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Letter to the Editor

Sjögren´s syndrome complicated with retroperitoneal Non-Hodgkin´s lymphoma: A case of an elderly woman during methotrexate treatment, treated with R-CHOP

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To the Editor,

Sjögren´s syndrome (SS) is an autoimmune disease characterized by a lymphocytic infiltration of the salivary and lacrimal glands, leading to a progressive destruction of these glands, and is frequently accompanied by systemic symptoms (1). Non-Hodgkin lymphoma (NHL) represents a major complication in the evolution of SS patients (2). We describe a case of retroperitoneal diffuse large B-cell lymphoma (DLBCL) occurring in a geriatric patient with an underlying SS of 8 years of evolution. A non-smoking 76-year-old female patient was diagnosed with SS in 2003 based on the American-European Consensus Group Criteria for Sjögren´s syndrome (3) (xerostomia, xerophthalmia, a positive Schirmer test (<5 mm), pathological salivary gland scintigraphy, positive antinuclear antibodies (ANA titer count 1:1280), positive rheumatoid factor (RF) 56 UI/mL (N=0-14), and positive anti-RO/SS-A and anti-La/SS-B). The patient had been under treatment with oral hydroxychloroquine and subcutaneous methotrexate for non-erosive polyarthritis since 2008. She was admitted to our hospital in May 2012 because of asthenia, intermittent fever, and 20 kg weight loss of 6 months of evolution. The physical examination demonstrated cachexia without palpable peripheral lymphadenopathy. Blood test has highlighted: erythrocyte sedimentation rate (ESR) 118 mm (N=3-12), leukocytes 3500/mm^3 (N=4000-12,900) (neutrophils 2560/mm^3), hemoglobin 10 g/dL (N=12-15), hematocrit 30% (N=37-47), hypergammaglobulinemia 23% (N=11.8-18.8), beta 2 microglobulin 7.2 mg/L (N=0.7-1.8), and circulating cryoglobulins were positive. Other tumoral markers were all negative. Serological tests of *human immunodeficiency virus, hepatitis B, hepatitis C, Epstein-Barr virus,* and *cytomegalovirus* were also negative. Computed tomography was done (Figure 1) and has shown a retroperitoneal paraaortic mass of 52x35x61 mm at the level of the left renal hilum with intratumoral central necrosis. A CT-guided needle biopsy of the retroperitoneal mass was obtained under local anesthesia. A histopathological diagnosis of DLBCL was confirmed according to the newly proposed revised European–American classification of lymphoid neoplasms (4). Methotrexate was suspended, and the patient was treated every 3 weeks for 8 cycles of R-CHOP scheme (rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone). Complete remission was achieved (no B symptoms) that was corroborated by CT 4 weeks after completion of the eighth course of R-CHOP and at the sixth month thereafter. SS is a chronic autoimmune disease that is at the crossroads of systemic autoimmunity and malignancy (2, 5). B-cell NHL represents the most serious complication in the evolution of SS patients (2, 5). The risk was estimated to be 44 times greater than that observed in a comparable normal population (6.4 cases per 1000 per year in 136 women with SS observed for an average of 8.1 years) (5). The majority of SS-associated NHL is preferentially low-grade and extranodal in salivary glands and in other mucosa-associated lymphoid tissues (MALT) (5). Moreover, high-grade transformation to DLBCL has been occasionally and uncommonly found in SS patients (5). In a systematic review by Váróczy L et al. (6) to assess the rate of associated malignant lymphomas to autoimmune diseases, of 421 NHL patients, 32 (7.6%) had an autoimmune disease (26 females, mean age 48.3 years). The most common diagnosis was Sjögren´s syndrome, with 11 cases (100% females). The evolution from benign lymphocytic infiltration characteristic of SS to malignant NHL is probably a multistep process, the underlying molecular events of which are still unknown (2, 5, 6). In searching for SS-associated NHL, several considerations have to be taken into account in our case: first, the presence of various autoantibodies, such as the RF and anti-SSA/SSB antibodies, as well as hypergammaglobulinemia and positive circulating cryoglobulins, reflects B-cell hyperactivity (5); second, causality between methotrexate and DLBCL is often difficult to prove, but it is likely that this drug might have a role in the development (6). In several studies, the combination of R-CHOP has a good safety-efficacy profile, inducing responses and long-term survival in over 90% of patients with

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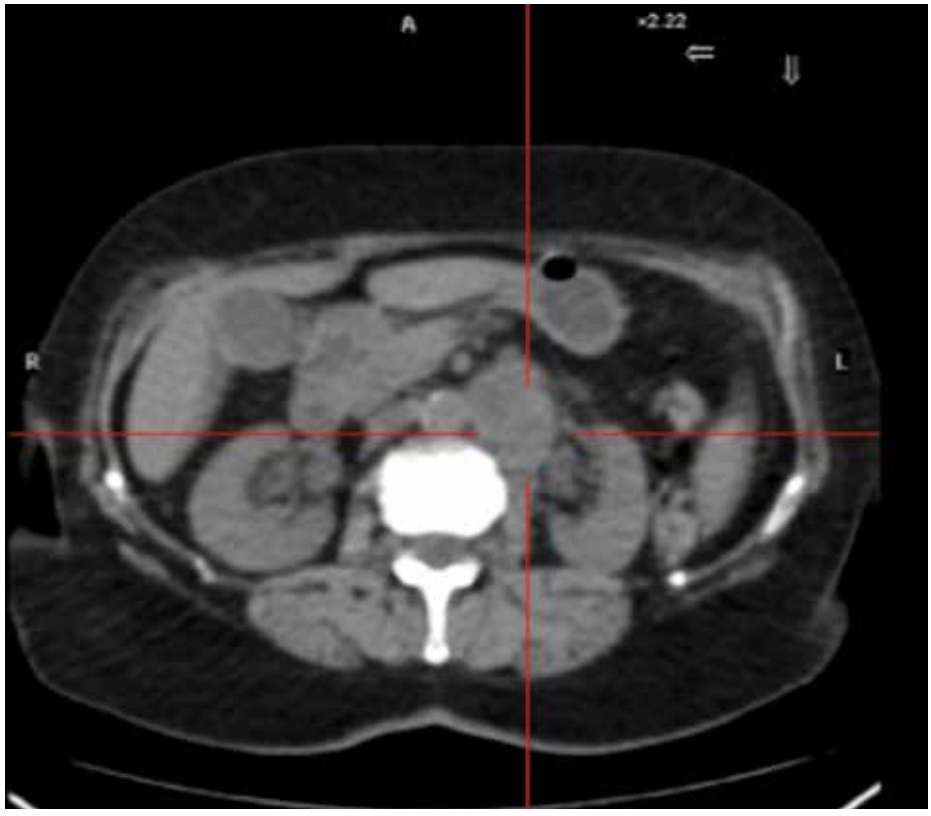

Figure 1. Computed tomography (axial) shows retroperitoneal paraaortic mass of 52x35x61 mm at the level of the left renal hilum with intratumoral central necrosis, suggestive of malignancy

aggressive SS-associated NHL compared with CHOP alone, as seen in our patient (7-9).

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