CASE REPORT

Serious Gastrointestinal Form of Henoch-Schönlein Purpura Induced by *Helicobacter pylori* Infection and Complicated by Bradycardia and Euthyroid Sick Syndrome

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ABSTRACT

Association between Henoch-Schönlein purpura and Helicobacter pylori *infection is rarely reported in the literature. We present a case of Henoch-Schönlein purpura with severe gastrointestinal manifestations, bradycardia and euthyroid sick syndrome, which resolved only after the eradication of* Helicobacter pylori *infection.*

Keywords: Bradycardia, euthyroid sick syndrome, *Helicobacter pylori*, purpura

INTRODUCTION

Henoch-Schönlein purpura (HSP) is the most common systemic vasculitis in children (10–30 cases per 100 000 children under 17 years) and usually occurs in children younger than 10 years (1). Henoch-Schönlein purpura is non-granulomatous, small-vessel vasculitis, which presents with palpable purpura on the lower extremities and buttocks with possible joint, gastrointestinal and renal involvement (1). In 75% of patients, an infection precedes HSP (2). *Helicobacter pylori* (HP) infection is rarely associated with HSP.

We present a case of HSP with severe gastrointestinal manifestations, bradycardia and euthyroid sick syndrome, which resolved after the eradication of *Helicobacter pylori* infection.

CASE REPORT

A five-year-old boy was hospitalized due to palpable purpura, abdominal pain and vomiting. The disease began four days earlier with petechial rash on the legs, followed by episodes of abdominal pain and vomiting. He was previously healthy.

On admission, he had palpable purpura on the legs and gluteus, and feet oedema. The abdomen was slightly meteoristic and sensitive in the paraumbilical region. Other findings were normal, like C-reactive protein 24.3 mg/L (0–5 mg/L), ESR 10 mm/h, WBC 20.5×10^9/L (78% granulocytes and 16% lymphocytes), ERC 5.49×10^{12}/L, HGB 133 g/L, HTC 43% and PLT 305×10^9/L. Coagulation profile, electrolytes, renal and liver function, immunoglobulins (Ig) A, M and G, complement components C3 and C4, anti-streptolysin O titre were normal. Viral serology was negative. Anti-nuclear antibodies (ANA), lupus anti-coagulant, anti-cardiolipin antibodies (ACLA) IgG and IgM, anti-ß2 glycoproteins IgM and IgG were negative. Urine showed proteinuria 2+, 15 erythrocytes; 24-hour proteinuria was 0.154 g/day. Throat swab was negative. Occult blood in the stool was positive. Copro-culture and clostridium difficile toxin were negative. Ultrasonography of the abdomen showed oedematous walls of the distal part of the terminal ileum (wall thickness: 5.3 mm) with intense regional blood flow (Power Doppler) and a moderate amount of free fluid in the abdomen (Fig. 1).

Our diagnosis was HSP, so we started therapy with methylprednisolone (1 mg/kg per day) and proton pump inhibitor. On the third day, palpable purpura re-emerged, now affecting all four extremities. This was accompanied by intense abdominal pain, colic, diarrhoea and haematochezia. Ultrasound examination of the abdomen showed advanced thickening of intestinal walls. Due to exacerbation of the disease, we administered

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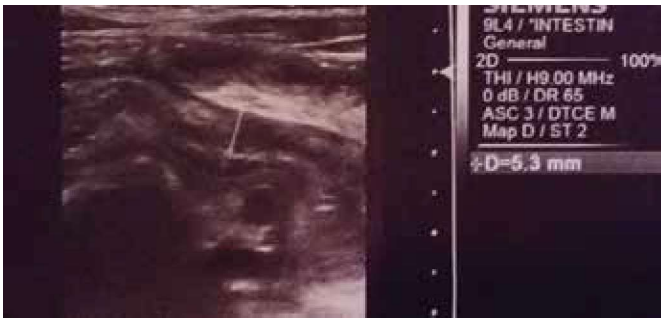

Fig. 1: Ultrasonography of the abdomen showing oedematous walls of the distal part of the terminal ileum.

methylprednisolone pulse therapy (30 mg/kg per day) for three days, and then proceeded with methylprednisolone at the standard dose of 1 mg/kg per day. Oral intake was suspended and total parenteral nutrition initiated. All these therapeutic measures gave only short-term effect.

On the ninth day, previous symptoms relapsed. Ultrasonography revealed further thickening of the intestinal walls. Intravenous immunoglobulins (IVIG) of 2 g/kg were given. This was followed by a significant clinical improvement, however, in attempts to reduce the doses of corticosteroids, abdominal pain and skin lesions relapsed.

