Renal Involvement of Human Parvovirus B19 in an Immunocompetent Host

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Human parvovirus B19, which is most commonly known to cause erythema infectiosum in children, is also known to cause infection in adults, with complications ranging from a self-limited polyarthritis in immunocompetent patients to hydrops fetalis in pregnant women, transient aplastic crises in patients with chronic hemolytic anemias, and chronic aplastic anemia in immunocompromised hosts. We describe a previously healthy immunocompetent woman who presented with manifestations of acute parvovirus B19 infection.

In July 1998, a 38-year-old woman was admitted to the University of Maryland Hospital, Baltimore, with a 3-week history of intermittent fevers (temperature, to 39.2°C), pleuritic chest pain accompanied by shortness of breath at rest, a discrete rash, fatigue, and diffuse joint pain. The illness started as a flulike syndrome marked by headache, fever, general malaise, and a violaceous rash on the face (sparing the nose); the syndrome had lasted 1 week. Despite a negative Lyme disease antibody titer, the patient had been treated 2 weeks before her admission for parvovirus were negative. Glomeruli examined by immunofluorescence stained strongly positive for IgG, IgM, C3, and Fibrinogen, predominantly in the mesangium, indicating an immune complex etiology.

The patient’s renal ultrasound appeared normal. A renal biopsy specimen showed a moderate diffuse endocapillary glomerulonephritis. Immunoperoxidase stain and in situ hybridization for parvovirus were negative. Glomeruli examined by immunofluorescence stained strongly positive for IgG, IgM, C3, and Fibrinogen, predominantly in the mesangium, indicating an immune complex etiology.
The patient was then tested for human parvovirus B19 DNA by PCR with Southern blot test confirmation (Viro-Med), which was positive. By the fifth day of hospitalization, the patient’s symptoms had so improved that she was discharged. On a follow-up visit 3 weeks later, the patient was still feeling weak but showed marked improvement of her dyspnea. Her fever had disappeared and her lungs were clear. Heart rate was 110 beats/min, and her edema was reduced to a trace in the ankles. Her hematocrit had increased to 34.9%. A urinalysis showed 3+ blood and 3+ protein, and results of hepatitis A, B, and C serological tests were all negative. A repeated 24-h urine collection revealed 1.75 g of protein per 24 h. In addition, the patient’s serological tests were all negative. A repeated 24-h urine collection done in March 1999 was negative 40 weeks after the beginning of her illness. A urinalysis performed 1 year from the onset of her symptoms was negative for both protein and blood, and results of hepatitis A, B, and C were 1+ positive for both blood and protein. A repeat Westergren sedimentation rate was 55 mm/h, and hematocrit was 33.5%. The patient returned 20 weeks after the onset of her illness feeling much improved; her rheumatological symptoms had disappeared. A urine dipstick test showed 1+ protein and blood of 177 g of protein per 24 h. A repeat spiral CT scan of the chest at this time revealed resolution of the pleural effusions. By week 26, the patient’s vital signs were back to baseline. Her proteinuria had resolved, and serum parvovirus B19 IgM was negative and IgG was positive. A parvovirus serum PCR done in March 1999 was negative 40 weeks after the beginning of her illness. A urinalysis performed 1 year from the onset of her symptoms was negative for both protein and blood, and the patient remained asymptotic.

Human parvovirus B19 (the only known parvovirus to infect humans), is a nonenveloped single-stranded DNA virus that can present with many protean manifestations. It is best known as the etiologic agent in erythema infectiosum or fifth disease, a common exanthematous disease of childhood usually occurring in epidemics in late spring [1, 2]. Commonly reported presentations are symmetrical polyarthropathy, hydrops fetalis after intrauterine infection, and chronic anemia in immunocompromised patients [3]. In patients with chronic hemolytic anemias (and occasionally in immunocompetent hosts) parvovirus B19 infection can cause a transient aplastic crisis. [1–3]. Many women infected with human parvovirus B19 develop an acute self-limited symmetrical arthropathy associated with a blotchy or lacylike rash and flulike symptoms [1]. On rare occasions, arthralgia, neuroarthropathy, and viremia may persist in healthy adults in the absence of anemia [4]. Infrequent manifestations of parvovirus infection include hepatitis [5], neuropa-thies [1], and papular-purpuric glove and socks syndrome [6]. In addition, chronic parvovirus infection in immunocompetent patients has been associated with systemic necrotizing vasculitis in patients with features of polyarteritis nodosa and Wegener’s granulomatosis [7, 8].

