

Acute massive pulmonary hemorrhage after craniotomy in a patient with systemic lupus erythematosus

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Acute massive pulmonary hemorrhage (AMPH) is a rare life-threatening complication of systemic lupus erythematosus (SLE). We report a lupus nephritis patient with active disease, in whom AMPH developed after craniotomy for brain injury. Computed tomography scan of the brain revealed a subdural hemorrhage and intracranial hemorrhage with a midline shift, indicating increased intracranial pressure (IICP). Neurogenic pulmonary edema (NPE) was suspected 5 days after operation due to dyspnea and chest radiograph findings of bilateral infiltrations. Seven days after the craniotomy, she had bloody sputum, a sudden drop in blood hemoglobin level (from 12.3 g/dL to 8.8 g/dL), and diffuse alveolar infiltrates in both lung fields. All of these features were characteristic manifestations of AMPH. Complete blood count disclosed mild thrombocytopenia (88,000/mm³). We believe that in an SLE patient, IICP or NPE might be risk factors in the development of AMPH.

Key words: Central nervous system diseases, intracranial pressure, pulmonary edema, systemic lupus erythematosus

Acute massive pulmonary hemorrhage (AMPH) is a rare and severe complication in systemic lupus erythematosus (SLE), and has a high mortality rate. The clinical manifestations of AMPH include sudden onset of dyspnea, shortness of breath, hemoptysis, a sudden drop in serum hemoglobin level, and increased infiltrates in both lung fields [1]. This pulmonary complication usually progresses very quickly [1,2]. The mechanism for the development of AMPH in SLE is yet to be elucidated, but a multifactorial theory is favored [1,2]. The contributory factors include the SLE disease, thrombocytopenia, vasculitis, congestive heart failure, and infection [3]. Increased intracranial pressure (IICP) has been considered as one of the possible precipitating factors in the development of AMPH. Neurogenic pulmonary edema (NPE) is a common manifestation after head injury and usually develops hours to days after head insults [4]. The mechanism for NPE development may be related to a sympathetic catecholamine discharge [4,5]. NPE can increase pulmonary artery pressure and

induce pulmonary microvascular vasoconstriction [4]. If an SLE patient has pulmonary artery wall damage, the raised pulmonary artery pressure caused by NPE might be a risk factor for pulmonary hemorrhage. Our patient had sudden onset of shortness of breath 5 days after craniotomy and NPE was suspected by chest image initially. The computed tomography (CT) scan of the brain revealed a midline shift indicating IICP. We believe that IICP or NPE might have played a role in the development of AMPH in this case.

Case Report

SLE was diagnosed in a 50-year-old woman in 1992 due to arthritis, proteinuria, positive antinuclear antibody (1:640, diffuse type), and a high level of anti-ds DNA (301 IU/mL; normal, <50 IU/mL). Impaired renal function with a serum creatinine level of 1.7 mg/dL and heavy proteinuria of 4.46 g/24 h were noted in October 1999. Renal biopsy disclosed diffuse proliferative glomerulonephritis with active changes in the subendothelial tissue and mesangial deposition of electron-dense materials and extensive proliferation of endocapillaries. Pulse methylprednisolone treatment (1 g for 3 days) was administered in October and

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November 1999, and cyclophosphamide (300 mg) was given 3 times per week during this period. She fell to the ground and lost consciousness on December 3, 1999. An emergency brain computed tomography scan disclosed a subdural hemorrhage in the right frontal-temporal area, and intracranial hemorrhage in the right temporal lobe, with a midline shift to the left side, indicating IICP. After craniotomy and removal of the hematoma, medical treatment with glycerol (300 mg every 8 h intravenously) and dexamethasone (5 mg every 8 h intravenously) were instituted and she quickly regained consciousness.

