Two Family Members With a Syndrome of Headache and Rash Caused by Human Parvovirus B19

Antonio Carlos M. Pereira, Roberto Alexandre Q. Barros, Jussara Pereira do Nascimento and Solange Artimos de Oliveira Department of Infectious Diseases, Antonio Pedro University Hospital and Department of Virology, Instituto Biomédico, University Federal Fluminense, Niterói, RJ, Brazil. Biomanguinhos, Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil

Human parvovirus B19 infection can cause erythema infectiosum (EI) and several other clinical presentations. Central nervous system (CNS) involvement is rare, and only a few reports of encephalitis and aseptic meningitis have been published. Here, we describe 2 cases of B19 infection in a family presenting different clinical features. A 30 year old female with a 7-day history of headache, malaise, myalgias, joint pains, and rash was seen. Physical examination revealed a maculopapular rash on the patient's body, and arthritis of the hands. She completely recovered in 1 week. Two days before, her 6 year old son had been admitted to a clinic with a 1-day history of fever, headache, abdominal pain and vomiting. On admission, he was alert, and physical examination revealed neck stiffness, Kerning and Brudzinski signs, and a petechial rash on his trunk and extremities. Cerebrospinal fluid analysis was normal. He completely recovered in 5 days. Acute and convalescent sera of both patients were positive for specific IgM antibody to B19. Human parvovirus B19 should be considered in the differential diagnosis of aseptic meningitis, particularly during outbreaks of erythema infectiosum. The disease may mimic meningococcemia and bacterial meningitis.

Key Words: Human parvovirus B19, aseptic meningitis, erythema infectiosum.

Human parvovirus B19 was discovered in 1975, by Cossart, et al. [1], and has been described as the causative agent of a broad range of diseases. These include erythema infectiosum [2], arthropathy [3], nonimmune hydrops fetalis and spontaneous abortion in pregnancy [4], transient aplastic crises in patients with chronic hemolytic disorders [5], and chronic anemia in individuals with underlying immunodeficiency illnesses [6].

Received on 13 July 2000; revised 16 November 2000. Address for correspondence: Dr. Solange Artimos de Oliveira - Department of Infectious Diseases, Hospital Universitário Antonio Pedro - Rua Marques do Paraná, 303, 2º andar, Niterói, RJ. CEP 24030-210. Brasil. Phone/Fax: +55 21 7197262. E-mail: artimos@vm.uff.br Support: CNPq (grant No. 52-0689/96-8)

The Brazilian Journal of Infectious Diseases 2001;5(1):37-39 © 2001 by The Brazilian Journal of Infectious Diseases and Contexto Publishing. All rights reserved. 1413-8670

Central nervous system (CNS) involvement by parvovirus B19 is rare, and only a few reports of encephalopathy [7-11] and meningitis [12-17, 21] have been reported. Other CNS abnormalities described in connection with parvovirus B19 includes numbness and tingling of fingers [18], and neuralgic amyotrophy [19]. The prognosis of meningitis and encephalitis due to parvovirus in otherwise healthy people appears to be good, and most of the cases have been benign and self-limiting [20, 21]. Here, we describe 2 cases of parvovirus B19 infection in the same family (mother and son) who presented different clinical aspects.

Case reports

<u>Case 1</u>. A previously healthy 30 year old female was seen at our hospital on December 18, with a 7-day history of headache, malaise, myalgias, joint

pains involving her hands, knees and ankles, and a 3-day history of body rash excluding her face. Physical examination revealed a maculopapular rash on the patient's extremities and trunk, and swelling and tenderness of both hands at the proximal interphalangeal joints. Her acute and convalescent phase sera had specific immunoglobulin IgM and IgG antibodies against parvovirus B19 confirmed by using, respectively, an antibody capture enzyme immunoassay [22], and an "in house" enzyme immunoassay using recombinant B19 capsids produced in insect cells (Sf9) as antigen [23, 24]. She became completely well in 1 week.

