

CASE REPORT

PAPULAR-PURPURIC “GLOVES AND SOCKS” SYNDROME DUE TO PARVOVIRUS B19: REPORT OF A CASE WITH UNUSUAL FEATURES

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SUMMARY

We present a case of papular-purpuric “gloves and socks” syndrome (PPGSS) in an adult male with acute parvovirus B19 infection. The patient displayed the classical features of fever, oral lesions, and purpura on hands and feet, but the purpuric lesions on the feet evolved to superficial skin necrosis, a feature not previously described in this syndrome. We believe this is the first reported case of PPGSS occurring in Brazil.

KEYWORDS: Parvovirus B19; Papular-purpuric “gloves and socks” syndrome; Rash; Purpura

INTRODUCTION

The papular-purpuric “gloves and socks” syndrome (PPGSS) was first described in 1990 by HARMS *et al.*¹⁰ based on clinical features of five Swiss young adults presenting with a pruritic erythema and edema of the hands and feet, sharply margined on the wrists and ankles, rapidly evolving to petechial purpura associated with fever and oral aphthoid lesions. The illness was self-limited, lasting 1 to 2 weeks. An infectious origin, probably viral, was suggested, but could not be proven. In 1991, BAGOT & REVUZ³ reported a case of PPGSS in a woman with primary parvovirus B19 infection. Since 1990, more than 50 cases of PPGSS have been published. In many cases no cause could be found⁷. B19 is the only virus clearly established as an etiologic agent of PPGSS^{9,19}, although occasional cases associated with Coxsackie B virus, measles virus, cytomegalovirus, hepatitis B virus, Epstein-Barr virus, and human herpesvirus 6 infection suggest that PPGSS could be a nonspecific manifestation of a viral infection¹⁸. A case of PPGSS developing after intake of trimethoprim/sulfamethoxazol and after re-challenge with the same drug²⁰, and another one associated with pharyngitis due to *Arcanobacterium haemolyticum*⁸ suggest medications and bacteria as being other possible, although uncommon, triggers.

We present what we believe to be the first reported case of PPGSS occurring in Brazil: an adult man with acute B19 infection who displayed clinical features not previously described in PPGSS.

CASE REPORT

In October 1999, a previously healthy 54-year-old white man was

admitted to the hospital with a five-day history of itching, swelling, and reddening of the hands, suddenly followed by painful purpuric skin lesions involving hands and feet. He experienced fatigue, anorexia, intense myalgia, fever and chills. Sore throat, odynophagia, dysuria, and painful swelling of the glans penis developed the day before admission. Prednisone was initiated three days before admission because a drug reaction had been considered, but brought no clinical improvement. The patient denied having used any kind of medicine before the onset of the disease, but reported that his 10-year-old daughter presented with a febrile rash about ten days before the onset of his illness.

On admission, he was febrile (37.8 °C) with conjunctival injection and mild jaundice (+/4+). He had multiple grouped vesicles on the upper lip, a white plaque coating his tongue, buccal enanthema with small erosions on labial mucosa, and petechiae on the hard palate. A maculopapular rash was noted on the trunk and extremities with purpuric lesions on the groins and occasional petechiae on the inner surface of the thighs. A confluent purpuric-petechial eruption involving both the palmo-plantar and dorsal surfaces of the hands and feet extended to the wrists and ankles in a “gloves and socks” distribution. Hemorrhagic bullae were present on the lateral aspects of his feet. His glans penis was painful, swollen and reddened. The remainder of the physical examination was unremarkable.

Laboratory tests disclosed the following values: hemoglobin, 16.9 g/dL; leukocytes, 11,200/mm³ (92% granulocytes, 4% lymphocytes, 3% eosinophils); platelets, 143,000/mm³; erythrocyte sedimentation rate, 5 mm/h; prothrombin and partial thromboplastin times, normal. Serum chemistry analysis was normal, except for a total bilirubin value of 2.3

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mg/dL (unconjugated bilirubin, 1.8 mg/dL). Blood cultures collected on admission revealed growth of a coagulase-negative *Staphylococcus* in one of three blood samples. A skin biopsy specimen from the left foot showed extravasated red blood cells and a mild perivascular lymphoid infiltrate, without evidence of vasculitis.

