

SHORT REPORT

Atypical bleeding due to idiopathic thrombocytopenia in association with low factor VIII levels

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Arch Dis Child 2002;87:227-228

Two children with bleeding from idiopathic thrombocytopenia with low factor VIII levels are described. The presence of a double haemostatic defect in an otherwise healthy individual presenting with bleeding is extremely rare. In both cases the atypical bleeding raised the suspicion of dual pathology.

Idiopathic thrombocytopenic purpura (ITP) has an estimated annual incidence of three cases per 100 000 children in the United Kingdom. It is generally a self limiting illness, which rarely requires intervention.¹ A typical case presents with a petechial rash and a history of increased bruising following knocks or falls. Less commonly this is accompanied by epistaxis or mucosal bleeding.

Haemophilia A is an X linked deficiency of factor VIII, with a prevalence of five cases per 100 000 males.² Severe haemophiliacs have spontaneous bleeding into joints and soft tissues. Bleeding from cuts or mucosal surfaces is less common. The severity of bleeding varies widely and 20-30% of patients will have a clinically mild form of the disease. Female carriers of haemophilia A can have reduced FVIII:C and abnormal bleeding.

In our first case we report the unmasking of a previously asymptomatic haemophilia A by an episode of ITP. In our second case idiopathic thrombocytopenia was complicated by partial FVIII:C deficiency.

CASE 1

A 2 year old boy with a two week history of increased bruising grazed his left eyelid on a car seat belt. Over the course of the day he had developed a large haematoma over both his upper and lower lids. Although there was no family history to suggest an inherited bleeding disease a maternal uncle had died of an intracranial haemorrhage following a cycling accident.

On examination there were widespread petechiae and numerous small bruises, of varying age, over his lower legs. Although these features are consistent with ITP, the large haematoma was not. By the time he attended he was unable to open the affected eye and it was evident that the haematoma was continuing to increase in size; this was suggestive of an underlying coagulopathy, and clotting studies and a full blood count were performed.

The platelet count was $4 \times 10^9/l$ and the blood film also showed immature lymphocytes. A bone marrow aspirate confirmed that he did not have leukaemia but normal haemopoiesis with increased numbers of megakaryocytes compatible with peripheral platelet consumption. Coagulation studies (table 1) were compatible with a diagnosis of mild haemophilia; further investigations, performed later, excluded von Willebrand's disease (table 1). Thrombocytopenia was a complicating factor as there were insufficient platelets available to perform a ristocetin induced platelet aggregation.

In view of the severity of bleeding and the need to do a bone marrow aspirate the child was treated with intravenous vasopressin. Coagulation studies pre- and post-infusion showed a significant therapeutic response (table 1). Because of his symptoms high dose immunoglobulin (0.8 g/kg) was given to treat the ITP. Over the course of three days the platelet count increased to $180 \times 10^9/l$ and the haematoma decreased in size.

CASE 2

A 5 year old white girl, the niece of a severe haemophiliac, was referred because of bruising. Coagulation studies (table 2) excluded von Willebrand's disease and confirmed that she was a carrier of haemophilia A.

Aged 9 she had an epistaxis lasting 45 minutes as well as a one month history of easy bruising. She was treated with

Abbreviations: FVIII, factor VIII; ITP, idiopathic thrombocytopenia purpura

Table 1 Investigations for case 1

<i>At presentation</i>		
Activated partial thromboplastin time	49 seconds	Normal 29-40 seconds
Partial thrombin time	13 seconds	Normal 11-15 seconds
Factor VIII:C assay	0.13 iu/ml	Normal 0.5-1.5 iu/ml
Factor IX assay	0.97 iu/ml	Normal 0.5-1.5 iu/ml
<i>Post-intravenous vasopressin</i>		
Activated partial thromboplastin time	39 seconds	Normal 29-40 seconds
Factor VIII:C assay	post 0.54 iu/ml	Normal 29-40 seconds
<i>Subsequent investigations</i>		
vWF:Ag	0.94 iu/ml	Normal 0.5-1.5 iu/ml
vWF:Act	0.54 iu/ml	Normal 0.5-1.5 iu/ml

