Massive Pulmonary Hemorrhage in a Patient with Systemic Lupus Erythematosus

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Abstract: Pulmonary hemorrhage is a rare and often fatal manifestation of systemic lupus erythematosus (SLE) and enters the differential diagnosis of diffuse lung disease in patients with SLE. We have recently seen massive pulmonary hemorrhage in a 24 year old SLE patient with diffuse proliferative lupus nephritis. Pulmonary hemorrhage was diagnosed by the clinical triad of hemoptysis, anemia, infiltration on chest X-ray and by elevated carbon monoxide diffusing capacity (DLCO/VA).

Key words: SLE, Pulmonary hemorrhage, DLCO/VA

INTRODUCTION

Pulmonary disease is one of the major complication of systemic lupus erythematosus (SLE) and occurs in as many as 50%-70% of patients during the course of their illness (Alarcon-Segovia et al. 1961; Estes et al. 1971). These include infection, pleurisy, interstitial fibrosis, diaphragmatic myopathy with consequent atelectasis, pulmonary edema and acute pneumonitis with or without pulmonary hemorrhage (Hunninghake 1979). However, massive pulmonary hemorrhage is a seldom appreciated aspect of the disease (Mintz et al. 1976).

We report one case to alert physicians to this rare but fatal complication of SLE.

CASE REPORT

First admission

She was well until September 1987, when she was admitted to the hospital because of catatonic posture. Because she showed psychosis, persistent proteinuria, high anti-DNA antibody titer and positive fluorescent antinuclear antibody, she was diagnosed as SLE based on the revised diagnostic criteria for SLE by the American Rheumatism Association. Serum creatinine was 1.2 mg/dl, and 24 hour urine protein was 778 mg. The kidney biopsy showed diffuse increase of mesangial matrix associated with mesangial hypercellularity in light microscopy and abundant subendothelial, mesangial deposits in electron microscopy, so it was classified as diffuse proliferative lupus nephritis (Fig. 1, Fig. 2). Treatment with prednisolone 50 mg per day was begun and tapered to 17.5 mg per day with improvement for one year.

Second admission

One month prior to the second admission on October 17th 1988, she had easy fatigability, alopecia, decreased urine amount with 15 kg weight gain in spite of prednisolone therapy 60 mg/day for 4 weeks. On admission, the chest
Fig. 1. Photomicrograph of the glomerulus. Diffuse increase of mesangial matrix associated with mesangial hypercellularity is demonstrated. Rather severe mesangial sclerosis is noted in portions. Peripheral capillary lumens are well opened with minor change of the wall. (H & E)

Fig. 2. Electron microscopic picture of the glomeruli, showing abundant subendothelial and mesangial deposits with areas of subepithelial deposits. Patchy effacement of foot process is seen.
roentgenogram was normal. The hemoglobin was 7.7 g/dl, hematocrit 23.6%, the leukocyte count 7,000/mm³ and platelet 170,000/mm³. The coagulation profile was normal. The serum creatinine was 3.6 mg/dl, 24 hour urine protein was 2.76 g. The creatinine was 3.6 mg/dl, 24 hour urine protein was 2.76 g. The fluorescent antinuclear antibody (FANA) was positive with homogeneous type. Serum complement levels were total gross hematuria with dysuria. In the morning of October 29th, she had fever, hemoptysis and dyspnea, and she was readmitted. On admission, the patient appeared to be acutely ill and dyspnea. Her temperature was 39°C, respirations 28/min, heart rate 108/min, and blood pressure was 170/100 mmHg. Chest examination revealed bilateral rales especially or; blood 3+, RBC 2-51HPF. The patient was treated with ultrafiltration once and 10 mg nitrogen mustard twice (October 26th, 22nd). She was discharged with improvement on October 26th, 1988.

Third admission

In the evening of October 26th, she voided total gross hematuria with dysuria. In the morning of October 29th, she had fever, hemoptysis and dyspnea, and she was readmitted. On admission, the patient appeared to be acutely ill and was dyspneic. Her temperature was 39°C, respirations 28/min, heart rate 108/min, and blood pressure was 170/100 mmHg. Chest examination revealed bilateral rales especially or; blood 3+, RBC 2-51HPF. The patient was treated with ultrafiltration once and 10 mg nitrogen mustard twice (October 26th, 22nd). She was discharged with improvement on October 26th, 1988.

