J Anesth (2008) 22:460–463
DOI 10.1007/s00540-008-0656-9

Journal of
Anesthesia

An adult patient with Kabuki syndrome presenting with Henoch-Schönlein purpura complicated with pulmonary hemorrhage

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Abstract
We present a case of a 33-year-old woman with Kabuki syndrome (KS) presenting with Henoch-Schönlein purpura (HSP). She was admitted to our hospital with a brain abscess in the lateral ventricle and meningitis. She had been diagnosed with KS. Skin eruptions had appeared on her lower extremities, with arthralgia, cough, and hemoptysis. She suddenly developed pulmonary hemorrhage and respiratory failure. We intubated her trachea and started mechanical ventilation in the intensive care unit (ICU). Skin biopsy revealed leukocytoclastic vasculitis with granular depositions of immunoglobulin A (IgA) in dermal vessel walls, and she was diagnosed as having HSP. Supportive management and prednisolone at 20 mg·day^{-1} cured the pulmonary hemorrhage and respiratory failure. On ICU day 27, she was weaned from mechanical ventilation. Pulmonary hemorrhage as a complication of HSP is rare and sometimes fatal. KS is often associated with an increased incidence of infection and congenital heart disease. Susceptibility to infection and pulmonary hypertension due to congenital heart disease in this patient may have led to the development of the pulmonary hemorrhage. Supportive care and steroid therapy appeared to be beneficial in the treatment of this patient with HSP with pulmonary hemorrhage.

Key words Kabuki syndrome · Henoch-Schönlein purpura · Pulmonary hemorrhage

Introduction

Henoch-Schönlein purpura (HSP) is an immune-mediated vasculitis associated with immunoglobulin A (IgA) deposition [1,2]. Although the underlying cause of HSP remains unknown, a variety of infectious diseases and/or drugs have been proposed to trigger HSP [1–4]. It is typically characterized by a purpuric rash on the lower extremities, arthralgia, abdominal pain, and renal involvement [1,2], while pulmonary hemorrhage is rare [5–10].

We treated a 33-year-old woman with Kabuki syndrome (KS) who had a pulmonary hemorrhage due to HSP. KS is characterized by multiple malformations with unusual facial features, skeletal anomalies, congenital heart disease, postnatal growth deficiency, and mental retardation [11–13]. The incidence of several types of infection is high in KS because of the autoimmune dysfunction found in this condition [11]. To our knowledge, this is the first case of a patient with KS who developed HSP; however, we are not sure about the relationship between HSP and KS.

Case report

A 33-year-old woman was admitted to our hospital because of a brain abscess in the left lateral ventricle and meningitis. Abscess drainage and the administration of antimicrobial agents for 3 months cured the abscess and meningitis. She showed multiple malformations, with characteristic facies (i.e., long palpebral fissures with eversion of the lower lateral eyelids, arched eyebrows with lateral sparseness, depressed nasal tip, lower lip pitting, and prominent and cupped ears), of KS. Fingertip pads, atrial septal defect (ASD), and mental retardation were also observed. She had been diagnosed with KS. During her stay in our hospital, she complained of right ankle-joint pain, cough, hemoptysis, and a purpuric rash on her lower extremities.

Ten days after the onset of right ankle-joint pain, she suffered from respiratory distress and Hypoxemia, and was transferred to the intensive care unit (ICU). On admission to the ICU, her blood pressure was 152/93 mmHg; heart rate, 140/min; respiratory rate, 40·min^{-1}; pulse oximetry saturation (Sp_{O_2}), 88%; and body temperature, 38°C. Blood gas analysis showed pH, 7.42; Pa_{O_2}, 60 mmHg; Pa_{CO_2}, 26 mmHg; and base excess,

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Received: April 23, 2008 / Accepted: June 9, 2008

