

Pulmonary Hemorrhage in a Patient initially presenting with Discoid Lupus

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As a cutaneous variant of lupus erythematosus, discoid lupus erythematosus (DLE) is thought to have a good prognosis; however, the involvement of internal organs with a transition to systemic disease may occur. The progression from DLE to systemic lupus erythematosus has been reported in up to 28% of patients. This progression to systemic disease has been associated with a benign course. Herein, we report the case of a 31-year-old woman with a 10-year history of discoid lupus, now presenting with dyspnea and pleuritic chest pain of 1 month's duration. A significant drop in hemoglobin and hematocrit levels was observed in association with leukopenia, lymphopenia, a positive ANA, and hypocomplementemia. Chest radiography and computed tomography revealed bilateral infiltrates. An open lung biopsy confirmed the presence of intra-alveolar hemorrhage. Based on the results of the tests and analyses detailed herein, a diagnosis of pulmonary hemorrhage secondary to systemic lupus erythematosus was made. To our knowledge, pulmonary hemorrhage as the initial manifestation of the systemic involvement of discoid lupus has not been reported before. [*PR Health Sci J* 2013;4:203-205]

Key words: Systemic lupus erythematosus, Discoid lupus, Pulmonary hemorrhage

Discoid lupus erythematosus (DLE) is characterized by well-defined, scaly, patchy lesions (primarily on the head, neck, and other areas that are exposed to the sun) of variable sizes that tend to heal with atrophy, scarring, and pigmentary skin changes. Although limited to the skin, these changes can lead to disfigurement and significant social impairment (1). DLE patients usually have an isolated cutaneous disease, without systemic involvement. However, up to 28% of these patients subsequently develop systemic lupus erythematosus (SLE) (2,3). Leukopenia, lymphopenia, thrombocytopenia, and/or positive antinuclear antibodies (ANA) have been identified as risk factors for the development of systemic disease (4-6).

Pulmonary involvement in DLE is uncommon. Conversely, over 50% of patients with SLE may have pulmonary manifestations, including, but not limited to, pleuritis, interstitial lung disease, pulmonary embolism, infections, and pulmonary hemorrhage (7). Pulmonary hemorrhage occurs more commonly in patients with active disease and 1 or more extrapulmonary manifestations, the most common being serious renal involvement (7-9). We report the case of a 31-year-old woman with long-term DLE who progressed to severe SLE with pulmonary hemorrhage.

Case report

A 31-year-old Hispanic woman with biopsy-proven DLE of 10-year duration presented with dyspnea and pleuritic chest pain that had been continuous for 1 month. Her DLE was manifested in the form of erythematous, scaly papules and plaques occurring on sun-exposed areas. Her disease was well controlled with photo-protective measures and topical corticosteroids. She

was admitted because of progressively worsening dyspnea and pleuritic-type chest pain. She had no fever, chills, productive cough, or hemoptysis. One month before, she was treated with intravenous azithromycin and ceftriaxone for an acute pneumonic process, which treatment resulted in a partial improvement of her symptoms.

On physical examination the patient had discoid lesions on her right malar and nasal regions. The lesions were erythematous with hyperpigmented margins and flattened and scarred central areas. There were no mucosal lesions, scarring alopecia, alopecia areata, skin thickening, digital pitting scars, palpable purpura, or Raynaud's phenomenon. A pulmonary examination revealed increased tactile fremitus, dullness to percussion, and decreased breath sounds at the right pulmonary base. The rest of the physical examination was unremarkable. The patient's laboratory evaluation revealed leukopenia ($2,600/\text{mm}^3$) and lymphopenia ($676/\text{mm}^3$). By the eighth day of hospitalization, her hemoglobin level had decreased from 12.8 g/dl to 10.2 g/dl, associated with a hematocrit drop to 29.5%, without any obvious evidence of bleeding. With those exceptions, her complete blood count and coagulation profile were within normal limits. The corrected erythrocyte sedimentation rate (ESR) was 48mm/hr. She had a positive ANA at 1:160 with a homogenous pattern. Further serologic tests, including anti-

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dsDNA, anti-RNP, anti-histone, anti-Jo-1, and anti-Scl-70 antibodies, were negative. Complement analysis revealed a low level of C3, 77mg/dl (normal being 90-180mg/dl), while the C4 complement level was normal. No abnormalities in the renal function parameters were noted, and the urinalysis did not reveal proteinuria, hematuria, or urinary sediments. Extensive laboratory evaluations, including blood and sputum cultures, mycoplasma antibodies, and a Mantoux tuberculin skin test, were all negative.

Chest radiography revealed bilateral interstitial infiltrates. Computed tomography of the chest confirmed the presence of bilateral pulmonary infiltrates and consolidations with air bronchograms (Figure 1). Because of the diagnosis of bronchopneumonia, broad spectrum intravenous antibiotic therapy (moxifloxacin and ceftriaxone) was promptly initiated. There was no favorable response over the next several days, as a result of which a bronchoalveolar lavage was performed. Microscopic analysis of the lavage sampling showed macrophages and many acute inflammatory cells but no malignant cells. Special stains for *Mycobacteria*, fungi, and *Pneumocystis jiroveci* were negative.