On the fifth day of hospitalization, leukocyte count dropped to 4,280/mm³ (62% granulocytes, 17% lymphocytes, 12% monocytes, 8% eosinophils) and serum bilirubin value was normal. The patient's condition rapidly improved with conservative treatment, but skin lesions on the feet changed from purpuric to brown-black with a few areas of superficial skin necrosis. Two weeks after discharge the patient was well with scaling of the hands and black eschars replacing the necrotic skin areas of the feet (Fig. 1). A cell blood count showed 8,400 leukocytes/mm³, with 27% eosinophils.

Serologic tests were performed in sera from days 7 and 29 of illness. Serology for syphilis, hepatitis B and C, Epstein-Barr virus (Monotest), and HIV were negative; serology for measles, rubella, cytomegalovirus, and herpes simplex virus excluded recent infections. Antistreptolysin O level in serum from day 29 of illness was 104 IU/mL. Serologic tests for parvovirus B19 were performed by an "in house" IgM capture enzyme immunoassay (MACEIA-FIOCRUZ) using native virus antigen¹⁶, and by immunofluorescence to detect B19-specific IgG antibody¹⁷. Both serum specimens yielded B19-specific IgM and IgG antibodies, confirming an acute B19 infection. B19 DNA was not demonstrated in serum specimens by dot-blot hybridization assay¹⁵.

At the time of the patient's illness, an outbreak of B19 infection was occurring in the metropolitan area of Rio de Janeiro⁵.

COMMENTS

PPGSS is a rare, but clearly defined clinical entity with distinctive characteristics which permit its rapid recognition and diagnosis, even considering that diverse acral dermatitis and disorders associated with acral petechiae have to be considered in the differential diagnosis, such as Gianotti-Crosti syndrome, atypical measles, rickettsial diseases, Kawasaki disease, and meningococemia^{10,14}. Cutaneous manifestations of PPGSS are characteristic. Initially, edema and erythema appear on the hands and feet in a "gloves and socks" distribution, followed by isolated or confluent erythematopapular and purpuric lesions on the same sites, frequently accompanied by pruritus and pain. In some cases, similar lesions may also be observed on other sites, including face, trunk, buttocks, groin, elbows, knees, and thighs²¹. Systemic symptoms, such as asthenia, headache, anorexia, and arthralgia usually accompany skin eruptions. Fever occurs frequently. A variety of oral manifestations have been described, including pharyngeal erythema, small erosions of the oral mucosa, petechiae and vesiculopustules on the hard and soft palates, and even Koplik spots⁶. Genital mucosa may also be affected, with painful edema and erythema of glans penis¹⁰ and vagina^{9,11}, sometimes with small ulcerations on these sites. Laboratory findings are nonspecific, with occasional leukopenia, neutropenia, monocytosis, eosinophilia², thrombocytopenia, and mild elevations of transaminase levels⁷. Histologic findings include edema of the papillary dermis, extravasation of red blood cells, and a predominantly lymphocytic perivascular infiltrate, without vasculitis¹⁹, although a leucocytoclastic vasculitis has been demonstrated in some cases¹⁴.

The present case is noteworthy because the patient displayed atypical clinical features of PPGSS. Jaundice noted at presentation has not been previously reported. The predominantly unconjugated hyper-



Fig. 1 - Scaling of the feet during convalescence of PPGSS: black eschars replace necrotic skin areas.

bilirubinemia and its spontaneous resolution in a few days could be due to a clinically inapparent destruction of red blood cell precursors in bone marrow, due to B19-induced lytic infection of erythroid progenitor cells⁴. However, Gilbert's syndrome could not be discarded.

The most striking feature of this patient's eruption was the presence of hemorrhagic bullae associated with purpuric lesions on the feet, that progressed into cutaneous necrosis with superficial ulcerations. Purpura associated with skin necrosis and superficial ulcerations was reported in a case of arthritis and vasculitis due to B19 infection¹³. Although some PPGSS patients develop desquamation of the involved areas as the syndrome resolves²¹, healing with thick black eschars has not to our knowledge been previously described in this syndrome.