–6.0 mmol·l^{-1} under 15 l·min^{-1} supplemental oxygen via a face mask. Her trachea was intubated and mechanical ventilation was started. Physical examination showed skin eruptions on her lower extremities (Fig. 1), axilla, and buttocks. Bloody secretions were aspirated through an endotracheal tube (ETT). Chest X-ray exhibited bilateral pulmonary infiltrates, and chest computed tomography (CT) scan revealed a consolidated, patch-like appearance and air bronchograms in both lungs (Fig. 2). Laboratory studies disclosed white blood cell (WBC), 10 200 · mm^{-3}; hemoglobin 15.5 g·dl^{-1}; platelets 16.4×10^4/mm^{-3}; prothrombin time international normalized ratio (PT-INR), 1.37; partial thromboplastin time (APTT), 28.8 s; fibrin degradation products, 16 µg·ml^{-1}; blood urea nitrogen, 16 mg·dl^{-1}; creatinine, 0.63 mg·dl^{-1}; and C-reactive protein (CRP), 16.5 mg·dl^{-1}.

The time courses of antibiotic and steroid therapy, CRP, and respiratory parameters when the patient was in the ICU are shown in Fig. 3. Anti-DNA antibody, antineutrophil cytoplasmic antibodies (ANCA), and myeloperoxidase-specific ANCA were negative. Echocardiography revealed 24-mm ASD leading to left-to-right shunt and pulmonary hypertension (estimated pulmonary artery systolic pressure, 39 mmHg), and normal systolic cardiac function (ejection fraction, 61%). On ICU day 7, a skin biopsy specimen obtained from her left lower leg revealed leukocytoclastic vasculitis in the small vessels throughout the dermis, with IgA deposition (Fig. 4), and She was diagnosed with HSP. The skin lesion and hemoptysis resolved spontaneously. On ICU day 10, her skin lesion reappeared, and WBC and CRP were increased, to 21 900 · mm^{-3} and 22.4 mg·dl^{-1}, respectively. Sputum grew methicillin-resistant *Staphylococcus aureus* (MRSA) on culture and she was treated with teicoplanin. On ICU day 17, she developed hemoptysis, resulting in deoxygenation. The Pa_{O_2}/fraction of inspired oxgen ($F_{I_{O_2}}$) ratio was 140 mmHg at positive end-expiratory pressure (PEEP) 12 cmH_2O. She coughed out blood via the ETT over the next 3 days. Hemoglobin was decreased from 9.8 to 7.6 g·dl^{-1}. PT-INR, APTT, and platelet count were within normal limits. She was treated with prednisolone 20 mg·day^{-1}, and the pulmonary hemorrhage and lung infiltrates gradually disappeared. On ICU day 27, the $Pa_{O_2}/F_{I_{O_2}}$ ratio had improved to 260 mmHg and she was successfully weaned from mechanical ventilation. She was discharged from the ICU on ICU day 34. Prednisolone was tapered and continued at 5 mg·day^{-1}. About 2 months later, she was discharged from our hospital.

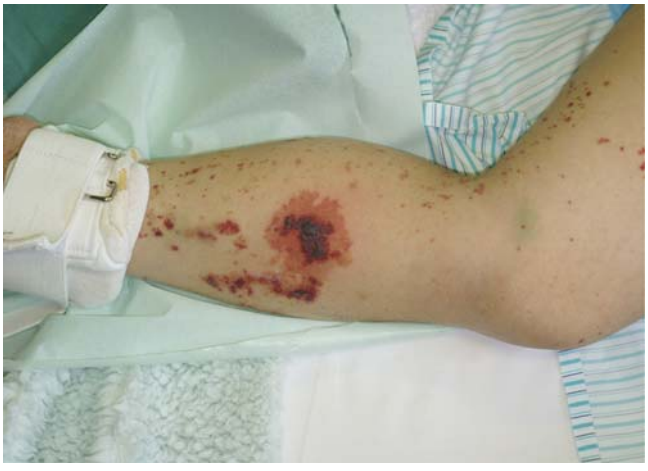

Fig. 1. Palpable purpura with hemorrhagic vesicles on lower extremities

Discussion

We have presented an adult patient with KS, with HSP complicated with pulmonary hemorrhage. Although rare pulmonary hemorrhage can be a fatal complications of this disease in HSP.

