DOI:10.21276/sjpm.2017.2.3.2

Saudi Journal of Pathology and Microbiology
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: http://scholarsmepub.com/

ISSN 2518-3362 (Print)
ISSN 2518-3370 (Online)

Case Report

Monoclonal gammopathy in systemic lupus: a case report

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Abstract: The occurrence of monoclonal gammopathy of undeterminate significance (MGUS) in an autoimmune disease such as systemic lupus is not common but it is not as rare as the occurrence of a malignant disease such as Multiple myeloma. The complexity of this association lies in the challenges of monitoring MGUS's patients who are likely to progress towards malignant hemopathy. Some risk factors for this progression have been described (rate of monoclonal compound, paraprotein isotype, medullary plasmacytosis or even light chains). However, none of these factors taken independently allows us to correctly categorize patients. Scores combining several of these factors have been proposed to define groups of patients with different evolving risks. The aim of this work is to report this association (systemic lupus and MGUS) in a 52 year old woman, in order to alert the clinicians about this eventuality when monitoring their lupus patients**.**

Keywords: Systemic Lupus, MGUS, Monitoring.

INTRODUCTION

Systemic lupus is the archetype of systemic autoimmune diseases. It is a disease of immunological whose precise causes remain unknown. The occurrence of this autoimmune disease results from a genetic predisposition associated with exposure to a particular environment. The presence of antinuclear autoantibodies is observed in practically all lupus patients. An anomaly of the physiological clearance of apoptotic bodies seems to be the main source of autoantigens. The interactions between these autoantigens, dendritic cells (plasmacytoides pCD and myeloid mCD), B lymphocytes and T lymphocytes lead to the production of antibodies and T lymphocytes deleterious to the organism. Thus, innate and adaptive immune systems are involved, and various amplification loops subsequently maintain the autoimmune reaction [1]. The occurrence of monoclonal gammopathy in systemic lupus is not common, hence the interest to report the observation of this 52 year old patient followed for lupus since 17 years. Monoclonal gammopathies are frequent in the general population and their frequency increases with age. Monoclonal gammopathy testifies proliferation of a plasmocyte clone producing a monoclonal immunoglobulin which may be indicative of malignant haemopathy or undetermined significance (MGUS for Monoclonal Gammopathy of Undetermined Significance), as the case here presented.

CASE REPORT

It's about a 52-year-old female patient whose pathological history is limited to a tonsillectomy in childhood. She is treated for systemic cortico-dependent lupus for 17 years. This diagnosis was retained on the association of a bundle of clinical and para-clinical arguments: a chronic acro-arthritis, hair loss, renal involvement (glomerulonephritis stage II b) and pericarditis. The whole is accompanied by dry eye syndrome and asthenia. The patient had a biological inflammatory syndrome: sedimentation rate was 85 mm/hour, normochromic normocytic anemia (hemoglobin at 9.2 g /dL, MCV at 94 fL and MCHC at 34.3 g/dL), peripheral fluorescent antinuclear antibody with anti DNA antibodies positive, rheumatoid factor at 42 IU/ml, complement was low C3 at 0.67 g/L (0.90-1.80), 24 hours protein urine at 1426 mg/L, C4 complement and renal status were normal. The corticosteroids dose was 1mg / kg / day with gradual decrease. Currently the patient is stable with 10 mg per day of prednisone as the lowest effective dose.

During this year, a gamma globulin peak was revealed by biological assays.The serum protein electrophoresis showed gamma globulins at 16.9 g/L (8-

13, 5 g/L) with M Spike. The immunofixation determinated a monoclonal immunoglobulin, IgA kappa class. The molecular weight of immunoglobulin showed an IgA at 8.44 g/L (0.63-6.45 g/L).

Clinically, the disease was quiescent and the patient hasn't bone pain. The myelogram showed plasmocyte population (7% of medullary cells) essentially made by dystrophic plasmocytes (Figure 1) in a hypocellular bone marrow. Inflammatory studies revealed normocytic normocytic anemia (HB at 11.7 g / dl, MCV at 93.4 fL and MCHM at 34.3g/dL), sedimentation rate at 87 mm in the first hour, C reactive protein at 1.84 mg/L. The renal function was good: urea at 0.32 g/L and creatinine at 6.70 mg/L and 24 hours protein urine at 235 mg/24h. Serum calcium was at 91 mg/L. Bence jones protein test was negative. Standard radiographs of the skull, thorax and long bones didn't show bone lesions.

Medullary MRI did not show any myelomatous lesions. Osteodensitometry in the lumbar spine and femoral neck revealed osteopenia at 2 sites (T score = -1 on Lumbar spine and T score = -1.3 on the femoral neck).

