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Could it be Henoch-Schönlein purpura?

Background
Henoch-Schönlein purpura is the most common form of systemic vasculitis in the paediatric setting with 90% of cases occuring in childhood. Although diagnosis in the primary care setting may be difficult, it is vital in order to avoid significant complications.

Objective
This article outlines the pathogenesis, clinical manifestations and classification of Henoch-Schönlein purpura and details evidence based investigations and management.

Discussion
Henoch-Schönlein purpura is a self limiting disease characterised by a tetrad of clinical manifestations that vary in occurrence and order of presentation. There is no single diagnostic test to confirm Henoch-Schönlein purpura; diagnosis depends on recognition of clinical manifestations. Management usually occurs in the ambulatory setting and is mainly supportive. Priorities include symptom relief and preventive therapy to reduce the risk of complications. Further trials to clarify the role of glucocorticosteroids are needed before a definitive role for steroids in the management of Henoch-Schönlein purpura can be established.

Case study

CM, 12 years of age, presented to a hospital emergency department with his father. He had a referral letter from his family doctor with him which read: 'Fevers, legs + lower abdomen rash 2/7, neck lymphadenopathy. ? systemic disease ? meningitis ? septic arthritis'.

On presentation, CM was unable to weight bear and complained of a painful left leg. During the preceding week he had experienced symptoms of an upper respiratory tract infection, including cough. He also had diarrhoea for 2 days but no nausea or vomiting was noted.

Initial observations were:

- temperature 37.8°C (last paracetamol 5 hours ago)
- pulse 108 bpm
- respiratory rate 24/min
- oxygen saturation 98% on room air.

There was a petechial and purpural skin rash over CM's arms and buttocks; lesions were multiple, nonblanching painful and palpable. Other positive findings included enlarged cervical nodes, suprapubic tenderness, left ankle swelling and tender joints in his lower limbs bilaterally.

Henoch-Schönlein purpura (HSP) is the most common form of systemic vasculitis in the paediatric setting with 90% of cases occurring in childhood.[1] In the majority of patients, HSP is self limiting. It is characterised by four features:

- **palpable purpura in patients without thrombocytopenia or coagulopathy**
- **arthritis or arthralgia**
- **abdominal pain, and**
- **renal disease.**

Epidemiology

Henoch-Schönlein purpura is commonly found in children aged 3–15 years and has a higher prevalence in Caucasians and Asians than in those of African descent.[2] Studies reveal a lower incidence of 10/100 000 in children aged <17 years in Taiwan and the Czech

Republic,[3,4] compared with 20–70/100 000 per annum in the United Kingdom. There is a male predominance with a male:female ratio of 1.8:1.[2,3] Henoch-Schönlein purpura occurs more often in the colder months and is usually preceded by an upper respiratory infection, particularly streptococcal.[5]

Pathophysiology

The exact aetiology of HSP remains unknown. Histologically, HSP exhibits an immune mediated leukocytoclastic vasculitis, with deposits of immunoglobulin A (IgA) and its immune complexes within the walls of involved vessels and organs. Patients have elevated serum levels of IgA, IgA immune complexes, IgA anticardiolipin antibodies and transforming growth factor-ß, as well as altered IgA glycosylation.[6,7]

Clinical manifestations

Clinical manifestations are illustrated in *Figure 1*. These can develop over days to weeks and may vary in the order that they present. Palpable purpura and joint pain are the most common and consistent presenting symptoms; initial diagnosis of HSP in the absence of these symptoms may not be obvious. For, example a misdiagnosis of infection may occur in patients with significant joint or abdominal pain but no skin manifestations.

Skin manifestations

The classic rash (*Figure 2*) of HSP begins as erythematous, urticarial and macular wheals. It then coalesces and develops into the typical ecchymoses, petechiae, and palpable purpura. The rash often manifests in a symmetrical pattern at pressure dependant areas, such as the lower extremities in adults and the buttocks in toddlers. In nonambulatory children the face, trunk, and upper extremities may be more affected.

