Case Report

Management of Henoch-Schonlein Purpura with Gastrointestinal Manifestations in Children

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ABSTRACT
Henoch-Schonlein Purpura (HSP) is systemic vasculitis in children, hallmark by inflammatory infiltration of polynuclear leukocytes in small blood vessels, followed by IgA1 immune deposits. HSP prevalence is approximately 3-27 cases per 100,000 children. The inflammatory process in HSP causes an ischemia and hemorrhagic process characterized by non-thrombocytopenia purpura, arthralgia, gastrointestinal problems, and kidney impairment. This process is called leukocytoclastic vasculitis. A 10-year-old boy came to ER of Dr. Sayidiman Magetan Hospital presenting with diffuse abdominal pain and purpura skin lesions in body. The complaint started with a red rash on both legs, then progressively extended to both hands, thighs, and buttocks, and continued with severe abdominal discomfort, nausea, dizziness, fever, and the patient also experienced a brownish-black stool. The patient was diagnosed with Henoch-Schonlein purpura with gastrointestinal manifestations based on medical examination. The patient stayed for six days at the hospital, and the condition improved.

Keywords: children, HSP, purpura, vasculitis

INTRODUCTION
Henoch Schoenlein purpura or IgA vasculitis (IgAV) is the most common systemic vasculitis in children, characterized by inflammatory infiltration of polynuclear leukocytes in small blood vessels, followed by predominance of IgA1 immune deposits (1,2). The inflammatory process that occurs in the small blood vessels in this disease causes an ischemia and/or hemorrhagic process, characterized by purpura without a decrease in platelet levels, arthralgia, gastrointestinal problems, and kidney impairment, so this process is called leukocytoclastic vasculitis (3).

The disorder can affect all ages. It is most frequently seen in children, especially aged 2-11 years, but it can also manifest in adolescents and adults. The disease can be severe and may lead to long-term kidney disease in adults (4). The prevalence of HSP is approximately 3-27 cases per 100,000 children (4). The overall incidence is predicted to be 9/100,000 population (5). It is presented in children with a high rate of occurrence at 4-6 years of age, with 90% of cases developing at <10 years of age (4). HSP is more common in males than females with a ratio of 1.5:1 (6).

The disease usually follows an upper respiratory tract infection with the most common triggering factors are group A- β hemolytic Streptococcus, Staphylococcus Aureus, or
Mycoplasma. The case is characterized by specific skin lesions of palpable non-thrombocytopenic purpura, along with arthritis, abdominal pain and gastrointestinal bleeding, and may also be accompanied by nephritis. Reddish spots appear in areas predominantly affected by gravity, such as the lower extremities and upper extremity extensors, along with pressure point areas, such as the buttocks (7).

Gastrointestinal manifestations are an initial feature of the disease, seen in 35-85% of HSP cases. Gastrointestinal symptoms may include nausea, vomiting, severe abdominal pain, and bleeding (8). Severe complications involving edema, erosion, and bleeding of the stomach and duodenum are intestinal perforation, intussusception, and pancreatitis. Manifestations of renal impairment in HSP are found in 20-50% of cases, characterized by hematuria with or without proteinuria, to glomerulonephritis leading to renal failure (3).

HSP has no definitive diagnostic test. The diagnosis of HSP can be confirmed by evaluating the manifestations that appear and adjusted to the existing criteria. According to the American College of Rheumatology (1990), the diagnosis of HSP has criteria including age of onset <20 years, non-thrombocytopenia purpura, gastrointestinal tract impairments, and granulocyte biopsy results on the walls of arterioles or venules (9,10).

Furthermore, the diagnosis criteria based on the latest classification of the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology Society (PReS) in 1994 are palpable-purpura (absolute criteria), followed by one or more symptoms: 1. acute abdominal pain, 2. arthralgia, 3. gastrointestinal disturbances or bleeding, 4. IgA deposits on skin biopsy, 5. and renal abnormalities (finding blood or protein in the urine) (4,11).

In this case, the patient has fulfilled the diagnosis of HSP based on both of the criteria. So the author wants to discuss in more detail the case of Henoch Schoenlein Purpura with gastrointestinal manifestations in pediatrics. HSP is a generally self-limiting disease. There is no specific treatment, except for supportive therapy. Corticosteroids are commonly used to treat HSP with gastrointestinal manifestations and renal impairment. The prognosis of the disease is good, and the average recovery is 4 weeks after onset (4,7).