On day 5 after the craniotomy, she had sudden onset of cough and shortness of breath. Physical examination revealed basal rales in both lower lung fields. Arterial blood gas showed hypoxemia and oxygen saturation dropped to 88%. Diuretics were prescribed due to suspected acute pulmonary edema but had little effect. The dyspnea worsened very quickly and she received endotracheal intubation the next day. On day 7 after the craniotomy, bloody sputum was suctioned out from the endotracheal tube. Emergency chest X-ray disclosed diffuse alveolar infiltrates in both lung fields (Fig. 1). Complete blood count showed a white blood cell count of 10,300/mm³, mild thrombocytopenia (88000/mm³), and a sudden drop in hemoglobin from 12.3 g/dL to 8.8 g/dL (Fig. 2). Activated partial thromboplastin

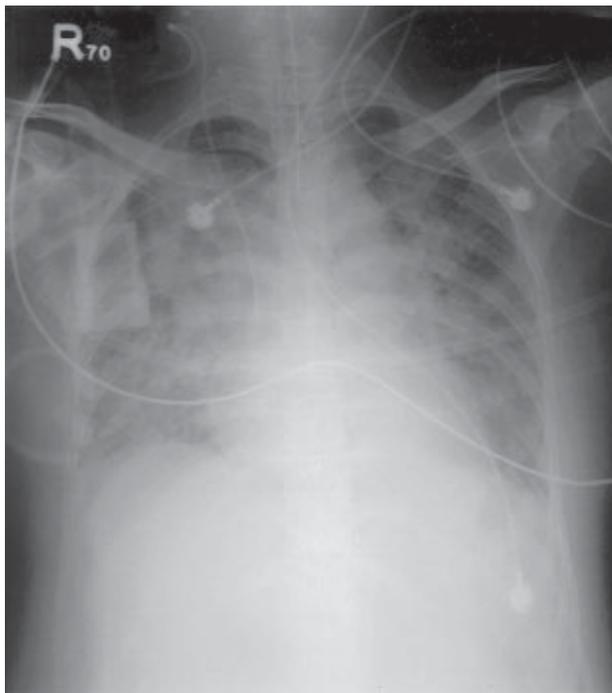


Fig. 1. Chest X-ray 7 days after craniotomy shows bilateral diffuse pulmonary infiltrates in an alveolar pattern.

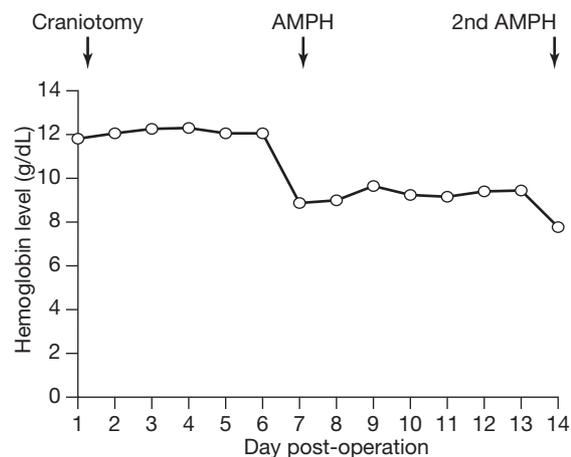


Fig. 2. Serial follow-up of blood hemoglobin level post-craniotomy shows a sudden drop of hemoglobin at the development of acute massive pulmonary hemorrhage (AMPH) on day 7 and day 14.

time and prothrombin time were within normal limits, Coombs' test was negative and the reticulocyte count was 0.8%. There was no evidence of active bleeding from the gastrointestinal, genitourinary or nasal area. Laboratory data also revealed an anti-ds DNA of 17 IU/mL, C3 of 40 mg/dL, C4 of 17 mg/dL, blood urea nitrogen of 33 mg/dL, creatinine of 1.7 mg/dL, erythrocyte sedimentation rate of 52 mm/h and C-reactive protein of 2.0 mg/dL. Results were negative for D-dimer test (<1.0 µg/mL), and sputum smear and culture for bacteria. Blood and urine culture were also negative for bacteria growth. Under the impression of AMPH, she was treated with dexamethasone (10 mg every 6 h intravenously) and an immediate platelet transfusion. Antibiotic treatment with first-generation cephalosporin was prescribed for prophylaxis, although she did not have a fever.

Her pulmonary condition did not improve after the above treatment. Unfortunately, another episode of bloody sputum developed and the hemoglobin dropped further to 7.7 g/dL on day 14 after operation. Due to suspicion of a recurrence of AMPH, aggressive treatment with cyclophosphamide at a dose of 300 mg was given, and plasmapheresis was begun on day 15 after the craniotomy. Her condition did not improve even after intensive therapy. Pulmonary hemorrhage with secondary infection was suspected due to the persistent pulmonary infiltrates. Her sputum culture finally grew *Pseudomonas aeruginosa* and the urine culture grew *Candida albicans*. She died of sepsis and pneumonia in February 2000.

