Case report

An unusual cause of death of a Hb E/β thalassaemia patient

H M D Moratuwagama, A Jayathilake , T Somarathna, J Hewavisenthi

Introduction

Thalassaemias are a group of genetic disorders common in many tropical countries. Haemoglobin E/β thalassaemia results from coinheritance of a β thalassaemia allele and a Hb E allele and represent 50% of cases of severe β thalassaemia. The cerebrovascular manifestations of thalassaemia and the underlying pathophysiology are not well understood. There are a few case reports and case series describing ischaemic episodes and intracranial haemorrhages including a syndrome of hypertension, convulsions and cerebral haemorrhage following blood transfusion.

We describe the post-mortem findings of a child with Hb E/β-thalassaemia who died following sudden onset headache and an increase in blood pressure followed by convulsions. A subarachnoid haemorrhage was found at autopsy. Some of the poorly understood cerebrovascular manifestations of thalassaemia and the possible underlying pathophysiological mechanisms are discussed.

Case report

A 13 year old girl with E/β -thalassemia on regular blood transfusion and iron chelation treatment, presented with an episode of acute cholecystitis which responded to intravenous antibiotics. As the frequency of blood transfusions in this child had increased over the preceding few months, hypersplenism was suspected and a splenectomy was planned. She was given top up transfusions in preparation for surgery and her Hb improved from 7.3g/dl on admission to 16.4g/dl.

Ten days later, while awaiting surgery, she suddenly developed severe headache and vomiting. She was afebrile and the neurological examination was normal. She had an elevated blood pressure of 180/100mmhg. Subsequently,

Department of Pathology, Faculty of Medicine, University of Kelaniya, Ragama.

Correspondence: H.M.D.Moratuwagama, Department of Pathology, Faculty of Medicine, University of Kelaniya, Ragama, Email: moratuwagama@yahoo.com

she developed generalized tonic clonic seizures which progressed to status epilepticus. As neither the seizures nor the blood pressure could be controlled, she was paralysed and ventilated.

A CT scan of the head could not be performed as the machine was out of order. All the other investigations done at this stage did not provide a reason for the sudden deterioration. The child died thirteen hours after the onset of the status epilepticus. The postmortem examination revealed the following significant findings; a subarachnoid haemorrhage over the left frontal and parietal lobes (Fig.1), hepatomegaly and massive splenomegaly, the latter two organs showing evidence of extramedullary haemopoeisis on histology. There was early fibrosis of the liver.

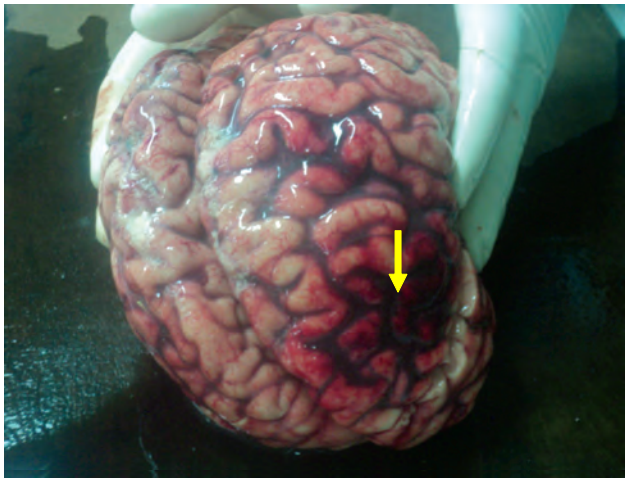

Fig.1: Sub arachnoid haemorrhage (arrow)

Discussion

Thalassaemia are a group of genetic disorders common in many tropical countries. Haemoglobin E/β thalassaemia represent 50% of severe β thalassaemia. The cerebrovascular manifestations of thalassaemia and the underlying pathophysiology are not well understood. There are a few case reports and case series describing ischaemic episodes and intracranial haemorrhages including a syndrome of hypertension, convulsions and cerebral haemorrhage following blood transfusion (1, 2, 3, 4).

The cause for a bleeding tendency in Thalassaemia is poorly understood and several hypotheses have been proposed. These include the presence of circulating coagulation factor inhibitors (2), platelet function defects (5), loss of high molecular weight multimers of von Willebrand factor (6), Pseudoxanthoma elasticum (7), rupture of extramedullary haemopoietic tissue masses (8) and a syndrome of hypertension, convulsions and haemorrhage after blood transfusions (1,3,4).

In 1978, Wasi et al described a syndrome characterised by various combinations of severe headache, hypertension, convulsions and cerebral haemorrhage in eight patients (1). Six of them had E/β-thalassaemia. They had been given multiple blood transfusions in preparation for

splenectomy and none had a history of previous seizures or hypertension. He believed that this syndrome began with hypertension leading to hypertensive encephalopathy and cerebral haemorrhage. The episodes in most cases began many days after blood transfusion (as long as 15 days) and he thought this was unlikely to be due to volume overload. He postulated that this might have been triggered by vasopressor substances introduced by or related to multiple blood transfusions. At necropsy, no pathological blood vessels which might have allowed leakage were observed. Brain changes were similar to those seen in hypertensive cerebral haemorrhage and hypertensive encephalopathy. In some cases, only brain oedema and minute extravasations of red cells were seen.

Incorpora et al reported a case series of β thalassaemia major patients with intracranial haemorrhage. He identified two groups, early onset (within 48 hours) and late onset (7-15 days). The majority (77%) belonged to the latter group. He hypothesized that prolonged anaemia could lead to aseptic venous thrombosis resulting in haemorrhagic strokes. The inability of the blood vessel walls, weakened by chronic exposure to low viscosity blood, to handle sudden increase in viscosity attained through blood transfusions may also be a potential explanation.

Sonakul et al reported the brain pathology in six fatal cases of post transfusion hypertension, convulsion and cerebral haemorrhage syndrome found in a series of 76 thalassaemic patients. Findings included brain oedema and congestion. Visible cerebral haemorrhages were seen in half the cases. Microscopically, all showed small focal or perivascular haemorrhages. None had underlying vascular diseases (3). Wiwanitkit V, reviewing Thai patients with this syndrome reports 9 similar cases (4).

Cerebrovascular complications in Thalassaemia syndrome are poorly understood and rare. This patient shared some of the features of the syndrome of hypertension, convulsion and cerebral haemorrhage even though microscopic changes consistent with hypertensive cerebral haemorrhage or hypertensive encephalopathy were not observed.

This case emphasises that caution should be exercised in transfusing thalassaemia patients, especially when optimising Hb within a short time and that blood pressure should be closely monitored during the post transfusion period.

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