

Henoch-Schonlein purpura(IgA vasculitis)

Summary

IgA vasculitis (IgAV), previously referred to as Henoch-Schonlein purpura (HSP), is an acute immune complex-mediated small vessel vasculitis that most commonly occurs in children. Onset is often preceded by an upper respiratory tract or gastrointestinal infection; IgAV in adults may be idiopathic. Affected individuals typically develop palpable purpura, arthritis and/or arthralgia, and abdominal pain. Renal involvement (i.e., IgAV nephritis) is more common and usually more severe in adults than in children, typically manifesting with hematuria. While IgAV is a clinical diagnosis, laboratory studies are used to identify organ involvement and exclude differential diagnoses, and skin biopsy can confirm the diagnosis in patients with atypical presentations. IgAV is usually self-limited; treatment is generally supportive. Systemic glucocorticoids may be required depending on severity of manifestations (e.g., in IgAV nephritis, orchitis). IgAV has an excellent prognosis in children, usually resolving within one month when not complicated by IgAV nephritis. Adults often manifest with more severe features and have lower remission rates. All patients require follow-up assessments to rule out the development of chronic renal disease.

A. **Definition.** A systemic IgA-mediated vasculitis that primarily involves the skin, joints, gastrointestinal (GI) tract, and kidneys.

B. **Epidemiology**

1. HSP is primarily a disease of children (ages 3–15 years); the peak incidence is at 4–6 years.
2. HSP is the most common form of vasculitis of childhood.
3. Males are more likely to be affected.
4. HSP occurs primarily in the fall, winter, and spring.

ETIOLOGY

- HSP is a vasculitis of unknown etiology characterized by inflammation of small blood vessels with associated leukocytic infiltration of tissue, hemorrhage, and ischemia.
- The immune complexes associated with HSP are predominantly composed of IgA, raising the suggestion that this illness may be allergy mediated.
- HSP is associated with group A streptococcal infection, but no causal association has been proved.
- often follows an upper respiratory tract infection.

Pathophysiology

- Hypothesized pathophysiological mechanism: exposure to allergen/antigen (e.g., infection, drugs) → stimulation of IgA production → deposition of IgA immune complexes in vascular walls (e.g., in the skin, GI tract, joints, kidneys) → activation of complement → vascular inflammation and damage

CLINICAL MANIFESTATIONS

- HSP is characterized by rash, arthritis, gastrointestinal or renal vasculitis.
- Low-grade fever and fatigue are present in more than half of affected children.
- The hallmark of HSP is the rash of PALPABLE PURPURA
 - ✓ caused by small vessel inflammation in the skin leading to extravasation of blood into the surrounding tissues.
 - ✓ IgA often is deposited in the lesions.
 - ✓ begin as small macules or urticarial lesions, but rapidly progresses to purpura with areas of ecchymosis.
 - ✓ classically found in dependent areas, below the waist on the buttocks and lower extremities.
 - ✓ accompanied by edema, particularly of the calves and dorsum of the feet and the scalp and scrotum or labia.
 - ✓ last from 3–10 days, and may appear at intervals that vary from a few days to as long as 3–4 mo.
 - ✓ In <10% of children, recurrences of the rash may not end until as late as a 1yr.
- ARTHRITIS occurs in ⅓ of children with HSP, most commonly the ankles and knees.
 - ✓ effusions are serous, not hemorrhagic, in nature and resolve after a few days without residual deformity or articular damage.



- Edema and damage to the vasculature of the GASTROINTESTINAL TRACT may also lead to (50%):

- intermittent abdominal pain (colicky)
- peritoneal exudates
- enlarged mesenteric lymph nodes
- segmental edema
- hemorrhage into the bowel
- 50% patients= occult heme-positive stools, diarrhea ($\pm$ blood), or hematemesis.
- Intussusception, suggested by an empty right lower abdominal quadrant, currant jelly stools, complete obstruction or infarction with bowel perforation. Ttt: hydrostatic reduction during a contrast study vs. surgical intervention.

NOTE:

Palpable purpura can occur in meningococemia if there are pre-existing coagulation abnormalities such as factor V Leiden, protein S, or protein C deficiency

- PANCREATITIS, and ORCHITIS.

- RENAL INVOLVEMENT: Most cases of glomerulonephritis occur within the first few months of presentation occurs in 25-50% of children and manifest with:

- hematuria
- proteinuria
- nephritis or nephrosis
- acute renal failure
- chronic hypertension
- end-stage renal disease.

- Others:

- HEPATOSPLENOMEGALY and LYMPHADENOPATHY may also be present during active disease.
- NEUROLOGICAL INVOLVEMENTS: seizures, encephalopathy,, mononeuropathies ,paresis, or coma.
- rheumatoid-like nodules
- cardiac and eye involvement
- pulmonary or intramuscular hemorrhage.

NOTE:

ACUTE HEMORRHAGIC EDEMA (AHE)

- ✓ ≤ 2 yr of age that may be confused with HSP.
- ✓ fever; tender edema of the face, scrotum, hands, and feet; and ecchymosis (usually larger than the purpura of HSP) on the face and extremities .The trunk is spared.
- ✓ urinalysis is normal.
- ✓ The younger age, nature of the lesions, absence of other organ involvement, and biopsy may help distinguish AHE from HSP

LABORATORY AND IMAGING STUDIES (neither specific nor diagnostic)

- HSP show evidence of systemic inflammation with elevated ESR, CRP, and WBC count.
- The platelet count is the most important test because HSP is characterized by nonthrombocytopenic purpura with a normal, or even high, platelet count.