HSP is the most common form of systemic vasculitis in children, and more than 90% of patients with HSP are younger than 10 years old [1,2]. It is an immune-mediated vasculitis associated with IgA deposition [1,2]. Although the underlying causes of HSP remain unclear, a recent history of upper respiratory infection and the

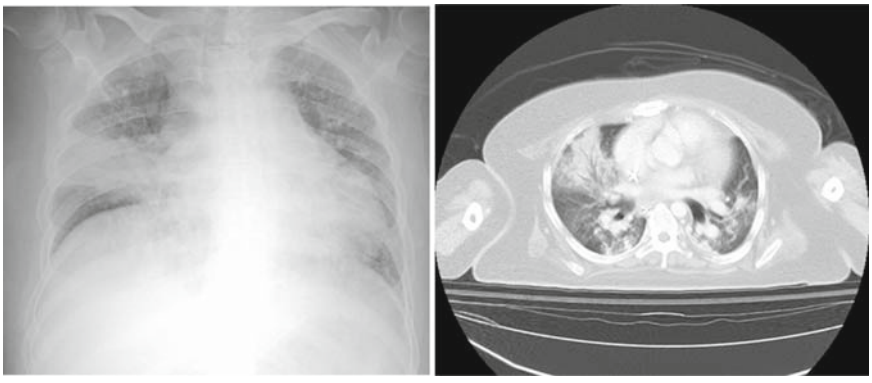

Fig. 2. Chest radiograph and chest computed tomography, done on admission to the intensive care unit (ICU). Chest radiograph shows bilateral alveolar infiltrates. Chest computed tomography shows consolidated, patch-like appearance in both lungs

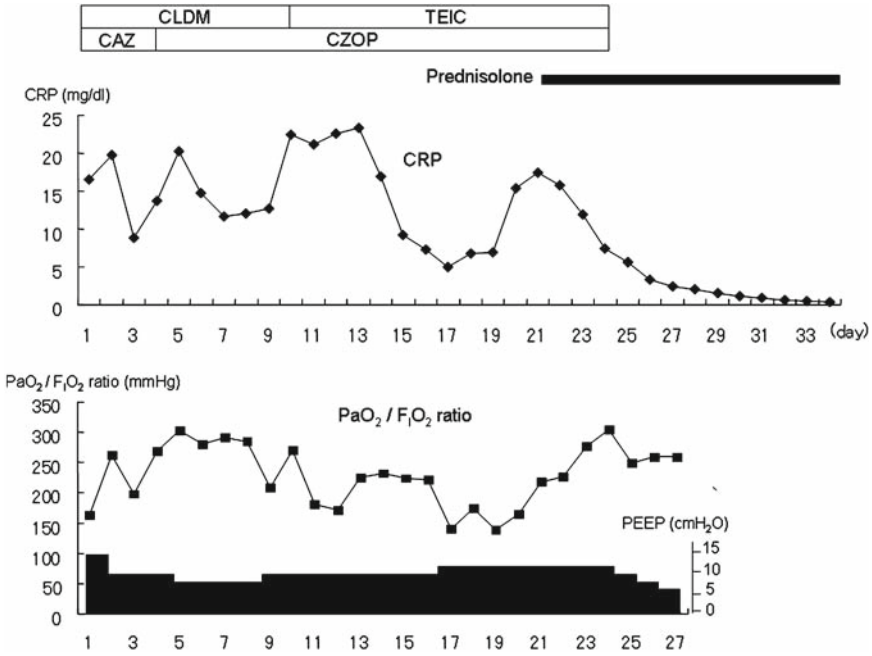

Fig. 3. Time courses of antibiotics and steroid therapy (*top*), C-reactive protein (*CRP*; *middle*) and respiratory parameters (*bottom*) in the ICU. After steroid therapy, CRP started to decrease and Pa_{O_2}/fraction of inspired oxygen ($F_{I_{O_2}}$) ratio gradually improved. *CLDM*, Clindamycin; *TEIC*, teicoplanin; *CAZ*, ceftazidime; *CZOP*, cefozopran; *PEEP*, positive end-expiratory pressure

