PREDNISOLONE THERAPY FOR LUPUS ANTICOAGULANT IN B-THALASSEMIA MAJOR

D Sinniah
J Bosco
A Kamaruddin

SYNOPSIS

Screening of patients with B-thalassemia major at the University Hospital, Kuala Lumpur revealed the presence of a circulating lupus anticoagulant in 5 children of whom 4 suffered intracranial haemorrhage while a fifth was asymptomatic. Spontaneous disappearance of the anticoagulant was observed in one patient but two others with persistent inhibitor suffered recurrent hemorrhage which resulted in one fatality. An empirical 14-day trial of prednisolone in 3 patients resulted in clearance of the anticoagulant in each case. Report of a similar response to steroids in a thalassemic patient with the lupus inhibitor in Bangkok and successful suppression of lupus anticoagulant activity in non-thalassemic patients with prednisolone suggest that steroid therapy may have a role in the management of thalassemic patients who are at increased risk of hemorrhage because of circulating lupus anticoagulant.

INTRODUCTION

The presence of the lupus anticoagulant has been reported in a variety of disorders like lupus erythematosus, rheumatoid arthritis, penicillin allergy and in some instances without demonstrable underlying disease (1-3). It has been suggested that the inhibitor interferes with the coagulation phase involved in the activation of prothrombin probably at the level of the phospholipid fraction of platelets (1, 4-6). Patients with the lupus anticoagulant have undergone major surgery without excessive postoperative bleeding, paradoxically some have manifested thrombotic manifestations (4, 6). Although significant bleeding is considered rare, the risk may be increased in the presence of thrombocytopenia or hepatocellular damage which can occur in patients with B-thalassemia. Prednisone and aspirin have been used successfully in the treatment of pregnant women with the lupus antlcoagulant (7).

Lupus anticoagulant (prothrombinase inhibitor) has recently been found in association with intracranial hemorrhage in 4 thalassemic patlents (8). Two of these patients have since suffered further episodes of bleeding resulting in one fatality. We describe here our experience with prednisolone in the treatment of 3 thalassemic children with the lupus inhibitor.

Department of Paediatrics and Medicine
Faculty of Medicine
University of Malaya
Kuala Lumpur

D Sinniah, MA, MD, FRACP, FRCPI, DCH
Associate Professor

J Bosco, MBBS, MRCP
Associate Professor*

A Kamaruddin, MBBS, MRCP
Lecturer

PATIENT AND METHODS

Screening of 20 consecutive children with B-thalassemia major attending the Paediatric Haematology Clinic of the University Hospital, Kuala Lumpur for regular blood transfusion, using the prothrombin (PT) and partial thromboplastin time (PTT) performed by standard methods using platelin as a source of partial thromboplastin and simplastin as the thromboplastin for the prothrombin time, revealed abnormal results in 8 patients. 50:50 mixing experiments described previously (8) yielded abnormal findings indicative of the presence of a lupus inhibitor of the IgM class in 5 patients. Results of tests for antinuclear factor by immunofluorescence method and C3 and C4 by radial immunodiffusion and for Hepatitis B antigen were negative.

REPORT OF CASES WITH LUPUS ANTICOAGULANT

Case Nos. 1-4
Four of the cases with circulating anticoagulant suffered intracranial hemorrhage and have been reported elsewhere (8). Serial follow up of these patients over a 2 year period has revealed spontaneous disappearance of the inhibitor in case no. 2, 6 months after the initial episode of intracranial hemorrhage. The anticoagulant however has persisted in the other 3 cases; case no. 1 suffered recurrent intracranial hemorrhage while case no. 3 died of pneumonia complicated by hemothorax.

Case No. 5
A 5 year old Chinese boy with B-thalassemia receiving 6 weekly blood transfusions had no symptoms of bruising or bleeding and was found to have abnormal PT, PTT and 50:50 mixing experiments on routine coagulation screening. Platelet count was normal.

STEROID THERAPY

Because of recurrent life threatening bleeding observed in 2 of the cases (cases nos. 1 and 3), prednisolone 2 mg/kg body weight/day was administered for 14 days to 3 children (case nos. 1, 4, 5). The rationale for this therapy is based on the observation that corticosteroid therapy can suppress the activity of the lupus anticoagulant. (5, 7) PT, PTT and 50:50 mixing experiments were monitored both before and after prednisolone therapy and at regular intervals thereafter.

RESULTS

The results of coagulation studies before and after prednisolone therapy on the 3 cases of B-thalassemia major with the lupus anticoagulant are recorded in Table I. Complete disappearance of the inhibitor was noted in all 3 children given prednisolone and no side effects were observed. Serial studies over a one year period have failed to demonstrate the reappearance of the lupus anticoagulant. Mild prolongation of PT and/or PTT correctable with normal plasma however persisted suggesting the presence of liver dysfunction independent of the lupus anticoagulant. As none of our patients received desferrioxamine the hepatic dysfunction can be attributed to the effects of iron deposition in the liver.

DISCUSSION

Mild impairment of the coagulation of mechanism has been described in children with B-thalassemia major between 7 and 10 years of age and is similar to that observed in patients with liver disease of any aetiology (9). The coagulation abnormality is usually mild and rarely causes bleeding (10). Eight of twenty children with thalassemia screened by us had prolonged PT and/PTT. Five of these children also had a lupus inhibitor of the IgM class and of these four suffered intracranial hemorrhage. While the presence of the inhibitor alone may not cause symptoms, we have not observed serious bleeding in its absence. The risk of life threatening hemorrhage appears to be increased when the presence of the inhibitor is associated with infection, liver dysfunction or thrombocytopenia.

The reason for the emergence of the lupus anticoagulant is not clear as none of our patients had SLE but allosensitisation following blood transfusion may be a possible explanation (11). While spontaneous disappearance of the inhibitor can sometimes occur (4)

TABLE I COAGULATION STUDIES BEFORE AND AFTER PREDNISOLONE

Patient No.	1		4		5	
Coagulation tests	Before/After PNSL		Before/After PNSL		Before/After PNSL	
PT (sec)						
NP	15.0	13.8	15.0	13.5	13.0	13.6
PP	22.5	15.6	21.5	15.6	17.3	15.5
50:50 (NP + PP)	17.8	14.5	16.5	13.6	14.9	-
PTT (sec)						
NP	40	36.0	40.0	35.4	36.7	39.4
PP	66.5	49.4	90.0	40.8	42.5	45.1
50:50 (NP + PP)	50.5	38.8	54.0	38.3	43.5	39.8
Platelet count (ul)	80 – 113 X 10^3		54 – 148 X 10^3		Normal	

PNSL = Prednisolone

as observed in one of our patients, recurrent hemorrhage is a problem and has resulted in fatality and permanent neurological deficit.

In view of the increased risk of recurrent life threatening bleeding in thalassemic patients with the lupus anticoagulant, a trial of prednisolone was started in three patients with complete clearance of the anticoagulant. These observations confirm other reports of the beneficial effects of corticotropin (5) and prednisolone (1, 7) in suppressing lupus anticoagulant activity. Lupus anticoagulant has recently been confirmed in a patient with B-thalassemia major at the Sri Raj Hospital in Bangkok and a similar response to steroid therapy has also been observed (Personal Communication - Dr. Sutbat Fucharoen MD).

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