Case 2. A 6 year old boy was admitted to a private clinic on December 16, with a 1 day history of high fever (40°C), headache, abdominal pain and vomiting. On admission, he was alert and oriented; physical examination revealed slight neck stiffness, Kernig and Brudzinski signs, oropharyngeal erythema, tender occipital lymphadenopathy, and a petechial rash on the patient's trunk and extremities. His peripheral white cell count was 3.7 x 10³/mm³, with 11% band cells, 63% segmented cells, 21% lymphocythes. Platelet count was 325,000 mm³. Cerebrospinal fluid (CFS) analysis showed normal cell count and protein and glucose concentrations. Gram's stained smear, latex agglutination for Neisseria meningitidis (Groups A, B, C, YW135), Streptococcus pneumonia, Streptococcus "B", Escherichia coli (K1), and culture of CSF were negative. Serum samples from acute and convalescent phases were positive for IgM antibodies to parvovirus B19. Radiography of the facial sinus and chest did not show any abnormalities. Other investigations, including detection of IgM for measles, rubella and dengue, was negative for both patients. A 2-day course of treatment with intravenous ceftriaxone was started for 7 days because of the clinical hypothesis of meningococcal disease. The clinical signs of meningitis and fever completely disappeared in 2 days. However, the petechial rash remained for 3 more days.

Discussion

Despite major advances in pediatric intensive care, meningococcemia remains an important cause of morbidity and mortality in Brazilian children. Because the outcome of the disease depends on rapid diagnosis and immediate institution of antibiotics, the diagnosis of meningococcemia is best made clinically [25].

Bacterial meningitis is diagnosed in a patient with clinical evidence of meningeal irritation and inflammatory response to infection in the CSF [26]. However, confirmation of the clinical diagnosis may sometimes be difficult as bacterial meningitis with normal CSF has been reported by several authors [25, 26, 28, 29]. Since, at the time of hospital admission, the clinical manifestations of patient 2 were considered to be suggestive of meningococcal infection, he received early treatment with antibiotics. As the child made a rapid uneventful recovery, no other lumbar puncture was done.

The suspicion that both patients were suffering from the same disease was highly suggestive and was confirmed by the detection of anti-B19 IgM in sera of both cases. The occurrence of the diseases at the same time, the CSF results, and the prompt recovery of the boy were important clues to consider a viral etiology for both patients.

In immunocompetent individuals, IgM antibody to B19 appears about 10 to 14 days after infection. IgG antibody also appears about 2 weeks after infection [30]. The 6 year old boy failed to mount an IgG response during the period evaluated. The early collection of the samples might explain this result. However, it was not possible to collect another specimen to detect or demonstrate a rise in B19-specific IgG antibodies.

Our patient presented 2 unusual clinical manifestations of parvovirus B19 infection: meningitis and petechial rash [31]. This case demonstrates that this infection should be considered in the differential diagnosis of patients with aseptic meningitis, particularly during outbreaks of erythema infectiosum.

Acknowledgements

We thank Dr. Marilda M. Siqueira for measles and rubella tests, Dr. Rita M. Nogueira for the dengue test, and Dr. João M. Joceli for clinical support. We also thank Conselho Nacional de Pesquisa e Desenvolvimento (CNPq – grant No. 52-0689-96-8) for providing financial support for this research.

References

- 1. Cossart Y.E., Field A.M., Cant B., Widdows D. Parvovirus-like particles in human sera. Lancet **1975**;1:72-3.
- 2. Anderson M.J., Jones S.E., Fisher-Hoch S. P., et al. The human parvovirus, the cause of erythema infectiosum (fifth disease)? Lancet **1993**;1:1378.
- 3. White D.G., Woolf A.D., Mortimer P.P., et al. Human parvovirus arthropathy. Lancet **1985**;1:419-21.
- 4. Brown T., Anand A., Ritchie L.D., et al. Intrauterine parvovirus infection associated with hydrops fetalis. Lancet **1984**;2:1033-4.
- Serjeant G.R., Mason K., Topley J.M., et al. Outbreak of aplastic crises in sickle cell anaemia associated with parvovirus-like agent. Lancet 1981;2:595-7.
- 6. Kurtzman G.J., Cohen B.J., Field A.M., et al. Immune response to B19 parvovirus and an antibody defect in persistent viral infection. J Clin Invest **1989**;84:1114-23.
- 7. Yoto Y., Kudoh T., Asanuma H., et al. Transient disturbance of consciousnouss and hepatic dysfunction associated with human parvovirus B19 infection. Lancet **1994**;344:624-5.
- 8. Balfour H.H. Jr., Schiff G.M., Bloom J.E. Encephalitis associated with erythema infectiosum. JAMA 1970;77:133-6.
- 9. Hall C.B., Horner F.A. Encephalopathy with erythema infectiosum. Am J Dis Child **1977**;131:65-7.
- 10. Watanabe T., Satoh M., Oda Y. Human parvovirus B19 encephalopathy. Arch Dis Child **1994**;70:71.
- 11. Umene K., Nunoue T. A new genome type of human parvovirus B19 present in sera of patients with encephalopathy. J Gen Virol **1995**;76:2645-51.
- 12. Brass C., Elliott L.M., Stevens D.A. Academy rash. A probable epidemic of erythema infectiosum (fifth disease). JAMA **1982**;248:568-72.
- Lefrère J.J., Olivier C., Couroucé A.M., Soulier J.P. Erythroblastopénie et syndrome méningé fébrile dus à parvovirus chez un enfent drépanocytaire homozygote. Presse Méd 1985;14:228-9.