DISCUSSION

One of the salient clinical manifestations of this patient was the sudden development of diffuse pulmonary infiltrates, so the differential diagnoses in this patient were infection, congestive heart failure, uremia, drug reaction and lupus pneumonitis with or without pulmonary hemorrhage (Eagen et al. 1979; Churg et al. 1980) and often these factors may coexist. The common clinical features of pulmonary hemorrhage are hemoptysis, shortness of breath, cough, rales, severe hypoxemia usually accompanied by fever. In this patient, all of these features had been observed but begun with total gross hematuria and dysuria. It is possible that the cause of total hematuria may be the hemorrhagic complication of hyperheparinemia during nitrogen mustard treatment (Gilman et al. 1985). But that is less likely because of its delayed time onset. It is also possible that it was caused by the urinary bladder involvement of SLE. Alarcon-Segovia et al. (1984) reported that histologic changes of the urinary bladder were found in 16 of 35 necropsies from SLE patients. These included hemorrhage, interstitial cystitis, congestion, and vasculitis. And patients with histologic changes of the bladder were found to have more frequent pulmonary hemorrhage than those without. When this patient visited the hos-
pital on October 29th, pulmonary hemorrhage was suspected due to abrupt hemoptysis, decreased hematocrit, abnormal chest roentgenogram and severe hypoxemia. To rule out other diagnostic possibilities except pulmonary hemorrhage, we tested the carbon monoxide uptake expressed as DLOC/VA. DLOC/VA is a useful technique for detecting acute pulmonary hemorrhage (Ewan et al. 1976; Bowely et al. 1979; Rees 1984). Recent alveolar hemorrhage provides an extravascular pool of viable erythrocytes such that the amount of CO uptake is greater than predicted (Bowely et al. 1979). Rees (1984) has found the DLOC/VA to be more sensitive than the chest roentgenogram in detecting fresh alveolar hemorrhage. Ewan et al. (1976) examined serial changes in DLOC/VA in Goodpasture's disease and proposed that a 30% increase over the baseline value is highly suggestive of acute alveolar hemorrhage but a single value which is markedly elevated also seems to have diagnostic merit. As in this patient who had SLE and uremia, DLOC/VA is usually lower than the predicted value. In uncomplicated uremia, the mean baseline value is on the average 30 to 40% less than predicted (Lee and Streeton 1975) and average value of DLOC/VA of SLE patient was 66% of the predicted value (Holgate et al. 1976). This is readily explained by histological fibrinoid change, necrosis and hyaline degeneration of interstitial tissues, alveolar walls and endothelial lining of the capillaries, all of which are frequently observed in the lungs of SLE patients (Koldes et al. 1946; Huang et al. 1965). In this patient, the DLOC/VA of November 1st was 129.1% which was markedly ele-
Fig. 4. Serial chest radiographs of the patient.
A. Initial chest radiograph showed ill-defined patchy air-space densities in right upper and both para-hilar area (arrows). Cardiomegaly is seen.
B. Chest radiograph taken 12 hours after (A) showed diffuse bilateral air-space consolidation, especially in right side.
C. Chest radiograph taken 2 days after (B), following methylprednisolone pulse therapy, showed improved air-space consolidation especially in right lower and left upper lung fields.
D. Chest radiograph taken 1 day after (C), showed aggravated air-space consolidation in both upper lung fields as compared with (C).
E. Chest radiograph taken 10 hours after (D), 7 hours before death, showed extensive air-space consolidation occupying the entire lungs.
vitated in spite of azotemia (BUN 131 mg/dl, creatinine 4.5 mg/dl) and SLE. After three day's methylprednisolone pulse therapy, the first pulmonary hemorrhage began to decrease. Hemoptysis decreased, the hematocrit and pO2 level were stable and a chest roentgenogram showed improvement on November 1st (Fig. 3, Fig. 4-C). When evidence of the second pulmonary hemorrhage such as increased hemoptysis, decreased hematocrit, hypoxemia and aggravated chest roentgenogram (Fig. 3, Fig. 4-D) appeared in the morning of November 2nd, the DLCO/VA increased further to 138.6% from 129.1% of November 1st.

The sequence of events responsible for massive pulmonary hemorrhage in SLE is not well defined. However its pathogenesis may be related to immune complex deposition, especially Ig G (Foldes 1946; Gould et al 1975; Churg et al 1980). These deposits were usually present in the alveolar septa, capillary loops and adjacent interstitium in the wall of small blood vessels and bronchioles in a granular pattern (Eagen et al. 1978; Myers et al. 1986). Electron dense deposits were observed at the alveolar capillary basement membrane by electron microscopy (Elliott et al 1970; Kuhn 1972; Gould and Soriano 1975; Katz et al. 1983).

Factors other than immune complex deposition may also play in precipitating diffuse alveolar damage and pulmonary hemorrhage. Twenty three cases of pulmonary hemorrhage in SLE have been reported in English written literature (Eagen et al. 1978; Carette et al. 1984; Leatherman et al. 1984). And factors which might precipitate pulmonary hemorrhage (e.g., infection, coagulopathy, uremia, volume overload and thrombocytopenia) were present in these cases. In this patient, although urine culture and blood culture were negative, it can not be ruled out that this patient had infection. And she had coagulopathy and uremia, so the pulmonary hemorrhage in this patient can be due to any or combination of these factors such as coagulopathy, uremia, thrombocytopenia, infection.

The prognosis of pulmonary hemorrhage of SLE patient is grave, and successful treatment is rarely feasible, even if treatment is initiated early. It is therefore important to suspect pulmonary hemorrhage even in the absence of hemoptysis in severely ill patients with bilateral pulmonary infiltrates and a sudden drop in hematocrit. We recommend that as soon as a presumptive diagnosis of pulmonary hemorrhage is reached, corticosteroid therapy should be started promptly and/or raised to high doses in pulse form with the simultaneous addition of cytotoxic agents.

REFERENCES
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전신성 홍반성 낭창 환자에서 관찰된 광범위한 폐출혈 1예

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전신성 홍반성 낭창 환자에서의 폐출혈은 매우 드물고 치명적이며 임상상으로 이런 질환의 환자에서 흉부 X-선 사진상 전반적인 패 القضية가 나타날 때 반드시 감별 진단해야 할 임상상의 하나이다. 저자들은 최근 전신성 홍반성 낭창으로 치료받고 있던 24세의 여성환자에서, 폐출혈 의 3예 발생의 소견이 펼쳐진 후, 흉부 X-선 사진상 패출혈 양상과, 증가한 DLCO/VA로 진단된 폐출혈이, 매우 심하게 진행되면서 사망한 증례를 관찰하였기에 보고하는 바이다.