**CASE DESCRIPTION**

A 10-year-old boy, came to pediatric emergency room (ER) of, Dr. Sayidiman Magetan Hospital presenting with diffuse abdominal pain and purpuric and petechial skin lesions in body. The complaint started with a red rash on both legs progressively extended to both hands, thighs, buttocks, and back for 6 days. The rash was red to blackish in color, prominent, palpable, with no itching or pain. The rash was followed by pain, discomfort and swelling in the knees, it caused the patient incapable to walk. The complaints get worse when the patient do activity and decrease when resting by lying down.

He also complained of severe abdominal discomfort, especially in the lower right abdomen, followed by nausea, dizziness, and fever for 3 days before entering the hospital. These complaints of abdominal pain arised and disappeared, felt twisted, and could last 15-30 minutes. The next day 6 hours before admission to the hospital, the patient vomited 6 times every time he ate and drank. The patient experienced a brownish black stools 2 days earlier as much as 2 times.
The patient and family have no history of similar diseases and denied any history of allergies, autoimmune, nor gastrointestinal diseases. The patient said that 2 weeks before the first symptoms appeared, the patient had experienced a fever, cough, and runny nose. During the complaint, the patient had been treated by a doctor, but the complaint was temporarily reduced. The patient's delivery history was normal, basic immunization history was complete, and growth and development history was normal.

Clinical examination revealed the kid was moderately ill, alert, and the vital sign shows blood pressure 110/95 mmHg, respiratory rate 20x/min, pulse 97 x/min, and temperature 37°C. On general status examination of the head, neck, and thorax were normal. For abdominal examination, on inspection found flat, no distended, auscultation intestinal peristaltic within normal limits, on palpation found diffusely painful without rebound tenderness in epigastrium (VAS scale 3), without signs of abnormal mass, hepatomegaly and splenomegaly. On examination of the extremities, there was non-blanching palpable erythematous purpura, not relieved by pressure, intermediate in size between miliary and lenticular, diffusely spreading across both feet going to both hand, thighs, back, and buttocks, with indistinct borders, and no tenderness.

The blood test laboratory examination showed Hb 16.4 g/dL, leukocytes 16,800/µL, platelets 620,000/µL and hematocrit 47.3%, erythrocytes 6.35 x 106uL, segment neutrophils 84.6%, lymphocytes 6%, NLCR 13.28%. Renal function tests were normal. Histopathologic examination shows a hypocellular smear consisting of hyperkeratosis, red blood cell extravasation, with a distribution of squamous epithelial cells among extensive neutrophilic inflammatory cells and lymphocytes.

![Figure 1. Non-thrombocytopenia purpura lesion on hand of the patient](image-url)
Based on history, physical examination, and supporting examination, the patient was diagnosed with Henoch-Schonlein Purpura with gastrointestinal manifestations. This case fulfills the criteria for the diagnosis of HSP according to the American College of Rheumatology (1990): age of onset < 20 years, palpable erythematous purpura, diffuse acute abdominal pain, and leukocytoclastic vasculitis biopsy results. We didn’t find any renal involvement manifesting in the form of hematuria, hypertension or nephritis, also any neurological manifestations.

During medical treatment, the patient was given therapy including: IVFD D1/2 NS 23 gtts/min, ranitidine 0.2mg/kgBW IV, ondansetron 2-5mg/kgBW IV, and methylprednisolone 55.5mg IV for 3 days, followed by methylprednisolone 8mg tablet oral 3x for 4 days. , then the dose will be reduced gradually. The patient was hospitalized for 6 days, and his condition improved.

**DISCUSSION**

Henoch-Schonlein Purpura is an autoimmune disease of IgA-mediated hypersensitivity vasculitis often identified in children. HSP has been defined as a clinical syndrome of generalized inflammatory vasculitis of small blood vessels of the skin, joints, gastrointestinal
tract, and kidneys, characterized by nonthrombocytopenic purpuric lesions, abdominal pain or gastrointestinal bleeding, arthritis, arthralgia, and sometimes followed by nephritis to hematuria (4,6,9,12).