- Tsuji A., Uchida N., Asamura S., et al. Aseptic meningitis with erythema infectiosum. Eur J Pediatr 1990;149:449-50.
- Okumura A., Ichikawa T. Aseptic meningitis caused by human parvovirus B19. Arch Dis Child 1993;68:784-5.
- Cassinoti P., Schultze D., Schlageter P., et al. Persistent human parvovirus B19 infection following an acute infection with meningitis in an immunocompetent patient. Eur J Clin Microbiol Infect Dis 1993;12:701-4.
- 17. Susuki N., Terada S., Inoue M. Neonatal meningitis with human parvovirus B19 infection. Arch Dis Child **1995**;73:F196-7.
- Faden H., Gary G.W., Korman M. Numbness and tingling of fingers associated with parvovirus B19 infection. J Infect Dis 1990;161:354-5.
- Pellas F., Olivares J.P., Zandotti C., Delarque A. Neuralgic amyotrophy after parvovirus B19 infection. Lancet 1993;342:503-4.
- Heegaard E.D., Peterslund N.A., Hornsleth A. Parvovirus B19 infection associated with encephalitis in a patient suffering from malignant lymphoma. Scand J Infect Dis 1995;27:631-3.
- 21. Koduri P.R., Naides S.J. Aseptic meningitis caused by parvovirus B19. CID **1995**;21:1053.
- Cubel R.C.N., Alferes A.C.R., Cohen B.J., Nascimento J.P.
 Application to immunoglobulin M capture hemadherence assays of hemagglutination of monkey erythrocytes by native and recombinant human parvovirus B19 antigens.
 J Clin Microbiol 1994;32:1997-9.
- Bansal G.P., Hatfield J.A., Dunn F.E., et al. Candidate recombinant vaccine for human B19 parvovirus. J Infect Dis 1993;167:1034-44.
- Cubel R.C.N., Siqueira M.M., Santos E.O., et al. Human parvovirus B19 infections among exanthematic diseases notified as measles. Rev Soc Bras Med Trop 1997;30:15-20.
- Kirsch E.A., Barton P.R. Kitchen L., Giroir B.P. Pathophysiology, treatment and outcome of meningococcemia: a review and recent experience. Pediatr Infect Dis J 1996;15:967-79.
- Coll M.T., Uriz M.S., Pineda V., et al. Meningococcal meningitis with "normal" cerebrospinal fluid. J Infect Dis 1994;29:289-94.
- 27. Klein J O., Feigin R.D., McCracken G.H. Jr. Report of the Task Force on diagnosis and management of meningitis. Pediatrics **1986**;78(Suppl).
- 28. Moore C.M., Ross M. Acute bacterial meningitis with absent or minimal cerebrospinal fluid abnormalities. Clin Pediatr **1973**;12:117-8.
- Domingo P., Mancebo J., Blanch L., et al. Bacterial meningitis with "normal" cerebrospinal fluid in adults: a report on five cases. Scand J Infect Dis 1990;22:115-6.
- 30. Brown K.E., Young N.S. Parvovirus B19 in human disease. Annu Rev Med **1997**;48:59-67.
- 31. Mortimer P.P., Cohen B.J., Rossiter M.A., et al. Human parvovirus and purpura. Lancet **1985**;2:730-1.