Table 2 Investigations for case 2, aged 5

Activated partial thromboplastin time	42 seconds	Normal 29–40 seconds
Partial thrombin time	14 seconds	Normal 11–15 seconds
Factor VIII:C assay	0.39 iu/ml	Normal 0.5–1.5 iu/ml
vWF:Ag	0.64 iu/ml	Normal 0.5–1.5 iu/ml
vWF:Act	0.76 iu/ml	Normal 0.5–1.5 iu/ml

intravenous vasopressin, which controlled the bleeding. In view of the unexpected severity of her bleeding further investigations were arranged. Her FVIII:C level after 1-deamino-8-D-arginine vasopressin was 0.54 units/ml and her platelet count $37 \times 10^9/l$. The blood film was otherwise normal and a bone marrow aspirate was not deemed necessary.

Four months later she presented once more with severe soft tissue bleeding following a fall from a bicycle. Her platelet count at this time was $43 \times 10^9/l$. She was treated with a vasopressin infusion. A trial of oral steroids produced a rapid but unsustainable rise in her platelet count. She went on to develop chronic idiopathic thrombocytopenia.

DISCUSSION

The presence of a double haemostatic defect in an otherwise healthy individual presenting with bleeding is rare. These are the first reported cases of idiopathic thrombocytopenia presenting with atypical bleeding as a result of mild haemophilia A or reduced factor VIII in a haemophilia carrier.

The practice of performing routine coagulation studies on children presenting with thrombocytopenia has been deemed unnecessary.³ Where bruising accompanying thrombocytopenia is exacerbated by an underlying coagulation defect the atypical nature of this bruising, as in these two children, is likely to suggest the need for additional investigation.

Mild haemophilia A can be asymptomatic until it is unmasked by accidents or elective operations complicated by excessive bleeding. In our first case the affected child's older asymptomatic brother was shown to have haemophilia A. With two affected sons his mother is an obligatory carrier and it is possible that unrecognised haemophilia A contributed to the intracranial bleeding following her brother's cycling accident.

Other causes for this combination of haemostatic defects are uncommon. HIV related thrombocytopenia is well recognised and can pose an enormous problem to patients with severe haemophilia.⁴ Thrombocytopenia is also seen in HIV negative haemophiliacs who have received multiple transfusions of blood products and is strongly associated with liver disease.³ Severe mucosal bleeding has been described in a

patient with thrombocytopenia and acquired factor VIII deficiency secondary to acute myelomonocytic leukemia.⁶ Thrombocytopenia as a result of Fanconi's anaemia in a patient with haemophilia A has also been reported. The reported case that most resembles ours is that of a Russian baby who developed extensive, spontaneous bruising over the spine and buttocks over the first week of life as a result of isoimmune thrombocytopenia and haemophilia A. He was treated with clotting factor concentrate and responded well.⁷

ACKNOWLEDGEMENTS

We would like to thank Dr Philipp Conradi for his assistance in translating reference 7.

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Accepted 23 April 2002

REFERENCES

- Bolton-Maggs PHB**, Moon I. Assessment of UK practice for management of acute childhood idiopathic thrombocytopenic purpura against published guidelines. *Lancet* 1997;**350**:620–3.
- Davies AEM**, Billson, HR Jenkins. *Key topics in paediatrics*. BIOS Scientific Publishers, 1994.
- Eden OB**, Lilleyman JS. Guidelines for management of idiopathic thrombocytopenic purpura. *Arch Dis Child* 1992;**67**:1056–8.
- Sloand EM**, Klein HG, Banks SM, *et al*. Epidemiology of thrombocytopenia in HIV infection. *Eur J Haematol* 1992;**48**:168–72.
- Eyster ME**, Whiethurst DA, Catalano PM, *et al*. Longterm follow-up of hemophiliacs with lymphocytopenia or thrombocytopenia. *Blood* 1985;**66**:1317–20.
- Meek JC**, Haak HL. Acute myelomonocytic leukaemia and acquired haemophilia A with severe cutaneous haemorrhage. *Scand J Haematol* 1986;**37**:168–73.
- Bushmarina TA**, Papaian LP, Fedorova ZD, *et al*. Combination of hemophilia A and isoimmune thrombocytopenia in a newborn infant. *Problemy Gematologii i Perelivaniia Krovi* 1978;**7**:56–7.