Cases are most prominent in children, primarily aged 2-11 years. The prevalence of HSP is estimated to be 3-27 cases per 100,000 children. HSP is highly prevalent in children with an incidence peak at 4-6 years of age, with 90% of cases occurring at <10 years of age. The HSP occurrence follows a seasonal variability with a fall-winter incidence peak, hinting at the role of climate-related environmental triggers, specifically for infections (4-6).

The etiology of HSP remains unknown, but genetic predisposition and environmental factors may impact pathogenesis of the disease. Some hypotheses suggest a connection between HSP and infection, 50% of patients with HSP have acute upper respiratory infections (AURI) with the common cause Group A beta-hemolytic streptococcus (GAS) found in 20-50% of patients with serologic culture or bacterial culture (2,11,13).

Some case of HSP can also be caused by Mycoplasma pneumonia, Helicobacter pylori, Mycobacterium tuberculosis, Epstein Barr virus, Campylobacter jejuni, Shigella sp., Epstein Barr virus, Yersinia, hepatitis A,B and C viruses, varicella, Parvovirus B19, CMV, measles, rubella, and adenovirus. HSP might occur after cholera, measles and typhoid vaccinations although these risks are rare. Other triggers can be related to chemical toxicants and drugs such as penicillin, erythromycin, and anticonvulsants (2,9,12).

In this patient, it is suspected that HSP originated from an upper respiratory tract infection, because the patient had symptoms of cough, runny nose, and fever 2 weeks before the redness on the body appeared. HSP arises from the inflammatory infiltration of polymononuclear leukocytes in IgA-mediated small blood vessels as a prime response to extraneous or endogenous antigens, resulting in the formation of predominant IgA1 immune deposits in small vasculature, which include arterioles, capillaries, and venules (4,15).

Immune complex deposits and complement activation led to local inflammation and destruction of surrounding tissues mediated by complement and Fc receptors (14). The IgA complexes created and deposited in the skin, kidneys, joints, and abdomen will cause clinical purpura in the skin, nephritis, arthritis, and severe abdominal pain. Leukocytoclastic vasculitis (LCV) occurs with necrosis in small blood vessels (1,14,16). Moreover, elevated serum levels of galactose-deficient IgA1 and abnormal IgA1 glycosylation are trusted as the main pathogenesis mechanisms in the HSP patients (4).

There are several abnormalities involving IgA in HSP, including elevated serum IgA levels, IgA-containing macromolecular aggregates, IgA immune complexes, IgA antineutrophil cytoplasmic antibodies, IgA Anti endothelial cell antibodies, IgA rheumatoid factor, IgA fibronectin complexes, and IgA anticardiolipin antibodies (8).

The vascular lesions occur when lymphokines contribute to the inflammatory response. The acute phase of HSP in children has higher levels of non-specific pro-inflammatory cytokines such as tumor necrosis alpha (TNF-α), interleukin (IL)-6 and IL-1β. IL-1 and TNF-α stimulate the endothelium to activate intrinsic and extrinsic coagulation pathways and reduce
fibronolytic activity. This reason explains the thrombosis process that takes place in vasculitis (14,16).

Patients with HSP have clinical symptoms of a non-pruritic erythematous macular rash, which rapidly turns into papules and urticaria, and progresses to petechiae and purpura. Purpura is commonly referred to as non-blanching cutaneous hemorrhage (17).

Clinical symptoms begin with a symmetrical erythematous macular eruption on the skin of the lower extremities that progresses to palpable purpura without thrombocytopenia. The rash is originally confined to the skin of the malleolus, then extends to the dorsal surface of the legs, buttocks and outer arms. Within 12 - 24 hours the macules will transform into purpuric lesions that are dark red in color and have a diameter of 0.5 - 2cm (13,15).

Palpable purpura rash and subcutaneous edema are the characteristics of HSP or cutaneous IgA. Purpura has a hallmark acute onset, symmetrical distribution Eruptions usually present in the lesions, not disappear with pressure, clear lesion borders, with sizes ranging from pinpoint to several centimeters (2).

The lesions change from red to purple before the lesions gradually disappear in around 10 days. The rash is often located in areas that depend on pressure e.g. lower extremities, beltline and buttocks (17). Skin lesions were the hallmark of HSP disease found in 90% of cases, often accompanied by abdominal and joint symptoms. Purpura is reported in all HSP patients to be widespread and diffuse in 56%, but in 11% of purpura is localized to the lower extremities (gluteus and legs) (2,18).

