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Case Report

Case report of multiple relapses of Henoch-Schönlein purpura

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Henoch-Schönlein Purpura (HSP) is the most common systemic vasculitis disease in children. The prognosis is generally good, as the disease course is usually benign and self-limited. The HSP reccurences occured in 2.7-51.7% of cases. Reccurences are usually lighter and shorter than the first episode; and occur in 6 weeks to years after the first diagnosis. The gastrointestinal manifestations at the onset of disease have contributerd to HSP relapses.

Corticosteroid administration early in the course of HSP affects both acute (pain, surgical intervention) and chronic (reccurence, renal disease) complication of HSP. **[Paediatr Indones. 2023;63:134-8; DOI: https://doi.org/10.14238/pi63.2.2023.134-8**].

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Henoch-Schönlein Purpura (HSP) is an acute immunoglobulin A (IgA)-mediated disorder characterized by generalized vasculitis. HSP commonly occurs in children. The annual worldwide incidence is 13-20 per 100,000 children under 17 years of age.[1-3] It is characterized by non-thrombocytopenic palpable purpura mostly located on the dependent parts like lower extremities and buttocks, arthralgia/arthritis, bowel angina, and hematuria/proteinuria. HSP pathophysiology is not yet completely understood. Genetic factors are thought to drive the fundamental susceptibility and clinical manifestations. Proposed triggering factors include upper respiratory tract infections, medications, vaccinations, and malignancies. Disease course is usually benign and self-limited. Even though the prognosis is generally good, recurrences or relapses are common within 1 year of initial presentation.[4]

The frequency of relapses reported in previous studies range from 2.7% to 51.7%.[5,6] In most cases, relapses present as new episodes of cutaneous rash often accompanied by gastrointestinal and renal manifestations. The predictive factors for HSP relapse are joint and gastrointestinal manifestations, as well as a history of previous infection at the time of HSP diagnosis.[7] Consistent follow-up is important because complications such as hypertension or chronic kidney disease have been reported up to 10 years after the first HSP episode.[8]

Here we report a case of a nine-year-old boy diagnosed with multiple HSP relapses. For 26 months, he was comprehensively managed both medicamentosa (methylprednisolone and immunosuppressive therapy) and non-medicamentosa with psychosocial support to achieve optimal quality of life.

The case

A 9-year-old boy was referred to our hospital with a diagnosis of Henoch-Schönlein purpura (HSP) and persistent palpable purpura that lasted longer than

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one month. His complaints at presentation were palpable purpura from the lower extremities to the abdomen and gastrointestinal complaints, such as nausea and vomiting. These complaints occurred after he had received a diphtheria tetanus vaccine. Physical examination revealed that the patient was in conscious state, and had blood pressure 90/58 mmHg, heart rate 94 beats per minute, respiratory rate 24 times per minute, and body temperature 37°C. A large amount of palpable purpura were scattered across his lower extremities (**Figure 1**) to his abdomen. Laboratory results showed white blood cells count of 10,910/L, hemoglobin level 14.7 gr/dL, platelet count 443,000, with normal urinalysis results: specific gravity 1.005, pH 6.0 with negative protein, ketones, glucose, bilirubin, and nitrites.

The patient had been previously treated with oral methylprednisolone for 10 days, but the purpura persisted. In our hospital, the patient continued oral methylprednisolone with dose 0.2 mg/kg/day, which was then tapered down slowly over 4 weeks. The symptoms gradually improved.

Four months after the first episode of HSP, the patient returned with same complaint of purpura that did not improve with oral methylprednisolone therapy. In this episode of HSP, abdominal pain was predominant, along with palpable purpura in his lower extremities. From his history, he had no other complaints such as fever, cough, or cold that preceded the purpura. The patient had no history of allergies or diseases with genetic predispositions. The boy was again diagnosed with relapsing HSP since he met 3 out of 4 criteria: age under ≤20 years,palpable purpura, and diffuse abdominal pain (**Table 1**).[9] Physical examination revealed that the child was awake, alert, and fully conscious, and had blood pressure 90/60 mmHg, heart rate 98 beats per minute, respiratory rate 24 times per minute, and temperature 37°C. In this episode of HSP, laboratory and urinalysis results