B19 infection has been associated with a broad spectrum of dermatological and systemic problems, that vary with the age and clinical conditions of the host, and include erythema infectiosum, polyarticular arthralgias and arthritis, transient aplastic crisis in persons who have underlying hemolytic anemia, hydrops fetalis and fetal death, and chronic anemia resulting from persistent infection in immune compromised patients¹². Acute B19 infection may be an asymptomatic or subclinical infection, or may manifest as a biphasic illness with symptoms during the viremic and immune complex-mediated stages of the disease.

In experimental parvoviral infection in humans¹, B19 DNA is detected in serum by dot-blot hybridization after the sixth day from the intranasal inoculation of the virus and may be detected for up to seven days thereafter. A B19-specific IgM response develops during the second week after inoculation whereas IgG develops at the end of the second week and early in the third week after inoculation¹. Since B19 DNA is detectable in serum by dot-blot hybridization for only a few days, and, on the other hand, by polymerase chain reaction for more than 4 months after acute infection, the diagnosis of acute B19 infection in immunocompetent persons is based on serologic assays for B19-specific IgM⁴. Several commercial tests for specific IgM have been developed and used to diagnose acute infection. These tests can produce false positive and false negative results, and IgM detection using native antigen in a capture assay format should be therefore performed as a confirmatory test. In acute B19 infection, the capture assay by enzyme immunoassay (MACEIA-FIOCRUZ) has been 100% concordant with the referential capture assay by radioimmunoassay (MACRIA-CPHL-UK)¹⁶.

In the present case, both B19-specific IgG and IgM were detected in sera from days 7 and 29 of illness. B19 DNA was not detected in sera by dot-blot hybridization, as expected as the patient had already mounted an antibody response at that time¹⁵. The diagnosis of acute B19 infection was reinforced because the patient lived in a community known to be experiencing an outbreak of B19 infection⁵, and by the fact that his daughter had an exanthematic disease days before the onset of his illness. In Rio de Janeiro, incidence of B19 cases peaks between August and November, with outbreaks occurring at 5-year intervals⁵.

The pathogenesis of PPGSS remains incompletely defined. In the cases associated with B19 infection, the virus has been found in the endothelial cells of skin vessels and cells of the basal epidermis at the time of the exanthem, which suggests that the rash is directly related to viral presence²⁹. However, it is not known whether the rash is a manifestation of primary viremia or a consequence of immune complex

formation¹⁹. In several B19-related PPGSS cases, B19-specific IgM antibody has not been demonstrated in serum at the time of the initial presentation with rash and pruritus, suggesting that the mucocutaneous lesions develop during the period of viremia^{2,19,21}. In the present case, both B19-specific IgG and IgM were detected in serum collected on the seventh day of illness, which might suggest that the rash occurred when an antibody response had already developed. This finding is similar to that observed in patients with erythema infectiosum, in whom IgG and IgM are detected in serum at the time of the rash, and contrasts to that observed in patients with transient aplastic crisis, in whom B19 DNA is detected in serum by dot-blot hybridization, and IgM but not IgG antibodies may be detected at the time of the aplastic crisis^{4,17}.

This case report illustrates the variability of clinical features displayed by B19 infection, emphasizes the need of further investigations into the pathogenesis of PPGSS, and reinforces B19 as the principal etiologic agent of PPGSS.

RESUMO

Síndrome purpúrico-papular em "luvas e meias" por parvovírus B19: relato de caso

Um caso de síndrome purpúrico-papular em "luvas e meias" devido à infecção aguda por parvovírus B19 é descrito em um homem adulto que, além das manifestações clássicas de febre, lesões orais e púrpura em mãos e pés, evoluiu com icterícia e necrose cutânea superficial dos pés, características até então não descritas nesta síndrome. Acreditamos tratar-se do primeiro caso descrito no Brasil.

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