

A case report of papular-purpuric gloves and socks syndrome: A manifestation of the parvovirus B19

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ABSTRACT

Introduction: The majority of parvovirus B19 infections are asymptomatic. In childhood, however, they may present as the fifth disease and in adults their manifestations can vary from mild, non-specific, cold-like symptoms to other forms of presentations. Papular-purpuric gloves and socks syndrome (PPGSS) is an uncommon form of parvovirus B19 infection, characterized by symmetric, pruriginous and painful erythema and edema of feet and hands. Generally, systemic symptoms are usually mild and dissemination to other body regions occurs in only 50% of the cases. The rash gradually progresses to petechiae and purpura delineating well demarcated “socks” and “gloves” on both feet and hands. The diagnosis is predominantly based on the clinical features. Serologic conversion is not considered as evidence of parvovirus B19 infection and histopathological findings from lesional skin are not specific. There are no definite antiviral

drugs or vaccines against parvovirus. Patients with PPGSS require only symptomatic therapy. **Case Report:** We report the case of a 30-year-old female with this characteristic erythema caused by the parvovirus B19. Nevertheless, this case is remarkable because the patient had significant systemic manifestations and an exuberant perineal and oropharyngeal involvement. Further, the erythema assumed a bullous expression that has not been so commonly reported. A biopsy was performed which was unspecific and the diagnosis was confirmed with the serology and molecular detection of the virus in blood sample as well as on mouth swab. Our patient needed treatment to control pain and pruritus, fever was self-limited. **Conclusion:** A high index of suspicion is essential to diagnose patients with this syndrome. Early recognition can prevent unproductive measures and the good management of this infection.

Keywords: Human parvovirus B19, Parvovirus B19 infection, Papular-purpuric socks and gloves syndrome, Viral infection

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INTRODUCTION

Parvovirus B19 is a small DNA virus of the *Parvoviridae* family that causes a worldwide infection [1]. The incubation period varies from 4–21 days and usually affects children and young adults [2]. The majority of the parvovirus B19 infections are asymptomatic, but panoply of manifestations can also occur [3]. In childhood, it may manifest itself as the fifth disease, or megalocytosis, with a macular-papular erythematous rash typically involving cheeks, trunk and extremities [1, 3]. In adulthood the disease can vary from mild, non-specific, cold-like symptoms to other uncommon presentations like cutaneous manifestations similar to children's rash, hematological disorders such as transient aplastic crisis and chronic red cell aplasia, rheumatoid manifestations resembling non-erosive polyarthritis and also the so-called gloves-socks syndrome, or papular-purpuric gloves and socks syndrome (PPGSS) [1, 3].

The PPGSS is characterized by symmetric, pruriginous and painful erythema and edema of feet and hands that gradually evolves to petechiae and purpura, and may progress to vesicles and bullae with skin desquamation [3, 4]. The rash typically delineates socks and gloves involving palms and soles and can also involve other areas, such as the perineum region and oral mucosa [3]. Systemic symptoms like fever, arthralgias, asthenia and anorexia can also accompany this condition [4, 5].

The diagnosis is based on the dermatological features and confirmed with one of two possible laboratory tests: Parvovirus B19-specific antibody testing and viral DNA testing [6].

There are no specific definite antiviral drugs or vaccines against parvovirus. But generally parvovirus infection is a self-limited disease that resolves in one to three weeks without any treatment [7].

Motivated by the rarity of this syndrome and by the unusual presentation in this patient, the authors decided to report this case of PPGSS.

CASE REPORT

A 30-year-old female presented to the emergency department complaining of edema and a violaceous, painful and very pruriginous exanthema on both hands and feet. She described that the rash had begun three days before on both soles and progressively extended acquiring a socks pattern (Figure 1). Simultaneously, in both hands the erythema rapidly assumed gloves forms (Figure 2). By the second day, she developed a perineal painful erythematous rash also accompanied by a greenish leucorrhea as well as began to have fever (38–39°C) that responded to antipyretic medication.

