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TOPIC HIGHLIGHT

Bullous Henoch-Schönlein Purpura: A Case Series

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ABSTRACT

Henoch-Schönlein purpura (HSP) represents the most common vasculitis in children. Typically, HSP manifests with palpable purpura and edema, usually following an urticarial or erythematous maculopapular eruption. Bullous HSP represents an uncommon presentation of "classic" HSP, exhibited by only 2% of affected children. We here present three cases of bullous HSP. This variant seems due to an excess of production of neutrophilic matrix metalloproteinase-9, a lytic enzyme that degrades basement membrane components, eventually leading to dermoepidermal detachment and blister formation. Notably, American College of Rheumatology (ACR), Paediatric Rheumatology European Society (PRES), European League against Rheumatism (EULAR), and Paediatric Rheumatology INternational Trials Organization (PRINTO) do not encompass blisters and/or bullae into HSP classification criteria. Outcome of bullous HSP does not differ from "classic" purpuric HSP. The former, however, demands special care measures: local pain control, topic antibiotic therapy, and protective dressings over areas of open or blistered skin.

Key words: Bullous Henoch-Schönlein purpura, Pediatrics, Dermatology

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Abbreviations
HSP: Henoch–Schönlein purpura; CBC: Complete blood count; ED: Emergency Department; WBC: White blood cells; CRP: C-reactive protein; MMP-9: matrix metalloproteinase-9; ACR: American College of Rheumatology; PRES: Paediatric Rheumatology European Society; EULAR: European League against Rheumatism; PRINTO: Paediatric Rheumatology INternational Trials Organization

INTRODUCTION

Henoch-Schönlein purpura (HSP) represents the most common vasculitis in children. Its hallmarks are cutaneous purpura, arthritis, abdominal pain, and nephritis[1]. Skin manifestations of HSP are very characteristic of the disease and consist of palpable purpura and edema, possibly following an urticarial or erythematous maculopapular eruption. Lesions typically appear on pressure-prone surfaces like ankles, feet, and buttocks. Purpuric rash is the presenting symptom in more than 50% of cases[1].

Pediatric bullous HSP represents a much rarer variant of "classic" HSP, exhibited by only 2% of affected children according to literature[1]. Conversely, haemorrhagic bullous rash is present in up to 60% of adult cases of HSP.

Patient 1

A 5-year-old girl presented with a three-day history of purpuric rash over both lower extremities and bilateral ankle pain. Three weeks before rash onset she presented an upper respiratory tract infection. General examination revealed good overall condition; body temperature was 36.5°C, and blood pressure 100/60 mmHg. Palpable purpura over the buttocks and lower extremities was evident. Both ankles and feet were swollen and tender. Complete blood count (CBC) was normal. Urinalysis showed microhematuria. Renal function was normal. Further laboratory investigation revealed a low level of complement component C3 and a high level of streptolysin O. After two days, the rash increased and tender vesicles along with small bullae appeared on left foot arch. A few days later, the lesions coalesced into a large bulla of 2.5 cm of diameter (Figure 1). No other lesions became evident thereafter. The skin bullous lesions resolved completely in a few days with no need for steroid therapy. We re-evaluated the patient regularly in the following 6 months, with no recurrence of skin lesions. Urinalysis continued to be positive for microhematuria at 6-month follow-up control visit, with persistently normal renal function.