Lupuslike presentation has been reported in the literature with patients presenting with arthritis, fever, polyarthralgia, pleuritic chest pain, and macular rash; some of those cases had laboratory features of low complement and cross-reactivity to autoantibodies such as a transient positive anti-nuclear antibodies [9–15]. Chia and Jackson [16] describe a patient with significant myopericarditis and strongly positive serum tests for parvovirus B19 DNA and IgG in the absence of any demonstrable immune defects. Orth et al. [17] report another case of severe perimyocarditis in a previously healthy 34-year-old man with transient anemia and no documented immunosuppression. More recently, a case of pulmonary involvement leading to respiratory failure and mechanical ventilation was reported in a previously healthy 47-year-old woman with acute parvovirus B19 infection [18]. Review of the literature revealed reports of parvovirus B19–associated focal segmental glomerulonephritis in patients with sickle cell disease, nephrotic syndrome, and preceding aplastic crisis [19–21].

The pathogenesis of cardiac, pulmonary, and renal involvement in the setting of parvovirus B19 infection has not been fully elucidated. It may be related to an immune complex deposition type process. Such a process has been described in glomerulonephritis associated with several other viruses, including hepatitis B and hepatitis C. A mammalian parvovirus that is the etiological agent of Aleutian mink disease, a chronic infection in mink, presents with severe immunocomplex glomerulonephritis [22]. The role of a direct viral cytopathic effect in the pathogenesis of parvovirus B19–associated organ involvement is more controversial. We were unable to detect parvovirus antigen in the renal tissue of this patient; this fact, along with the lack of cytolysis on pathology, makes it unlikely that the virus was directly cytotoxic. Similarly, Chia and Jackson [16] and Wierenga et al. [19] failed to detect any parvovirus DNA or viral inclusions in their patient’s myocardial and renal biopsy, respectively. However, in other cases, a direct viral cytopathic effect was suggested by several reports describing positive hybridization studies in the myocardium of fetuses with lethal parvovirus B19 infection [23] and immunocytochemical studies in the myocardium of an infant with lethal myocarditis [24].

Several authors have reported the development of autoantibodies during the course of parvovirus B19 infection in patients with chronic or recurrent arthritis and persistent IgM antibodies against parvovirus, including antibodies to cardiolipin, keratin, collagen type II, double-stranded DNA, and phospholipids [25–27]. We speculate this patient’s parvovirus may have triggered the production of an as-yet unidentified autoantibody that led to the deposition of immune complexes.
into the various tissues. This autoantibody may have caused multifocal pathology until the clearance of parvovirus infection by the patient downregulated its production. Clearance of parvovirus along with the fall of IgM usually occurs ~8 weeks after initial infection; however, low titers may persist 4–6 months after acute infection, which seemed to be the case in this patient [4].

Several cases of successfully treated parvovirus-induced anemia have been documented that used commercial Ig preparations at 440 mg/kg. Most of these patients, unlike the patients we studied, lacked parvovirus antibodies and or were HIV positive [3, 28]. We chose not to treat this patient with immunoglobulin or immune modifying agents because: (1) her symptoms began to resolve within a reasonable amount of time, (2) her body demonstrated an ability to raise antibodies against parvovirus, and (3) her renal biopsy was more consistent with that of a reversible process.

We think that human parvovirus B19 had a direct effect on this patient’s process because of the onset of acute infection occurring in the endemic season that correlated with the onset of her anemia, her pulmonary and rheumatological symptoms, and her renal pathology; and because the resolution of these findings occurred at the same time as the clearance of her parvovirus B19 IgM and DNA from her serum. This, in conjunction with the absence of any other detectable agents or processes and the detection of immune complexes on renal biopsy, suggests that parvovirus played a direct role in the etiology of her illness. We encourage other clinicians to be alert to this as well as the other various manifestations of human parvovirus B19 infections.

References