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CASE REPORT

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Reliability of anti-TNF treatment in a patient with chronic lymphocytic leukemia and ankylosing spondylitis

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ABSTRACT

Anti-tumor necrosis factor alpha (anti-TNFα) agents are second-line treatment modalities for patients with ankylosing spondilitis after non-steroidal anti-inflammatory drugs, and are commonly used for different inflammatory rheumatic diseases. Development of malignancy is still one of the most feared side effects, with controversial results. In this paper, we present an ankylosing spondylitis patient with concomittant early stage chronic lymphocytic leukemia (CLL) who is currently under treatment with infliximab without progression for the past 5 years.

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Introduction

Chronic lymphocytic leukemia (CLL) is the most common lymphoproliferative disease in developed western countries, characterized by slow progressive accumulation of CD5+ B lymphocytes in peripheral blood and lymphoid organs [1]. Recent studies have shown that slowing of apoptosis rather than an increase in mitosis plays a culprit role in the pathogenesis of the disease, and that tumor necrosis factor alpha (TNFα) is a central mediator in the regulation of apoptosis [2]. TNFα has been shown to play an important role in progression of the disease by increasing the growth and life capacity of CLL cells [3].

A comprehensive literature review, including fourteen randomized, controlled, double-blind studies did not show an increased risk for malignancy development compared to a placebo arm in ankylosing spondylitis (AS) patients under anti-TNFα treatment [4]. In addition, there have been case reports in the literature with early hematological malignancy for whom anti-TNFα therapy could be used safely. Kuşkonmaz Ş et al have reported a 66 year old man diagnosed with ankylosing spondilitis and stage 1 CLL who was successfully treated with etanercept for 5 years without progression [5]. Anna Balata et al stated that they also followed a patient with psoriasis accompanied by CLL for 3 years without progression, and successfully continued treatment with etanercept and infliximab, respectively [6].

Case Presentation

A 35-year-old man diagnosed with ulcerative colitis (pancolitis) in 2003 was followed for 4 years in remission with azathiopurine, oral sulfasalazine and steroid therapy in our tertiary health care center. Ankylosing spondylitis was detected in 2012. Between 2012 and 2015, his treatment was continued with infliximab and azathiopurine. In 2016, an exact hematological evaluation was performed upon the detection of persistent absolute lymphocytosis in routine laboratory tests. Presence of absolute lymphocytosis (lymphocyte ≥ 5000/μL), peripheral smear findings (presence of mature lymphocytosis, absence of atypical blast or bone marrow precursor cells) and peripheral blood flow cytometry results (clonality of B-cell expansion, CD3, CD5, CD19, CD23 co-expression with low levels of CD20) suggested a diagnosis of chronic lymphocytic leukemia. He did not describe constitutional symptoms, and neither cytopenia nor organomegaly was detected. Possible risks were explained to the patient. He chose to continue the treatment with infliximab. For the recent five years, he was followed up in remission for ankylosing spondilitis and without progression of early stage CLL.

Discussion

Here we aim to emphasize that early stage CLL patients with concomittant inflammatory rheumatic disease can be treated with biological agents without progression or complications for a long follow-up time.

In 2016, the Assessment in SpondyloArthritis International Society (ASAS) and the European League Against Rheumatism (EULAR) recommended the use of biological therapies (first choice being anti-TNFα drugs in daily practice) for ankylosing spondylitis patients with high disease activity despite conventional treatment. In the same guideline, it was emphasized that the decision of treatment should be obtained by an agreed decision of the patient and the rheumatologist [7]. Also, randomized, controlled and observational studies revealed that use of long-term biological agents did not increase the risk of malignancy in AS patients. However, it should be kept

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in mind that the follow-up period of observational studies was short [8]. Biological treatment recommendations in ankylosing spondylitis patients with malignancy differ between the guidelines. In the 2018 axial spondyloarthropathy treatment recommendations of APLAR, attention was paid to the careful use of these drugs in the patient group with a high risk of skin cancer [9]. In the Portuguese group recommendations, a history of hematological malignancy in the last five years constitutes a contraindication for biological treatment including anti-TNFα drugs [10]. As a result, the decision of appropriate treatment should be considered on a case-by-case basis.

CLL is more common in older people, and the vast majority of patients are detected in an asymptomatic early stage [11]. In addition, due to defects in humoral and cellular immunity, susceptibility to infection may lead to infectious complications in these patients [12]. Our case was a young man in the asymptomatic phase who was diagnosed at an early stage, but despite receiving biological treatment he was not complicated with serious infection or sepsis. This may be attributed to his young age, early stage of the disease and no requirements for additional immunosuppressive treatment for CLL. While symptomatic CLL patients require active treatment, observation is recommended for patients in an early asymptomatic phase. Physical examination and routine check-up with complete blood count (organomegaly and/or cytopenias) should be followed every 6 months for progression [13]. In the literature, there are no studies or case reports showing that biological treatment shortens the early asymptomatic phase or accelerates transition to the blastic phase.

To our knowledge, we report the second case of CLL under anti-TNFα treatment among ankylosing spondylitis patients. We emphasize that biological treatment can be used safely for a long time with early-stage hematological malignancy.

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