

# Henoch-Schönlein Purpura With Hemoptysis: Is It Pneumonia or Something Else?

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## KEY WORDS

Henoch-Schönlein purpura, pulmonary hemorrhage

## ABBREVIATIONS

CT: computed tomography

CXR: chest radiograph

GPA: granulomatosis with polyangiitis

HSP: Henoch-Schönlein purpura

Ig: immunoglobulin

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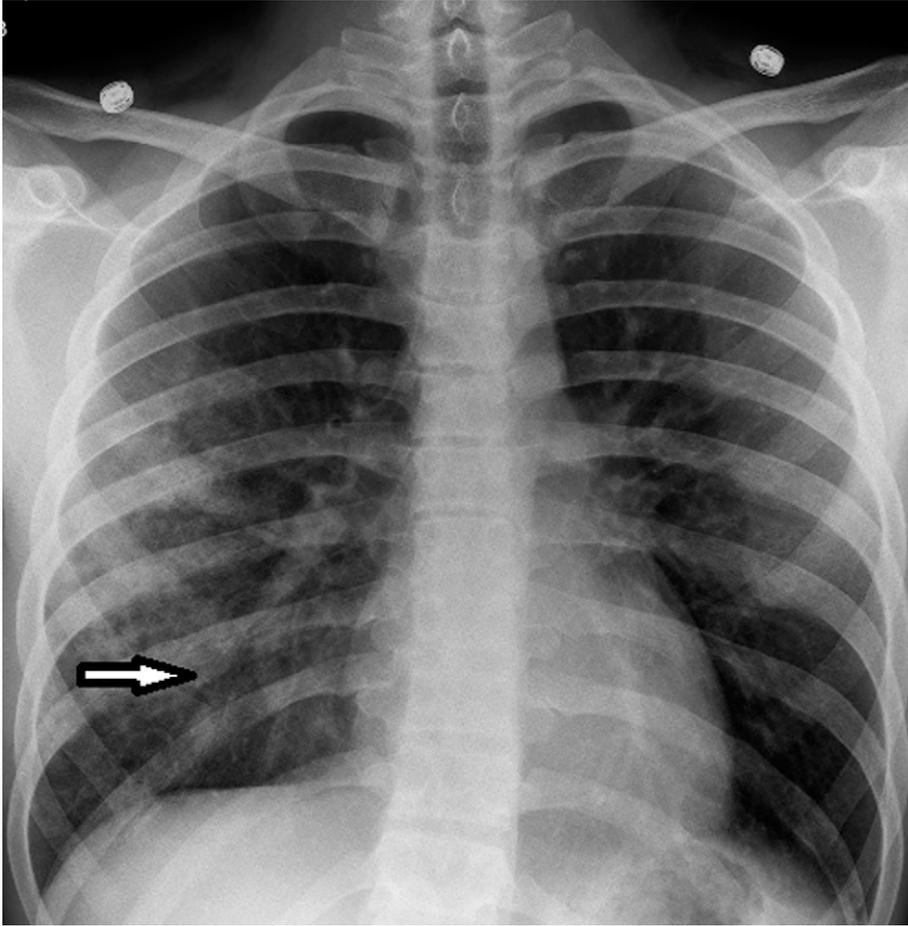
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**Case:** An 18-year-old male presented to the emergency department with a 5-day history of a palpable purpuric rash, arthralgias, dark-colored urine, and severe abdominal pain. The patient was admitted to the hospital medicine service for further management. A urinalysis showed mild hematuria and trace proteinuria. An abdominal ultrasound was normal. He was diagnosed with Henoch-Schönlein purpura (HSP) and was started on prednisone by the hospital medicine team. His symptoms improved significantly, and he was subsequently discharged from the hospital on hospital day 4 (day 9 of illness) to complete a 2-week taper of prednisone (initially started on 80 mg/day with instructions to decrease the dose by 20 mg every 5 days) and to follow up with his primary care physician. On day 15 of illness, the patient presented to the emergency department with worsening upper and lower extremity edema, arthralgia, and palpable purpura, new-onset shortness of breath, hemoptysis, and epistaxis. No fever was reported. He was at the time taking 60 mg of oral prednisone per day. On physical examination, the patient was pale in appearance but was not in acute distress. Vital signs showed elevated blood pressure of 148/69 mm Hg, temperature of 36°C (96.8°F), heart rate of 89 beats per minute, respiratory rate of 18 breaths per minute, and oxygen saturation of 99% on room air. He had normal respiratory effort, and lungs were clear on auscultation with good air movement. A new systolic ejection murmur best heard at the left upper sternal border was appreciated, and the patient was also noted to have pitting edema in the lower extremities bilaterally. Abdominal examination was reassuring, and there were normal bowel sounds with no abdominal tenderness or distention. Laboratory evaluation revealed a slight increase in the serum creatinine level from 0.59 to 0.68 mg/dL, significant proteinuria (300 mg/dL; urine protein to creatinine ratio of 3.9 mg/mg compared with 0.16 mg/mg during his recent admission), hematuria with >50 red blood cells per high-power field, and hyaline and white blood cell casts in his urine. Furthermore, the patient was noted to have hypoalbuminemia (albumin: 2.8 g/dL) and normocytic anemia (hemoglobin: 10.6 g/dL [reduced from 14.9 g/dL 1 week previously]). Platelets, prothrombin time, partial thromboplastin time, and international normalized ratio were all within normal limits. A chest radiograph (CXR) showed a right lower lobe opacity (Fig 1). Consequently, the patient was started on ceftriaxone and was admitted for further evaluation.

