CASE REPORT

Acute parvovirus B19 infection in identical twins unmasking previously unidentified hereditary spherocytosis

Donall G Forde,¹ Alison Cope,² Ben Stone³

¹Department of Infectious Disease and Virology, Birmingham Heartlands Hospital, Birmingham, UK

²Department of Virology, Northern General Hospital, Sheffield, UK

³Department of Infectious Disease and Tropical Medicine, Royal Hallamshire Hospital, Sheffield, UK

Correspondence to

Dr Donall G Forde, donallforde@gmail.com

Accepted 10 July 2014

SUMMARY

Identical Caucasian male twins, previously fit, presented 1 week apart with short histories of fever and lethargy. The twins were febrile at presentation with profound pancytopenia and evidence of haemolysis. There was no rash or arthralgia. Both required multiple red cell transfusions. The twins had positive IgM serology for Epstein-Barr virus (EBV), cytomegalovirus (CMV) and parvovirus B19. EBV viral capsid antigen and Epstein-Barr nuclear antigen IgGs were also positive however, suggesting past EBV exposure. Parvovirus B19 DNA was detected from peripheral blood PCR; CMV and EBV DNA PCRs were negative. Convalescent serology demonstrated no evolution of the CMV serological response, that is no IgG to CMV developed which implies an initial non-specific polyclonal IgM response. The twins recovered fully over 7 days, the first with a course of prednisolone and the second spontaneously. They were diagnosed with hereditary spherocytosis on convalescent blood films. On further questioning, a family history of hereditary spherocytosis was eventually revealed. The twins' maternal grandmother was known to have the condition asymptotically. Their mother had prior to this never been tested, but later bloods would reveal a compatible biochemical picture.

BACKGROUND

This case highlights three key learning points:

1. In patients presenting with evidence of acute parvovirus B19 infection and concurrent aplastic crisis, common underlying causes for disordered red cell production or destruction should be sought.
2. While virological diagnoses can be made by single serological screening tests, multiple positive IgMs can be misleading; these should be supported by confirmatory PCR testing and convalescent serology samples to look for development of specific IgG in response to the acute infection.
3. The importance of thorough history taking including a family history.

CASE PRESENTATION

Identical Caucasian male twins, previously fit and well, presented 1 week apart with short histories of fever and lethargy. They were febrile at presentation with profound pancytopenia and evidence of haemolysis. There was no rash, arthralgia or neurological symptoms. Examination was unremarkable. The twins had weekly contact with each other.

INVESTIGATIONS

The first twin underwent a bone marrow examination, which excluded haematological malignancy, but did demonstrate appearances consistent with an aplastic crisis.

Nadir haemoglobin was 5.9 g/L, platelets of $44 \times 10^9/L$ and total white cells of $2 \times 10^9/L$.

The first twin had positive IgM serology for Epstein-Barr virus (EBV), cytomegalovirus (CMV) and parvovirus B19. EBV viral capsid antigen and Epstein-Barr nuclear antigen IgGs were also positive however, suggesting past EBV exposure and therefore polyclonal B-cell reactivity. Parvovirus B19 DNA was detected from peripheral blood PCR. CMV and EBV DNA PCR were negative. A similar serological picture was seen with the second twin, with evidence of acute parvovirus B19 infection also confirmed by PCR (see [figure 1](#)).

The twins tested negative for HIV infection.

Convalescent serology demonstrated evolution of the parvovirus B19 response with appearance of specific IgG, but no evolution of the CMV serological response.

The twins were diagnosed with hereditary spherocytosis on convalescent blood films (see [figure 2](#)).¹

DIFFERENTIAL DIAGNOSIS

- ▶ Acute myeloid leukaemia
- ▶ Acute lymphoid leukaemia
- ▶ Lymphoma
- ▶ Paroxysmal nocturnal haemoglobinuria

TREATMENT

Treatment was supportive, with no specific antiviral available. The twins needed multiple red cell transfusions due to their profound anaemia. The first twin received steroids while investigations to exclude haematological malignancy and primary EBV infection were ongoing. A less invasive and more supportive management plan was adopted for the second twin presenting 1 week later, as the initial presenting twins diagnosis had by that time been confirmed.