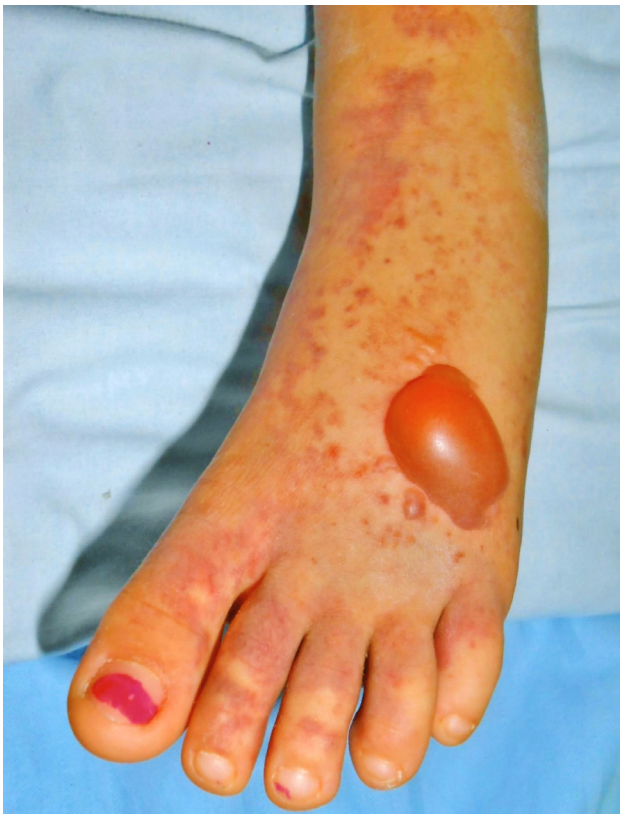

Figure 1 Large (2.5 cm of diameter) hemorrhagic bullous lesion on left foot arch of a 5-year-old girl with bullous HSP.

