Case Report:
Henoch-Schonlein Purpura in A Child Complicated by Fatal Pulmonary Hemorrhage

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Abstract
We report an 11-year old, Saudi boy who was diagnosed as Henoch-Schonlein Purpura (HSP). During the course of his illness he suffered from severe HSP nephritis and had been managed by steroids and mycophenolate mofetil. Later on, he developed cough with low oxygen saturation, followed by severe pulmonary hemorrhage and deteriorating respiratory status for which he needed to be ventilated. Cyclophosphamide was added and peritoneal dialysis was started, but the boy died within few days due to respiratory failure secondary to massive pulmonary hemorrhage. Pulmonary hemorrhage is a rare yet, severe complication of HSP. Only 19 pediatric cases were reported in literature with 5 deaths including our case. Early recognition of this complication is important so as to start proper management. Cyclophosphamide with steroids are essential for treatment of such cases, especially when associated with renal impairment.

Key Words: Henoch-schonlein purpura – Complications – Pulmonary hemorrhage – Cyclophosphamide – Methylprednisolone – Saudi Arabia.

Introduction
HENOCHE-SCHONLEIN Purpura (HSP) is a common pediatric disease with multisystem involvement. It is characterized by IgA-dominant immune deposits, which affect small vessels, especially in skin, gastrointestinal tract, kidney and joint [1].

The diagnosis of HSP is easy in the presence of typical purpuric or petechial rash (without thrombocytopenia), mainly on the extensor services of the lower limbs and buttocks, which is a mandatory criterion by the European League Against Rheumatism/Pediatric Rheumatology European Society criteria. The criteria request at least one of the following findings: Diffuse abdominal pain, leukocytoclastic vasculitis with predominant IgA deposits on skin biopsy, acute arthritis or arthralgia in any joint, and renal involvement as evidenced by proteinuria and/or hematuria [2].

Except for nephritis, HSP has an excellent outcome with complete and spontaneous resolution of symptoms and signs. Renal involvement is a mild disease, characterized by microscopic hematuria and minimal proteinuria, with <1% risk of progression to End-Stage Kidney Disease (ESKD) [3]. Other complications, such as gastrointestinal bleeding and intracranial bleeding may lead to mortality in some cases [4].

Moreover, pulmonary involvement rarely occurs in HSP, with pulmonary hemorrhage being the most severe lung manifestation [5]. Therefore, this case report aims to raise the awareness of physicians toward this serious complication which might complicate other common pediatric diseases.

Case Report
In May, 2014 an 11-year old Saudi boy presented to the emergency room of Aseer Central Hospital (a tertiary care hospital in Abha, Kingdom of Saudi Arabia), with extensive purpuric rash, abdominal pain and painful ankles. He was in a good health till 3 days before coming to the emergency room, when he started to have purpuric rash over his lower limbs and buttocks with few rashes on the upper limbs. His ankles became swollen with severe pain preventing him from walking. He had mild swelling of both elbows with mild pain. He started to have moderate colicky abdominal pain over the peri-umbilical area in the same day of presentation to medical service. The pain was associated with 2 attacks of vomiting in small amounts without blood and no abdominal distension or change in bowel habits. There were no respiratory symptoms.
His urine was normal in amount and color. There was no family history of any significant diseases.

Physically, he was in pain with pain score of 5/10. He was fully conscious and oriented. All of his vital signs were normal (BP 108/72mmHg, pulse rate: 93 beats per minute, RR: 20/min and temperature 36°C). His oxygen saturation in room air was 96%. He had normal growth parameters. Throat examination was normal. His central nervous system was intact. Cardiac examination was normal and he had no signs of respiratory distress and both lung fields were clear. His abdomen was not distended. However, he had mild periubilical tenderness with no palpable organs or masses. The bowel sounds were normal. Both testicles appeared normal in shape, size and color without any tenderness. His ankles were swollen, hot and tender with restriction of movement. He could move both arms around his elbow joints with mild discomfort. He had extensive purpuric rash all over the lower limbs extending to his buttocks and few rashes on his arms. No lower limbs edema.

Laboratory investigations on admission showed the following: White blood cells count 14,300/gL, red blood cell count 5,990 X 10^3/gL, platelet count 473 X 10^3/µL, hemoglobin 15.5g/dL, erythrocytes sedimentation rate 24mm/minute, urea 24mg/dL, creatinine 0.4mg/dL. All electrolytes were normal. Albumin was 3.7g/dL and total protein was 6.4g/dL. His liver enzymes were normal. Urine analysis showed mild hematuria and trace proteinuria.

