Gingival bleeding, epistaxis and haematoma three days after gastroenteritis: the haemorrhagic lupus anticoagulant syndrome

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Abstract A 3 year and 9 month-old girl presented with gingival bleeding, epistaxis, and multiple haematomas 3 days after an acute episode of gastroenteritis. Prothrombin time and activated partial thromboplastin time were prolonged with reduced clotting activity of factor II (<10%), VIII (<1%), IX (3%), XII (10%) and evidence of a high titre inhibitor. Prothrombin (factor II) level was below the detection limit, both in a functional and immunological assay. It did not increase after administration of vitamin K or fresh frozen plasma. Further studies revealed presence of a strong lupus anticoagulant and a specific IgG antibody against prothrombin. Factor VIII antigen levels also were reduced (31%), but to a lesser extent than functionally determined factor VIII (<1%). Blood coagulation normalised following clinical recovery 6 weeks after admission. The pathophysiology of this acquired inhibitor phenomenon (accelerated clearance of complexes of clotting factors and phospholipids) is discussed.

Conclusion The haemorrhagic lupus anticoagulant syndrome (acquired hypoprothrombinaemia lupus anticoagulant syndrome) is a rare presentation of acquired bleeding diathesis in childhood. Since most cases in post-infectious children are asymptomatic, it might be underdiagnosed. In children with newly appearing bleeding symptoms or unclear prolonged prothrombin time or activated partial thromboplastin time, one has to consider this syndrome which could lead to relevant bleeding.

Key words Bleeding disorder · Gastroenteritis · Lupus anticoagulant · Anti-prothrombin antibodies

Abbreviations ACL anti-cardiolipin · aPTT activated partial thromboplastin time · β2GP β-2-glycoprotein · FFP fresh frozen plasma · LA lupus anticoagulant · SLE systemic lupus erythematosus

Introduction

Gastroenteritis is one of the most frequent problems encountered by a paediatrician. Some bloody diarrhoea is often a concomitant finding but other bleeding symptoms are very rare. Recently we were confronted with a 3 year and 9 month-old child with a transient bleeding disorder following an episode of gastroenteritis.
Further studies revealed a transient haemorrhagic lupus anticoagulant syndrome with hypoprothrombinaemia. The clinical relevance and the pathophysiology of this syndrome are discussed.

Case report

A previously healthy 3 year and 9 month-old girl, without a history of a haematological disorder in her family, presented with acute gastroenteritis in our emergency ward. She showed slight dehydration and subfebrile temperature but no haematomas or petechiae. No laboratory tests were done. Three days later she presented again with multiple haematomas of 1–4 cm diameter, ecchymoses, gum bleeding, and epistaxis (Fig. 1). Temperature was 37.4 °C. Initial laboratory evaluation showed prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT) (Table 1). Blood smear and all routine chemistry were normal. Intoxication with rodenticide or coumarin, although unlikely because of normal results for factor VII, was ruled out by toxicological screening (urine). No signs of malignant disease were found. Biopsy of the haematomas (size and appearance seemed to be unusual) ruled out lymphoma and sarcoma. Administration of fresh-frozen-plasma (FFP) and large doses of vitamin K could only marginally shorten PT and aPTT. Gum bleeding stopped after administration of tranexamic acid.

Reduced clotting activity of factor II (< 10%), VIII (< 1%), IX (3%), XII (10%) and the presence of a high titre lupus anticoagulant (LA) were found. The diluted Russel viper venom test showed a high ratio in spite of dilution with normal plasma. In comparison to the reduction of most phospholipid dependent coagulation assays, an unusually low prothrombin level was found which did not increase after vitamin K/FFP administration (Table 1). Low prothrombin levels determined functionally in a one stage assay (Dade Behring) corresponded with those antigenetically determined (Laurell electrophoresis with an anti-prothrombin antiseraum, Stago Inc.). Bethesda test revealed an inhibiting phenomenon with identical results before and after incubation. Further investigations demonstrated high titre anti-prothrombin IgG antibodies by a specific solid phase dot blot method (Biomedical Diagnostics). The titres decreased spontaneously during the 1st week. As functional determined factor VIII was also markedly reduced (< 1%), factor VIII antigen levels (Asserachrom Inc.) were determined and found to be reduced to a lesser extent (31%). Anti-prothrombin IgM antibodies, anti-cardiolipin antibodies (ACL) and antibodies against beta-2-glycoprotein (β2GP) were consistently negative. Viral serology revealed a borderline titre of 1:80 for adenovirus on two occasions. All other serological studies, bacterial cultures and stool antigen tests were negative.

On follow-up, no life threatening bleeding occurred. On day of discharge, 8 days after admission, factor II level were 20%. Three weeks later both PT and factor II level had normalised and 6 weeks after hospitalisation, no LA or anti-prothrombin antibodies were detectable. At 24 months after discharge, the child is healthy, has normal coagulation parameters and shows no signs of systemic lupus erythematosus (SLE) or other auto-immune diseases.

Discussion

LA are heterogeneous antibodies directed against phospholipids and phospholipid binding plasma proteins with an activity to prolong the clotting time of phospholipid dependent tests. They occur in a variety of underlying diseases. Thrombotic complications as observed in adults are rare in children. Mostly, LA are transient and without any clinical symptoms [5, 6, 7, 10]. On some occasions they can be observed as one of the presenting symptoms in childhood SLE. In a series of 95 children with positive LA, 85% were asymptomatic but 10% had bleeding symptoms and only 5% had a history of thrombosis [10]. It has been shown that prothrombin can be one of the phospholipid-bound antigenic targets to LA. Severe hypoprothrombinaemia can occur, and on some occasions, cause bleeding.

Since its first description in 1960 by Rapaport et al. [13] in an 11-year-old girl with SLE and severe bleeding, acquired hypoprothrombinaemia in combination with LA has been documented in the literature in 27 paediatric patients [2, 3, 4, 8, 9, 10, 13, 16]. All had mild (bruising, purpura, haematomata) to severe haemorrhagic symptoms (gastrointestinal bleeding, untreatable epistaxis, excessive gum bleeding, haemarthrosis in two cases). In 16 patients (aged 1.5 to 10 years) this syndrome was preceded by a viral infection (respiratory infection or gastroenteritis; in 50% adenovirus infection). None of the 16 patients developed SLE or other collagen vascular disease. Most of them recovered spontaneously after 3 months, although corticosteroids had been used in a few cases. In 3 of 27 reported patients, no underlying disease or preceding illness was found. Eight paediatric patients from the literature, all

Fig. 1a, b  Bleeding disorder in a 3 year and 9 month-old girl due to a transient LA and severe hypoprothrombinaemia 3 days after gastroenteritis. The photos show the unusually large haematomas and ecchymoses on admission