Figure 1. High-resolution computed tomography of the chest showing a right lower lobe pulmonary infiltrate and consolidations with air bronchograms. There are smaller left lower lobe pulmonary infiltrates and consolidations present, as well. There is no evidence of pleural effusion.

A lung biopsy through video-assisted thoracoscopic surgery was performed in view of persistent respiratory symptoms. The biopsy revealed intra-alveolar hemorrhages (Figure 2). No evidence of bronchopneumonia, interstitial pneumonitis, pleural involvement, or vasculitis was reported. A diagnosis of pulmonary hemorrhage secondary to SLE was made, as the patient fulfilled American College of Rheumatology (ACR) criteria for the classification of SLE (10). She was treated with 60 mg/day (1mg/kg/day) of oral prednisone, resulting in a marked and rapid clinical improvement without the need of cytotoxic agents or plasmapheresis. She recovered over the course of 1 month under low-dose prednisone (40mg/day) and hydroxychloroquine (400mg/day) therapy. The

prednisone dose was progressively tapered, and no other clinical manifestation of SLE or exacerbation has since occurred.

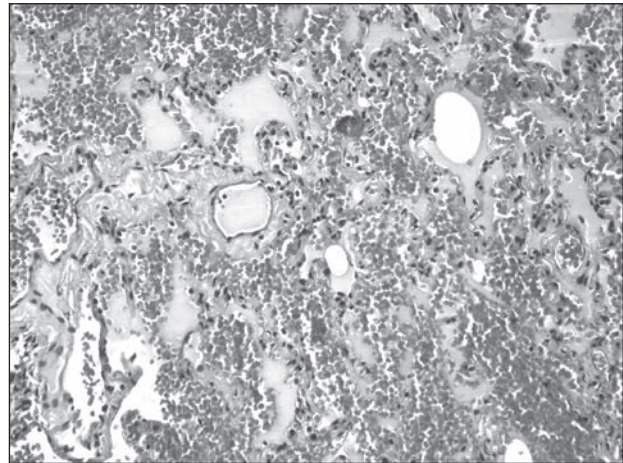


Figure 2. Lung tissue stained with hematoxylin and eosin reveals intra-alveolar hemorrhages and edema. The alveolar septa are unremarkable. Focal alveolar macrophages can be seen in the alveolar septa.

Discussion

We report the case of a young woman with a 10-year history of DLE (limited to the face), who developed a life-threatening lupus complication, namely, a pulmonary hemorrhage. Although unusual, DLE can progress to SLE in up to 28% of cases (3). Studies have shown that progression to SLE sometimes occurs within 5 years of having acquired DLE (2-4). However, the time frame for this complication can be up to 34 years (3). Pulmonary involvement as part of this evolution has been reported, but to our knowledge has never been associated with pulmonary hemorrhage.

Patients with DLE confined to the head and neck usually present with few laboratory abnormalities (2). The extent of skin involvement in DLE is a criterion for prognosis, since such involvement has been associated with a higher risk for systemic complications (3). Some authors have linked widespread cutaneous involvement with systemic complications such as nephropathy and hemolytic anemia (11,12). Furthermore, several laboratory findings have been linked to an increased risk of progression to SLE (4,5). Our patient had leukopenia, lymphopenia, elevated ESR, and positive ANA with high titers; however, her skin involvement was limited to the face. Although discoid lupus usually has a good prognosis, studies have shown that its patients are still at risk for systemic complications (11-13). Recently in a large multiethnic study analyzing SLE patients with DLE, the presence of discoid lupus was linked to more damage accrual and serious clinical features, such as seizures and vasculitis (14). However, pulmonary complications were reported to have occurred infrequently in this study.

A pulmonary hemorrhage is a catastrophic complication of SLE characterized by the presence of new infiltrates on a chest radiograph and an acute decrease in hemoglobin levels without any other bleeding source. Pulmonary hemorrhage as the initial presentation of SLE is very rare. The cases reported thus far have occurred mainly in patients who evince severe renal involvement as the most common extra-pulmonary manifestation (15, 16). However, our patient developed a pulmonary hemorrhage in the absence of renal involvement.

Interestingly, despite the grim ramifications of developing such a hemorrhage, our patient responded well to oral corticosteroids alone. She did not require aggressive therapy with another immunosuppressive agent and/or plasmapheresis, either or both of which are the mainstay treatments for pulmonary hemorrhage. This clinical course is in agreement with the fact that discoid lupus has been previously identified to have a protective role for severe renal disease (17).

Given the potentially fatal outcome of an unrecognized pulmonary hemorrhage, physicians should remain mindful of the possibility of this complication in patients with DLE. Therefore, patients with DLE should be monitored for signs of systemic involvement, even in the absence of overt symptoms. Early treatment with anti-malarial agents should be considered for patients with DLE. Besides controlling cutaneous disease, hydroxychloroquine retards the development of systemic involvement. (18).

