Haemorrhagic Bullous Lesion in Henoch-Schonlein Purpura

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ABSTRACT

Background: Henoch-Schonlein purpura (HSP) is a vasculitis of the small vessels and the most common type of vasculitis in children. Vesicles and haemorrhagic bullae were thought to be rare in HSP and maybe difficult to diagnose. Purpose: To describe the rare case of haemorrhagic bullous lesion in HSP. Case: A 15-year-old Javanese girl was admitted to Dr. Soetomo General Hospital Surabaya with one week history of multiple haemorrhagic blisters on her extremities, accompanied with joint pain, abdominal pain, and severe nausea. Firstly, it’s only a few redness patches then become numerous and changed to haemorrhagic blisters. A dermatological examination shown multiple bullae and vesicles on multiple palpable erythematous purpura. There were hypokalemia on laboratory examination and histopathological examination concluded a leukocytoclastic vasculitis. Discussion: Fluid balance, oral corticosteroid, oral antihistamine, antiemetic injection, and potassium correction were administered to the patient. Dexamethasone was discontinued because there was a presence of melena. Symptomatic treatment was given and significantly improvement was achieved in one month after treatment. Conclusion: Henoch-Schonlein purpura is diagnosed based on history, physical, clinical, and histopathological examination. Vesicles and haemorrhagic bullae are rare in HSP, and it does not seem to have any prognosis value in the outcome of HSP.

Key words: Henoch-Schonlein purpura, haemorrhagic bullous lesion, small vessel vasculitis.

INTRODUCTION

Henoch-Schonlein Purpura (HSP), also known as anaphylactoid purpura, is an inflammatory vascular disease and the most common form of vasculitis affecting children.1,2 It is an acute, systemic immune complex-mediated and leukocytoclastic vasculitis.3,4 Vasculitis in HSP is mediated by immunoglobulin (Ig) A-immune complex deposition. HSP characterized by the clinical tetrad of non-thromboticopenic palpable purpura, abdominal pain, arthritis, and renal involvement.5,6,7 Skin lesion, usually presents as erythematous maculopapules, petechiae, and purpura.6 Haemorrhagic bullae lesions are seen only 2% in childhood HSP. Trancede-Bohin et al. reported that about 60% of adult with HSP showed these manifestation.1,8

The annual incidence of HSP in children (0-14 years) shows geographical variations; 13.5 per 100,000 population in Ireland, 18 per 100,000 in Denmark, and 21.75 per 100,000 in France, 8.5 per 100,000 in Jordan. Males are affected twice as often as females.9 The cause of HSP is unknown. It is sometimes precipitated by an infections, in particular by a streptococcal infection. It is commonly follows
an upper respiratory tract infections. The pathogenesis of HSP is not yet clearly understood although it is known to be an immune complex-mediated disease. IgA complexes are formed and deposited in the skin, gut, and glomerulus, thus triggering a localized inflammatory response. Necrosis of the small blood vessels develop into leukocytoclastic vasculitis. The diagnosis is usually straightforward clinically, with the typical skin rash (predominantly lower limb purpura) being the main clue, often accompanied by abdominal pain and arthralgia. No single laboratory test is available for the diagnosis of HSP. In 1990, the American College of Rheumatology developed criteria for the diagnosis of HSP. The criteria are (1) palpable purpura (2) age ≤ 20 years at disease onset (3) bowel angina (4) wall granulocyte on biopsy. A patient is said to have HSP if at least 2 of the 4 criteria are present. In 2006, the European League Against Rheumatism (EULAR) and Pediatric Rheumatology European Society (PRES) define, a patient is classified as having HSP in the presence of purpura or petechiae that are dominant in lower limb plus one of the four following criteria (1) abdominal pain (2) histopathology showing typical leukocytoclastic vasculitis with predominant IgA deposit or proliferative glomerulonephritis with predominant IgA deposit (3) arthritis or arthralgia (4) renal involvement (proteinuria, hematuria, or presence of red blood cell cast). The acute, active phase of HSP resolves spontaneously in 94% of children and 89% of adults. Patient often requires admission to hospital, particularly for symptom control. Bed rest maybe necessary for those with arthralgia and abdominal pain. The vasculitic skin manifestation rarely needs therapy but particularly in bullous lesion, there are reports of the successful use of steroid.

