

A Syndrome Resembling Thrombotic Thrombocytopenic Purpura Associated with Human Parvovirus B19 Infection

R. H. J. Kok,¹ M. J. H. M. Wolffhagen,² G. Klosters²

¹Department of Internal Medicine and ²Laboratory of Medical Microbiology and Infectious Disease, Isala Clinics 'de Weezenlanden,' Zwolle, The Netherlands

This is the first report of a patient with a syndrome resembling thrombotic thrombocytopenic purpura associated with a recent human parvovirus B19 infection.

Human parvovirus B19 (B19) is a nonenveloped, single-strand DNA virus that can cause a diverse range of clinical manifestations. Erythema infectiosum (fifth disease) is the most commonly recognized disorder caused by B19 infection. B19 is also associated with polyarthropathy, transient aplastic crisis in patients with hemolytic anemia, chronic infection and anemia in immunocompromised hosts, and hydrops fetalis [1]. Renal involvement in cases of B19 infection is rare [2, 3]. B19 infection has been described in association with glomerulonephritis in patients with sickle-cell disease [4, 5]. We present a patient with B19 infection and thrombotic thrombocytopenic purpura (TTP).

A 37-year-old man who had no relevant medical history and who was not using any medication was admitted to our hospital because of fever and purpura. He had been well until 3 days earlier, when nausea, headache, fever, rash, and joint pain had developed. The patient was married and had 3 children, 1 of whom had recently been ill, with rash and fever.

At admission the patient's temperature was 39.2°C, pulse was 100 beats/min, and blood pressure was 150/100 mm Hg. Physical examination revealed an ill, confused man with generalized rash and purpura on his shoulders, upper arms, and upper legs. Further examination showed no abnormalities—in particular, no focal neurological signs. Results of laboratory tests performed at admission (day 1) are shown in Table 1. Peripheral blood film examination showed leukocytosis with a

left shift and red cell fragmentation. We measured the activated partial thromboplastin time, the prothrombin time, and fibrinogen levels repeatedly; all were normal, which made a diagnosis of disseminated intravascular coagulation (DIC) less probable. The results of urine examination were normal. A bone marrow biopsy was performed, and the specimen showed no red cell hypoplasia, no maturational arrest, and no giant pronormoblasts. These findings are typical in cases of B19 infection. Chest radiographs and the findings of abdominal echography were normal.

A diagnosis of TTP and/or sepsis with DIC was considered. After aerobic and anaerobic cultures of blood specimens were performed, the patient received iv imipenem and clindamycin. After 1 day the skin lesions developed into extensive purpura with full-thickness skin necrosis (which was proven by examination of biopsy specimens). The patient developed anuria and the results of laboratory tests worsened (Table 1, day 2). Continuous veno-venous hemodiafiltration (CVV-HDF) was started, with bicarbonate-buffered hemofiltration solution as the substitution fluid, followed by administration of fresh frozen plasma and intermittent plasmapheresis (exchange of 3.5 L of plasma per run). Cultures were performed with specimens of blood, throat, feces, and urine obtained at admission; results were negative for bacterial growth. Results of serologic testing (enzyme-linked immunosorbent and immunofluorescence assays) for B19 were positive for IgM and IgG antibodies. Furthermore, a PCR analysis of serum samples showed the presence of B19 DNA. (The PCR analysis was performed at the Central Clinical Laboratory, Academic Hospital Leiden, The Netherlands).

Table 1. Results of laboratory tests performed at 2 time points for a patient with thrombotic thrombocytopenic purpura associated with human parvovirus B19 infection.

Laboratory test	Normal value	Value on	
		Day 1	Day 2
Hemoglobin level, mM/L	8.7–11.1	7.8	5.6
Leukocyte count, cells × 10 ⁹ /L	4.0–10	4.6	3.7
Platelet count, cells × 10 ⁹ /L	150–350	30	13
Urea nitrogen level, mM/L	1.8–6.4	23.6	28.5
Creatinine level, μM/L	75–110	494	631
Lactate dehydrogenase level, U/L	<320	786	2440
Aspartate aminotransferase level, U/L	<30	39	86
Alanine aminotransferase level, U/L	<30	47	82
Alkaline phosphatase level, U/L	<100	45	49
Total bilirubin level, μM/L	<17	24	73

Received 27 December 1999; revised 30 May 2000; electronically published 28 December 2000.