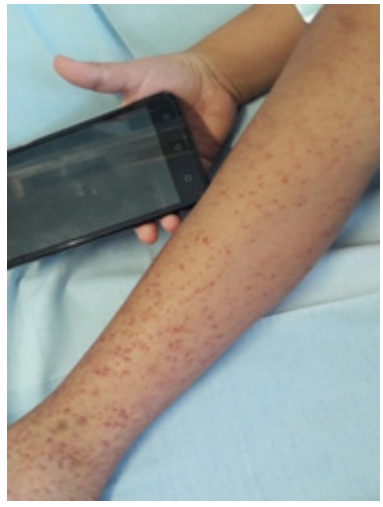

Figure 1. Palpable purpura in the lower extremities

were normal. The C3 level was 129 mg/dL, C4 level 35.4 mg/dL, ALT 17 U/L, AST 33U/L, BUN 24 mg/dL, and creatinine level 0.67 mg/dL. Laboratory results included blood glucose 107 mg/dL (<200), total cholesterol 203 mg/dL (<200), triglycerides 69 mg/dL (<150), HDL 102 mg/dL (> 40), and LDL 87 mg/dL (<100). The patient's abdominal ultrasound showed no complications of HSP relapse such as nephritis or gastrointestinal abnormalities. The patient received a HSP relapse treatment protocol using cyclophosphamide-mesna intravenously for 3 months and oral methylprednisolone for 12 weeks, followed by slowly tapering over 18 weeks.

Six months after the last treatment, the patient was diagnosed again with HSP relapse. His clinical symptoms were much milder; palpable purpura occurred only in the lower extremities and there were no gastrointestinal symptoms. To limit methylprednisolone side effects, the patient was treated with another immunosuppressive agent such as mycophenolate mofetil (MMF) 30 mg/kg/day as bridging therapy for 12 weeks and methylprednisolone

Table 1. *The 1990 American College of Rheumatology Criteria* for the diagnosis of HSP[9]

Criteria	Definition
Palpable purpura	Slightly raised "palpable" hemorrhagic skin lesions, not related to thrombocytopenia
Age ≤ 20 at disease onset	Patient 20 years or younger at onset of first symptoms
Bowel angina	Diffuse abdominal pain, worse after meals, or the diagnosis of bowel ischemia, usually including bloody diarrhea
Wall granulocytes on biopsy	Histologic changes showing granulocytes in the walls of arterioles or venules

0.5 mg/kg/day, followed by slowly tapering over 18 weeks. The symptoms improved by the 4th week of therapy.

Unfortunately, the patient relapsed again 3 months after the last therapy. No evidence of prior infection was recorded for this episode. Despite the milder symptoms, he still received oral methylprednisolone 0.5 mg/kg/day for 8 weeks, and remission was finally achieved after completing the therapy.

Overall, the patient suffered 4 episodes of HSP. We performed an anti streptolysin O (ASTO) test to evaluate for a possible upper airway infection as the trigger of relapse, but the result was negative. The predictors of relapsing HSP in our patient were persistent purpura as well as joint and gastrointestinal involvement at the first HSP episode. Multiple recurrences of HSP increased the probability of renal and abdominal complications in our patient, so during the illness, he was monitored for proteinuria by monthly urinalysis. Fortunately, despite multiple recurrences, the child had no renal complications.

One of the factors that affected the patient's quality of life are side effects of the methylprednisolone and mycophenolate mofetil. At the beginning of the clinical course, the patient had no signs of methylprednisolone side effects. During his consumption of methylprednisolone, his blood pressure was monitored closely at each visit. He had no hypertension until the last observation (24 months after diagnosis). The child also had no hyperglycemia, another side effect of methylprednisolone; random blood glucose tests showed that it was maintained at normal levels. The lipid profile at the end of the observation was abnormal, with total cholesterol 214 mg/dL, triglyceride 68 mg/dL, HDL 61.79 mg/dL, and LDL level 138 mg/dl. We intervened by educating the patient to limit his consumption of high cholesterol foods and engage in physical activity.

Long-term use of methylprednisolone can decrease the plasma half-life of vitamin D. The patient's vitamin D level was 24.4 ng/dL, which was diagnosed as vitamin D insufficiency. He was then given 1,000 IU/day of vitamin D supplementation. Eye examinations were done annually during the consumption of methylprednisolone, and we found no signs of cataracts or glaucoma.

At the beginning of the observation, the child had a possible risk of overweight, with BMI 19.5 kg/m2 and normal height (HAZ -1.9 SD). During treatment and at the end of observation, his nutritional status remained at possible risk of overweight.

