Acute infantile thrombocytosis and vitamin K deficiency associated with intracranial haemorrhage

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SUMMARY A 5-week-old breast-fed girl presented unconscious and convulsing with heavily blood-stained CSF under increased pressure. This was associated with oozing from venepuncture sites, a grossly prolonged prothrombin time, and a raised platelet count. The prothrombin time became normal 18 hours after she had been given parenteral vitamin K and a transfusion of fresh plasma and red cells, but the thrombocytosis persisted. A moderate communicating hydrocephalus also remained and was treated, and one year later health and development appeared normal. The thrombocytosis resolved after a few weeks and has not recurred.

Thrombocytosis in infancy accompanying intracranial haemorrhage is rare and in the few cases that have been recorded was not associated with a clinical bleeding tendency or blood coagulation deficiency (Sanyal *et al.*, 1966).

We describe the case of a 5-week-old infant with an intraventricular haemorrhage who was found to have a high platelet count and was also noted to have a bleeding disorder with a grossly prolonged prothrombin time. This triad of intracranial bleeding, thrombocytosis, and possible late vitamin K deficiency has not been reported before.

Case report

The patient, the first child of healthy parents, was born after a normal pregnancy. The delivery was normal and her birthweight was 2.86 kg. Vitamin K was not given at birth. She was breast fed and in good health until age 5 weeks when she vomited and was irritable for 3 days, before becoming comatose. On admission

to hospital she was unconscious, moaning, very pale, rigid, and had a tensely bulging anterior fontanelle. She also had two small bruises in the popliteal fossa and was seen to ooze excessively from venepuncture sites but there was no evidence of external injury.

Lumbar puncture showed blood-stained and markedly xanthochromic CSF under increased pressure. Subsequently, a ventricular tap also yielded heavily blood-stained CSF. Hb was 7.1 g/dl; WBC $14.3 \times 10^9/l$ (differential counts showed a neutrophilia); and platelets $1154 \times 10^9/l$. The prothrombin time was grossly prolonged, as were partial thromboplastin and plasma recalcification times, but the thrombin time and concentration of fibrin/fibrinogen split products were normal.

Immediate transfusion of 50 ml fresh plasma and 90 ml stored blood was given together with 2 mg parenteral vitamin K; 18 hours later there was total correction of the prothrombin and recalcification times, with the partial thromboplastin time returning to normal in 42 hours. The platelet count, however, remained high at $900 \times 10^9/l$, and a further legacy of the event was a moderate, freely communicating hydrocephalus, which was treated with ventricular drainage and, subsequently, by isosorbide by mouth.

Platelet function studies were normal, and the thrombocytosis was last noted 4 weeks after presentation ($760 \times 10^9/l$) but had disappeared 7 months later ($340 \times 10^9/l$). The relevant haematological parameters are given in the Table.

Clinically the child has no apparent sequelae, and is well at the time of writing (2 years). Prothrombin time, partial thromboplastin time, and plasma recalcification time have apparently remained normal since correction after plasma and vitamin K on the one occasion, and the thrombocytosis has not recurred.

Table Summary of haematological abnormalities after admission

Time after admission	Hb (g/dl)	Platelets ($\times 10^9/l$)	Prothrombin time (British corrected ratio)	Partial thromboplastin time (ratio to control)	Fibrin degradation products ($\mu g/ml$)
0	7.1	1154	>10.0	>10.0	<10
18 hours	11.1*	750	1.15†	1.4	—
42 hours	9.2	510	1.0	0.9	<10
4 days	10.2	900	—	—	—
13 days	10.4	1015	—	—	—
1 month	11.3	760	—	—	—
8 months	13.0	340	—	—	—

*After transfusion, †after vitamin K and fresh plasma.

Discussion

High platelet counts are rarely found in babies, and conditions associated with them have been reviewed (Addiego *et al.*, 1974). The thrombocytosis in this patient was discovered at the same time as a subarachnoid and intraventricular haemorrhage and a gross coagulopathy, and how these relate to each other is not certain. A likely sequence of events is that the coagulopathy allowed bleeding which provoked an unusually pronounced reactive platelet increase. If the high platelet count was the *cause* of bleeding, as paradoxically can occur in some myeloproliferative disorders, the coagulopathy would have to have been coincidental, which seems improbable.

Infantile central nervous system disease associated with thrombocytosis alone has been recorded by Sanyal *et al.* (1966) and Huttenlocher and Smith (1968) and has been implicated as being causally related (by precipitating cerebral thrombosis) as the high platelet count was seen to precede an acute hemiplegia in one case (Huttenlocher and Smith, 1968). In no previous report has a coincidental disorder of coagulation been noted.

Late vitamin K deficiency in infants has been described (Nammacher *et al.*, 1970; Cooper and Lynch, 1979), and while the evidence for its existence in our case is entirely circumstantial, it is hard to offer an alternative explanation for such rapid permanent *in vivo* correction of a clinically obvious bleeding tendency associated with a prolonged prothrombin time in the absence of intravascular coagulation. There was no reason to suppose that the production of liver

coagulation factors was impaired from any other cause, but no estimation of protein induced by vitamin K absence was made, which would have helped to clarify this aspect.

Quite why this child should be lacking vitamin K is hard to say, as breast feeding is the only reason to suppose a deficient supply. It must be acknowledged that it is possible some other factor provided permanent correction of the observed and apparently acquired bleeding tendency, but to define such a factor is not possible.

We thank Dr B. L. Priestley for referring this infant to us.

References

- Addiego, J. E., Jr, Mentzer, W. C., Jr, and Dallman, P. R. (1974). Thrombocytosis in infants and children. *Journal of Pediatrics*, **85**, 805-807.
- Cooper, N. A., and Lynch, M. A. (1979). Delayed haemorrhagic disease in the newborn with extradural haematoma. *British Medical Journal*, **1**, 164-165.
- Huttenlocher, P. R., and Smith, D. B. (1968). Acute infantile hemiplegia associated with thrombocytosis. *Developmental Medicine and Child Neurology*, **10**, 621-625.
- Nammacher, M. A., Willemin, M., Harmann, J. R., and Gaston, L. W. (1970). Vitamin K deficiency in infants beyond the neonatal period. *Journal of Pediatrics*, **76**, 549-554.
- Sanyal, S. K., Yules, R. B., Eidelman, A. I., and Talner, N. S. (1966). Thrombocytosis, central nervous system disease, and myocardial infarction pattern in infancy. *Pediatrics*, **38**, 629-636.

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Premature menarche without other evidence of precocious puberty

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SUMMARY We describe 4 young girls with recurrent vaginal bleeding in the absence of other signs of precocious sexual development. Investigation showed low oestrogen levels in 2 of them, and basal gonadotrophins were in the upper part of the prepubertal range. We believe that the isolated early menstruation in these patients was possibly related to increased sensitivity of the endometrium to oestrogens.

Cyclical vaginal bleeding in the absence of other signs of secondary sexual development is rare and little has been written about the clinical and laboratory aspects of this condition. We describe 4 young

girls seen at The Hospital for Sick Children because of recurrent menstrual bleeding; they had no other stigmata of precocious puberty or evidence of an underlying genital disorder.

Case reports

Case 1 (born 14.11.1960). When she was 10 months, this girl began to have episodes of vaginal bleeding which lasted for 2 or 3 days and recurred every 4 to 5 weeks. She had been born 2 weeks after the expected date of confinement, but her neonatal history and developmental progress were normal.

She was admitted to hospital at age 1·2 years for