



Stage-IV Kaposi's Sarcoma During Abatacept Therapy: A Case Report

Eugene Jalbert*, Robert DiGiovanni and Randal Worth

Nova Southeastern University: Largo Medical Center, Largo, FL, USA

*Corresponding author: Eugene Jalbert D.O., Nova Southeastern University: Largo Medical Center, Largo, FL, USA, Tel: 7276000841; E-mail: Genejalbert@gmail.com

Received date: January 05, 2015; Accepted date: January 31, 2015; Published date: February 10, 2015

Copyright: © 2015 Jalbert E, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Patients with rheumatoid arthritis (RA) are traditionally treated with disease modifying anti-rheumatic drugs (DMARDs). DMARDs have evolved throughout the years with an accelerated rate. Better understanding of molecular biology has made it possible to develop newer drugs with newer mechanisms of action. One of these drugs is abatacept, inhibiting the CD80 and CD86 on the antigen presenting cell from binding to the CD28 of the T cell. For some, this drug works amazingly. There are however side effects to these drugs, including increased risk for opportunistic infections and malignancies. The case we present in this paper is a gentleman with RA who was treated effectively with abatacept who then developed stage-IV Kaposi's sarcoma.

Keywords: Abatacept; Rheumatoid arthritis; Kaposi's sarcoma; HHV-8

Introduction

Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease which primarily causes a symmetric erosive arthritis of the peripheral joints but can also have debilitating systemic effects as well. Treatment of RA in years past has included very high dose aspirin and gold salts which are now very foreign to the newer generation of rheumatologist who are more apt to prescribe methotrexate and tumor necrosis factor inhibiting drugs. Using newer agents to treat RA is exciting, but clinicians must be cognizant of the fact that these drugs all carry risks.

Kaposi's sarcoma (KS) is an angioproliferative disorder that is caused by infection of human herpes virus 8 (HHV-8) also known as Kaposi's sarcoma-associated herpes virus [1]. While this is true, HHV-8 alone does not cause KS. There are now recognized cofactors that play a vital role in the development of KS after infection with HHV-8 [2]. Traditionally Kaposi's sarcoma is thought to be caused by immunosuppression of an individual with HIV and a co-infection with HHV-8. This is not entirely true. There are, in fact four subtypes of Kaposi's sarcoma. HIV-induced immunosuppression is only one of these four subtypes. The four subtypes are classic, endemic, AIDS-associated, and iatrogenic [3]. We will focus on the iatrogenic subtype in this paper.

Abatacept is a soluble fusion protein that binds to the CD80 and CD86 on the antigen presenting cell, blocking its interaction with CD28 on the T cell [4]. This action inhibits T cell proliferation and B cell immunological responses [4,5]. Abatacept consist of a cytotoxic T-lymphocyte antigen 4 (CTLA-4) linked to a modified Fc portion of human IgG1 [6]. Abatacept is used for the treatment of moderate to severe rheumatoid arthritis in adults and moderate to severe juvenile idiopathic arthritis in pediatrics 6 years of age and older [7]. Abatacept can be used by itself and in combination with other disease modifying anti-rheumatic drugs (DMARDs) other than tumor necrosis factor inhibiting agents [7]. The package insert for abatacept warns that in

those treated with abatacept there are increased risks for certain malignancies such as lung cancer and lymphoma [7].

When considering a treatment for any condition it is of great concern to the physician and patient when the treatment itself is cause for illness. The same holds true for treatment of rheumatoid arthritis (RA). There was a recent publication sponsored and funded by Bristol-Myers Squibb on the 7-year safety and efficacy of abatacept and methotrexate for the treatment of rheumatoid arthritis [8]. The study showed that of 219 patients treated with abatacept and methotrexate, there was an incidence ratio (IR) of 1.78 events per 100 patient-years of developing non-melanoma skin cancers, solid organ malignancies, or hematologic malignancies [8]. Other studies have shown that the IR of developing malignancy while on abatacept is equivalent to developing malignancies while on non-biologic DMARDS [9]. Therefore, abatacept in general has been considered relatively safe when treating RA.

According to Bristol-Myers Squibb, abatacept has been approved for use in rheumatoid arthritis (RA) since 2005 [7]. A search for any publications about Kaposi's sarcoma caused by abatacept was completed. There have never been any case reports of Kaposi's sarcoma caused by abatacept. This paper presents the case of an RA patient, treated with abatacept who later went on to develop stage-IV Kaposi's sarcoma.

Case

Our patient was a 57 year old white male who had recently moved from Arkansas to Florida during the spring of 2010. He was originally from Houston, Texas where he was a pharmacist of 30 years duration. He was diagnosed with seropositive erosive rheumatoid arthritis (RA) which was cause for early retirement. He was a notable smoker with a 35 pack-year history and rarely used alcohol. He denied prior IV drug abuse. He originally presented to our rheumatology clinic March 22nd, 2010. Prior treatments for his RA included methotrexate 25 mg PO weekly, prednisone 5 mg PO daily, folic acid, meloxicam 15 mg daily and hydrocodone as needed for pain. Initial labs in our office showed CCP to be >250, rheumatoid factor of 44, ESR of 16, and CRP of less