Gastrointestinal manifestations occur after the skin lesion (1-4 weeks after onset) in 35-85% of cases (12). GI manifestations such as: abdominal pain in 62% of cases; may be followed by nausea, vomiting, hematemesis, melena, bloody diarrhea, duodenal ulcer. Gastrointestinal bleeding occurred in 33% of cases, and sometimes invagination happened (11).

Gastrointestinal (GI) tract manifestations occur in to 72% of patients and typically present with abdominal colicky pain, due to gut angina. This can progress to acute GI bleeding with symptoms of melena or hematemesis which could be severe and life-threatening. GI bleeding has been related to prolonged hospital stay and in severe cases, requires acute immunosuppressive treatment (4,9).

Musculoskeletal involvement is the second frequent manifestation of HSP disease, estimated to be seen in 70-90% of patients with symptoms of arthralgia or arthritis and in 5-25% of patients with onset prior to purpura (19). Arthralgia appeared in 43% of cases, and reported in 23% of HSP children (2). Knees and ankles are more often affected than small joints in HSP. Symptoms of arthritis include swelling, warmth and tenderness (17).

The renal impairment incidence is estimated at 30-50% and has a role in determining the long-term prognosis of HSP, including mortality and morbidity. Clinical manifestations in HSP nephritis starts from microscopic hematuria and/or proteinuria affecting the renal parenchyma, with characterized extrarenal deposition of IgA, C3 and other complement factors in the mesangium, subepithelial and subendothelial spaces, leading to an increased risk of chronic kidney disease (13,17,20).

In addition, HSP in the children has a risk of CNS disorders with onset 2-4 weeks after the symptom appears. The symptoms include headache, seizures, emotional instability, irritability and behavioral changes. Other symptoms may include ataxia, intracerebral
hemorrhage (ICH), hemiparesis, mononeuropathy and acute sensory-motor axon neuropathy (13).

The diagnosis of HSP is based on the American College of Rheumatology (ACR) criteria, including: 1) palpable purpura, 2) The age of onset ≤ 20 years, 3) acute abdominal pain, and 4) skin biopsy showing granulocytes in small arterioles or venules). The diagnosis of HSP can be made if 2 out of 4 criteria are identified with a sensitivity of 87.1% and specificity of 87.7% (10,11).

In 2005, the new European League Against Rheumatism (EULAR)/Pediatric Rheumatology European Society (PReS) developed criteria for the diagnosis of HSP : Purpura or petechia with lower extremity predominance (Main sign), followed by at least 1 of the following 4 criteria: 1) Acute onset of diffuse abdominal colicky pain (may include intussusception and gastrointestinal bleeding), 2) Histology showing leukocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposition, 3) Acute onset of arthralgia or arthritis, and 4) Renal abnormalities (characterized by proteinuria/hematuria (4,21).

In this case, the patient showed the classic symptoms defined by ACR as well as EULAR and PReS, including palpable erythematous purpura without thrombocytopenia, age of onset <20 years, diffuse acute abdominal pain, arthralgia, and leukocytoclastic vasculitis biopsy. HSP or IgAV is clinically diagnosed. Supportive investigations are important, especially to look for complications of renal impairment. Laboratory examination is also important to exclude the diagnosis of other diseases and to identify complications of renal impairment. Routine blood tests, renal function tests (such as urinalysis and determination of urea, creatinine, and electrolytes in the blood), complete blood count, coagulation profile, and ESR can help to confirm the diagnosis of HSP. Detection of antinuclear immunoglobulin G (ANA) or antineutrophil cytoplasmic auto antibodies (ANCA) may be assisted in ruling out other causes of vasculitis (13,20).

This patient has an increased leukocyte count and platelets. Hemoglobin in HSP cases is generally normal, because it depends on the presence or absence of bleeding. Increased blood urea nitrogen (BUN) and creatinine can be a clue to glomerulonephritis, and urine analysis can present hematuria with or without proteinuria, and blood can also be detected in the feces (6).