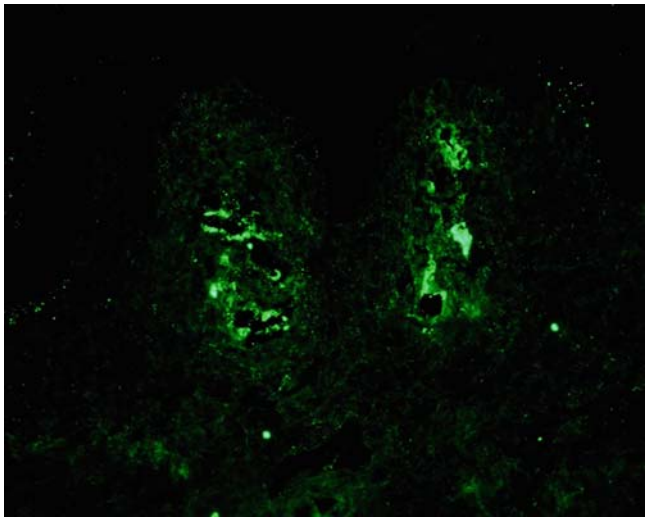

Fig. 4. Direct immunofluorescence microscopy shows immunoglobulin A (IgA) throughout the dermis. Immunofluorescent examination shows perivascular deposits of IgA (×100)

introduction of new medications have been implicated as possible triggers for HSP [3,4]. *Streptococcal* or *Staphylococcal* superantigens, and allergic reactions to drugs, may be responsible for the autoimmune phenomenon in HSP [3,4]. In our patient, brain abscess and *MRSA* pneumonia were prolonged, and antimicrobial agents were administered for 3 months. These factors may have induced HSP in our patient.

Pulmonary hemorrhage is a rare complication of HSP. It has been reported primarily in adults and adolescents and is associated with significant morbidity and mortality [5–10]. Of 29 HSP patients with pulmonary hemorrhage, 48% were over 18 years old [5–10]. The mortality of HSP with pulmonary hemorrhage was 50% in adults and 20% in pediatric patients [5–10]. The principal cause of pulmonary hemorrhage in HSP is vasculitis in the small pulmonary blood vessels. Pulmonary hemorrhage developed in our patient, but without severe renal dysfunction. In general, the causes of pulmonary hemorrhage include the use of drugs such as anticoagulants or thrombolytic agents, pulmonary infectious diseases, pulmonary hypertension, and systemic vascular diseases [14]. Our patient had no history of such drug use. She suffered from *MRSA* pneumonia and, at the same time, pulmonary hypertension due to ASD. These underlying diseases may have been risk factors for pulmonary hemorrhage.

The treatment of pulmonary involvement in HSP includes corticosteroids, cyclophosphamide, and azathioprine [5–10]. Our patient was treated with prednisolone 20 mg·day^{-1}. At the beginning, we hesitated to use corticosteroid because of the pneumonia. Fortunately, the pulmonary hemorrhage resolved spontaneously; however, it recurred once. Prednisolone was effective in controlling the pulmonary hemorrhage in our patient.

KS, which is associated with abnormalities in multiple organ systems shows unusual facial features, abnormal dermatoglyphics, skeletal anomalies, congenital heart disease, postnatal growth deficiency, and mental retardation [11–13]. The incidence of several types of infection is high in KS because of autoimmune dysfunction [11]. Congenital heart diseases, such as ASD and

ventricular septal defects, are common malformations associated with KS [12,13]. Although we are not sure whether HSP and KS have any common pathogenic features, it is possible that autoimmune disorders and pulmonary hypertension due to ASD may have been involved in the pathogenesis of pulmonary hemorrhage in our patient.

In conclusion, we presented a case of HSP complicated with pulmonary hemorrhage in a patient with KS. Steroid was beneficial in the treatment of the pulmonary hemorrhage.

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