During the third week of illness, the boy become bradycardic (heart rate: 44 per minute) and constipated.

Standard ECG showed sinus bradycardia. 24-hour ECG Holter monitoring showed persistent bradycardia with a mean heart rate of 55 per minute, minimal heart rate of 39 per minute, without significant sinus pauses and conduction disorders (Fig. 2). Echocardiography was normal.

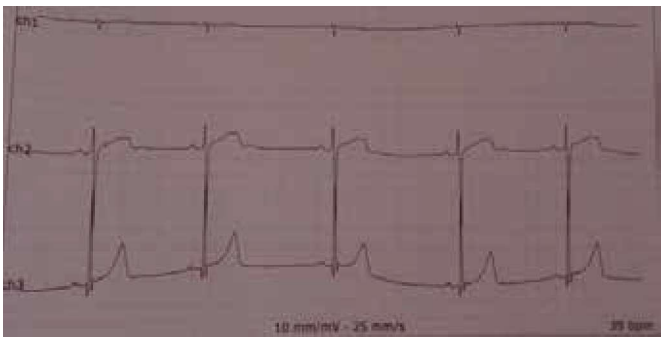

Fig 2. 24-hour ECG Holter monitoring showing bradycardia with heart rate of 39 per minute.

Thyroid function tests were indicative of euthyroid sick syndrome: (tri-iodothyronine [T3] – 0.72 nmol/L [reference range: 1.42–3.8 nmol/L], normal levels of thyroxine [T4] and thyroid-stimulating hormone [TSH]). Levothyroxine was introduced in the therapy and gradual normalization of the heart rate and hormones levels occurred.

Due to relapsing gastrointestinal symptoms, anti-*Helicobacter pylori* IgG and IgA antibodies were determined; and the results were positive for IgG antibodies (90.1 RJ/ml, reference < 22 RJ/ml), so a seven-day course of amoxicillin and metronidazole was administered. After the eradication of HP, there was no further re-occurrence of abdominal pain; findings of occult blood in the stool became and remained negative; abdominal ultrasound findings normalized and skin lesions permanently resolved. The corticosteroids were gradually reduced and discontinued after two months. Levothyroxine therapy has been discontinued after one month.

DISCUSSION

Gastrointestinal symptoms occur in 51%–74% of children with HSP and usually manifest as diffuse abdominal pain or colic, associated with nausea, vomiting and diarrhoea (3, 4). There is no consensus on the treatment of severe gastrointestinal manifestations of HSP and recommendations are based on small studies and case reports. The most commonly administered therapy are methylprednisolone pulses and IVIG, and sporadically—plasmapheresis, cyclophosphamide, methotrexate, mycophenolate mofetil, azathioprine, rituximab, factor XIII concentrate replacement therapy, *etc*. (5, 6). In our patient, relapsing episodes of gastrointestinal symptoms required complete cessation of oral intake and introduction of parenteral nutrition.

Several smaller studies and case reports that indicate an association between HSP and HP infection were recently published. In those cases, the eradication of HP led to a prompt resolution of HSP symptoms (7). In children, HP infections may be asymptomatic, as was the case with our patient. Increased IgA levels, decreased C3 levels, increased cryoglobulins and elevated levels of pro-inflammatory mediators caused by HP infection may have some role in the course of HSP (8). Previous studies indicate that the eradication of HP may lead to resolution and decreased recurrence of HSP. However, there is not enough evidence to substantiate the claim that HP infection may trigger HSP (8). In our case, resolution of all symptoms after the eradication of HP suggests an association between HP infection and HSP.

In our patient, the course of disease was complicated by persistent bradycardia. There are few described cases of adult patients treated with methylprednisolone, in whom bradycardia emerged within a few hours to

several days after the start of the therapy. Also, in the patients treated with conventional lower doses of corticosteroids, episodes of bradycardia were reported, but were extremely rare (9). The mechanisms by which corticosteroids may cause bradycardia have not been fully elucidated; however, there is speculation that corticosteroids may directly affect cardiomyocytes, modulating their sensitivity to catecholamines, or cause rapid electrolyte shifts across cell membranes, or indirectly—by inducing arterial hypertension. However, in our patient, the likely cause of bradycardia was decreased T3 levels. Possible mechanisms of decreased T3 availability may be corticosteroid-induced block of peripheral conversion of T4 to T3 or competition between corticosteroids and thyroid hormones for albumin-binding sites that decreases T3 levels despite normal T4 levels (10).

AUTHORS' NOTE

All the authors have participated in the concept and design, analysis, drafting and revising of the manuscript. Each author listed has seen and approved the submission of this version of the manuscript and takes full responsibility for the manuscript. The authors of this paper do not have any potential conflict of interest.

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