Male systemic lupus erythematosus, an overlooked diagnosis

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Abstract

Lupus erythematosus is a chronic autoimmune inflammatory disease of unknown cause that involves multiple systems. Autoimmune diseases that are prevalent in men usually manifest themselves clinically before the age of 50 years old and are characterized by an acute inflammation, whereas autoimmune diseases with predominance among women appear clinically in later stages of life, when chronic diseases, fibrosis and increased number of autoantibodies are present. Lupus erythematosus is more prevalent among women during the reproductive period, but the cause of this predilection is not fully established and little is known about the disease among men. We report a case of systemic lupus erythematosus (SLE) in a male patient whose diagnosis was delayed due to the systemic manifestations and because SLE is considered an uncommon disease in men.

Introduction

Autoimmune diseases affect approximately 8% of the population, 78% of whom are women. The reason for a high prevalence in women is unclear. Women are known to respond to infection, vaccination, and trauma with increased antibody production and more T helper (Th)2 predominant immune response, whereas a Th1 response and inflammation are usually more severe in men.[1]

Systemic lupus erythematosus (SLE) is a connective tissue disease of unknown etiology, generally considered a common occurrence in women of childbearing age and rare among men. It is estimated that out of every 10 people who have lupus only one is a man. Symptoms are equivalent in men and women, particularly skin rash, extreme fatigue and joint pain, but findings suggest that the disease in men has a more complex clinical course and some studies have shown that renal impairment, central nervous system and vascular diseases are more common in men when compared to women.[2]

Lupus erythematosus evolves with periods of activity and varying periods in which patients are asymptomatic or mildly symptomatic. The involvement of different organs or systems may occur simultaneously or sequentially.

Constitutional complaints such as adynamia, malaise, fatigue, weight loss and fever are frequently observed in the active phase of disease. Fever may be low and continuous, or high, peaked, and must be distinguished from intercurrent infection. Fatigue is a very frequent and nonspecific complaint. Weight loss is usually mild, however, in some cases it can be quite severe, leading to lupus cachexia.

Skin involvement occurs in 80% of cases throughout the disease course. Rash is frequent, but not always photosensitive. Butterfly rash or vespertilio is characterized by the acute onset of an erythematous rash located on the cheeks and dorsum. Other acute injuries are erythematous-macular, papular or maculopapular and bullous lesions, also with a preferential location to sun-exposed areas.

Arthritis in small joints of the hands, wrists and knees is usually symmetrical and intermittent. Most cases of anemia in SLE are normochromic and normocytic, and it has been attributed to the chronic aspect and the inflammatory activity of the disease. Less than 15% of the anemia cases are autoimmune hemolytic. Leukopenia and lymphopenia are listed in more than 50% of cases throughout the disease course and severe thrombocytopenia (less than 50,000 platelets/mm^3) occurs in less than 10% of cases. Renal involvement is characterized by proteinuria >0.5 g/24 h, casts and abnormal or rising serum creatinine levels, without other causes. Pleuritis and/or pericarditis are found in about 50% of the patients during the disease progression. In recent decades, three important phenomena have occurred and are little understood. Firstly, the incidence of SLE has had an apparent increase. Secondly, there has been an apparent dramatic increase in survival. Thirdly, there has been an apparent change in the manifestations of the disease.

Case Report

A 25-year-old male farmer presented with a 6-month history of swelling in the elbows, shoulders, hands, knees, metacarpophalangeal and proximal interphalangeal joints associated with lumbar pain, morning stiffness and an approximately 10 kg weight loss. Twenty days later, the patient developed a dry; sometimes yellow sputum-producing cough, evening fever and night sweats. Hospitalized, he was emaciated, had a generalized muscle wasting, as well as bilaterally reduced breath sounds, especially on the right side and crackles on the left base; spared joints. TST was non-reactive for AFB and sputum analysis was negative for fungus, normal bone marrow examination, electrocardiogram revealed a sinus tachycardia; endoscopy showed mild erosive antral gastritis without evidence of *H. Pylori*. Normal thyroid function was found. Electromyography: pattern of axonal polyneuropathy that was moderate in the sensory component and mild in the motor component. Computed tomography (CT) thorax: early lung inflammation, located in the anterior and lateral basal segments of the left lower lobe, as well as discrete fibroatelectasis-like laminar opacities in fibroatelectasis appearance, located in the posterior basal segment of the left lower lobe. Echocardiography: large-volume pericardial effusion of large volume (Figure 1). Pericardiocentesis was performed and the fluid analysis was negative for neoplastic cells and for tuberculosis, rare mesothelial cells, lymphocytes and cellular debris in a serohemorrhagic background. He was discharged after the administration of azithromicin and ceftriaxone. Two months later symptoms persisted and he was referred to our hospital. New analyses were conducted, which reavealed: Hb 8.3g%, leukocytes 4000/mm^3 (segmented 75, lymphocytes 24, monocytes 1), platelets 700,000, ESR 118 mm/^{1st} h, glucose 95 mg/dL, creatinine 0.8 mg/dL, C-reactive protein 114 IU, total protein 8.0 g% (albumin 2.6 globulin 5.4); unremarkable urinalysis; thorax radiography: left-sided pleural effusion; echocardiography: pericardial effusion with mild thickening located above the right atrium; rheumatoid factor reagent 1/2; ANF 1/640 fine dense cytoplasmatic pattern, positive anti ENA, positive anti RNP, positive anti Sm, positive anti-Ro (SSA). After the diagnosis of systemic lupus erythematosus, corticosteroids were prescribed and the