Patient 2

A 6-year-old boy presented to our Emergency Department (ED) for

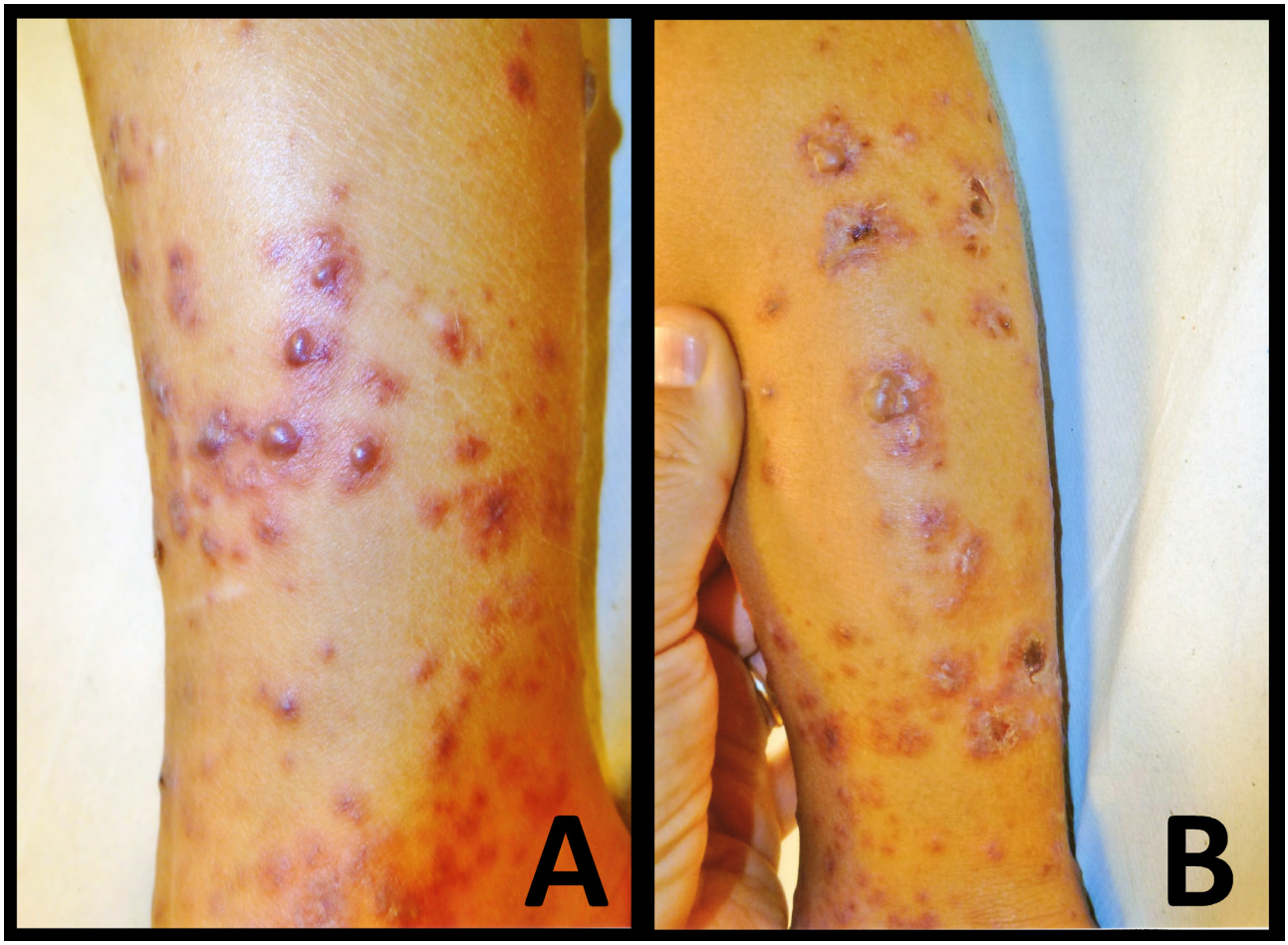

Figure 2 Multiple bullae and purpuric lesions on the right (2A) and left (2B) leg of a 6-year-old boy with bullous HSP. Several necrotic lesions are evident, particularly on the left leg.

arthralgia and purpuric rash on the lower extremities that started the day before. Several days prior, he was put on antibiotics for an upper respiratory tract infection. Physical examination revealed multiple palpable purpuric lesions over the buttocks and lower limbs. The boy was discharged with anti-inflammatory drug therapy. Two days later, the patient came back to the ED for worsening rash, persistence of arthralgia, and new-onset abdominal pain. Multiple vesicles and bullae were now evident on the lower limbs (Figures 2A and 2B). Laboratory investigations including CBC, serology for EBV and Mycoplasma pneumoniae, liver and renal function tests were normal. Steroid treatment (prednisone) was carried out for 7 days, with regression of the abdominal pain and arthralgias.

The purpura and vesicles spread for a few days further to upper extremities, and several necrotic lesions became evident (see Figure 2B). Skin manifestations completely regressed after 15 days; no recurrence was evident at 6-month follow-up evaluation.

Patient 3

A 4-year-old boy was brought to our ED because of fever and two-day history of a painful rash over his lower extremities. Recent medical history was unremarkable. Physical examination revealed multiple palpable purpuric lesions over his buttocks and lower limbs. His ankles, feet, and hands were swollen and tender. His abdomen was soft and nontender. CBC revealed leukocytosis [white blood cells (WBC) 12 × 10^9/L]; an increase in C-reactive protein (CRP) was also documented (149 mg/L). Urinalysis was normal. A diagnosis of HSP was made, and the patient was hospitalized. Three days later, his eruption continued to spread; blisters and hemorrhagic bullae began to appear on hands (Figure 3) and feet, and his arthritis also worsened. Therapy with intravenous prednisolone (1 mg/kg once daily) was then started and maintained for two weeks. Skin bullous lesions started to regress (some of them becoming necrotic) and eventually completely vanished without sequelae. The child was followed monthly for 6 months; during this period microhematuria was persistently absent at urinalysis, and clinical HSP did not recur.

DISCUSSION

HSP is a small-vessel vasculitis resulting from immunoglobulin A-mediated inflammation. It represents the most common acute systemic vasculitis in childhood; most targeted sites are skin, gastrointestinal tract, joints, and kidney. Skin lesions, usually presenting as erythematous maculopapules, petechiae, and purpura, often involve lower extremities and buttocks, but may also extend to upper extremities, trunk, and face. The occurrence of hemorrhagic bullae in children with HSP is uncommon (only 2% of total HSP-affected children according to literature)[1], and may therefore pose a diagnostic challenge. In contrast, up to 60% of adults with HSP may present with bullous lesions.