**Question:** *Is this pneumonia or HSP with pulmonary involvement?*

**Discussion:** The likelihood of the patient having pneumonia was low given that he remained afebrile, had a nonfocal lung examination, and was not hypoxic or tachypneic. In addition, the respiratory symptoms were associated with worsening



**FIGURE 1** Results of CXR showing right lower lobe air space opacity.

of his HSP symptoms and anemia, thus putting HSP with pulmonary involvement higher on the differential. HSP is an immunoglobulin (Ig) A–mediated small-vessel necrotizing vasculitis commonly seen in childhood. Ninety percent of cases are seen in children aged  $\leq 10$  years, with peak incidence between 4 and 6 years of age.<sup>1</sup> The etiology of the illness is unknown, but 75% of cases are preceded by an upper respiratory illness.<sup>1–3</sup> However, the pathophysiology of HSP involves the deposition of antigen-antibody complexes (especially IgA) in small vessels activating the alternative complement pathway, resulting in neutrophil accumulation that causes inflammation and vasculitis.<sup>1</sup> Clinical manifestations

usually include nonthrombocytopenic purpura, arthralgia, gastrointestinal manifestations, and renal involvement.<sup>4</sup> HSP is a self-limited disorder with an average duration of 4 weeks, with the extent of renal involvement being the main predictor of prognosis. Relapse occurs in 55% of patients and is usually within 3 months of the initial presentation.<sup>3,5,6</sup>

Pulmonary involvement is a rare complication seen in 5% of all HSP cases.<sup>7</sup> It usually presents as pulmonary hemorrhage. A review of the literature has shown that pulmonary hemorrhage can be the first manifestation of HSP in 88% of cases with pulmonary involvement.<sup>4,7</sup> Pulmonary hemorrhage is commonly

seen with the first episode of HSP, although it can occur with recurrent episodes. Studies have shown that clinical manifestations of pulmonary hemorrhage in HSP vary greatly, ranging from mild cough to acute severe dyspnea and respiratory failure.<sup>4</sup> Most patients present with dyspnea, and only about one-third of patients present with hemoptysis.<sup>4,5</sup> Most cases, regardless of the clinical manifestations, are temporally associated with an acute drop in hemoglobin levels and abnormal CXR findings.<sup>2,5,6,8</sup> Because a drop in hemoglobin can also be attributed to other manifestations of HSP such as gross hematuria and bloody stools, CXR findings in HSP patients presenting with respiratory symptoms and no fever may be the key in the early identification of pulmonary hemorrhage.

