Case Report

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Etanercept-induced thrombocytopenia in a patient with ankylosing spondylitis

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ABSTRACT

Objectives: Tumor necrosis factor alpha (TNF-α), which is produced by macrophages and activated T lymphocyte cells, plays a main role in inducing further stimulation of other inflammatory cells. Anti-TNF-α drugs are used for induction and preservation of remission in patients with Ankylosing spondylitis. Etanercept, it is possible that the use of its inhibitors may cause cytopeniabut isolated thrombocytopenia is an uncommon adverse event. We report the case of a 40-year-old man diagnosed with Ankylosing spondylitis who developed Etanercept-induced isolated thrombocytopenia.

Keywords: Thrombocytopenia, Ankylosing Spondylitis, adverse effect, biological agents

Ankylosing spondylitis (AS), a spondyloarthropathy, is a chronic inflammatory arthritis affecting the axial skeleton, sacroiliac joints and nonarticular structures to a different degree. One of the aims of the treatment of AS is to ease the symptoms and nonsteroidal anti-inflammatory drugs (NSAIDs), decreasing the stiffness and pain of inflammation, are the central component of AS treatment, However, many patients with AS have symptoms unresponsive to NSAID treatment and benefit from anti-TNF-α therapy. TNF-α inhibitors etanercept, adalimumab, golimumab, certolizumab and infliximab have proved to be efficient treatment options for patients with AS [1], but might have cause some adverse events including local injection reactions, demyelinating disease, heart failure, hepatotoxicity, malignancy and cytopenias.[2, 3] Although TNF-alpha inhibitors can lead to pancytopenia and occasionally leukopenia as reported in clinical trials, etanercept-induced thrombocytopenia is rarely seen.[4] TNFα regulates some pro-inflammatory cytokines such as interleukin (IL)-1, IL6, IL8 and granulocyte-macrophage-colony-stimulating factor, therefore, in theory, have the potential to block stem-cell differentiation with resultant bone marrow failure. Herein we report a patient who experienced thrombocytopenia induced by etanercept used for treatment of AS.

CASE

Fourty-years-old male patient diagnosed as Axial Spondyloarthritis in 2001, was started on etanercept (25 mg S.C. two times in a week) in April 2017 after failing several DMARDs including methotrexate and sulfasalazine. His pre-treatment blood counts were normal with a platelet count of $155x10^9$/l) and he was not using any other drug that could cause thrombocytopenia. After two doses of etanercept his platelet count fell to $79x10^9$/l and thrombocytopenia confirmed by examination of peripheral blood smear. His vitamin

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B 12 and folate levels were normal, anti-nuclear antibody (ANA) and antibodies to double-stranded DNA (anti-dsDNA) as well as anti-platelet antibodies were negative. Etanercept was discontinued due to the possibility of etanercept induced thrombocytopenia. His platelet count improved 12 days after stopping the etanercept (platelet count 162x10^9/l). There was no finding in the peripheral blood smear to explain other causes of thrombocytopenia. He started on adalimumab, after this treatment he has been no recurrence of the thrombocytopenia or any other side effects.

DISCUSSION

We present a case of patient who experienced pure thrombocytopenia during his treatment with etanercept. Cytopenia, which is also not common, is one of the well-known adverse effects of anti-TNF-α treatment. Hematologic side effects due to etanercept are generally seen as bicytopenia as leukopenia and thrombocytopenia in the literature.[5, 6] Our case is reported as the second isolated thrombocytopenia and the first patient who has AS while under treatment with anti-TNF-α drugs in the literature. The mechanism of anti-TNF-α therapy induced isolated thrombocytopenia is unclear. Several mechanisms have been proposed to explain this. According to a theory, TNF-α regulates some pro-inflammatory cytokines and granulocyte-macrophage colony- stimulating factor (GM-CSF), for this reason this blockage causes block stem-cell differentiation.[7] Another hypothesis is anti-TNF-α treatments contribute to formation of immune complexes, which in turn bind to the surface of platelet cells, so activating the complement cascade and subsequent platelet destruction.8 Another probable mechanisms include a lupus-like syndrome, associated with the production of ANA and anti-dsDNA.[9] The serum lupus antibodies were negative in our case. The temporal connection between the drug administration and the following development of trombocytopenia and between stopping of the drug and analytical recovery was clear. Pathare et al. described a case of isolated thrombocytopenia.[9] Etanercept was discontinued, and the platelet count recovered like other cases. Anti-TNF-α drugs have an important role in the treatment of rheumatic diseases in spite of their hematological side effects. We recommend that routine blood cell count must be performed for detect hematological changes before and shortly after etanercept or other anti-TNF treatment have started.

Authors' Contribution

Study Conception: AÖ,; Study Design: AÖ,; Supervision: GA,; Materials GA,; Literature Review: GA,; Manuscript Preparation: AÖ and Critical Review: BÖ, TA.

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