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Caso clinico

Case report

Petechial rash associated with Parvovirus B19 in children: case report and literature review

Rash purpuro-petecchiale associato a Parvovirus B19 in età pediatrica: caso clinico e revisione della letteratura

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INTRODUCTION

Parvovirus B19 (B19V) infection is widespread and associated with a heterogeneous clinical spectrum, ranging from asymptomatic to potentially life-threatening events, such as aplastic crisis in chronic haemolytic anaemia, hydrops fetalis, neurologic diseases and arthropathy [1]. This infection usually causes erythema infectiosum (EI), a benign self-limiting disease characterized by typical cutaneous manifestations (slapped cheek appearance with perioral sparing followed by a diffuse maculopapular rash evolving to a reticular pattern) [2].
Unusual rash, generally with focal acral petechial eruption (papular purpuric gloves and socks syndrome, PPGSS), has also been reported [3]. Nevertheless, several studies suggest that B19V-associated cutaneous haemorrhagic manifestations are more common than generally appreciated, and that they can have heterogeneous characteristics justifying a new nosological entity (B19V-associated purpuric-petechial eruption, PAPPE) [4]. We describe an unusual paediatric case of B19V associated with generalized petechial eruption, and review the recent literature.

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MATERIALS AND METHODS

We performed a retrospective analysis of the literature over the last decade (2003-2012) of paediatric reports of B19V-associated purpuric-petechial rash. We analysed the English literature over the last 10 years, using the following keywords in Pubmed: "Parvovirus B19", "purpuric", "petechial", "haemorrhagic", "atypical/unusual cutaneous/skin manifestation/eruption".
The following parameters were established as an additional selection: age under 18 years, confirmed B19V infection, immunocompetent patients, infection acquired after birth. For each selected case the following data were evaluated: age, gender, clinical and laboratory data, and microbiological diagnosis.

CASE REPORT

A previously healthy 12-year-old boy came to our attention in June 2012 for sudden petechial eruption. About 10 days earlier he had been bitten by a tick in the left axilla.
Symptoms onset was characterized by cramping in the lower limbs, followed by itching, swelling and petechiae at the dorsa of hands and feet. Because of fever and progressive extension of the rash, the patient was admitted to the Paediatric Unit of the Hospital of Siena (Italy). A physical examination revealed gener-

al good conditions with an axillary temperature of 37.8°C. Skin inspection revealed generalized purpuric eruption with a large number of confluent petechiae on the trunk and accentuated on the limbs (especially at the distal extremities and at the limb roots).
The remaining physical examination was normal, except for mild splenomegaly and painful left axillary lymphnode, not associated with skin inflammation or "tache noire". Laboratory tests revealed leukopenia with neutropenia (white blood cells count was 2,980 cells/mm^3, with a 32.3% neutrophils), and some activated lymphocytes and rare monocytes.
Erythrocytes (4.8 mil/mm^3), haemoglobin (13.6 g/dl), C reactive protein (<0.5 mg/dl), liver and kidney function tests and urine analysis were within normal limits. The faecal occult blood search was negative. An empiric therapy with doxycycline 4 mg/kg/day was started due to the suspicion of rickettsial infection, while waiting for microbiological test results.
The results of microbiological tests showed B19V acute infection (positivity of B19V DNA by polymerase chain reaction amplification on blood and throat swab, with antibody seroconversion on duplicate blood samples, collected on day 4 and on day 18).
The serology for Rickettsia, *Borrelia burgdorferi*, Epstein-Barr virus were negative. The PCR (polymerase chain reaction) search for genetic material of Adenovirus, Cytomegalovirus, Epstein-Barr virus and Picornavirus was negative on throat swab and on serum for Borrelia spp., Chikungunya virus and West-Nile virus. The patient rapidly improved with a complete re-

Table 1 - Reported paediatric cases of purpuric-petechial cutaneous eruption during B19V infection (2003-2012) (n=34).