OUTCOME AND FOLLOW-UP

Evolution of parvovirus B19 serology on convalescent testing (with no evolution of CMV serology) supported the diagnosis of acute parvovirus B19 infection. Each twin made a full recovery. No long-term sequelae were observed.

CrossMark

To cite: Forde DG, Cope A, Stone B. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202957

Serology	Acute	Convalescent
EBV IgM	Detected	Detected
EBV VCA IgG	Detected	Detected
EBV EBNA IgG	Detected	Detected
CMV IgM	Detected	Detected
CMV IgG	NOT Detected	NOT Detected
Parvovirus IgM	Detected	Detected
Parvovirus IgG	NOT Detected	Detected
HIV Ab	NOT Detected	NOT Detected
EBV PCR	NOT Detected	NOT Detected
CMV PCR	NOT Detected	NOT Detected
Parvovirus PCR	Detected	NOT Detected

Figure 1 Serology and PCR results (identical for both twins) confirmed acute parvovirus B19 infection.

DISCUSSION

The family Parvoviridae, in the genus *Erythrovirus*, contains a virus called parvovirus B19. It is the only single stranded DNA virus known to infect humans. The virus is toxic to erythroid progenitor cells. It is spread via the respiratory route with 50% of young adults showing evidence of past exposure.²

Consequences of infection range from asymptomatic to the childhood viral exanthem fifth disease (also known as ‘slapped cheek syndrome’), to the fatal hydrops fetalis in utero.

Cases of acute parvovirus infection causing pancytopenia in immunocompetent adults are described in the literature.³ Additionally, chronic parvovirus causing anaemia has been described in immunocompromised patients.⁴

Hereditary spherocytosis is the most common haemolytic anaemia; it is caused by defects in the ankyrin gene coding for the red cell membrane skeleton. In total, 75% of cases are autosomal dominant. It affects 250/million people in Northern Europe. The diagnosis is made based on anaemia with reticulocytosis and spherocytosis, in the setting of a familial history of haemolytic anaemia and an abnormal osmotic fragility test.⁵

Our case adds to this cohort by demonstrating the spectrum of severe clinical manifestations in a uniquely at-risk set of identical twins with an almost definite path of infection between them.

Figure 2 Blood film demonstrating spherocytes.

Learning points

- ▶ In patients presenting with evidence of acute parvovirus B19 infection and concurrent aplastic crisis, an underlying cause for disordered red cell production or destruction should be sought.
- ▶ While virological diagnoses can be made by serological screening tests, multiple positive IgMs can be misleading; these should be supported by confirmatory PCR testing and follow-up samples to look for specific evolution of the serological response over time.
- ▶ All patients with a cytopenia should undergo HIV testing.⁶
- ▶ The importance of contact tracing in the evaluation of patients with an infectious disease allows for a more tailored management approach.
- ▶ Taking a thorough family history can be invaluable.

Acknowledgements The authors would like to acknowledge Nicole Brumpton ID secretary for administrative help and the twins for their consent.

Contributors DGF is the guarantor of the article. All authors were involved in the clinical care and writing of the case.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Image taken from: <http://www.wadsworth.org/chemheme/heme/microscope/spherocyte.htm>
- 2 Collier L, Kellam P, Oxford J. *Chapter 13: parvoviruses*. In: Human virology. 4th edn. New York: Oxford University Press, 2011.
- 3 Barlow GD, McKendrick MW. Parvovirus B19 causing leucopenia and neutropenia in a healthy adult. *J Infect* 2000;40:192–5.
- 4 Frickhofen N, Abkowitz JL, Safford M, et al. Persistent B19 parvovirus infection in patients infected with human immunodeficiency virus type 1 (HIV-1): a treatable cause of anemia in AIDS. *Ann Intern Med* 1990;113:926–33.
- 5 Bolton-Maggs PH, Langer JC, Iolascon A, et al. Guidelines for the diagnosis and management of hereditary spherocytosis—2011 update. *Br J Haematol* 2012;156:37–49.
- 6 UK National Guidelines for HIV testing. (2008). British HIV Association.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow