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Original article

Pulmonary hemorrhage in patients with systemic lupus erythematosus. Clinical manifestations and prognosis☆

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ABSTRACT

Background and objective: Pulmonary hemorrhage (PH) in systemic lupus erythematosus (SLE) is a rare but potentially fatal complication that occurs most frequently in the context of active lupus with involvement of other organs. The objective of this study is to report the clinical features and prognosis of patients with SLE who had PH.
Methods: Patients with SLE (1982 American College of Rheumatology criteria) and PH under monitoring between June 1999 and November 2011 were studied. Demographic, clinical, laboratory, treatment and prognosis data related to PH were analyzed.
Results: Eleven patients with SLE developed 14 episodes of PH. PH was the first manifestation of SLE in 2 patients. The most frequent symptoms and clinical signs were dyspnea, fever and cough, which occurred in 12 (85%), 11 (77%) and 7 (50%) patients, respectively. Hemoptysis was also observed in 5 (35%) episodes, tachycardia in 2 (14%), pallor in one (7%) and chest pain in one (7%). All patients had other concomitant organ involvement, and were treated with glucocorticoids. In addition, intravenous cyclophosphamide was indicated in 12 episodes and plasma exchange in 4. Overall mortality was 64%. Factors associated with mortality were infection, mechanical ventilation and dialysis.
Conclusions: PH continues to be a rare and severe complication of SLE. Its suspected presence forces us to quickly study these patients, since early diagnosis and aggressive treatment have been shown to improve survival in them.

Hemorragia pulmonar en pacientes con lupus eritematoso sistémico. Características clínicas y pronóstico

Palabras clave:
Lupus eritematoso sistémico
Hemorragia pulmonar
Manifestaciones clínicas
Pronóstico

RESUMEN

Fundamento y objetivo: La hemorragia pulmonar (HP) en el lupus eritematoso sistémico (LES) es una complicación rara pero potencialmente mortal, que se presenta con mayor frecuencia en el contexto de un lupus activo con afectación de otros órganos. El objetivo de este estudio es comunicar las características clínicas y el pronóstico de pacientes con diagnóstico de LES que presentaron HP.
Pacientes y método: Se incluyeron pacientes con diagnóstico de LES (criterios del *American College of Rheumatology* de 1982) y HP, en seguimiento entre junio de 1999 y noviembre de 2011. Se analizaron datos demográficos, clínicos, de laboratorio, tratamiento y pronóstico relacionado con la HP.
Resultados: Once pacientes con LES desarrollaron 14 episodios de HP. La HP fue la primera manifestación del LES en 2 pacientes. Los síntomas y signos clínicos más frecuentes fueron disnea, fiebre y tos, que se presentaron en 12 (85%), 11 (77%) y 7 (50%) pacientes, respectivamente. También se observó hemoptisis en 5 (35%) episodios, taquicardia en 2 (14%), palidez en uno (7%) y dolor torácico en otro (7%). Todos los pacientes presentaron otro compromiso orgánico concomitante, y todos fueron, asimismo, tratados con glucocorticoides. Además, en 12 episodios se indicó ciclofosfamida intravenosa, y en 4, recambio plasmático. La mortalidad general fue del 64%. Los factores que se asociaron a mayor mortalidad fueron infección, ventilación mecánica y diálisis.

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Conclusiones: La HP continúa siendo una complicación rara y grave del LES. La sospecha de su presencia nos obliga al rápido estudio del enfermo para realizar un diagnóstico y tratamiento intensivo, que han demostrado mejorar la supervivencia en estos pacientes.

Introduction

Pulmonary hemorrhage syndrome (PH) is a rare and life-threatening complication in systemic lupus erythematosus (SLE). Its presence is usually accompanied by other organs involved and is clinically characterized by the presence of dyspnea; hemoptysis; diffuse and bilateral alveolar infiltrates on chest X-ray and decreased hemoglobin (Hb).[1–4] It involves 2–5% of patients with SLE and can also be the initial manifestation of the disease.[5]

Due to the high mortality and the lack of signs and symptoms presented by the patient (particularly at the beginning of the disease), high suspicion for diagnosis is required, particularly in patients where PH is the SLE presentation.

In this paper we describe the clinical features and prognosis of 11 patients with SLE who presented PH, and we have reviewed the literature of the main cases series published to date.

Patients and methodology

Patients with a diagnosis of SLE (criteria of the American College of Rheumatology [ACR] 1982) and PH were included, followed up by the Rheumatology Department of J. M. Cullen Hospital, in the city of Santa Fe from June 1999 to November 2011.