Author	*Year*	*No. patients*	*Cutaneous manifestations*	*Diagnosis**
Alfadley [7]	2003	1	Petechiae, oedema	PPGSS*
Pavlovic [3]	2003	1	Macules, papules, purpura, petechiae	PPGSS
Messina [11]	2003	1	Purpura, petechiae	PPGSS
Hsieh [12]	2004	1	Oedema, erythema, purpura	PPGSS
Ferraz [13]	2005	1	Macules, papules, petechiae	-
Huerta-Brogeras [9]	2005	1	Petechiae	BATH-TRUNK
McNeely [5]	2005	1	Macules, papules, petechiae	-
Butler [14]	2006	1	Erythema, pustoles, purpura	BATH-TRUNK
Aguilar-Bernier [8]	2006	1	Macules, papules, purpura, oedema	PPGSS
Aydinoz [1]	2006	1	Papules, petechiae	PPGSS
Chinsky [2]	2006	2	Purpura, petechiae	-
Chatproedprai [15]	2006	1	Purpura	-
Segura-Saint Gerons [6]	2007	1	Papules, purpura	PPGSS
Parez [16]	2008	1	Papules, purpura, oedema	PPGSS
Fretzayas [17]	2009	1	Papules, erythema, purpura	PPGSS
Shah [18]	2010	1	Papules, petechiae	PPGSS
Edmondson [10]	2010	8	Petechiae	PAPPE*
Meyer [19]	2010	1	Macules, papules, petechiae	-
Hashimoto [4]	2011	2	Papules, purpura, petechiae	PAPPE
Conde-Montero [20]	2012	1	Papules, erythema, purpura	PAPPE

PPGSS, Papular purpuric Gloves and Socks Syndrome; PAPPE, PVB19-Associated Purpuric-Petechial Eruption.

gression of the rash. On day 6 he was discharged in good general conditions and the blood tests were within the normal range.

DISCUSSION

The only Parvovirus capable of causing disease in human beings is B19 (B19V), a small DNA virus that typically infects and replicates in the erythroid progenitor cells [5]. Found worldwide, it has a high prevalence of infection in young children [6]. At this age the virus usually causes erythema infectiosum (EI) (slapped cheek appearance with perioral sparing followed by a diffuse maculopapular rash evolving to a reticular pattern) [7].

During the last two decades an increasing number of reports describing purpuric-petechial eruptions linked to B19V infection have been published. These eruptions are defined as: "papular purpuric gloves and socks syndrome" (PPGSS), "acropetechial syndrome", "unilateral laterothoracic exanthem", "asymmetric periflexural exanthem of childhood", "bathing trunk distribution", emphasizing the distinctively focal distribution.

Few reports describe the generalized purpuric-petechial eruptions associated with B19V infection [4]. In 2011, Hashimoto and Yuno proposed the term "PVB19-associated purpuric-petechial eruption" (PAPPE), to describe a polymorphous eruption with the following features: papular-purpura and/or petechial rash accompanied by fever, arthro-myalgia, lymphadenopathy; focal or generalized involvement; frequently prominent acral and/or intertriginous distributions; usually preceded, accompanied or followed by enanthema and/or exanthema such as pruritic erythema, oedema and/or papules; occasionally followed by EI; confirmation of primary/recent B19V infection [4].

Our clinical case meets all criteria for "PVB19-associated purpuric-petechial eruption" (PAPPE).

We performed a retrospective analysis of the literature over the last decade (2003-2012) of paediatric reports of B19V-associated purpuric-petechial rash. We found 34 paediatric case reports of B19V-associated cutaneous haemorrhagic manifestations (Table 1). Demographic, clinical and laboratory features from all the included patients are shown in Table 2. Additionally, we also found that haemorrhagic rash is frequently associated with school-age children (no patients under 2 years of age) and is more common in males.

Purpuric petechial cutaneous manifestations, although involving the trunk in about half of cases, are more frequently distributed on the extremities and on the limb roots (as in our pa-

Table 2 - Clinical and laboratory features from pediatric cases of B19V-associated purpuric-petechial cutaneous manifestations (n=34).