Recurrence and chronicity that occurred in this patient indirectly affected his quality of life. The child's Peds-QL score at the beginning of the observation was 72.5, but it decreased to 65 during the observation. The lowest score occurred when the patient had a third HSP relapse. However, the patient's social and educational aspects were not affected by the disease. The child received psychosocial support. And at the end of the observation, his Peds-QL score improved to 88.125, indicating that the patient had a good quality of life.

Discussion

Here we describe an unusual case of HSP in a nine-year-old boy who relapsed three times. HSP is the most common childhood vasculitis, affecting 10-20 children per 100,000 per year. More than 90% of patients are under 10 years of age, with a mean age of 6 years. HSP is a leukocytoclastic vasculitis involving small vessels.[3] Its clinical presentation includes cutaneous palpable purpura, joint pain, renal involvement, colicky abdominal pain, and gastrointestinal bleeding. A diptheria-tetanus vaccination was believed to be the trigger of HSP in our patient.

Henoch Schonlein purpura is an acute disease with a good prognosis, as a complete resolution can usually be achieved in 4 to 6 weeks. Median remission was reportedly achieved within 2 weeks in 83%, and within 4 months in 17% of children, including those with renal failure.[10] The frequency of recurrence varies from series to series. Recurrences are usually lighter and shorter than the first episode. In our patient, the times between relapse episodes were 6, 7, and 10 months, respectively, after the initial episode. Recurrence in HSP reportedly occurs in 6 weeks to years after the first diagnosis.[11]

A relapse is defined to occur when a patient previously diagnosed with HSP and becomes asymptomatic for at least 4 weeks, presents again with a new flare of cutaneous lesions or other systemic manifestations of vasculitis. The pathogenesis of relapse in HSP still remains elusive. The gastrointestinal

manifestations at the time of HSP diagnosis in our patient may have contributed to his multiple relapses. In contrast, an infection shortly before the onset of HSP appears to be a protective factor for relapsing disease,[12] but that did not occur in our patient.

The typical goals of treating HSP are to: (1) ameliorate acute symptoms, (2) mitigate short-term morbidity (such as abdominal complications that require surgery), and (3) prevent chronic renal insufficiency.[13] Because HSP is characterized by leukocyte infiltration of the blood vessel walls along with immunoglobulin A deposition (with resulting vascular injury and necrosis), and because corticosteroids inhibit inflammatory processes, early treatment with corticosteroids has been postulated to be effective for all three therapeutic goals, but controversy remains. In a systematic review, the potential benefit of corticosteroid administration early in the course of HSP may be more prominent than previously suggested for both acute (pain, surgical intervention) and chronic (recurrence, renal disease) complications of disease.[13] Our patient received corticosteroids early as treatment for his first HSP episode, resulting in improvement of acute HSP symptoms and prevention of gastrointestinal and renal complications, despite the multiple recurrences. With rigorous monitoring during the treatment, corticosteroid side effects were not been observed in our patient, except for vitamin D insufficiency, which was addressed by giving vitamin D supplementation.

Other reported treatment choices in complicated and severe HSP patients vary from combined heavy immunosuppressive (cyclosporine, cyclophosphamide) therapy to plasmapheresis. MMF is known to have less adverse effects than other immunosuppressive drugs, with a distinct benefit in the treatment of many immunologically mediated renal diseases, combined with antifibrotic and antiproliferative effects. MMF can be extremely valuable for treating complicated HSP.[14] We chose MMF to treat our patient to minimize the adverse effects of immunosuppressive therapy.

Chronicity and multiple relapses affect patient quality of life, not only from the disease itself, but also from side effects of methylprednisolone. *The PedsQL™* questionnaire was used to assess our patient's quality of life.[15] At the beginning of treatment, his *PedsQL* score was 72.5, but during the illness his score decreased. The child's risk of psychosocial problems was increased because of chronicity in HSP. His physicians noted the boy's overt and covert signs of psychosocial distress, so the adjusted approach and care given to patient and his family resulted in an improved *PedsQL* score at the end of treatment.[16] It is crucial to intervene in situations causing distress, so that in addition to resolving the illness, the disease did not seem to cause further psychosocial impacts.

Multidisciplinary and comprehensive continuous monitoring is needed for children with HSP, considering that renal complications can occur. In our case, chronicity and multiple relapses were unusual problems of HSP. The possible side effects of corticosteroids (hypertension, hyperglycemia, gastrointestinal problems, vision problems, and infection) should be carefully monitored since our patient relapsed several times. Ultimately, support from medical personnel, child psychologists, and parents are important to prevent complications and improve the quality of life of children with HSP.

Conflict of interest

None declared.

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