Pulmonary alveolar hemorrhage in systemic lupus erythematosus

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Abstract Pulmonary alveolar hemorrhage (PAH) is a rare complication of systemic lupus erythematosus (SLE), with mortality rates exceeding 70% (1-4). We describe the occurrence of pulmonary alveolar hemorrhage in a patient with active SLE and successful outcome with prompt diagnosis and aggressive therapy.

Keywords: SLE; pulmonary alveolar hemorrhage; case report.

A 27 year old Filipino lady was diagnosed with SLE in the USA two months prior to her presentation at our hospital. She was placed on corticosteroids, but unfortunately discontinued them. She gave a history of malar rash, alopecia, pleuritic chest pain, history of leukopenia, thrombocytopenia and arthralgias.

Physical examination revealed a young, sick looking lady who was confused and delirious.

Temperature 38.2 °C; pulse 110/minute, and BP 120/90. Skin showed purpuric areas, petechiae, ecchymosis and nail fold vasculitic lesions.

Examination of the heart and abdomen was unremarkable. Chest revealed bilateral rales diffusely. Musculoskeletal examination revealed bilateral swelling and tenderness of hands, wrists, elbows, knees and ankles.

Shortly thereafter she had a sudden onset of cough, hemoptysis and dyspnea.

Laboratory tests revealed the following: Initial hemoglobin of 8.9 grams/dL, which dropped within 24 hours to 6.8 grams/dL; WBC 18,900/mm³ platelets 37,000; westergren sedimentation rate 127 mm/hour. Arterial blood gases revealed severe hypoxemia pH 7.38, PO2 47.8 mmHg, PCO2 36.6 mmHg, HC03 21.8 mmol/L.

Normal EKG and echocardiogram.

Slightly elevated prothrombin time with normal activated partial thromboplastin time.

Total protein 51 grams/L (64-82 grams/L); albumin 17 grams/L (34-50 grams/L); C30.16 grams/L (0.83-1.77 grams/L), C4 <0.08 grams/L (0.15-0.45 grams/L), CH50 <21 U/ml (>70 CH100 U/ml).

BUN 9.3 mmol/L, creatinine 59 Ummol/L (44-133 Ummol/L). LDH 1161 U/L (100-230 U/L).

Twenty-four hour urine protein was 1.62 grams/d (0.0-0.14 grams/d).

Urinalysis revealed besides proteinuria, 10-15 granular casts, 2-4 hyaline casts.

ANA titer 1:320 (<40), speckled pattern, anti DNA and rheumatoid factor were negative, anti SM titer 1:200 (<1:50). Normal anti SS-A, anti SS-B and antinuclear antibodies, ANCA and antibodies to glomerular basal membrane were negative.

Initial CXR showed extensive mixed alveolar and interstitial infiltrates. On the next day the abnormality was more interstitial favoring the strong probability of pulmonary hemorrhage (Fig.1a).

Patient course In view of the patient’s grave condition she was admitted to ICU, intubated and was placed on ventilatory support. She was covered with broad spectrum antibiotics after obtaining appropriate cultures.

She was started on methylprednisolone pulse therapy of one gram IV/day x 3 days followed by oral prednisolone of 60-120 milligrams daily in divided doses. She also received cyclophosphamide pulse therapy one gram/M2 IV, plasmapheresis daily x 5 days, then every other day for one week.

Patient responded well to the above modalities.

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Received April 1995. Accepted for publication in final form August 1995.

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with progressive resolution of the lung infiltrates and improved oxygenation. She was extubated, and ambulated with remarkable recovery in three weeks.

Her CXR 3 weeks after initiation of treatment revealed some utterly discreet interstitial infiltrates as residuals in the right lower lobe (Fig.1b).

Two months later her chemistry normalized. C3 0.97 grams/L, C4 0.29 grams/L. Urinalysis was negative for protein, cells and casts. Hemoglobin 15.6 grams/dL, WBC 11,200/mm³, platelets 232,000, westergren sedimentation rate 27 mm/hour.

Prednisolone was tapered down over the following four months to 7.5 milligrams/d and she was also maintained on plaquenil (Hydroxychloroquin sulfate).

She remained in remission and was doing remarkably well at 18 months follow-up.

Discussion Pulmonary alveolar hemorrhage (PAH), often occurs in active disease and in association with other features of SLE. In some patients it is the initial manifestation of SLE.
Symptoms of hemoptysis, dyspnea, hypoxemia, decrease in hemoglobin of 1.5 to 4 grams/dL in a 24-48 hour period, and appearance of alveolar or interstitial infiltrates as occurred with our patient direct the clinician to the diagnosis, especially in the setting of active SLE. The differential diagnosis of massive pulmonary hemorrhage is long. Good Pasture's syndrome, idiopathic pulmonary hemosiderosis, Wegner's granulomatosis and SLE are rare causes of PAH. Although pulmonary bleeding may occur in the setting of uremia, congestive heart failure, infection, pulmonary infarction and coagulopathy, Bronchoscopy demonstrating bleeding and bronchoalveolar lavage showing hemosiderin-laden macrophages is helpful in establishing the diagnosis. Open lung biopsies in some cases show a distinctive small vessel vasculitis. The lesion is characterized by acute inflammation and necrosis involving capillaries, arterioles, and small muscular arteries and termed microangiitis to reflect the small size of the affected vessels.

A proposed mechanism in PAH is an immune-mediated disruption of small blood vessels and alveolar septae. Some authors have detected granular-immune deposits and complement within alveolar septa and blood vessel walls by electron microscopy and immunofluorescence as well as microangiitis under light microscopy while others however, have not detected any immunoglobulin, complement deposits, or evidence of vasculitis.

Moreover, patients with SLE and pulmonary abnormalities other than hemorrhage may show these immune deposits as well.

Other well known pleuro-pulmonary manifestations of SLE include lupus pneumonitis, lymphocytic interstitial pneumonia, pulmonary embolism associated with lupus anticoagulant, pulmonary hypertension, lupus pleuritis and weakness of the diaphragm.

The clinical presentation of our patient is similar to those in previously described anecdotal reports and case series. Evidence of hemoptysis, dyspnea, hypoxemia and alveolar or interstitial infiltrates as well as a decrease in hemoglobin of 2.1 grams/dL in a 24 hour period.

Based on the clinical presentation, laboratory findings and patient's course, we believe that pulmonary vasculitis was the underlying mechanism of pulmonary alveolar hemorrhage in our patient.

It is essential to recognize and exclude concomitant illnesses that can also cause PAH such as infection, uremia, coagulopathy, congestive heart failure, and pulmonary infarction which may also complicate the picture.

Several authors have recommended the use of high-dose corticosteroids and cytotoxic agents as well as plasmapheresis as soon as the diagnosis of hemorrhage is established.

Our patient clearly had very active SLE and PAH, was diagnosed promptly and treated aggressively with successful outcome.

References

نزيف الحويصلات الرئوية في مرضى الذبحة الإحمرارية العام

ملخص:
نزيف الحويصلات الرئوية هو مضاعفة نادرة الحدوث لمرض الذبحة الإحمرارية العام مع معدلات الوفاة التي تزيد عن 27% (مرجع رقم 1-4)، وننح نصف حدوث نزيف الحويصلات الرئوية في مريضة بداء الذبحة الإحمرارية العام والنشط مع النجاح في العلاج بالتشخيص السريع والعلاج المكثف.