In conclusion, DLE patients who present with leukopenia, lymphopenia, or a positive ANA should be monitored closely as they may be at risk for developing further systemic involvement, which involvement could include pulmonary hemorrhage, a serious complication.

Resumen

El lupus eritematoso discoide, como una variante cutánea, es considerado de buen pronóstico; sin embargo el involucramiento de órganos internos, progresando a enfermedad sistémica, puede ocurrir. Progresión a lupus eritematoso sistémico se ha reportado en hasta un 28% de los casos. Esta progresión a enfermedad sistémica se ha vinculado a un curso benigno. Presentamos el caso de una mujer de 31 años con lupus eritematoso discoide por diez años que presenta con disnea y dolor pleurítico, de un mes de evolución. Además se observaron, una disminución significativa en los niveles de hemoglobina y hematocrito, al igual que leucopenia, linfopenia, niveles bajos de complementos, y anticuerpos antinucleares. La radiografía y la tomografía computarizada del tórax demostraron infiltrados bilaterales. Una biopsia abierta de pulmón confirmó la presencia de hemorragia intra-alveolar y se hizo el diagnóstico de hemorragia alveolar secundaria a lupus eritematoso sistémico. Hasta nuestro

conocimiento, hemorragia pulmonar como presentación inicial de involucramiento sistémico en pacientes con lupus eritematoso discoide no ha sido reportado previamente.

References

1. James WD, Berger TG, Elston DM. Connective Tissue Diseases. In: Andrews' Diseases of the Skin: Clinical Dermatology. 10Th ed. Philadelphia, PA: WB Saunders; 2005:156.
2. Tebbe B, Mansmann U, Wolina U, et al. Markers in cutaneous lupus erythematosus indicating systemic involvement. A multicenter study on 296 patients. *Acta Derm Venereol* 1997;77:305-8.
3. Chong BF, Song J, Olsen NJ. Determining risk factors for developing systemic lupus erythematosus in patients with discoid lupus erythematosus. *Br J Dermatol* 2012;166:29-35.
4. Beck JS, Rowell NR. Discoid lupus erythematosus. A study of the clinical features and biochemical and serological abnormalities in 120 patients with observations on the relationship of this disease to systemic lupus erythematosus. *Q J Med* 1996;35:119-36.
5. Wallace DJ, Pistiner M, Nessim S, Metzger AL, Klinenberg JR. Cutaneous lupus erythematosus without systemic lupus erythematosus: clinical and laboratory features. *Semin Arthritis Rheum* 1992;21:221-6.
6. Trucker LB, Menon S, Schaller JG, Isenberg DA. Adult and childhood-onset systemic lupus erythematosus: a comparison of onset, clinical features, serology, and outcome. *Br J Rheumatol* 1995;34:866-72.
7. Eagen JW, Memoli VA, Roberts JL, Matthew GR, Schwartz MM, Lewis EJ. Pulmonary hemorrhage in systemic lupus erythematosus. *Medicine (Baltimore)* 1978;57:545-60.
8. Müller NL, Miller RR. Diffuse pulmonary hemorrhage. *Radiol Clin North Am* 1991;29:965-71.
9. Travis WD, Colby TV, Lombard C, Carpenter HA. A clinicopathologic study of 34 cases of diffuse pulmonary hemorrhage with lung biopsy confirmation. *Am J Surg Pathol* 1990;14:1112-25.
10. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982;25:1271-7.
11. Callen JP. Chronic cutaneous lupus erythematosus. Clinical, laboratory, therapeutic and prognostic examination of 62 patients. *Arch Dermatol* 1982;118:412-6.
12. Healy E, Kieran E, Rogers S. Cutaneous lupus erythematosus--a study of clinical and laboratory prognostic factors in 65 patients. *Ir J Med Sci* 1995;164:113-5.
13. Gilliam JN, Prystowsky SD. Conversion of discoid lupus erythematosus to mixed connective tissue disease. *J Rheumatol* 1977;4:165-9.
14. Santiago-Casas Y, Vilá LM, McGwin G Jr, et al. Association of discoid lupus erythematosus with clinical manifestations and damage accrual in a multiethnic Lupus cohort. *Arthritis Care Res (Hoboken)* 2012;64:704-12.
15. Santos-Ocampo AS, Mandell BF. Systemic lupus erythematosus-associated alveolar hemorrhage: presentation, treatment, and outcome. *J Clin Rheumatol* 2000; 6:350-5.
16. Sengul E, Eyiletlen T, Ozcan A, Yilmaz MI, Yenicesu M. Diffuse alveolar hemorrhage as an unusual presentation of systemic lupus erythematosus. *Rheumatol Int* 2011;31:1085-7.
17. Merola JF, Chang CA, Sanchez MR, Prystowsky SD. Is chronic cutaneous discoid lupus protective against severe renal disease in patients with systemic lupus erythematosus? *J Drugs Dermatol* 2011;10:1413-20.
18. James JA, Kim-Howard XR, Bruner BF, et al. Hydroxychloroquine sulfate treatment is associated with later onset of systemic lupus erythematosus. *Lupus* 2007;16:401-9.