Kobayashi *et al* found high concentrations of matrix metalloproteinase-9 (MMP-9) in blister fluid[2]. MMP-9 is a zinc-dependent endopeptidase produced by polymorphonuclear neutrophils that gather on the dermal side of the dermoepidermal junction after migration out of inflamed microvasculature; excessive production of MMP-9 degrades basement membrane components (including type VII collagen), eventually leading to dermoepidermal detachment and blister formation. This occurs particularly on surfaces subject to pressure like the ankles (due to shoe pressure against malleoli), foot arches (due to pressure exerted by tight shoelaces), and buttocks (due to sitting pressure).

Notably, American College of Rheumatology (ACR)[3], Paediatric Rheumatology European Society (PRES)[4]. European League against Rheumatism (EULAR)[4] and Paediatric Rheumatology INternational Trials Organization (PRINTO)[4] do not encompass blisters and/or bullae into HSP classification criteria.

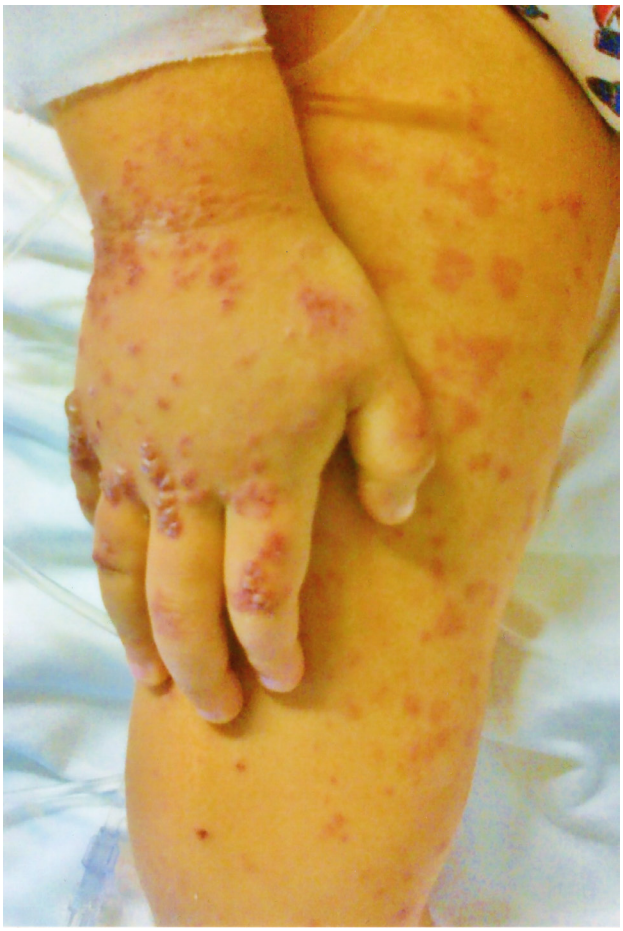

Figure 3 Blisters and haemorrhagic bullae on the right hand back of a 4-year-old boy with bullous HSP.

Since the course of HSP is usually benign, first line treatment is most often symptomatic and encompasses rest, analgesia, and nonsteroidal anti-inflammatory drugs (albeit this last measure has to be avoided in case of renal or gastrointestinal involvement). Efficacy of corticosteroid therapy as well as of novel strategies including the use of other immunosuppressant agents (colchicine, azathioprine, mycophenolate mofetil, cyclosporin A, cyclophosphamide, rituximab), other immunomodulatory approaches (intravenous immunoglobulin, plasma exchange), sulfonamides (dapsone), and anti-leukotriene agents (montelukast) remains controversial, with no incontrovertible evidence of improved long-term outcome in the pediatric or adult population[5].

Outcome of bullous HSP does not differ from "classic" purpuric HSP. Anyways, bullous HSP lesions demand special care measures: local pain control, topic antibiotic therapy, and protective dressings over areas of open or blistered skin.

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