

A case of chronic lymphocytic leukemia still taking etanercept for ankylosing spondylitis

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ACTA REUMATOL PORT. 2016;41:90-91

To the Editor:

Anti-TNF agents are second line drugs in AS coming after non-steroidal antiinflammatory drugs (NSAIDs)¹. Malignancies have been discussed as major adverse events associated with anti-TNF drugs. How to behave when a hematologic malignancy is diagnosed in the course of anti-TNF treatment remains unanswered².

A 66-year-old male patient consulted us for routine control of AS. He had AS for 30 years and had been on etanercept for the last two years. On physical examination a submandibular lymphnode of about 2 cm was palpated. He had no hepatosplenomegaly. He denied any weight loss, night sweats or fever. His white blood cell count was 14400/µL with 60% lymphocytes. The peripheral blood smear showed small mature lymphocytes with dense nuclei. Flow cytometric analysis revealed B cells co-expressing CD19/CD5 as well as CD20, CD22 and CD23 antigens. B cell CLL stage 1 was diagnosed and follow-up was planned. The patient was informed about the diagnosis and possible association with biologic agents. He preferred to continue with etanercept. He is doing well on etanercept without any progression in CLL for five years.

Several case reports describe appearance of acute myeloid leukemia in patients on etanercept with no prior history of hematologic disease³ or transformation of known diseases to more aggressive forms such as leukemic transformation in follicular lymphoma⁴.

A recent study analyzed the data from 49 observational studies addressing the safety of biologic DMARDs in RA. The authors detected no excess risk of lymphoma or other cancers in general except for a slight increase in the risk of melanoma⁵.

The 2008 guideline of American College of Rheuma-

tology and the 2011 Portuguese recommendations (under review) for the use of biological therapies in patients with axial spondyloarthritis still consider that anti-TNF use is contraindicated in patients with a history of lymphoproliferative disease in the past five years^{6,7}. In contrary, guidelines issued in 2010 by EULAR, does not mention any contraindications for anti-TNF use in patients with previous hematological disease⁸.

CLL is a hematologic malignancy, which is characterized with monoclonal proliferation of B-lymphocytes. Treatment is indicated in active symptomatic disease only; with B symptoms, cytopenias or rapid progression⁹. Interestingly, etanercept had been tried in the treatment of hematologic malignancies. In a phase I/II study etanercept was added to rituximab in patients with chronic lymphocytic leukemia and small B cell lymphoma and the combination was found to provide durable remission in non-del (17p13.1) CLL patients¹⁰.

Our patient had stage 1 CLL. To our knowledge, this is the first rheumatologic patient continuing treatment with TNF inhibitors while complicated with hematologic malignancy. We observed that continuing with etanercept may be safe in case of early stage CLL.

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