CASE REPORT
Acute encephalopathy with parvovirus B19 infection in sickle cell disease
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A 13 year old girl with haemoglobin Sβthalassaemia developed simultaneous aplastic crisis and encephalopathy associated with parvovirus B19 (PB19) infection. Brain magnetic resonance imaging findings were consistent with central nervous system (CNS) vasculitis and her symptoms resolved with steroid therapy. Thus, PB19 induced CNS hypersensitivity vasculitis must be considered in the differential diagnosis of encephalopathy.

Human parvovirus B19 (PB19) is a well known cause of aplastic crisis in sickle cell disease (SCD). Other manifestations such as myocarditis, arthritis, and glomerulonephritis have been reported with PB19 infection in patients with or without SCD.

The proposed role of PB19 in vasculitis is based on serological evidence of acute PB19 infection and/or the documentation of PB19 DNA in the blood in few patients with various vasculitic syndromes, but no aetiological relation has yet been proven. We report a patient with haemoglobin Sβthalassaemia who developed acute encephalopathy secondary to a vasculitic process in association with PB19 infection.

CASE REPORT
A 13 year old African-American female, with haemoglobin Sβthalassaemia, was admitted with recent onset thoracolumbar region pain without any fever. The child was alert but appeared in pain, without any obvious focus of infection. Her white blood cell (WBC) count was 9200/mm³, haemoglobin 96 g/l, platelet count 188 000/mm³, and reticulocyte count 0.1%. She was treated with morphine and non-steroidal anti-inflammatory drugs for pain. She developed fever on the second day of admission and was started on cefuroxime for probable occult bacteraemia. Her blood and urine cultures remained sterile.

On the third day, she developed altered sensorium with poor responsiveness to auditory, tactile, and visual stimuli. There was associated hypertension and laboured respiration. Her physical examination was significant for the absence of papilloedema and focal neurological deficits. Metabolic parameters (including electrolytes, blood glucose, and renal and liver function tests), chest radiograph, and computed tomography scan of the brain were normal. Her haemoglobin dropped to 79 g/l; a partial exchange transfusion was given, but she was haemodynamically unstable with persistent altered sensorium, requiring ventilatory support for one week. Following intubation she had a cardiac arrest and required inotropic support. She developed acute renal failure for which she underwent haemodialysis. Urine analysis showed 1+ proteinuria, 3+ haematuria, with 10–20 WBC/high power field but no red blood cell (RBC) casts.

Cerebrospinal fluid (CSF) studies obtained on day 4 were normal, with WBC count of 1/µl, glucose 79 mg/dl, and protein 31 mg/dl. Oligoclonal bands were undetectable and immunoglobulin synthesis was <1.0 in the CSF. Antinuclear antibody was undetectable, cytoplasmic and perinuclear antineutrophil antibodies negative, C3 180 mg/dl (90–180 mg/dl), and C4 21 mg/dl (10–40 mg/dl). Initial magnetic resonance imaging (MRI) of the brain on day 15 of the illness showed multiple punctate areas of enhancement in the basal ganglia, periventricular white matter, and along the posterior parietal cortex predominantly on the right. The circle of Willis magnetic resonance angiography was normal. A follow up...

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid; EEG, electroencephalogram; MRI, magnetic resonance imaging; PB19, parvovirus B19; PCR, polymerase chain reaction; RBC, red blood cell; SCD, sickle cell disease; WBC, white blood cell

Figure 1 Sagittal T1 images before [A] and after contrast [B], showing punctate enhancement. Unenhanced scan two weeks later shows punctate areas of perivascular haemorrhage (C).
MRI two weeks later showed development of punctate haemorrhages in the previous areas of perivascular enhancement. The distribution (deep grey matter as well as cortex) and configuration (enhancing punctate lesions together with subsequent development of punctate haemorrhage in those areas) are most consistent with a vasculitic process (fig 1). An electroencephalogram (EEG) showed diffusely slow, moderate amplitude theta and delta waves, clinically correlating with encephalopathy.

In view of the developing anaemia in combination with reticulocytopenia, PB19 IgM and IgG antibody titres were determined by enzyme linked immunosorbenetassay (ELISA) initially and in the convalescent phase (table 1). Anti-PB19 IgM was undetectable in CSF; however, anti-PB19 IgG was detected at a level of 0.14, the significance of which is unknown. PB19 DNA was not detected in the serum two weeks after hospitalisation by polymerase chain reaction (PCR).

The neurological manifestations and MRI findings were attributed to vasculitis secondary to an infectious process, and she was treated with steroids for four weeks. Over the next 3–6 weeks, she recovered from the renal failure, and her neurological state improved to normal. EEG normalised after three weeks. She continues to be clinically well two years after the episode.

**DISCUSSION**

Although aplastic crisis is seen in 67% of cases of PB19 infection in SCD, neurological complications from PB19 have rarely been reported. In a recent report, cerebrovascular events, either in the form of stroke or encephalitic disease, are most consistent with a vasculitic process (fig 1). An electroencephalogram (EEG) showed diffusely slow, moderate amplitude theta and delta waves, clinically correlating with encephalopathy.

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The patient’s renal failure was attributed to acute tubular necrosis because of the preceding events of cardiac arrest and hypotension, presence of mild proteinuria (1+), and the absence of RBC casts and hypocomplementaemia. However, a kidney biopsy was not performed to look for glomerulonephritis. PB19 infection has been associated with endocapillary glomerulonephritis.12 13

Cerebrovascular vaso-occlusive events are rare in patients with haemoglobin Sβ thalassaemia. Our patient had no evidence of meningitis or meningoencephalitis, based on CSF studies. Her brain MRI findings and resolution of symptoms with steroid therapy supports a vasculitic process. A detailed investigation for known autoimmune vasculitic diseases was negative. These findings in conjunction with seroconversion for PB19 can be explained by parainfectious hypersensitivity vasculitis, most likely to be caused by an abnormal immune reaction against PB19 with CNS autoantigen binding properties. The lack of detection of PB19 DNA in the serum may have been owing to the convalescent phase of the disease. Further studies on the anti-PB19 specific antibodies and viral proteins would reveal the mechanisms involved in viral hypersensitivity.

**REFERENCES**

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doi: 10.1136/adc.87.6.541

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