He was diagnosed as Henoch-Schönlein Purpura (HSP), admitted to the general pediatric ward and started on prednisolone 2mg/kg/day. However, on the second day, he passed bloody stool for 2 times and his abdominal pain got worse. So, he was shifted to the Pediatric Intensive Care (PICU) for close observation and management. Both pediatric surgery and rheumatology teams were involved in the management of the case. In PICU, his vital signs were stable. Urgent abdominal ultrasonography was done which showed no signs of intussusception.

Eventually, he was started on pulse methylprednisolone 30mg/kg/day. He was kept for 3 days in the PICU without further bleeding and his abdominal pain almost disappeared. Moreover, the swelling of joints and rashes got improved as well, and he was shifted back to the general ward. Skin biopsy was done which showed leukocytoclastic vasculitis Figs. (1,2), while immunofluorescence studies were not available.

Fig. (1): Photomicrograph of skin punch biopsy showing perivascular neutrophilic infiltrate involving the superficial and mid dermis, associated with extravasation of erythrocytes and nuclear dust. The overlying epidermis is unremarkable (Hx & E stain X40).

Fig. (2): Photomicrograph of the skin biopsy showing leukocytoclastic vasculitis with vascular damage, endothelial swelling, vascular wall fibrinization, karyorrhexis and red blood cells extravasation (Hx & E stain X400).

After 4 days, he started to pass dark urine with high blood pressure recordings with edematous lower limbs. His renal functions deteriorated, creatinine and urea increased to 1.7mg/dL and 62 mg/dL, respectively. His albumin dropped to 2.5 mg/dL and urine protein creatinine ratio increased to 1.6 with numerous red blood cells casts. So, mycophenolate mofetil was added to prednisolone, which he was on since admission.

The condition of his renal functions remained poor. The family was hesitant to accept doing renal biopsy. He remained having stable blood pressure with anti-hypertensive medications and other vital signs were normal. Anti-nuclear antibodies, anti-DNA antibodies, c-ANCA and p-ANCA, all were negative. After 12 days of admission, he developed progressive cough followed by hemoptysis for the first time with respiratory distress and hypoxia.
Again, he was shifted to the PICU for close observation. Chest X-ray was done and showed mild infiltration bilaterally Fig. (3). There was a high possibility of pulmonary hemorrhage, especially that his hemoglobin dropped for 1.5g/dL from baseline.

Oral prednisolone was stopped and we started pulsed methylprednisolone plus mycophenolate mofetil. On the second day, he started to have severe hemoptysis and his hemoglobin dropped further to 8.6gm/dL with normal coagulation profile. So, he was ventilated and required high ventilatory settings. Repeated chest X-rays showed diffuse patchy infiltration bilaterally Fig. (4).

Peritoneal dialysis was started and cyclophosphamide replaced mycophenolate mofetil. Nevertheless, he died after a week with respiratory failure secondary to massive pulmonary hemorrhage despite of aggressive management.

Fig. (3): Bilateral patchy infiltration of the apical lobes and middle lobe with air-bronchogram.

Fig. (4): Diffuse significant patchy nodular infiltration more homogeneous on the left mid-thoracic and right upper lobe. Findings are suggestive of diffuse alveolar infiltration.

**Discussion**

Till now, data on pulmonary hemorrhage associated with HSP are limited. There are few reports about the disease in adults and children [6-13]. Chen et al., did a search of the literature (from 1966 till 2010) and found only 16 cases of HSP with pulmonary hemorrhage in children in addition to his reported case. All reported cases presented with typical HSP findings including characteristic rash with or without arthritis, abdominal pain and renal involvement. The symptoms of pulmonary hemorrhage include cough, dyspnea, hemoptysis, chest pain and anemia.

Ren et al., stated that HSP can be associated with pulmonary hemorrhage without any respiratory symptoms or signs [7]. In most cases there were bilateral diffuse infiltrations on chest X-rays [8].

Our patient initially presented with typical purpuric rash, arthritis and abdominal pain which progressed to gastrointestinal bleeding and was managed successfully with pulse steroids. He started to have renal involvement on the 9th day of admission. Mycophenolate mofetil was added to the treatment regimen. His renal functions did not come back to normal. He suffered from respiratory symptoms and his condition deteriorated quickly. This is the 5th reported case of death secondary to HSP with pulmonary hemorrhage in pediatric age group [6]. Rapid deterioration and death can happen in less than 24 hours from the onset respiratory symptoms [9,10]. The diagnosis of such complications should be suspected in patients who present with HSP with any respiratory symptoms or signs. Keeping in mind that respiratory symptoms and signs could be mild [6] or absent [7].