CXR findings are varied and include mild perihilar infiltrates, and unilateral or bilateral opacities with pleural effusions.<sup>4</sup> These varied findings may divert treatment efforts toward other respiratory illnesses and thus delay diagnosis and targeted therapies for pulmonary hemorrhage. In the case of our patient, the CXR was initially interpreted as most consistent with lobar pneumonia, and he was subsequently started on antibiotic therapy. However, lack of fever, new-onset hemoptysis, and history of HSP in the setting of abnormal CXR findings should heighten suspicions for pulmonary hemorrhage. One case report made note of an adult patient with patchy interstitial and alveolar infiltrates bilaterally suggestive of pulmonary edema treated with diuretic and acute hemodialysis, with minimal improvement initially.<sup>6</sup> Computed tomography (CT) scan and biopsy results later suggested hemorrhage rather than fluid overload in that case.

Previous studies have shown baseline lung function decline with HSP pulmonary vasculitis without any clinical or radiographic evidence of parenchymal lung involvement.<sup>9</sup> One study demonstrated decreased lung diffusion capacity in 96% of patients with HSP that eventually normalized on follow-up testing. Previous research also found lower transfer factor for carbon monoxide in 15 patients with HSP compared with the control group.<sup>10</sup> Findings were attributed to early subclinical lung impairment secondary to temporal alteration of the alveolar capillary membrane by IgA deposition during time of disease. This condition resolved with recovery from the acute illness and had no association with development of pulmonary hemorrhage. It is unclear why only a very small proportion of children with HSP will develop pulmonary hemorrhage.<sup>9,10</sup> Furthermore, results of the pulmonary function tests obtained for our patient were normal, highlighting the unclear role of these tests in the diagnosis and follow-up of pulmonary hemorrhage in HSP patients because they may not be a reliable screening method to predict progression to pulmonary hemorrhage.

**Case Continuation:** The patient initially continued to have significant hemoptysis that gradually improved but lasted for a total of 9 days. The patient's hemoglobin level was at its lowest on hospital day 5 of the second admission (9.1 g/dL). Pulmonology, nephrology, and rheumatology consults were obtained. Results of pulmonary function tests and a ventilation/perfusion scan were normal. Flexible bronchoscopy showed normal anatomy with no acute hemorrhage, but the bronchoalveolar lavage specimen was noted to be bloody. Cytology

showed low inflammatory profile (cell differential: 80% macrophages, 20% neutrophils, <1% lymphocytes, and <1% eosinophils) and 30% hemosiderin-laden macrophages. Results of respiratory culture, fungal cultures, acid-fast stain, and viral polymerase chain reaction were negative.

On day 3 of admission, the patient was noted to have increased lower extremity edema with worsening hematuria and proteinuria (protein-creatinine ratio increased to 8.9 mg/mg), an uptrending serum creatinine value (1.07 mg/dL from a baseline of 0.6 mg/dL), and a serum albumin level of 2.2 g/dL.

**Question:** *Is it still HSP or could it be something else?*

**Discussion:** The association of glomerulonephritis with pulmonary hemorrhage raises the suspicion of pulmonary-renal syndrome, a term used to describe a multisystem disease dominated by pulmonary and renal involvement.<sup>11</sup> Only a few diseases can present with pulmonary-renal syndrome in children. The differential diagnosis includes Goodpasture syndrome, granulomatosis with polyangiitis (GPA) (formerly known as Wegener granulomatosis), and systemic lupus erythematosus. HSP is also a cause of pulmonary-renal syndrome in children.

Goodpasture syndrome is a rare autoimmune disease caused by antiglomerular basement membrane antibodies.<sup>12</sup> These antibodies attack both the glomerular and alveolar basement membranes, leading to glomerulonephritis and alveolar hemorrhage. The antibodies can be detected in the blood to confirm the diagnosis.<sup>11</sup> Systemic lupus erythematosus is a multisystem disease and can present as pulmonary-renal syndrome. Antinuclear antibodies are

usually positive in lupus, and complement C3 and C4 levels are low. GPA is an idiopathic vasculitis that may present as pulmonary-renal syndrome in children but usually involves the upper airways, including sinusitis and nasal disease. Antineutrophil cytoplasmic antibodies are usually positive in children with GPA.<sup>13</sup>

**Case Continuation:** The evaluation for pulmonary-renal syndromes in our patient was negative for antinuclear antibodies, antiglomerular basement membrane, and antineutrophil cytoplasmic antibodies. A serum protein panel revealed normal complement levels, low transferrin, albumin, and IgM levels. Sinus CT scan was normal. A lung high-resolution CT scan (Fig 2) revealed a patchy mixed ground-glass appearance, concerning for inflammatory process versus diffuse alveolar hemorrhage. An echocardiogram (performed to evaluate for the new murmur on presentation) was normal, and the murmur was attributed to anemia.