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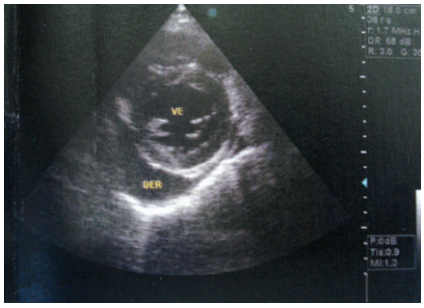

Figure 1. Echocardiography showing pericardial effusion of large volume.

patient evolved with clinical improvement and was discharged with an outpatient prescription of prednisone 20 mg/day and hydroxychloroquine 400 mg/day.

Discussion

Lupus erythematosus is a chronic inflammatory disease that affects multiple organs or systems. It has an unknown, multifactorial etiology, in which the interaction of genetic predisposition and various hormonal, environmental and infectious factors appear to lead to a loss of immunological tolerance.

The importance of sex hormones in the pathogenesis of SLE is well shown in animal models. In humans, exacerbations of SLE during pregnancy, post partum and menstrual periods due to rapid hormonal changes are well documented, as there are numerous reports associating the use of estrogen-containing oral contraceptives and disease exacerbations.[2] In contrast, it has been shown that men with lupus do not produce abnormal estrogen levels, which suggests that estrogens can not be considered an isolated determinant of lupus.[3] Stahl and Decker studied 12 men with SLE and observed that there was no evidence of hypogonadism or androgen deficiency. Men with lupus are fertile, sexually active and have normal reproductive history.[4]

Because of the predominance of women in most studies, little is known about the disease in men. Recent studies suggest that the impairment occurs in older men have higher mortality in one year than women with SLE, suggesting that even men with lupus have a more complex clinical course than women.[5]

It has become increasingly clear that men with SLE have more seizures, immune-mediated anemia (low hemoglobin level) and lupus anticoagulant level that may lead to thrombogenesis. On the other hand, men appear to be less likely to have Sjögren's syndrome and even though men appear to have more severe manifestations, these can occur in both sexes.

Miller *et al.* studied 50 male patients with lupus erythematosus and reported a lower prevalence of neurological involvement, thrombocytopenia and alopecia when compared to female patients. However, pleuritis was more common among men.[6] Our patient had pleutritis and pneumonitis likely. Hochberg *et al.* observed no significant differences in the major organ involvement in 12 male patients and 138 female patients affected with SLE, except for peripheral neuropathy, which appeared to be more common in men.[7] In our case, the patient had electromyographic changes. In a multicenter study by Cervera *et al.*, no difference in vital organ involvement was observed among men and women affected with SLE, although they observed that men had less serosistis early in the disease and more arthritis during the disease course.[8] There is no consensus on the presence of differences in the clinical manifestations between men and women with systemic lupus erythematosus. Further studies are warranted and more awareness should be given once sex differences affect the drug activity and it has been suggested that specific therapies should be developed based on gender.[9] In addition, the diagnosis of SLE should always be considered in patients with systemic involvement, which would certainly avoid delay in management and prevent irreversible damage to target organs.

References

1. Fairweather D, Frisancho-Kiss S, Rose NR. Sex differences in autoimmune disease from a pathological perspective. AMJ Pathol 2008;173:600-9.
2. Mok CC, Lau CS, Chanz TM, Wong RWS. Clinical characteristics and outcome of southern Chinese males with systemic lupus erythematosus. Lupus 1998;8:188-96.
3. Ramsey-Goldman R, Mattai SA, Schilling E, et al. Increased risk of malignancy in patients with systemic lupus erythematosus. J Investig Med 1998;46:217-22.
4. Stahl NI, Decker JL. Androgenic status of males with systemic lupus erythematosus. Arthritis Rheum 1978;21:665-8.
5. Prete PE, Majlessi A, Gilman S, Hamiden F. Systemic lúpus erythematosus in men: a restrospective analysis in a Veterans Administrations Healthcare System population. J Clin Rheum 2001;7:142-50.
6. Miller MH, Urowitz MB, Gladman DD, et al. Systemic lúpus erythematosus in males. Medicine (Baltimore) 1983;62:327-34.
7. Hochberg MC, Boyd RE, Ahearn JM, et al. Systemic lúpus erythematosus: a review of clinico-laboratory features and immunogenetic markers in 150 patients with emphasis on demographic subsets. Medicine (Baltimore) 1985;64:285-95.
8. Cervera R, Khamashta MA, Font J, et al. Systemic lupus erythematosus: clinical and immunologic patterns of disease expression in acohort of 1000 patients. Medicine (Baltimore) 1993;72:11-24.
9. Lu LJ, Wallace DJ, Ishimori ML, et al. Male systemic lupus erythematosus: a review of sex disparities in this disease. Lupus 2010;19:119-29.