**CASE REPORT**

A 15-year-old Javanese girl was admitted to emergency ward of Dr. Soetomo General Hospital Surabaya on March 3rd, 2011 with chief complaint multiple haemorrhagic blisters on her extremities since one week before admission, accompanied with joint pain (especially on her knees and ankles), abdominal pain, and severe nausea. Ten days before admission, she noticed a few itchy redness patches that were especially concentrated on her lower extremities after she had suffered from cough and common cold one day before. Firstly the redness patches were appeared on her upper extremities then rapidly spread into her lower extremities. At the same time she also complained about sore throat, fever, and malaise. Some of these skin lesions had become numerous and changed to haemorrhagic blisters. She was given an analgesic medication from the general practitioner but there was no improvement. She also complained about nausea and abdominal pain but there was no vomiting. The patient had experienced the same disease one year before admission, but the complaint was milder and healed spontaneously without specific medication. She did not experience any disturbances of ears, nose, but there was complaint of sore throat. She also did not complain about leukorrhea or any spontaneous bleeding on her nose or in other area. There were no complaint about pain in mixturation or defecation. There were no history of the same disease in her family, no history of taking oral traditional medication before, no history of receiving any injection medication, no history of applying topical medication before or after the lesion appeared, and no history of food or drug allergy before.

General physical examination at the first day of admission revealed an alert girl but look weak, no sign of anemic, cyanotic, icteric, and respiratory distress. The blood pressure was 100/70 mmHg, pulse rate was 100 times per minute, and body temperature was 37.2°C. There were no abnormality on thorax and abdominal examination. The dermatological examination on both of lower extremities (Figure 1), there were multiple tense and flaccid bullae and vesicles on multiple palpable erythematous purpura bases, unsharply marginated that were varying in size (2-4 cms). Some of bullae and purpura were confluent and became larger. There were also punctate lesion on some part of the lesion (Figure 2). There were edema and pain on the lesion. There were no necrotizing tissue and spontaneous bleeding on the lesion. On both of upper extremities (Figure 3), there were purpuric rash, unsharply marginated that distributed especially in the lower arms. There were no necrotizing tissue, punctate lesion, or spontaneous bleeding on the lesion.
Figure 1. On both of lower extremities: multiple tense and flaccid bullae and vesicles on multiple palpable erythematous purpura bases. Edema was also noted.

Figure 2. Multiple punctate lesions on some part of the lower extremity.

Figure 3. Purpuric rash on upper extremities.

Laboratory examination on the first day of admission revealed the increase of liver function test (SGOT/SGPT: 72/48), hypokalemia (3.0), and slightly leukocytosis (10.4). Patient was consulted to Internal Department because of abdominal pain and the conclusion was drug allergy, dyspepsia, and hypokalemia. Based on history, physical examination, laboratory result, and consultation from Internal Department, the temporary diagnosis was erythema multiforme with differential diagnosis suspect HSP, dyspepsia, and hypokalemia. Based on this diagnosis, the patient was decided to treat with intravenous line RL:D5% infusion 1:1 for the fluid balance, dexamethasone 1 mg orally (three times a day), mehidroline napadisilat 50 mg orally (three times a day), intravenous injection omeprazole 80 mg once per day, and KCl 25 Meq/500 cc RL. Patient was also consulted to Odontology Department and Ear, Nose, Throat Department to find the focal infections. The result from Odontology Department concluded there was no focal infection. Ear, Nose, and Throat Department revealed patient with acute pharyngitis. They only gave gargarisma khan. Some diagnostic procedures were performed to establish the diagnosis and rule out the differential diagnosis. Anti-streptolysin O (ASO) titer was elevated at 200. Histopathological examination was performed and revealed leukocytoclastic vasculitis (Figure 4). Based on this findings, previous history, and physical examination, erythema multiforme can be ruled out and the final diagnosis is HSP.
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On third day of admission, patient was suffered from profuse vomit with the frequency of vomit was more than five times in a day, abdominal pain was getting worsened but the joint pain was improved. In the same day, dermatological examination revealed that there was slightly improvement on her lower extremities. Some tense bullae became flaccid, some of the old bullae was not ruptured yet and there was no new bullae formation, edema in both legs decreased, erythematous macule also slightly faded over. On both of upper extremities region, all of purpuric rash almost diminished.

Because of profuse vomit, we added domperidone two times a day orally, antacid three times a day orally, sucralfate syrup. After those treatments the vomit was improved. The laboratory examination on fourth day of admission indicated that hypokalemia and LFT were normal (K: 3.5 with LFT: SGOT/SGPT 29/26). Coagulation function test were within normal limit. Leukocyte, nitrogen, protein, glucose, and keton were negative in urinalysis. Urine sedimentation revealed erythrocyte 1-2, leukocyte 1-2, and epitel 1-2.