Clinical data		
Average age (ys)	8.4	(range 2-18)
Gender		
Female	15/34	(44%)
Male	19/34	(56%)
Haemorrhagic rash		
Trunk	19/34	(56%)
Extremities	31/34	(91%)
Local accentuation		
Axillae	3/34	(9%)
Groin	10/34	(29%)
Distal Extremities	6/34	(18%)
Slapped-cheek	5/34	(15%)
Oral mucosa involvement	14/34	(41%)
Fever	25/34	(73.5%)
Other symptoms		
Headache	9/34	(26%)
Sore throat	7/34	(20.5%)
Fatigue	6/34	(18%)
Myalgia	5/34	(15%)
None	10/34	(29%)
Laboratory data		
Leukopenia (<5000 cells/mm^3)	18/30*	(60%)
Thrombocytopenia (<150000 cells/mm^3)	9/29**	(31%)
Anaemia (Hb<11.5 g/dL)	6/29***	(21%)
B19V diagnosis		
IgM +	27/34	(79%)
PCR +****	11/34	(32.5%)
Diagnosis		
PPGSS*****	10/34	(29%)
PAPPE******	16/34	(47%)
Not defined	8/34	(23.5%)

*Leukocytes not available for 4 patients. **Thrombocytes not available for 5 patients. ***Haemoglobin not available for 5 patients. ****Polymerase Chain reaction for BV19 DNA on blood. *****Papular Purpuric Gloves and Socks Syndrome. ******PVB19-Associated Purpuric-Petechial Eruption.

tient). Fever and other systemic symptoms are often associated with rash in about 75% of patients and the laboratory tests commonly show also leukopenia and (less frequently) thrombocytopenia.
The purpuric-petechial rash is closely related to the viraemic phase of the B19V primary infection, as documented in approximately 30% of the analysed cases and in this case report, and it differs from typical EI, which can be considered a post-viraemic manifestation of Parvovirus infection. These subjects are contagious during the rash time.
The pathogenesis of the cutaneous and extracutaneous symptoms is not yet clear. The B19V-DNA has been detected in the epithelial cells of sweat ducts and glands, in relation to the pathologic finding of perivascular lymphocytic infiltrate and the evidence of erythrocyte extravasation [8]. In other cases, direct immunofluorescence revealed granular deposits of IgM and C3 components in the walls of dermal vessels, suggesting a vascular reaction to antigenic triggers, without vasculitis [9]. According to Hashimoto and Yuno, our data confirm that paediatric B19V infection is commonly associated with a self-limiting disease characterized by fever, systemic symptoms and polymorphous purpuric-petechial eruption [4]. Moreover, the review of the recent literature indicates that B19V-associated haemorrhagic cutaneous manifestations are much more frequent than generally appreciated, as reported by Edmondson et al. [10]. Early diagnosis of B19V infection is essential in order to avoid misdiagnosis, which can lead to complications in high risk patients and to delayed diagnosis of severe diseases such as meningococcal sepsis, rickettsia and anaphylactoid purpura.

Conflict of interest
The authors declare that they have no conflict of interest.

Keywords: Parvovirus B19, exanthem, paediatric rash, purpuric-petechial eruption.

SUMMARY

Human Parvovirus B19 (B19V) infection usually causes erythema infectiosum (EI). In recent decades, several uncommon exanthems have been described in association with B19V.
Recently, haemorrhagic manifestations such as purpuric-petechial rash have been reported. We describe an unusual paediatric case of B19V associated with generalized petechial eruption, and a review of the recent literature.

RIASSUNTO

L'infezione da Parvovirus B19 umano (B19V) è comunemente associata all'eritema infettivo, tuttavia manifestazioni esantematiche atipiche sono riportate in letteratura e recentemente sono state descritte anche eruzioni cutanee emorragiche. In questo studio descriviamo, unitamente a una revisione della letteratura recente, un raro caso pediatrico di infezione da B19V associata a manifestazione petecchiale diffusa.

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