In the absence of hemoptyis a low or falling hematocrit and sequential BAL fluid samples which are persistently hemorrhagic secure the diagnosis in patients with an acute pulmonary syndrome and pneumonic-type radiographic infiltrates [14].

Initially, our patient did not suffer from any respiratory symptoms or signs. Hence, we did not do chest X-rays. In previous reported cases [6-7], chest X-rays was helpful for early diagnosis of pulmonary hemorrhage, in spite of normal respiratory status. This demonstrates that pulmonary involvement in HSP can be subclinical and signs of pulmonary hemorrhage could appear on chest X-rays before clinical signs.
Chaussain et al., found that 28 out of 29 patients had decreased lung transfer for carbon monoxide (TLCO) as measured by a steady-state method in patients with HSP [18]. In the same study, they observed slight radiologic signs of interstitial lung involvement in 18 out of 26 patients.

Cortese et al., retrospectively studied the chest X-rays of 20 patients with diffuse pulmonary hemorrhage because of different pathologies. They identified consolidations or ground-glass opacities in 16/20 patients, mainly in the middle fields (73%). They concluded that diffuse alveolar hemorrhage is characterized by nonspecific alveolar filling pattern and CT is superior in detecting ground glass opacities and is required in cases of suspected diffuse pulmonary hemorrhage with normal chest X-ray findings [16].

Our patient developed severe pulmonary hemorrhage while he was on steroids and mycophenolate mofetil. Then, we added pulsed cyclophosphamide to steroids plus other supportive care, but without any improvement. Mycophenolate mofetil did not help in this condition as well. Matsubayashi et al., stated that it seems that steroids are unhelpful in preventing pulmonary hemorrhage to occur [13].

It is to be noted that pediatricians’ knowledge and experience are limited regarding treatment and prognosis due to the rarity of this condition. Cyclophosphamide pulse therapy should be considered if respiratory failure occurs [6]. Chen et al., suggested that steroid (pulse or non-pulse) therapy should be the first-line treatment for patients when no respiratory failure is present, considering the significant adverse effects of immunosuppressant therapy. Because of high mortality in such conditions, we suggest to start pulse cyclophosphamide early, especially in patients with significant renal involvement. Cyclosporine A can be a good alternative for cyclophosphamide [13].

Children with HSP who have glomerulonephritis tend to have poorer long-term outcome [17]. Such patients need to be observed closely for any respiratory symptoms, keeping in mind that pulmonary hemorrhage can occur without symptoms or signs. HSP patients who develop renal and pulmonary involvement tend to have poor outcome. Chest X-rays can be helpful in patients with subclinical pulmonary hemorrhage by demonstrating patchy infiltrations, which can help to establish the diagnosis earlier.

In conclusion, pulmonary hemorrhage secondary to HSP is rare among children, but still can cause mortalities. High index of suspicion is needed to recognize cases early enough to start the treatment before deterioration. Cyclophosphamide or cyclosporine A should be considered earlier in the treatment with steroids especially if the patient has concomitant renal involvement. More studies are needed to establish risk factors, best treatment modalities and prognosis.

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References


ملخص العرabi

يعرض هذا التقرير حالة طفل سعودي عمره 11 سنة، شخص بمرض فرفزة هينوخ شونلاين، نتج عنه إتهاب حاد بالكلى مما استدعي علاجه بالكورتيزيون، والميوكينتولات موفيتيلا. وفي نفس الوقت بدأ الطفل يعاني من كحة وانخفاض في معدل نسبة الأكسجين وعند ذلك نزيف رئوي شديد وتفتقر في وظائف الجهاز التنفسي، مما أدى إلى اعتماده على جهاز التنفس الصناعي، وتم إضافة عقار السايكلوفوسفاتاميد وكذلك إجراء الغسيل البروتيني، ولكن الطفل توفي بعد أيام قليلة نتيجة لفشل تنفسي بسبب نزف رئوي شديد. إن النزيف الرئوي هو أحد المضاعفات النادرة المصاحبة لفرفزة هينوخ شونلاين، وهذه 19 حالة تم نشرها لأطفال عانوا من هذا المرض توفي منها 5 حالات، بما فيها حالة هذا الطفل. لذلك فإنه من الضروري تشخيص مثل هذه الأعراض والمضاعفات مبكرًا ليتسنى البدء بمعالجتها. كما أن استخدام السايكلوفوسفاتاميد مع الكورتيزون ضروري جدًا عند حدوث مضاعفات النزيف الرئوي المصاحبة لمرض هينوخ شونلاين، لا سيما إذا صاحب هذا المرض اتهام بيفاعل الكلى.