Reprints and correspondence: Ronald Kok, Isala Clinics 'de Weezenlanden,' Department of Internal Medicine, Postbus 10500, 8000 GM Zwolle, The Netherlands (rhjkok@worldonline.nl)

Clinical Infectious Diseases 2001;32:311–2

© 2001 by the Infectious Diseases Society of America. All rights reserved.
1058-4838/2001/3202-0023\$03.00

The patient's child, who had recently been ill and had a rash, was also tested for B19 infection. However, results of the same tests were all negative. Serologic testing and PCR analysis were performed before the administration of FFP and other blood products. Results of serologic tests for antinuclear antibodies, immune circulating complex, hepatitis B, leptospirosis, and rickettsiosis were all negative, as were antistreptolysin titers and the results of Coombs' test.

Our patient became afebrile rapidly. CVV-HDF was changed to intermittent hemodialysis. After 12 days, the patient's platelet count had increased to $>100 \times 10^9$ cells/L. Renal function improved slowly, and, after 4 weeks, hemodialysis could be stopped. The necrotic skin lesions were repaired with skin grafts. The results of laboratory tests normalized completely, except for a mild renal impairment. Six months after discharge the patient remained without complaints with near normal kidney function.

Our patient presented with a characteristic set of clinical and laboratory findings that suggested TTP and an acute B19 infection. TTP is a life-threatening disease, characterized by fever, thrombocytopenia (often with purpura), microangiopathic hemolysis, and microvascular thrombotic occlusions that affect the brain, kidneys (causing acute renal insufficiency), and other organs [6]. This combination of symptoms can also be seen in certain other severe disorders, such as sepsis with DIC. However, in cases of DIC, the results of coagulation tests are usually not normal; in cases of TTP, they are normal. Although many cases of TTP are idiopathic, a variety of underlying infectious causes have been identified. The best known is TTP following

infection with cytotoxin-producing bacteria, such as *Escherichia coli*, *Shigella dysenteriae*, *Salmonella typhi*, *Campylobacter jejuni*, *Streptococcus pneumoniae*, and *Yersinia pseudotuberculosis*. TTP accompanying viral infections, such as infection with HIV, has also been described. B19 infection has not previously been reported in association with TTP. There is a recent report of hemolytic-uremic syndrome (a syndrome closely related to TTP) following B19 infection [7]. The case we describe demonstrates that the diagnosis of B19 infection should be considered for patients with TTP.

References

1. Portmore AC. Parvovirus (erythema infectiosum, aplastic crisis). In: Mandell GJ, Bebbet JE, Dolin R, eds. Principles and practice of infectious diseases. 4th ed. New York: Churchill Livingstone, 1995;1439–46.
2. Leray H, Canaud B, Cristol JB, et al. Parvovirus B19 infection revealed by acute renal insufficiency. *Nephrologie* 1992;13:123–5.
3. Scholbach T. Kidney involvement in parvovirus B19 infection in a child. *Kinderarztl Prax* 1992;60:156–8.
4. Wierenga KJ, Pattison JR, Brink N, et al. Glomerulonephritis after human parvovirus infection in homozygous sickle-cell disease. *Lancet* 1995;346:475–6.
5. Tolaymat A, Mousily F, MacWilliam K, Lammert N, Freeman B. Parvovirus glomerulonephritis in a patient with sickle cell disease. *Pediatr Nephrol* 1999;13:340–2.
6. Ruggenti P, Remuzzi G. The pathophysiology and management of thrombotic thrombocytopenic purpura. *Eur J Haematol* 1996;56:191–207.
7. Seward EW, Rustom R, Nye FJ, Bone JM. Haemolytic-uraemic syndrome following human parvovirus infection in a previously fit adult. *Nephrol Dial Transplant* 1999;14:2472–3.