Histopathologic examination of skin in HSP shows segmental inflammation of vessels, swollen endothelial cells, fibrinoid necrosis of blood vessel walls and infiltrates around vascular, called leukocytoclastic vasculitis. In this patient, the skin biopsy results revealed a hypocellular smear consisting of hyperkeratosis, red blood cell extravasation, with a distribution of squamous epithelial cells along with extensive neutrophil inflammatory cells and lymphocytes compatible with leukocytoclastic vasculitis (22,23).

Some cases of Henoch-Schonlein Purpura (HSP) are self-limiting and do not require treatment. However, it can recur in 1/3 of cases followed by 1/100 cases can lead to renal damage. (15) The onset of the disease ranges from 2-6 weeks (4,6).

The treatment given is symptomatic and supportive, including maintenance of hydration, electrolyte balance, nutrition, pain management with analgesics (9). Generally, all HSP patients are given NSAIID: prednisone and methylprednisolone. Although controversial, these drugs can control joint pain, and can be given in the setting of severe symptoms, such as persistent
purpura, severe abdominal pain, gastrointestinal bleeding, edema, manifestations of vasculitis in the central nervous system, lungs, and testis, and persistent nephritic syndrome. Some researchers use corticosteroids to prevent nephritis (8,9,17). The initial treatment of prednisone at a dose of 1-2mg/kg/day for 7-14 days helps reduce abdominal pain and joint pain intensity in children by decreasing resolution time (3,9,17).

On the other hand, the medication can prevent bleeding, obstruction, and perforation of the gastrointestinal tract which can worsen the patient's condition. Corticosteroids can inhibit T-cell proliferation, T-cell dependent immunity, and cytokine gene transcription (IL-1, IL-2, IL-6, interferon gamma, TNF-α) (20,23,24). If HSP patients have renal complications, called nephritis, then the corticosteroids treatment can be combined with immunosuppressants. IV methylprednisolone may help prevent early deterioration of renal disease (9,11). The treatment using azathioprine, cyclophosphamide, and cyclosporine is controversial (4,11).

The drug was given IV methylprednisolone at a dose of 250-750mg/day for 3-7 days in combination with cyclophosphamide 100-200mg/day. Followed by daily oral prednisone 100-200mg and cyclophosphamide 100-200mg/day for 30-75 days, until cyclophosphamide is stopped immediately and tapering off steroids for 6 months. In addition, close control of the side effects of the steroids should be monitored (9,13).

In this case, the patient was hospitalized due to severe pain, vomiting, reddish body rash, arthralgia, and there was concern of continued worsening of the disease. However, the patient had rapid improvement in abdominal and joint pain on day 2 of corticosteroid therapy, followed by purpura that dried up and disappeared.

HSP has a good prognosis and can spontaneously recover within a few days or weeks (usually 4 weeks after onset), if it is not combined with severe gastrointestinal disorders and renal impairment (9,12). HSP cases recover in 94% of children and 89% of adults. Recurrence can occur in the first 4 months after the attack in children <10 years old in 1/3 of cases. Exacerbations can generally occur between 6 weeks to 2 years after first onset, and renal disease as a sign of bad prognosis occurs 3 weeks after onset. Recurrences may occur in 40% of patients (4,8,9).

**CONCLUSION**

Henoch-Schonlein purpura is one of the systemic vasculitis in children. The hallmark of HSP is inflammatory infiltration of polymonuclear leukocytes in small blood vessels, followed by IgA1 immune deposits characterized by non-thrombocytopenic purpura, arthralgia, gastrointestinal manifestation, and renal impairment. The incidence rate is majorly at the age of 2-11 years, with 90% of cases developing at the age of <10 years. This is a case of a 10-year-old boy with diffuse abdominal pain and red purpura on both legs, progressively extending to both hands, thighs, buttocks, and severe abdominal discomfort, nausea, dizziness, and fever. He also had brownish black stools. Based on medical examination, the patient was diagnosed with Henoch-Schonlein Purpura with gastrointestinal manifestations. The patient stayed for six days at the hospital, and the condition improved.
ACKNOWLEDGMENTS

The authors would like to thank Dr Sayidiman Magetan Hospital which has facilitated the author in the process of making this case report.

CONFLICT OF INTEREST

The author(s) declare that they do not have a conflict of interest and that they do not have affiliations or relationships with any organization or entity that could raise biased questions or statements in the discussion and conclusion sections of the paper.

REFERENCES


