JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Hematology

Letter to the Editor

Hemophilia A Induced by Omalizumab

Luis Alberto Guardado Sánchez*[1], Alba Redondo Guijo[1], Santiago Santa Cruz Ruiz[1], José Ramón González Porras[1]

*[1]Hospital Universitario de Salamanca and IBSAL, Spain

*Corresponding author: Dr. Luis Alberto Guardado Sánchez, Hospital Universitario de Salamanca e IBSAL, Paseo Rector Esperabé, Número 46, 2 A. 37008, Salamanca, Spain, Tel : 0034 696 36 54 40; Email: guardadosanchez@hotmail.com

Received: 06-30-2015

Accepted: 07-15-2015

Published: 07-20-2015

Omalizumab, a humanized monoclonal antibody that binds circulating IgE antibody, is a treatment option for patients with moderate to severe allergic asthma whose condition is poorly controlled by inhaled corticosteroids and inhaled long-acting ß2-agonist bronchodilators.

The most common side effects of omalizumab treatment are bruising, erythema and pain at the site of injection. However, the most serious adverse effect of omalizumab is anaphylaxis, although this occurs infrequently [1].

We report for the first time an unusual case of omalizumab-induced hemophilia A.

A 82-year-old man came to our hospital with extensive bleeding from his oral cavity. His medical history included hypercholesterolemia, benign prostatic hyperplasia, and severe persistent allergic asthma, which had been treated with omalizumab therapy (Xolair®) comprising a 150-mg dose every 4 weeks for 10 months. His drug regimen had not recently changed in any other way.

Our patient presented a bleeding lesion on the dorsal surface of his tongue that was persistent despite surgical placement of sutures on the tongue. The patient was afebrile and hemodynamically stable. Physical examination did not reveal any other active bleeding.

Coagulation studies showed a prolongation of activated partial-thromboplastin time (APTT) of 76.1 s (normal value, 32s) and a reduced level of factor VIII:C of 4.3% (normal range, 50–150%). His FVIII inhibitor titer (Bethesda assay) was 64 Bethesda units. He did not have any personal or family history of hemophilia A and no history of bleeding during previous surgeries. These findings suggest a diagnosis of acquired hemophilia A. The patient was started on plasma-derived factor VIII concentrate (Beriate®) at a dose of 4000 UI every 4 hours, which stopped the bleeding. Due to the presence of the acquired inhibitor 2 months later, the patient was started on Rituximab at a weekly dose of 100 mg/kg for 4 weeks. Complete disappearance of antibodies to FVIII was achieved 3 months after initiation of treatment.

Factor VIII autoantibodies may be associated with pregnancy, autoimmune diseases, malignancy, infections or medication, and are most common in the elderly. Several drugs are also known to induce the production of autoantibodies to FVIII. In this case, the inhibitor was diagnosed after 10 months of treatment with omalizumab therapy. Autoantibodies to factor VIII that are induced by chronic use of immunomodulating agents (e.g., interferon) have been reported in recent years [2]. Omalizumab has also been associated with various immune-related adverse events, such as idiopathic thrombocytopenia, serum sickness and Churg-Strauss syndrome [3]. Therefore, we conclude that this case of acquired hemophilia was related to omalizumab therapy.

Unexpected adverse reactions related to biological response modifiers have recently been reported. In this setting, a case of hemophilia A induced by ipilimumab, a monoclonal antibody against cytotoxic T-lymphocyte-associated antigen 4 used in melanoma metastatic, has been described [4].

Physicians should bear this reported side effect in mind. Acquired hemophilia should be considered in the differential diagnosis of any coagulopathy, especially in the presence of

an isolated prolongation of APTT and normal Prothrombin Time-International Normalized Ratio (PT-INR), and of spontaneous bleeding with no family or personal history of bleeding.

References

1. Neil C. Thomson ,Rekha Chaudhuri. Omalizumab. Clinical Use for the Management of Asthma. Institute of Infection, Immunity, and Inflammation, University of Glasgow, and Respiratory Medicine, Gartnavel General Hospital, Glasgow G12 OYN, UK.

2. Franchini M, Capra F, Nicolini N, Veneri D, Manzato F et al. Drug-induced anti-factor VIII antibodies: a systematic review. Med Sci Monit. 2007 ,13(4): RA55-61.

3. Thomson NC, Chaudhuri R. Omalizumab: clinical use for the management of asthma. Clin Med Insights Circ Respir Pulm Med. 2012, 6:27-40.

4. Delyon J, Mateus C, Lambert T. Hemophilia A induced by ipilimumab. N Engl J Med. 2011, 365: 1747-1748.