Previous medical history of the patient was unremarkable except for an untreated dyslipidemia, a spontaneous abortion at the age of 23 and gestational diabetes during other pregnancy. Her chronic medication

included only an oral contraceptive. She had no known allergies. Immunizations were in accord to the national program. She lived with her husband and her 3-year-old son in a suburban area of Portugal and was unemployed. She was monogamous with her husband, did not smoke or used illicit drugs, did not consume any alcohol, had not traveled recently or contact with any diseased person.

On physical examination, the patient was on a good general state of health. She presented symmetrical edema and confluent violaceous macules, papules and pustules on both sides of her hands and feet with well-defined borders delineating “gloves and socks” (Figure 3). The exanthema also developed bullae with skin desquamation on both soles (Figure 4). The perineal region surface was covered with a macular-erythematous and pruritic rash. No ulcers were visible and none satellite lymph nodes were found. The remainder of the physical examination was normal except for the presence of angular cheilitis.

Laboratory studies showed an elevation of the C-reactive protein (170 mg/L) and a decrease of the platelets count ($127 \times 10^3/\mu\text{L}$). Red and white blood cell counts were normal, as well as renal and hepatic function tests and electrolytes. She was admitted to the hospital for clinical monitoring and further diagnostic investigation.



Figure 1: Papular-purpuric exanthema and edema evolving plants in form of socks.

Empirical antibiotic therapy with doxycycline was started because of the possibility of rickettsiosis, a prevalent disease in Portugal.

On the first day of hospitalization she reported a sensation of burning mouth and difficulty in chewing and swallowing. On the oral exam, the patient had a “pinpoint” enanthema dispersed throughout the palate and the jugal mucosa (Figure 5). She had no ulcers or petechiae and no involvement of the pharynx or larynx. A swab of the enanthem was made for DNA-virus research.

The patient was evaluated by dermatology on the first day and a steroid therapy (prednisolone 1 mg/kg per day) was started for suspected vasculitis. At that time a cutaneous biopsy was performed.

Additional laboratory studies were requested with normal C3 and C4 complement, cryoglobulins and protein-electrophoresis. The erythrocyte sedimentation rate was 48 mm/h and the immunological study was also normal (antinuclear, antineutrophil, anti-DS-DNA, antiphospholipid and anticardiolipin antibodies). Serologic testing for viral hepatitis A, B and C, syphilis, rickettsia, Epstein–Barr virus, cytomegalovirus and rubella excluded recent infection. HIV serology was negative. ELISA tests for herpes virus and for parvovirus



Figure 4: Details of the exanthema with the formation of bullae.



Figure 5: “Pinpoint” oropharyngeal enanthema.



Figure 2: Papular-purpuric exanthema evolving palms in form of gloves.



Figure 3: Details of the palms emphasizing the pustules.

B19 were positive for IgM and IgG antibodies. The presence of parvovirus B19 DNA was then confirmed with blood polymerase-chain-reaction (PCR). Enterovirus, coxsackie included, were also excluded with PCR. Furthermore, the result of the oropharyngeal enanthem swab came out two days later and confirmed the

parvovirus B19 infection. The skin biopsy results was not specific, and revealed “mild acanthosis and keratinocyte apoptosis in the epidermis and capillary dilatation with perivascular infiltrate consisting in lymphocytes, histiocytes and eosinophils in the dermis”.

By the time of diagnosis, on the third day of hospitalization, the enanthems improved and the patient was able to eat. The cutaneous lesions became dryer and less pruritic. Doxycycline and prednisolone therapy were discontinued. The platelets count returned to normal and the C-reactive protein acquired a descending profile. Consequently, the patient was discharged home only with antihistamine therapy, on the seventh day of hospitalization.

In the follow-up consultation, one month later, a complete remission of the lesions on both perineal and oropharyngeal enanthems and the normalization of all analytical parameters were verified. The patient was able to return to her daily life.

DISCUSSION

Parvovirus B19 affects mostly children and young adults, has a high index of infectivity and is more frequent in winter and spring [1]. We report a case occurred on spring of a female patient with the PPGSS who had a three-year-old boy who recently started attending a nursery school.