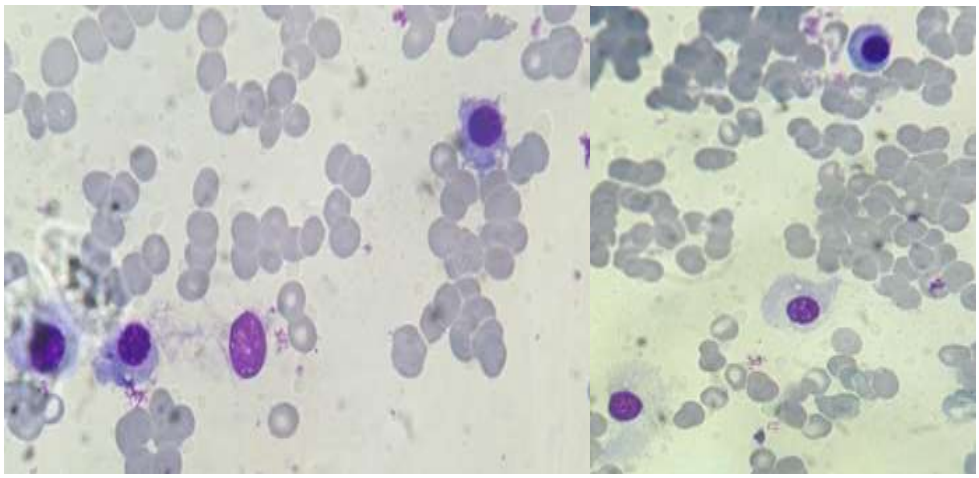

Fig-1: Bone marrow smear showing dystrophic plasmocytes

DISCUSSION

Systemic lupus is an autoimmune disease of unknown etiology that affects mainly women of reproductive age. It is characterized by hyperactivity of B lymphocytes. This activation is polyclonal and, at least in part, self-reactive [1].

Various non-neoplastic pathologies that can be associated with systemic lupus had been reported by various authors, often with connective tissue disease, with rheumatoid arthritis [2, 3]. In a study evaluating the risk of cancer in patients with Systemic lupus erythematous, it was associated to a high risk of non-Hodgkin lymphoma in comparison to general population [4].

The presence of a monoclonal protein in the peripheral blood without evidence of malignancy (multiple myeloma, macroglobulinemia ...) is in favor of a MGUS. The prevalence of monoclonal gammopathy is estimated to be 1% in patients less than 25 years, and increases to 3% in patients older than 70 years [5].

MGUS is defined by the presence of these 3 criteria, fulfilled by our patient:

- Serum monoclonal protein <30 g/L
- Medullary plasmacytes <10% and
- Absence of CRAB criteria (hypercalcemia, renal insufficiency, anemia, bone lesions) attributable to plasmacytic disorder.

A retrospective study of the Mayo Clinic of 21 079 monoclonal M spikes collected over a period of 35 years showed that monoclonal gammopathy corresponds to MGUS in 62% of cases and to myeloma in 18% of cases. Remaining 20% were: lymphoproliferative pathology (2%), Waldenstrom macroglobulin (2.5%), AL amyloidosis (2.5%), solitary plasmacytoma (2%), and other pathologies [6].

MGUS is a group of monoclonal plasmacytic pathologies with reduced malignancy, which can progress slowly towards malignant lymphoid hemopathy [7]. Approximately 25% of these patients, whith IgG or IgA gammopathies may develop myeloma (in 20 years), and those with IgM may develop malignant lymphopathy [2].

Monoclonal gammopathies occurring in lupus patients are not clearly a manifestation of disease activity, and their clinical significance is not yet clears [9]. Moreover, monoclonal gammopathy was discovered in the phase of remission of lupus in our patient. The prevalence of monoclonal gammopathy during lupus is 2.2% to 3.3% with an evolution that does not appear to be different from the general

population [10]. At the University of Toronto, reported prevalence was high by 5.4%, with predominance of IgA. This was also the case with our patient. On the other hand, it is less frequent for IgG or IgM. The association of lupus and multiple myeloma is more rarely described, and highlights the complexity of monitoring lupus patients with MGUS.

For MGUS with a low risk of progression defined by the presence of a monoclonal compound level of less than 15 g/L and an IgG isotype, patients will be monitored by protein electrophoresis every 6 months during the first year, Then every 2 to 3 years if the rate remains stable, or sooner if a symptom suggestive of scalability manifests itself [11]. Indeed, the systematic semi-annual blood follow-up of low-risk MGUS can only detect myeloma progression in 7% of cases [12].

Moreover, in the presence of a monoclonal protein level superior to 15 g/L, an IgA or IgM isotype or an abnormal kappa-lambda ratio, the risk of progression is higher. Medullary examination (with cytogenetic examinations) and x-rays of the skeleton will exclude an underlying malignant disease [11]. However, the bone radiograph is not very sensitive to detect bone invasion, unlike nuclear magnetic resonance, scanner or Pet-scan. However, the clinical significance of the asymptomatic lesions detected by this imaging mode is unclear. The realization of these examinations should be reserved for certain selected patients who present bone pain without abnormality in the standard radiological assessment [13].

Currently, there is no therapeutic means to prevent or delay the progression of an MGUS. Nevertheless, the identification of new markers should make possible the early detection ofhigh-risk individuals in the future. This will make it possible to propose therapeutic agents capable of destroying the abnormal clone, in order to prevent the appearance of irreversible organic damage [14].

CONCLUSION

Besides the unusual association of systemic lupus with monoclonal gammopathy, the interest of this work could extend to the problem of the monitoring of MGUS's patients, especially lupus ones. Regular and prolonged surveillance of MGUS is necessary not only because of the risk of progress towards malignant haemopathy which is estimated at 1% per year, but also because MGUS can be responsible for systemic manifestations that are sometimes disabling such us: AL amyloidosis, cryoglobulinemia, cutaneous manifestations and kidney damage.

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