To define PH, patients had to meet at least 4 of the criteria proposed by Barile et al.[5] and/or present hemosiderin/erythrocyte-laden macrophages (>20%) in the bronchoalveolar lavage (BAL) performed by fiberoptic bronchoscopy.

Barile et al.[5] criteria are as follows:

- Hb drops by at least 2 g/dl or anemia (Hb < 12 g/dl) related to the PH episode.
- Rapid onset respiratory failure.
- Hemoptysis.
- Dense pulmonary infiltrates in at least three quarters of the lung fields.
- Hypoxemia.

Demographic data, clinical symptoms, previous organ involvement and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) were analyzed at the time of PH, laboratory, cultures, X-ray and/or CT scan, treatment and prognosis associated with PH. Diagnostic delay was defined as the time in days from the first PH-associated sign/symptom recorded in the medical history until BAL diagnosis confirmation or criteria compliance.

We excluded patients with confirmed diagnosis of pulmonary edema, pulmonary embolism, congestive heart failure, uremia unrelated to renal failure secondary to collagen disorders, coagulopathies other than the antiphospholipid syndrome or drug-related PH.

The study design was a retrospective review of medical histories of patients with longitudinal follow-up.

Results

Eleven of the 192 SLE patients developed 14 PH episodes (3 were recurrent). Therefore, the PH accounted for 5.7% of our SLE patient population.

They were 10 females and one male, with a mean (SD) age at the time of bleeding of 29 (11) years and a median time to disease progression of 67 months (range 1–228).

PH was the first SLE manifestation in 2 patients, one of whom presented a pulmonary-renal syndrome. In the remaining patients PH occurred during the SLE evolution in a median time of 46 months (range 12–227). The average delay time at the time of diagnosis was 5 days (range 1–15).

The most frequent symptoms and clinical signs in the 14 PH episodes were dyspnea, fever and cough, which occurred in 12 (85%), 11 (77%) and 7 (50%) cases, respectively. Hemoptysis was also reported in 5 (35%) episodes, tachycardia in two (14%), paleness in one (7%) and chest pain in one (7%).

All patients, except one, had other concomitant organ involvement and received some SLE treatment (Table 1).

In the laboratory, patients had all their episodes with anemia or decreased Hb (mean 2.9 g/l; range 2–4); hypoxemia was reported in 11, and in 4 of the 14 episodes there was thrombocytopenia, but none was severe (<50,000 platelets/mm^3). At the time of PH, antinuclear antibodies were determined in 11/14 episodes (6 positive), anti-DNA antibodies in 7/14 (3 positive), anticardiolipin antibodies in 8/14 (2 positive IgG, 1 positive IgM) and AL in 7/14 episodes (all negative).

SLE disease activity, measured by SLEDAI at the time of PH, had a mean (SD) of 17,[10] with renal involvement, predominantly. In chest X-rays, 12 of the 14 episodes showed 1 diffuse alveolar infiltrate, and 2 had lobar infiltrate; one patient reported diffuse infiltrate and concomitant pleural effusion. In 7 of the 14 episodes these radiological findings were also reported on CT scan.

Only 5 patients met 4 of the 5 criteria proposed by Barile et al. to define PH. PH diagnosis was confirmed in the 14 episodes by fiberoptic bronchoscopy with BAL, finding hemosiderin and/or erythrocyte-laden macrophages in cytology (40% average [range 30–85]). At the same time, BAL samples were processed for germ culture. Bacterial infection was verified in 5 of 14 (36%) episodes simultaneously with PH, and in 2 patients as a complication during hospitalization. The isolated microorganisms were pneumococci in 3 cases and staphylococci in 2, while nosocomial bacteria were *Pseudomonas* in one case and *Acinetobacter* in the other.

All patients were treated with glucocorticoids: in 12/14 episodes with methylprednisolone in pulses, and then orally in decreasing rate, and 2 patients received oral glucocorticoids. Furthermore, in 12 episodes the indication was intravenous cyclophosphamide, and in 4, filtration plasmapheresis (range 5–10 sessions) (Table 2). Infected patients received specific antibiotic treatment.

All patients were admitted to the Intensive Care Unit; 5 of them required mechanical ventilation, and 3 hemodialysis. APACHE scoring was obtained in 9 episodes, being 14 the average value (range 9–22).

Overall mortality was 64% (7/11 patients). The cause of death was sepsis in 2 patients and PH in 5. Factors associated with higher mortality were infection, mechanical ventilation and dialysis. Two of the surviving patients discontinued follow-up a year after PH, one patient died from pneumonia at 2 years and the last one is on follow-up currently.