In fifth day of admission, patient suffered from melena. She complained about dark defecation and abdominal pain. Dexamethasone was discontinued immediately and nasogastric tube considered to be assembled to identify the bleeding location. From the tube draining a clear fluid and there was no haemorrhagic fluid. Intravenous line was administered for the nutrition replacement. In the same day, significantly improvement on the lesion was observed. Some of bullae were ruptured and leaving an erosion areas. Most of erythematous macule also faded over. Dressing with normal saline and fusidic acid cream were applied to erosion lesions. In sixth day of admission, we performed aspiration of the remaining bullae and the aspirate material was tested with Gram examination. Cocacobacil gram negative was found on Gram staining examination.

After eighth days of treatment, there were marked improvement of her symptoms. Abdominal pain getting better and there were no more joint pain. On her dermatological examination, all of the bullae were ruptured and leaving few shallow ulcers and erosion areas. Some erosion area became crusted. The clinically progression was displayed in Figure 5 and Figure 6. ASO titer was repeated after one month and the result was negative. The complete resolution was achieved after one month of treatment without any serious complication and none of the lesion become necrotic.
CONCLUSION

HSP is one of the common vasculitis syndrome in childhood. Although it primarily affects children (over 90% of cases), it may develop at any age. Cutaneous involvement always present and may appear as the initial symptom in more than 50% of HSP patients. Arthralgia or arthritis present in 60-70% of patients and appear to be the first manifestation in 25% cases. Gastrointestinal symptoms in children and adults is 46% and 66% respectively in case of HSP. Articular involvement occurs preferentially in the knees, ankles, wrist, elbows, fingers, shoulders, and toes. The etiology is still unclear, but it is commonly associated with infections (bacterial, viral, parasitic), medications, vaccination, and autoimmune mechanism.

We reported a case of bullous haemorrhagic in HSP. A 15-year-old Javanese girl was admitted with rashes on both lower and upper extremities, accompanied with arthralgia, abdominal pain, and nausea. She had history of common cold and cough preceeding the appearance of the rashes. Some of these rashes had become numerous and evolved to haemorrhagic blisters. Laboratory investigations including complete blood analysis, coagulation function test, and renal function test were within normal limit without leukocytosis and thrombocytopenia, except the kalium declined to the level 3.0 mmol/l, and we also noted slightly elevated of liver function test (OT/PT: 72/48) in the first examination. Urinalysis was normal. The histopathological examination from skin biopsy revealed leukocytoclastic vasculitis, so we diagnosed this patient with HSP.

The diagnosis of HSP in this case was based on history taking, physical, clinical examination, and histopathological investigation. Diagnosis HSP (EULAR/PRES consensus criteria) is palpable purpura (essential) in the presence of one of the following: diffuse abdominal pain, any skin biopsy showing predominant IgA, acute arthritis/arthralgia, renal involvement defined as any hematuria or proteinuria. The patient was classified as suffering HSP because of the presence of palpable purpura, diffuse abdominal pain, and acute athralgia. Palpable purpura was the first manifestation in this patient, followed by arthralgia and abdominal pain. We did not performed the skin biopsy to confirm the IgA deposit because the facility was not available yet at that moment in our center.

The association of HSP and group A β-haemolytic streptococcal infections remains controversial. Although there is no perfect serological tehnique to confirm group A β-haemolytic streptococcal infections, the most widely used assay is the ASO titer. In at least 50% of children with HSP, an upper respiratory tract infections may precede the onset of the disease by several days or weeks. Pharyngitis or rhinopharyngitis and tracheobronchitis have been frequently implicated in the development of the disease. Although many studies have identified beta-haemolytic streptococcus group A as a trigger for HSP, there are no controlled studies that confirm the benefit of benzathine penicillin for prophylaxis againsts relapse.

In this case, positive result (200) of ASO titer indicate that HSP may follow a bacterial infection especially Streptococcus β-haemolyticus. It is supported by the history of sore throat, upper respiratory tract infections and the conclusion from Ear, Nose, and Throat Department mentioned the existence of acute pharyngitis. ASO titer converted to negative one month after. Infection with Streptococcus β-haemolyticus in this patient may be a step in a series of changes that lead to the development of HSP in a predisposed individual.