Arthritis/arthralgia

Arthralgia occurs in 84% of HSP patients and often coexists with other symptoms.[8] The large joints of the lower extremities are most commonly affected. Transient oligoarticular arthritis and peri-articular swelling may cause pain, tenderness and restricted movement.

Figure 1. The four classic features of Henoch-Schönlein purpura

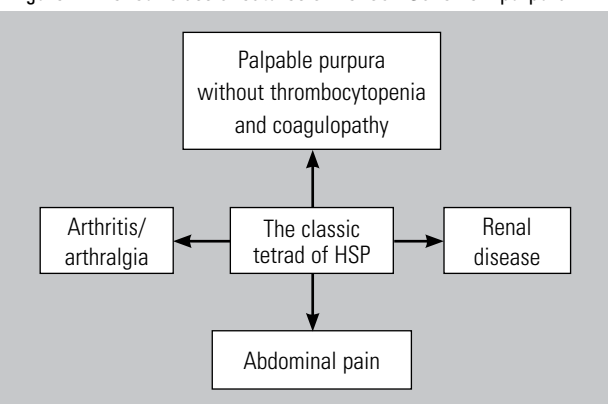
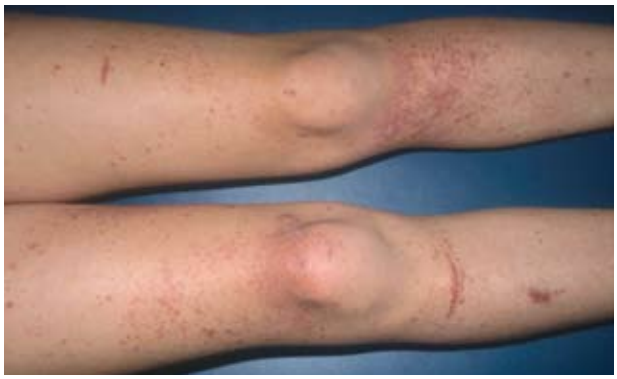


Figure 2. Classic rash of Henoch-Schönlein purpura



Renal manifestations

Retrospective cohort studies revealed some degree of initial renal involvement in about 20–54% of HSP patients, ranging from isolated haematuria and/or proteinuria (without any abnormality in renal function and blood pressure [BP]) to acute nephropathy with renal impairment.[8,9] Renal manifestations generally occur over a period of 28 days after the initial presentation of HSP. Gross or microscopic haematuria, proteinuria or nephritic syndrome may occur.[9]

Long term renal complications

In a 2005 systematic review, Narchi[10] followed up children with HSP and found an excellent overall renal prognosis. The review examined different lengths of follow up after the initial presentation of HSP and revealed that only 21 patients (which accounted for 1.8% of the total study population) developed subsequent renal impairment.

Follow up with urinalysis and BP measurement is recommended, however the ideal duration of follow up is unclear. Blanco et al[1] revealed a favourable short term prognosis for initial renal impairment in most HSP patients, with complete resolution of 94% in paediatric patients and 89% in adult patients at an average of 18 months follow up.

Gastrointestinal symptoms

Gastrointestinal (GI) symptoms such as nausea, vomiting, abdominal pain and transient paralytic ileus are found to precede skin manifestations in 15–35% of cases.[11] Complications include GI bleeding, bowel ischaemia or necrosis, intussusception and bowel perforation. Children with severe GI pain, and/or those requiring hospitalisation, may be at a greater risk of developing an intussusception. Ultrasonography should be the initial screening test for suspected intussusception; contrast enema may fail to detect the ileoileal intussusceptions typically seen in HSP.

Classification criteria

In 1990, the American College of Rheumatology established criteria to classify seven types of vasculitis, including HSP.[12,13] Criteria include:

- palpable purpura
- age ≤20 years at onset

- acute abdominal pain, and
- biopsy showing granulocytes in the walls of small arterioles and/or venules.

