



# CASE REPORT

## Side Effects of Adalimumab Masquerading as Lymphoma

Vishal Jain, M.D.<sup>1</sup>

David C Bodensteiner, M.D.<sup>2</sup>

<sup>1</sup>University of Kansas Medical Center

Department of Internal Medicine, Kansas City, KS

<sup>2</sup>Kansas City Veterans Administration Medical Center  
Kansas City, MO

### Introduction

Adalimumab (HUMIRA<sup>®</sup>) is a TNF- $\alpha$  blocking agent approved for several autoimmune conditions such as rheumatoid arthritis, psoriasis, ankylosing spondylitis, and Crohn's disease. The common side effects of adalimumab are headache, rash, upper respiratory tract infections, and injection site reaction. More cases of malignancies, especially lymphoma and non-melanoma skin cancer, have been observed among patients receiving TNF blockers compared to control patients in clinical trials.<sup>1</sup> The clinical manifestations of the side effects of adalimumab, at times, can be diagnostic dilemmas.

### Case Report

A 68-year-old man presented to the emergency room with a three-month history of unintentional weight loss, low-grade fevers, night sweats, and lymphadenopathy. He also reported generalized abdominal pain and anorexia. His past medical history was significant for rheumatoid arthritis (RA), hypertension, and depression. He had no previous surgery. Vital signs on admission were stable. The physical examination was remarkable for enlarged axillary, cervical, and inguinal lymph nodes. Initial laboratory tests results revealed pancytopenia and slightly elevated creatinine.

The differential diagnoses at this stage included, but was not limited to, malignancy (particularly lymphoma), tuberculosis (TB), HIV, and thyroid disorders. The patient also

had a history of depression which could explain some of his symptoms, such as anorexia and weight loss.

The patient was initially anemic and leukopenic. An HIV test was negative. A Quantiferon-Gold test for TB was also negative. A CT scan of the abdomen/pelvis showed multiple small lymph nodes in the aortocaval region. Subsequently, a bone marrow aspirate was normocellular. A lymph node biopsy did not reveal any evidence of lymphoproliferative disorder. The patient's abdominal symptoms improved with two days of supportive management.

The patient had been treated with adalimumab previously for rheumatoid arthritis. He stopped taking this medication five days prior to admission for anticipated knee replacement surgery. After three days of hospitalization, anemia and leukopenia improved spontaneously and the patient was discharged in stable condition. A rheumatology consult recommended discontinuing adalimumab and initiating steroids for rheumatoid arthritis. The patient's lymphadenopathy resolved after two weeks.

### Discussion

This case illustrated the potential for recognition of serious side effects of adalimumab in particular and biologic therapies in general. As reported earlier<sup>2</sup>, the risk of developing lymphoma is

increased in several autoimmune diseases. However, the French RATIO registry<sup>1</sup> suggested increased incidence of lymphomas with the use of anti-TNF monoclonal antibody.

Examining the risk of lymphoma with biologic use is complicated by several factors. First, although lymphoma is of public health importance (it is the fifth most common cause of cancer), it is statistically rare, affecting about 1 in 5000 people per year.<sup>3,4</sup> Therefore, very large studies are necessary to yield adequate statistical power to detect clinically significant lymphoma risks of biologics.

Second, many patients treated with biologics have received immuno-

suppressants such as methotrexate (MTX), cyclosporine, or azathioprine, either in the past, or concurrently with biologics, which themselves potentially can increase the risk of lymphoma. Consequently, it is difficult to determine which drug, or combination of treatments, meaningfully impacts lymphoma risk.

Although the patient described in the above case had a negative work-up for lymphoma, it was imperative to recognize such predictable side effects of adalimumab use. Identifying the side effects of biologic therapy is critical to the institution of appropriate management of acute illness and further follow-up.

## References

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