

# Erythema infectiosum following generalized petechial eruption induced by human parvovirus B19

Caterina Foti<sup>1</sup>, Domenico Bonamonte<sup>1</sup>, Anna Conserva<sup>1</sup>, Mauro Grandolfo<sup>1</sup>,  
Claudia Casulli<sup>1</sup>, Baldassarre Martire<sup>2</sup>

<sup>1</sup>Unit of Dermatology Department of Internal Medicine, Immunology and Infectious Diseases  
University of Bari Policlinico, Bari, Italy;

<sup>2</sup>Pediatric Department, University of Bari Policlinico, Bari, Italy

## SUMMARY

Parvovirus B19 is a DNA virus responsible for a wide spectrum of clinical illnesses. Among dermatological manifestations, the most common is erythema infectiosum, also known as the fifth disease. In 1990 Harms et al first described a papular-purpuric gloves and socks syndrome (PPGSS) due to parvovirus B19. It is an acute acral dermatosis characterized by an eruption of petechiae and small purpuric papules affecting the hands and feet in a gloves-and-socks distribution. Recently it was observed that PPGSS may be associated with involvement of the perioral region and the chin (acropetechial syndrome) and other sites provoking unusual presentation of the rash.

We describe a patient with an acral purpura with the features of the "acropetechial syndrome" involving the buttocks, genital and axillary regions who subsequently developed a maculopapular eruption with the characteristics of the fifth disease.

Parvovirus B19 DNA was detected by polymerase chain reaction (PCR) both in skin vasculitic lesions and in the serum during the petechial eruption, before the onset of antibodies. The immune response coincided with the development of the exanthem, suggesting a direct role of parvovirus B19 in the pathogenesis of endothelial cell injury.

**KEY WORDS:** Acropetechial syndrome, papular-purpuric gloves and socks syndrome (PPGSS), parvovirus B19, polymerase chain reaction (PCR).

Received Novembre 23, 2005

Accepted December 29, 2005

## INTRODUCTION

Parvovirus B19 is a small single-stranded DNA virus that causes a wide spectrum of clinical illnesses including dermatological, rheumatological and hematological manifestations. The dermatological manifestations are heterogeneous but the most common is erythema infectiosum (EI),

also known as the fifth disease or "slapped cheek". Other dermatological manifestations of parvovirus B19 infections include erythema multiforme, vasculitis, pustular eruptions and papular-purpuric gloves and socks syndrome (PPGSS) (Young *et al.*, 2004). PPGSS is an acute, self-limited condition first described in 1990 by Harms et al (Harms *et al.*, 1990). Skin lesions are quite characteristic and begin with edema and erythema symmetrically localized to the hands and feet. Subsequently, petechial and purpuric changes appear varying from a few millimeters in diameter to larger, confluent patches. Small erosions of the oral cavity may be present. Normally, the lesions of PPGSS spare the face. For cases with a prominent involvement of the perioral region and the chin the term

### Corresponding author

Caterina Foti, MD  
Department of Internal Medicine,  
Immunology and Infectious Diseases - Unit of Dermatology  
University of Bari  
Policlinico, Piazza Giulio Cesare, 11  
70124 Bari, Italy  
E-mail: c.foti@dermatologia.uniba.it

“acropetechial syndrome” has been proposed (Harel *et al.*, 2002). We describe the case of a patient with an acral purpura with the features of the “acropetechial syndrome” involving the buttocks, genital and axillary regions who subsequently developed a maculopapular eruption with the characteristics of the fifth disease.

### CASE REPORT

A 35-year-old male was admitted to our hospital with a two day history of fever and petechial rashes. On physical examination there was a sym-

metrical purpuric and petechial exanthem localized on his hands and feet in a gloves-and-socks distribution (Fig. 1) associated with multiple petechiae on buttocks, scrotum, axillae (Fig. 2), groin and perioral area. The hard and soft palate mucosa showed small petechiae. Physical examination revealed painful right cervical lymph nodes less than 0.5 cm in diameter. A laboratory examination showed lymphocytopenia (WBC:  $5.6 \times 10^9/L$ , lymphocytes: 10%, neutrophils: 78%, monocytes: 9%, eosinophils: 3%) with normal hemoglobin concentration, platelet count and levels of C3 (94 mg/dL), C4 (39 mg/dL) and serum immunoglobulins (IgG: 1230 mg/dL, IgA: 259



FIGURE 1 - Petechial exanthem of the hands and feet in a “gloves-and-socks” distribution.