When two out of the four criteria are present, a patient is said to have HSP, with a sensitivity of 87.1% and a specificity of 87.7%.[12,13]

Diagnosis

The diagnosis of HSP relies on clinical manifestations. However, in patients with incomplete manifestations or unusual presentations, a biopsy of an affected organ (eg. skin or kidney) that demonstrates leukocytoclastic vasculitis with a predominance of IgA deposition can confirm a diagnosis of HSP.

Biopsy

In the paediatric population, biopsy is reserved for patients with an unusual presentation of HSP (no rash or atypical rash) and patients with significant renal disease.

In adult patients, because of the lower incidence of HSP, biopsy has a more important role in establishing a diagnosis. Skin biopsies are performed to sample the small blood vessels from the superficial dermis. Light microscopy with haematoxylin and eosin (H&E) stains should demonstrate a classic leukocytoclastic vasculitis in postcapillary venules with IgA deposition. Immunofluorescence studies are essential to confirm a diagnosis and these often require biopsy from a second skin site.

Laboratory test

There is no single specific laboratory test that is diagnostic for HSP. However, serum IgA level may be an indicator (it has been reported to be elevated in 50–70% of patients with HSP).[14] Normal platelet count and coagulation profile help to differentiate HSP from other purpuric diseases. A normochromic anaemia may indicate occult GI bleeding. Urinalysis should be performed in all HSP patients as it can reflect the degree of renal involvement. In addition, renal involvement often becomes detectable after the other manifestations of HSP, so urinary screening should be continued beyond the acute presentation.

Management

Management is mainly supportive and symptomatic. Most patients can be managed as outpatients with treatment being directed at adequate oral hydration and pain relief. Oedema of the lower extremities, buttocks, and genital area are improved with bed rest and elevating the affected area. Clinicians need to be vigilant in assessing for severe complications that may require hospitalisation (*Table 1*).

Nonsteroidal anti-inflammatory drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) may have a role to play in HSP management. However, there are no randomised controlled trials evaluating their use in treating symptoms. In addition, due to their effects on platelets and renal perfusions, NSAIDs may be contraindicated in patients with active GI bleeding or glomerulonephritis.

Table 1. When hospitalisation is warranted for HSP patients

• Inability to maintain adequate hydration with oral intake
• Severe abdominal pain or significant GI bleeding
• Changes in mental status
• Severe joint involvement limiting ambulation and/or self care
• Renal insufficiency (elevated creatinine), hypertension, nephrotic syndrome

Table 2. Drug regimen commonly used in managing HSP patients

Drug	Dosage	Indications
Prednisone (oral)	1 mg/kg/day (maximum 60–80 mg/day)	Severe abdominal pain that affects oral intake and/or requires hospitalisation
Methyl-prednisolone (parenteral)	0.8–1.6 mg/kg/day (maximum 64 mg/day	As above in those who cannot tolerate oral medications

Glucocorticosteroids

The use of glucocorticosteroids in patients with HSP remains controversial and definite conclusions are yet to be drawn. The reported benefits include shortening the duration of abdominal pain, as well as decreasing the risk of intussusception, renal involvement, and recurrence.[15] However, most of these studies were retrospective in nature, definitions of renal involvement varied between the studies and dosing regimens, and mode of delivery also differed between studies. *Table 2* shows typical glucocorticosteroid regimens used in HSP.

Recurrence of HSP is reported in about one-third of affected children[8] and generally occurs within 4 months of the initial episode. Recurrence is more common in patients with nephritis, evidence of acute inflammation (eg. elevated ESR) and patients treated with corticosteroids.[8] This increased risk in those who receive corticosteroid therapy needs to be taken into account when considering whether or not to use steroids as part of initial management.

Summary of important points

- Henoch-Schönlein purpura is the most common systemic vasculitis primarily affecting children aged 3–15 years.
- HSP is characterised by palpable purpura without thrombocytopenia or coagulopathy, arthritis or arthralgia, abdominal pain, and renal disease.
- Diagnosis depends on clinical manifestations and no single diagnostic test can confirm the disease.
- Management is mainly supportive and symptomatic and can usually occur in the ambulatory setting.
- Clinicians need to be vigilant in assessing for complications that may require hospitalisation.

Conflict of interest: none declared.

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