than 8.6. X-Rays of the hands showed mild erosive changes in the MCP joints. MRI findings also showed synovitis with severe erosive changes in the distal radius and lunate with small erosive changes of the MCP joints. Patient was started on infliximab June 7th, 2010. Infliximab was continued and dosages were increased however patient was an inadequate responder. On February 3rd, 2011 it was decided to stop infliximab and start abatacept due to lack of efficacy. He continued to take methotrexate 15 mg weekly, folic acid and hydrocodone as needed for pain. He continued with this course of treatment for about three years with very good clinical response. May of 2014 the patient, now a 61 year old male, began to notice multiple telangiectatic lesions on his face and shoulder area. He was referred to a dermatologist. A shave biopsy was done of the right neck lesions. Pathology revealed Kaposi's sarcoma with HHV-8 and CD31 positivity. Because he was also having progressive dysphagia to liquids over the prior 6 months he was also seen by gastroenterology to evaluate the patient for possible gastrointestinal Kaposi's sarcoma. Biopsies were taken during an EGD which revealed gastric involvement of the Kaposi's sarcoma. CT scan of the chest, abdomen, and pelvis revealed innumerable periaortic, aortocaval and pericaval lymph nodes. Patient was seen by two separate oncology groups and was diagnosed with Stage-IV, HHV-8 positive Kaposi's sarcoma. Abatacept and methotrexate were both discontinued when he was diagnosed with Kaposi's sarcoma. HIV testing was done and was negative. Late June of 2014 it was decided to start pegylated liposomal doxorubicin 20 mg/m² given every three weeks. Without complication the patient had a total of four cycles of chemotherapy. At that point, exam showed that skin lesions and retroperitoneal adenopathy had improved considerably. He underwent repeat EGD with biopsy which showed resolution of the gastric Kaposi's sarcoma. From a rheumatology perspective abatacept and methotrexate were never restarted. Patient did continue to take prednisone 10 mg PO daily. During this period his HAQ and DAS-28 (CRP) scores indicated his RA in general was flaring with increased frequency. Sulfasalazine was started on August 5th, 2014. One month later prednisone was tapered slowly as the patient's rheumatoid arthritis symptoms were more controlled. Last office visit was December 2nd, 2014 which confirmed resolution of the skin lesions, and improved overall health.

Discussion

This case presents a patient who was diagnosed with rheumatoid arthritis and treated with various DMARDs. Originally an inadequate responder to infliximab, he was switched to abatacept. Abatacept offered considerable relief of the patient's symptoms. Methotrexate and low dose prednisone were continued during this time. After having been on abatacept for 39 months our patient started developing lesions which were confirmed to be Kaposi's sarcoma. As discussed

above, Kaposi's sarcoma is traditionally thought to be due to HIV however research shows that there are four types of Kaposi's sarcoma. By definition our patient has iatrogenic Kaposi's sarcoma.

Iatrogenic Kaposi's sarcoma is classically due to drugs given after organ transplant but has been associated with various biologic DMARDs such as rituximab [10] and infliximab [11]. While there have not been any prior publications on abatacept-induced Kaposi's sarcoma it is the purpose of this case presentation to make clinicians aware that there is an increased risk for developing opportunistic infections and malignancies alike.

Acknowledgement

A special thanks to Dr. Robert DiGiovanni and Dr. Randal Worth for their case contributions and manuscript review.

References

1. Gao SJ, Kingsley L, Hoover DR (1996) Seroconversion to antibodies against Kaposi's sarcoma-associated herpesvirus-related latent nuclear antigens before the development of Kaposi's sarcoma. *New England Journal of Medicine* 335: 233-241.
2. Brown EE, Fallin MD, Goedert JJ, Hutchinson A, Vitale F, et al. (2006) Host immunogenetics and control of human herpesvirus-8 infection. *J Infect Dis* 193: 1054-1062.
3. Szajerka T, Jablecki J (2007) Kaposi's sarcoma revisited. *AIDS Rev* 9: 230-236.
4. Herrero-Beaumont G, Martínez Calatrava MJ, Castañeda S (2012) Abatacept mechanism of action: concordance with its clinical profile. *Reumatol Clin* 8: 78-83.
5. Schiff M (2011) Abatacept treatment for rheumatoid arthritis. (*Oxford*) 50: 437-449.
6. Llorenç V (2014) T-Cell Costimulation Modulator: Abatacept. *E-Science Central*.
7. Orenia * (abatacept) [package insert]. Princeton NJ (2011) Bristol-Myers Squibb Company.
8. Westhovens R, Kremer JM, Emery P, Russell AS, Alten R, et al. (2014) Long-term safety and efficacy of abatacept in patients with rheumatoid arthritis and an inadequate response to methotrexate: a 7-year extended study. *Clin Exp Rheumatol* 32: 553-562.
9. Simon T, Smitten A, Franklin J (2009) Malignancies in the rheumatoid arthritis abatacept clinical development programme: an epidemiological assessment. *Ann Rheum Dis* 68: 1819-26.
10. Clifford KS, Demierre MF (2005) Progression of classic Kaposi's sarcoma with rituximab. *J Am Acad Dermatol* 53: 155-157.
11. Cohen CD, Horster S, Sander CA, Bogner JR (2003) Kaposi's sarcoma associated with tumour necrosis factor alpha neutralising therapy. *Ann Rheum Dis* 62: 684.