Vesicles and haemorrhagic bullae are fairly common as dermatological manifestation in HSP. Beside the typical purpura, other cutaneous manifestations may present in HSP as target-like lesion, subcutaneous nodules, and urticarial bullous, or vesicular rash. Bullous evolution represent an unusual but well-recognized cutaneous manifestation that maybe a source of diagnostic dilema, but does not seem to have any prognosis value in the outcome of HSP. The differential diagnosis of bullae includes erythema multiforme, toxic epidermal necrolysis, epidermolysis bullosa, bullous mastocytosis, or the
other bullous disease. Based on the criteria of HSP and the histopathological finding revealing a leukocytoclastic vasculitis, this patient finally was diagnosed with HSP. There are two point which could explain why the lesion become bullous haemorrhagic. First, vasculitis might have been severe in this case. It is reasonable to assume that the involvement of vessels in the deeper dermis may lead to the damage of corresponding skin region, leading to more severe skin manifestation. Second, HSP induced weakness and irritability of the skin and that pressure on the skin induced the severe lesion. It has been postulated that the gelatinase Matrix Metalloproteinase-9 (MMP-9) enzyme released from neutrophils accumulating around the blood vessels in the leukocytoclastic vasculitis associated with HSP may play a role in disrupting the surrounding basement membrane zone collagen, and this may lead to bullae or vesicles development.

In this case, we treated our patient with intravenous line RL: D5% infusion 1:1, dexamethasone 1 mg orally three times daily, mebhidroline napadisilat 50 mg orally three times daily, intravenous injection omeprazole 80 mg once per day, and pottasium chloride (KCl) 25 Meq/ 500cc RL. The dexamethasone was discontinued immediately on the fifth day because the patient suffered from melena since corticosteroid could be aggravate this condition. Supportive and symptomatic therapy were given to the patient. Fluid balance and nutrition replacement had been taken seriously because of the melena and profuse vomitting. Antacid, domperidone, and sucralfat were given to improve her nausea and reduce the vomit. Wet dressing with normal saline and antibiotic fusidic acid 2% cream were used for wound care. As a recovery ensues, the bullae were ruptured and leaving some erosion area in fifth day on admission, some erosion become crusted in eight day of admission and the postinflammatory hyperpigmentation was observed in one month after treatment. Over all, this patient was treated with symptomatic and supportive treatment. Complete resolution was achieved in one month after treatment without any sequelae event or serious complications and none of the lesion become necrotic.

The large majority of HSP cases were resolved spontaneously and required symptomatic treatment only. The goals of treating HSP are typically to ameliorate acute symptoms, mitigate short-term complication (such as abdominal complication), and prevent chronic renal insufficiency. Because HSP is characterized by leukocyte infiltration of the blood vessels walls along with IgA deposition, and also because corticosteroids inhibit inflammatory processes, early treatment with corticosteroid has been postulated to be effective for all therapeutic goals. However, corticosteroid treatment still remains controversial. A meta-analysis of four randomized controlled trial demonstrated no significant benefit of short-course prednisone, which administered at presentation of HSP for preventing persistent renal disease. However another meta-analysis, based on a comprehensive review literature, showed that corticosteroids given early in the course of illness, seemed to produce consistent benefits for several major clinically relevant HSP outcomes. Steroid treatment can decrease the intestinal wall edema and thus the symptoms improve. Furthermore, when a patient present with bullous lesion caused by HSP, the skin should be treated like that of a patient with bullous disease. That means the treatments consist of pain control, antibiotic ointment, and protective dressing applied to area of open or blistered skin, avoiding trauma, treatment of infections, and nutritional counseling if the skin is open. As recovery ensues, the lesion fade, leaving areas of postinflammation hyperpigmentation.

In general, the long term outcome of people with HSP is good. The long-term prognosis of HSP is closely associated with the severity of the renal involvement. Recurrences occur in 50% of cases, usually within six weeks and occasionally as late as seven years after the onset of illness. Approximately one third (20-30%) of patients have at least one recurrence, generally involving cutaneous and abdominal manifestation, especially during a 2-year period after the first outbreak. The skin and gastrointestinal manifestation in our patient appeared severe, but renal involvement was absence in this case. It is supported by the absence of proteinuria and hematuria in urine analysis, and RFT result was also within normal limit which mean there were no renal involvement. Therefore, the prognosis of this case is likely to be good. And there has been no recurrence of the bullous lesion or other manifestations of HSP over the ensuing 6-month of follow up.

REFERENCES


