival haemorrhage can occur after trivial trauma with disorders associated with thrombocytopenia and platelet dysfunction, such as thrombocytopenic purpura, leukaemia, hypersplenism, anticoagulant or antiplatelet therapy, and uraemia. Based on history and investigations, diseases other than thrombocytopenic disorders were excluded in this case. In the absence of features like fever, weight loss, bone pains, recent viral illness and drug toxicity, a diagnosis of ITP was made. Allo-immune ITP due to maternal alloimmunisation was ruled out as it occurs in the neonatal period. Drug

Figure 1 Right eye (A) and left eye (B) of an infant with massive subconjunctival haemorrhage which developed immediately after retinopathy of prematurity screening with scleral indentation. Petechial rash over bilateral cheeks can also be noted.

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toxicity due to bevacizumab was ruled out as it is associated with anaemia and neutropenia as well.

TREATMENT

Considering a strong possibility of ITP, the child was transfused one unit of Random Platelet Product (RDP). Intravenous immunoglobulin was also given for two consecutive days (4 g/day).

OUTCOME AND FOLLOW-UP

Following treatment, platelet count improved to $121.0 \times 10^9/L$ on day 3 of transfusion. Subconjunctival haemorrhage and petechial rash resolved gradually over the next 4 weeks. At last follow-up at 50 weeks, ROP had regressed with vascularisation reaching up to temporal ora serrata.

DISCUSSION

Scleral depression is an integral part of ROP screening as it allows visualisation of retinal periphery and ocular fixation under topical anaesthesia in a restrained yet actively moving baby. Manipulation during indentation may occasionally lead to minor subconjunctival and retinal haemorrhages. Factors responsible for such haemorrhages may be abrupt changes in intraocular pressure and fragile immature retinal vasculature with poor autoregulation.¹ However, large subconjunctival haemorrhages have not been reported after scleral depression in ROP, and this alarmed us to investigate for haematological abnormality in this case.

Subconjunctival haemorrhage can occur spontaneously or after trivial trauma with disorders associated with thrombocytopenia and platelet dysfunction. Based on history and investigations, a diagnosis of ITP was reached.

Systemic bevacizumab has been known to be associated with increased risk of thrombocytopenia but that is usually associated with anaemia and neutropenia.² Lee *et al* have reported a single case report of isolated thrombocytopenia after 4 weeks of intravitreal bevacizumab injection in an adult patient for branch retinal venous occlusion-related macular oedema.³ However, in our case, development of thrombocytopenia was too delayed (12 weeks) to be associated with bevacizumab injection.

Thrombocytopenia is known to play a part in etiopathogenesis of ROP.⁴ Platelets sequester vascular endothelial growth factor (VEGF) and regulate retinal angiogenesis. So thrombocytopenia could possibly permit greater unregulated retinal neovascularisation when IgF-1 levels rise and activate accumulated VEGF in proliferative phase of ROP.⁵ Correction of thrombocytopenia has been known to lead to spontaneous resolution of ROP.

ITP occurring in infants though rare resolves spontaneously within 6 months of diagnosis.^{6,7} Most cases of ITP are seen after infancy. ITP is a diagnosis of exclusion and routine testing for platelet antibodies is not recommended. Platelet recovery

occurs rapidly with treatment with intravenous immunoglobulins or corticosteroids. ITP was previously known as idiopathic thrombocytopenia, but being caused by an antiplatelet antibody of unknown aetiology, newer terminology is better accepted. Subconjunctival haemorrhage as the presenting feature of ITP has been described only once in an elderly woman.⁸ However, this was associated with additional complaints of haematuria.

Although occurrence of ITP in premature infant with ROP in our case is most likely coincidental, screening helped in earlier diagnosis and treatment of this potentially fatal condition.

Learning points

- ▶ Ophthalmologists performing retinopathy of prematurity (ROP) screening should be aware of possible association of thrombocytopenia with ROP.
- ▶ Although rare, immune thrombocytopenic purpura (ITP) can occur in infancy and should be promptly worked up if massive spontaneous haemorrhages occur.
- ▶ Platelet recovery occurs rapidly with treatment with intravenous immunoglobulins and/or corticosteroids in ITP.

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