Due to the severity of the kidney involvement characterized by nephrotic syndrome and elevated creatinine levels, the decision was made to proceed with renal biopsy. Results of the biopsy showed necrotizing segmental glomerulonephritis with strong positive IgA and C3 staining consistent with HSP nephritis. The final diagnosis was pulmonary hemorrhage associated with HSP.

**Question:** *What are the complications of pulmonary hemorrhage in HSP? What is the treatment?*

**Discussion:** Patients with pulmonary hemorrhage secondary to HSP have kidney involvement in up to 95% of the cases compared with 40% in those without pulmonary hemorrhage.<sup>7,14</sup> Renal involvement typically



**FIGURE 2** Chest CT scan showing diffuse patchy ground-glass opacities mainly on the right side.

manifests as IgA glomerulonephritis. Renal failure can be seen in 47% of cases compared with 1% to 2% in patients with no pulmonary involvement.<sup>6,7</sup> Nephrotic syndrome occurs in 8.3% of the cases, and our patient had nephrotic-nephritic syndrome.<sup>7</sup> Renal biopsy is reserved for patients in whom the diagnosis is uncertain or if there is clinical evidence of severe kidney involvement.<sup>15</sup> Although a skin biopsy is less invasive and is usually sufficient to confirm the diagnosis of HSP,<sup>16</sup> a renal biopsy was obtained in our patient to guide therapy and to provide prognostic information.

One-quarter of patients have other organ system involvement, including the cardiovascular and the central nervous system.<sup>7</sup> Upper airway involvement is seen in 11% of the cases and can present as epistaxis (as seen in our patient).

Acute respiratory failure is the most serious complication seen and may occur in up to 53% of patients with HSP and pulmonary hemorrhage.<sup>4</sup>

Respiratory failure is associated with a 33% mortality rate even with appropriate treatment, and 75% mortality has been noted when treatment is not initiated appropriately.<sup>2</sup> Early diagnosis and treatment significantly affect the clinical course of patients.

Although standard treatment of pulmonary hemorrhage associated with HSP has not been established, intravenous pulse methylprednisolone with high doses (ranging from 500–1000 mg) have been recommended as first-line therapy, with the addition of immunosuppressive therapy in the presence of respiratory failure.<sup>1,4,6,17</sup> As reviewed in the literature, combined therapy has been shown to improve survival rates from 25% to 75%.<sup>2,4</sup> Cytotoxic therapy has significant adverse effects; thus, it should be used judiciously based on sound clinical judgment. Our patient was on a typical prednisone regimen for HSP when he developed pulmonary hemorrhage, which suggests that the doses used in HSP may not prevent development of pulmonary hemorrhage.

**Case Continuation:** The patient was started on pulse intravenous steroid therapy at 1 g daily of methylprednisolone for a total of 5 days. He was then switched to oral prednisone 60 mg every other day for 6 months. Cyclophosphamide therapy was initiated at 750 mg/m<sup>2</sup>. The first dose was given during his hospital stay and continued monthly for a total of 6 months. The patient had complete resolution of hemoptysis, abdominal pain, arthralgias, purpura, edema, and gross hematuria before discharge on hospital day 13. The patient was followed by nephrology and rheumatology for immunosuppressive therapy. There have been no reports of hemoptysis on his follow-up visits after discharge from the hospital.

**Conclusions:** Pulmonary hemorrhage represents a rare but life-threatening complication of HSP. Respiratory symptoms in a patient with HSP should raise suspicion, especially if associated with a drop in hemoglobin level. Abnormal findings on CXR have been found in all the reported cases. Pulmonary hemorrhage indicates severe vasculitis and requires aggressive and early treatment. The mortality rate has decreased with the use of intravenous corticosteroids and immunosuppressive therapy. Early recognition of this uncommon complication of HSP by the pediatric hospitalist is crucial to prevent severe complications.

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