A child presented with excessive bruising and prolonged activated partial thromboplastin time. Mixing studies in plasma were positive for phospholipid dependence of the anticoagulant, confirming a diagnosis of lupus anticoagulant. Factor II level was reduced. Laboratory findings normalised after three months, with spontaneous resolution of bruising. This case demonstrates a transient antiphospholipid antibody syndrome as a rare presentation of bleeding diathesis in a previously healthy child, and should be considered in children with new onset bruising and prolonged activated partial thromboplastin time.

CASE REPORT

A previously well 3 year old white girl was referred by her general practitioner with a history of spontaneous bruising. On examination, she was a well child with multiple small bruises on her legs, back, and sides of thighs, forearms, and upper arms. There was no gum hypertrophy, lymphadenopathy, or hepatosplenomegaly.

Full blood count and blood film were normal. Repeat coagulation tests showed normal prothrombin time and thrombin time but a markedly prolonged aPTT (table 1). Mixing studies with 1:1 dilution of patient and pooled normal plasma performed did not fully correct the aPTT from 67.4/s to 53/s on mixing. This implied the presence of a circulating anticoagulant acting as an inhibitor in the intrinsic pathway. A modified Russell viper venom time (mRVVT) was prolonged at 118.1 seconds. There was significant shortening of the mRVVT after the addition of platelets, confirming the presence of LA. Anticardiolipin antibodies were not detected. Factor II activity was reduced to 40%. Factors V, VII, VIII, IX, X, XI, XII, and Von Willebrand factor were normal. Serological tests to detect underlying autoimmune disease were negative, including antinuclear antibodies, antibody to double stranded DNA, and rheumatoid factor.

She received no treatment, and her bruising resolved spontaneously over four weeks. Coagulation studies normalised in parallel with clinical recovery, with disappearance of the LA and Factor II level increased to normal by the time she was tested three weeks later. She remains well, three months later, with normal physical activity.

DISCUSSION

This case demonstrates the presence of antiphospholipid antibodies as a rare cause of transient haemorrhagic manifestations in children and emphasises the usefulness of coagulation studies in elucidating the diagnosis. LA may be associated with connective tissue disorders, malignancies, drug use, and infections, or with no underlying disease. Although patients may remain free of symptoms, LAs are commonly associated with deep vein thrombosis, placental infarction, and stroke in adults. Rarely, haemorrhagic symptoms have been reported, mainly in children. Estimated in 10%–20% of patients with LAs, levels of prothrombin will be decreased. It is now recognised that many APA are targeted to the prothrombin protein but it remains unusual for there to be

| Table 1 Laboratory findings in patient with lupus anticoagulant |
|-----------------|-----------------|-----------------|
|                 | Patient         | Normal range    |
|                 | (seconds)       | (seconds)       |
| aPTT            | 67.4            | 26–38           |
| aPTT after mixing | 53              | 26–38           |
| PT              | 12              | 9–14            |
| Factor II       | 40              | 50–140          |
| mRVVT           | 118.1           | 29–45           |
| mRVVT and platelets | 30.5       | 29–40           |
| β2 glycoprotein I | negative       |                  |
| Anticardiolipin antibodies (IgG and IgM) | negative |
| Adenovirus serology | negative |

APTT, activated partial thromboplastin time; PT, prothrombin time; mRVVT, modified Russell viper venom time.

Abbreviations: aPTT, activated partial thromboplastin time; LA, lupus anticoagulant; APA, antiphospholipid antibody
There have been three recognised components of the laboratory confirmation of LAs: (a) the use of sensitive screening reagents; (b) mixing studies to confirm the presence of a circulating anticoagulant; and (c) proof that the anticoagulant is phospholipid dependent. All were present in this case.

The addition of platelets as a rich source of phospholipids will neutralise the antiphospholipid antibody. Significant shortening of a prolonged mRVTT after the addition of platelets as seen in this child (table 1) supports the diagnosis of LA. With symptoms of bruising or bleeding, you would suspect an inhibitor against VIII, IX and XI resulting in a factor deficiency. However, these inhibitors are rare and usually occur spontaneously only in elderly people. However, in this case the finding was that of an antiphospholipid antibody, which is much more common than acquired factor inhibitors in individuals without a congenital factor deficiency.

Confirmation of LAs: (a) the use of sensitive screening tests to detect anticardiolipin IgG and IgM antibodies were both negative. A prothrombin time was by Rapaport et al, in 1960, describing an 11 year old girl with severe bleeding and systemic lupus erythematosus. However, the LA persists in autoimmune disorders and is not transient, as seen in our case. Because of the increasing frequency of occurrence of LAs with autoimmune disease, a high level of suspicion for the manifestations of systemic lupus erythematosus and other autoimmune diseases should be maintained, particularly if LA is persistent.

Becton et al reported six cases of previously healthy children with clinical signs of bleeding and prolonged aPTT resulting from positive mixing studies and evidence of phospholipid dependent coagulation tests. The autoantibodies are against negatively charged phospholipids or phospholipid binding proteins, including the phospholipid dependent clotting proteins such as PT and aPTT. At least two phospholipid bound plasma proteins are associated with LA, namely, prothrombin and β2 glycoprotein I. The assay of antibodies to these proteins are generally available in research laboratories rather than being widely available. In our case, β2 glycoprotein I and anticardiolipin IgG and IgM antibodies were both negative. A prothrombin antibody was not performed.

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Transient lupus anticoagulant: an unusual cause of bruising in children

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