The PPGSS in this patient assumed the characteristic papular-purpuric pruriginous eruption affecting hands and feet. Nevertheless, this case is remarkable because of the systemic manifestations and the exuberant perineal and oropharyngeal involvement. Generally, systemic symptoms are usually mild and patients may experience low-grade fever (52%), fatigue (20%), myalgias (16%), anorexia (16%), lymphadenopathy (16%) and arthralgias (12%). Dissemination to other body regions occurs in only 50% of the cases [8, 9]. Bullous skin lesions have not been so commonly reported [8]. In this case, when certain skin areas started to reveal bullae, our concern increased towards the possibility of developing Lyell-like syndrome characteristics or more severe infection complications. When the diagnosis was made that risk was considered lower since this disease is usually self-limited with resolution of the exanthema from one to three weeks [1, 7, 8]. Very occasionally, especially in cases of immunosuppression, the exanthema can persist for months [8] or even reappear without any particular trigger [10].

The rarity and unfamiliarity with this presentation of this disease led us to consider a wide range of alternative diagnosis, with multiple tests and exams being performed. PPGSS differential diagnosis should include other infections with cutaneous involvement, vasculitis, hematologic and rheumatic diseases [4]. Other viral infections such as Coxsackie B6 virus, human herpes virus 6 or 7, hepatitis B, Epstein-Barr, cytomegalovirus,

measles and rubella virus as well as the *Arcanobacterium haemolyticum* infection have been described as PPGSS [4]. Additionally, the trimethoprim/sulfamethoxazole [11] can also be related to this syndrome.

The detection of specific immunoglobulin M is helpful for the diagnosis. Its peak occurs within the first week, declines during the four subsequent weeks [1] and can be detectable until three months after infection [3]. Immunoglobulin G testing is not useful because it only indicates previous infection or immunity [1, 3, 6]. In the initial acute phase, the polymerase chain reaction is recommended to detect DNA virus, which can be detected even with very low viral load [1, 2]. However, normally there are no viruses in circulation when the symptoms emerge [3]. On average, the viremia period lasts 1 to 2 days, in general 7–9 days after exposure [1, 6].

In this case, IgG and IgM positivity to herpes virus and parvovirus B19 were observed. A cross reaction with other viruses is frequently found in recent parvovirus B19 infections, producing false-positive reactions in a variety of other infection diseases, specially Herpes virus and Epstein–Barr, virus infection [12].

As a consequence of a seroprevalence rate of 20–80%, in the American and European adult population [1], and the cross-reactions for the immunoglobulin M antibody class, serologic conversion is not considered as evidence of parvovirus B19 infection [8]. In our patient, the molecular detection of the virus in blood sample as well as on mouth swab strongly supports a causative role of the parvovirus B19 in PPGSS. In our hospital, the polymerase chain reaction is only qualitative and consequently we did not have access to the viral load. Nevertheless, with the favorable evolution of our patient and the positivity to the parvovirus B19, we thought it was not necessary.

Histopathological findings from skin lesions are not specific and therefore they are not useful to diagnose PPGSS. Thus, molecular detection of DNA virus in skin biopsy can be made, establishing the diagnosis [8].

Patients with PPGSS require only symptomatic therapy for fever, pain and pruritus. Corticosteroid therapy is not indicated because immunosuppressive therapy can promote the persistency of the virus [4].

We would like to highlight as particular strengths in this case, the epidemiology (seasonability and patient’s young child) and the rare but characteristic erythema. As limitations we emphasize the extreme rarity and unfamiliarity of this syndrome that can lead to misdiagnosis due to the huge variety of differential diagnosis. The misconduct of this disease can mask the clinic, lead to prolongation or even complications of the syndrome. In our particular case, the doxycycline and the prednisolone therapy could have been avoided if we knew the syndrome.

CONCLUSION

A high index of suspicion is essential to diagnose patients with this syndrome. Early recognition can prevent

unproductive measures and the good management of this infection.

Author Contributions

Inês Burmester – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

André Santa-Cruz – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Julietta Ramalho – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Maria João Regadas – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

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António Oliveira e Silva – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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