Discussion

AMPH is a potentially catastrophic, and fatal complication of SLE, with reported mortality rates from 23 to 92% [1,2,6]. Prompt diagnosis and treatment are essential to survival. Symptoms of hemoptysis, dyspnea, hypoxemia, a decrease in hemoglobin of 1.5 g/dL to 4 g/dL in a 24- to 48-h period without other sources of bleeding, and the appearance of alveolar or interstitial infiltrates should direct the clinician to the diagnosis [1,2]. Bronchoscopy demonstrating bleeding, and bronchoalveolar lavage showing hemosiderin-laden macrophages, are helpful in establishing the diagnosis [7-10]. Our patient had all of these features, thus meeting the criteria for the diagnosis of AMPH. She had shortness of breath and bloody sputum, and hemoglobin dropped from 12.3 g/dL to 8.8 g/dL in 48 h. Chest radiography revealed increased infiltrates bilaterally, but she did not undergo bronchoscopy. There are many possible causes for the development of AMPH in SLE, including the disease itself, infection, thrombocytopenia, coagulopathy, congestive heart failure, and renal failure [3]. Anticardiolipin antibody might contribute to the development of pulmonary hemorrhage in some cases [9]. Whether IICP can cause development of AMPH remains unclear, but IICP has been reported to cause pulmonary abnormality in SLE patients [11].

NPE can occur after virtually any form of central nervous system (CNS) insult, including head trauma, seizures, stroke, various types of intracranial hemorrhage, and infection [4]. Many pathophysiologic mechanisms have been proposed for the development of NPE, but the exact mechanisms remain unknown [4-6,12]. One of the most probable mechanisms seems to be a CNS insult followed by a massive sympathetic discharge, or "catecholamine storm" [4,5]. Catecholamine release has been shown to cause systemic arterial hypertension, peripheral vasoconstriction, increased pulmonary artery pressure, and pulmonary microvascular vasoconstriction. The rapid development of an intense, generalized, but transient vasoconstriction is thought to lead to a shift in the blood from high-resistance systemic circulation to low-resistance pulmonary circulation, and pulmonary edema is then formed [4,5]. There are 2 distinct types of NPE: an early form that develops within minutes to hours after the CNS insult, and a delayed form that may take days to develop [4,5,12,13]. Our patient had pulmonary symptoms on day 5 after the craniotomy, and chest radiogram showed a pulmonary

edema-like appearance characteristic of the delayed type of NPE. NPE may raise pulmonary artery pressure. If a patient has pulmonary artery wall damage or vasculitis due to SLE itself, or severe thrombocytopenia, then pulmonary hemorrhage could develop. Although NPE might have induced pulmonary hemorrhage in our patient, some studies have reported that active nephritis was a major risk factor for pulmonary hemorrhage in SLE patients [1,2]. In our patient, possible major contributory factors for the development of AMPH included active SLE disease activity (high serum anti-dsDNA and active lupus nephritis), thrombocytopenia, NPE, and IICP. All of these factors can interact with each other and precipitate the sudden development of AMPH.

Aggressive immunosuppressive drug treatment with high doses of corticosteroids (1-2 mg/kg/day) or pulse methylprednisolone therapy is the mainstay therapy for AMPH [2,3,9,10]. In severe cases, additional therapy with cyclophosphamide (2 mg/kg/day) and plasmapheresis may rescue patients from this catastrophic complication [2,10]. Since prolonged immunosuppressive drug treatment will lead to a higher rate of opportunistic infection, the risk of morbidity and mortality due to secondary infection after aggressive immunosuppressive therapy should be considered.

In conclusion, NPE can occur after any form of CNS insult. Whether it is a risk factor for AMPH remains unclear. IICP as a cause of AMPH has been rarely reported in SLE [11]. NPE or IICP can interact with many factors, such as the SLE disease itself, thrombocytopenia, or heart failure, to contribute to the development of the life-threatening complications of AMPH. In an SLE patient with active disease who develops dyspnea, hemoptysis, a sudden drop in the blood hemoglobin level without gastrointestinal bleeding, or increased infiltrates in both lung fields after head injury, AMPH caused by NPE or IICP should be highly suspected.

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