THE PRESENCE OF NORMAL PLATELET NUMBERS DIFFERENTIATES HSP FROM OTHER CAUSES OF PURPURA THAT ARE ASSOCIATED WITH THROMBOCYTOPENIA, SUCH AS AUTOIMMUNE THROMBOCYTOPENIA, SLE, OR LEUKEMIA.

- urine urinalysis for evidence of hematuria, and serum BUN and creatinine to evaluate renal function.
- Stool for occult blood.
- 50% of patients have elevated concentrations of IgA as well as IgM
- negative for antinuclear antibodies (ANAs), antibodies to nuclear cytoplasmic antigens (ANCAs), and rheumatoid factor.
- radiologic investigation? Gut perforation.
- Definitive diagnosis of vasculitis is confirmed by biopsy
- Renal biopsy may show mesangial deposition of IgA and occasionally IgM, C3, and fibrin.

CRITERIA FOR DIAGNOSIS OF HENOC-SCHÖNLEIN PURPURA

Criteria	Definition
PEDIATRIC age group	Age ≤ 20 years at onset of symptoms
Palpable PURPUR	Raised, palpable hemorrhagic skin lesions in the absence of thrombocytopenia
BOWEL angina	Diffuse abdominal pain or the diagnosis of bowel ischemia
Diagnostic BIOPSY	Histologic changes showing granulocytes in the walls of arterioles or venules

2P

2B

Differential diagnoses

Differential diagnosis of IgAV based on clinical features		
Clinical feature of IgAV	Differential diagnosis	Distinguishing features of the differential diagnosis
Purpura [17]	Hypersensitivity vasculitis	No IgA deposition on biopsy
	- Small vessel vasculitides such as: - Granulomatosis with polyangiitis - Eosinophilic granulomatosis with polyangiitis - Microscopic polyangiitis - Systemic lupus erythematosus (SLE)	- No IgA deposition on biopsy - Affects adults - Associated with specific antibodies (e.g., MPO-ANCA)
	Coagulopathies (e.g., hemophilia A)	Abnormal coagulation studies (e.g., ↑ aPTT)
	- Immune thrombocytopenia - Hemolytic uremic syndrome	- Low platelet count - Nonpalpable purpura
	- Meningococcal septicemia - Acute leukemia	- Low platelet count - Abnormal coagulation studies (e.g., ↑ PT)
Arthritis/arthralgia	- Autoimmune diseases such as: - SLE - Juvenile idiopathic arthritis (JIA) - Rheumatic fever	- No IgA deposition on biopsy - Associated with specific antibodies (e.g., anti-dsDNA)
	Septic arthritis	Arthritis typically in a single joint
	Reactive arthritis	No rash, abdominal pain, or renal symptoms
Renal disease	IgA nephropathy	- No rash, joint, or GI symptoms - Primarily affects (young) adults



IgAV is a unique cause of purpura without thrombocytopenia.

COMPLICATIONS

- Most cases of HSP are uniphasic in nature, lasting 3 to 4 weeks, then resolving completely.
- The rash can wax and wane, however, for 1 year after HSP, and parents should be warned regarding possible recurrences.
- The arthritis of HSP does not leave any permanent joint damage, and it does not typically recur.
- Renal involvement rarely may lead to acute renal failure.

PROGNOSIS

- The prognosis of HSP is EXCELLENT.
- Patients with HSP renal disease (elevated BUN, persistent high-grade protein-uria) are at highest risk for long-term complications, such as hypertension or renal insufficiency.
- There is a long-term risk of progression to end-stage renal disease in less than 1% of children with HSP.
- The rare patients who develop end-stage renal disease may require renal transplantation. HSP may recur in the transplanted kidney.

To Sum up:

A 5-year-old boy is seen with maculopapular lesions on the legs and buttocks. He complains of abdominal pain. He has recently recovered from a viral upper respiratory infection. Complete blood cell count, coagulation studies, and electrolytes are normal. Microscopic hematuria is present on urine analysis.

- IgA-mediated **vasculitis of small vessels** (IgA and C3 in skin, renal glomeruli, and gastrointestinal tract); most common cause of nonthrombocytopenic purpura in children
- Usually follows an **upper respiratory infection**
- Children usually 2–8 years of age; usually in winter, more males than females
- Clinical presentation
 - Low-grade fever and fatigue
 - Hallmark—**pink, maculopapular rash below waist; progresses to petechiae and purpura (red → purple → rusty brown); crops over 3–10 days** (at times in intervals up to 3–4 months)
 - Gastrointestinal:
 - Intermittent abdominal pain
 - Occult blood in stools
 - Diarrhea or hematemesis
 - **Intussusception** may occur
 - Arthritis unusually large, weight-bearing joints
 - Renal—25–50% with glomerulonephritis or nephrosis
 - Hepatosplenomegaly, lymphadenopathy
 - Rarely, CNS (seizures, paresis, coma)
- Laboratory studies
 - Increased platelets, WBCs, ESR
 - Anemia
 - **Increased IgA, IgM**
 - May have anticardiolipin or antiphospholipid antibodies
 - Urine—RBCs, WBCs, casts, albumin
- Diagnosis
 - Classic clinical presentation
 - Definitive diagnosis (rarely needed) with skin biopsy
 - Renal biopsy shows IgA mesangial deposition and occasionally IgM, C3, and fibrin
- Treatment
 - **Symptomatic treatment** for self-limited disease (constitutional symptoms, rash, arthritis)
 - Intestinal complications—**corticosteroids** oral or intravenous → dramatic improvement of gastrointestinal signs and symptoms (can recur for as long as 3 years)
 - Renal—same for any form of renal disease
- Complications—**renal insufficiency/failure, bowel perforation**, scrotal edema, and testicular torsion; chronic renal insufficiency occurs in <1% and of those, <0.1% result in failure