FIGURE 2 - Petechial lesions of the axillary regions.

mg/dL, and IgM: 163 mg/dL), Lymphocyte immunophenotyping was normal (CD3: 72%, CD4: 46%, CD8: 22%, CD19: 24%, CD16+ CD56+ CD3-: 14%). A chest radiograph and abdominal ultrasonogram showed no pathological findings. Histopathological examination of a skin biopsy specimen taken from the hand showed a superficial perivascular inflammatory infiltrate mostly made of lymphocytes, with numerous extravasated erythrocytes. Multiple blood and throat cultures were sterile. Antinuclear antibodies, antistreptolysin title and serological tests for a large panel of microorganisms, including cytomegalovirus, Epstein-Barr virus, hepatitis C virus, hepatitis B virus, herpes simplex virus, varicella zoster virus, human immunodeficiency virus, coxsackie B3 virus, *Toxoplasma gondii*, *Mycoplasma hominis* and *Rickettsia conorii* resulted negative. Parvovirus B19 specific IgM and IgG antibodies detected at the first and fifth days of hospitalization were negative, while parvovirus B19 DNA performed by PCR was demonstrated both in skin vasculitic lesions and serum of the patient, but not in involved skin. No specific treatment was instituted and the patient gradually improved. At day 7, the fever ceased but a maculopapular eruption appeared on the trunk. The eruption faded on the third day and the patient was discharged in good condition. Two days later serologic tests showed specific antibodies for parvovirus B19 IgM (8.877, n.v. <1) and disappearance of viremia (demonstrated by PCR).

## DISCUSSION

Infections with parvovirus B19 are common worldwide. It is usually spread through the respiratory route although transplacental and blood product transmission can also occur. The primary target of parvovirus B19 is the erythroid cell line, specifically near the pronormoblast stage (Takahashi *et al.*, 1990). The tropism for erythroid cells is related to the erythrocyte P blood group antigen, also expressed on endothelial cells, which serves as a cellular receptor for the virus (Brown *et al.*, 1993). Some manifestations of parvovirus B19 infection (such as transient aplastic crisis or PPGSS) appear to be as a direct viral effect (Loukeris *et al.*, 2005; Vafaie *et al.*, 2004),

whereas others, including exanthem and arteritis, appear to be post-infectious phenomena related to the immune response (Lehmann *et al.*, 2003). Humoral immunity is crucial in controlling infection. Specific IgM normally appears within 1-2 days after onset of the exanthem and persists for 6-8 weeks, followed by anti-parvovirus B19 IgG leading to control of the infection.

The PPGSS is an acute acral dermatosis characterized by an eruption of petechiae and small purpuric papules affecting the hands and feet in a gloves-and-socks distribution closely associated with parvovirus B19 infection (Harms *et al.*, 1990). Recently it has been observed that PPGSS may be associated with the involvement of the perioral region (acropetechial syndrome) or of other sites provoking unusual presentation of the rash (Harel *et al.*, 2002). In our case we observed a petechial rash with a distribution similar to that described in the acropetechial syndrome but with a prominent involvement of the genitals, buttocks and axillary region disclosing a new clinical picture of parvovirus B19 infection.

In most cases of PPGSS anti-parvovirus B19 IgG and IgM antibodies are usually absent at the time of the onset of the rash, while it is possible to detect parvovirus B19-DNA in skin biopsy specimens and in the serum of the patient (Loukeris *et al.*, 2005, Sklavounou-Andrikopoulou *et al.*, 2004).

An immunohistochemical study performed using specific anti-parvovirus B19 antibodies in skin biopsies of three patients with PPGSS disclosed viral antigens on the endothelial cells of the dermal vessel walls, on the epithelial cells of the sweat glands and ducts, and on the epidermal keratinocytes (Aractingi *et al.*, 1996).

Other observations suggest a direct role of parvovirus B19 in the evolution of vascular injury through a non-structural protein which it encodes, designated NS-1. In vitro studies show that NS-1 induces apoptosis of infected cells (Sol *et al.*, 1999).

The timing of the antibody response to B19 in PGSS appears to differ from that seen in EI. In patients with EI development of exanthem coincides with the appearance of antibody and disappearance of viremia. In contrast, patients with PPGSS may develop mucocutaneous lesions during the period of viremia and subsequently develop a humoral immune response.

The peculiar course of the disease in our patient, who developed a humoral response to the virus 2 days after a maculopapular eruption with the characteristics of the fifth disease supports these observations.

Moreover the detection of viral DNA in the skin specimen and in the serum of the patient confirms the direct implication of the virus in the pathogenesis of the mucocutaneous lesions of PPGSS.

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