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Case Report

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A RARE CASE OF ADENOCARCINOMA WHEN ON ADALIMUMAB BIOSIMILAR

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ABSTRACT

Ankylosing spondylitis is a chronic inflammatory disease of joints and number of cases burgeoning day by day in the world. Sacroiliitis is the main symbol of the disorder, peripheral joints, and hip and shoulder joints can be involved. It is predominantly associated with HLA B27 gene. The introduction of biological therapy have improved prognosis of patients with ankylosing spondylitis since last decade. Adalimumab is a human monoclonal antibody approved for treatment of ankylosing spondylitis. Here we present a case of 65-year-old male patient with ankylosing spondylitis who was developed adenocarcinoma after treatment of adalimumab.

KEYWORDS: Ankylosing spondylitis, Adalimumab, Adenocarcinoma.

INTRODUCTION

Ankylosing spondylitis is a chronic, systemic, inflammatory disease of joints mainly affecting axial skeleton and peripheral joints.[1] The etiology of disease is still not well known. But there is strong connection to a genetic component; HLA B27 gene associated with disease. [2] The disease is having early onset during second or third decade of life; and found predominantly two to three times more in men than women. The prevalence of disease in overall population is 1.9% reported.[1.2]

The management of disease is carried out by use of non-steroidal anti-inflammatory agents (NSAIDs), disease improving antirheumatic drugs (DMARDs) [3] and newly developed biological therapies against tissue necrosis factor-α (TNF-α).[2] Adalimumab is human monoclonal antibody acts by prevention of the interaction of TNF-α with the p55 and p75 cell surface TNF receptors. TNF-α is a key cytokine that facilitates inflammation and modulates the cellular immune response. US Food and Drug Administration (FDA) approved adalimumab in 2006 as anti-TNF-α agent for treatment of ankylosing spondylitis.[4]

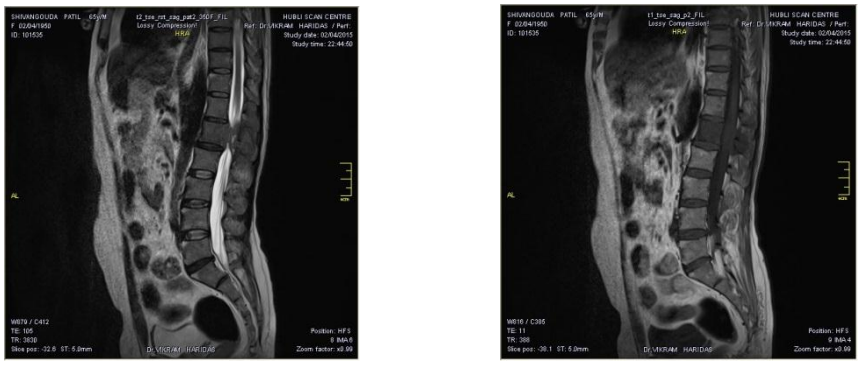
Here we report a rare case of adenocarcinoma after treatment of adalimumab for ankylosing spondylitis.

CASE REPORT

A 65-year-old male patient with ankylosing spondylitis having low back pain and morning stiffness visited to clinic. He was previously treated with Sulfasalazine 2g/day for 2 year duration with regular NSAID and low dose of methyl prednisolone of 5 mg/day. Even on treatment his back pain and stiffness persisted and continued to disturb his work. He had to quit his job and was at home since last 6 months. His hemoglobin: 11.2gm/dl, TC: 11,300 cells /dl, ESR: 110 mm/1hr, liver function tests (LFT) and creatinines were normal. Hence biological therapy with adalimumab was planned. As a routine screening for latent tuberculosis chest X-ray done was normal and QuantiFERON-TB gold was strongly positive. He was started on isoniazid and rifampicin daily for one month and later adalimumab 40 mg/every 15 days was started. Patient was better after 2 injections with improvement in back pain, and stiffness. Later after the 3rd dose he developed a swelling and severe pain in the left lower lumbar region radiating to the left foot with weakness in both the lower limbs. Initial clinical assessment was spinal tuberculosis with cold abscess.

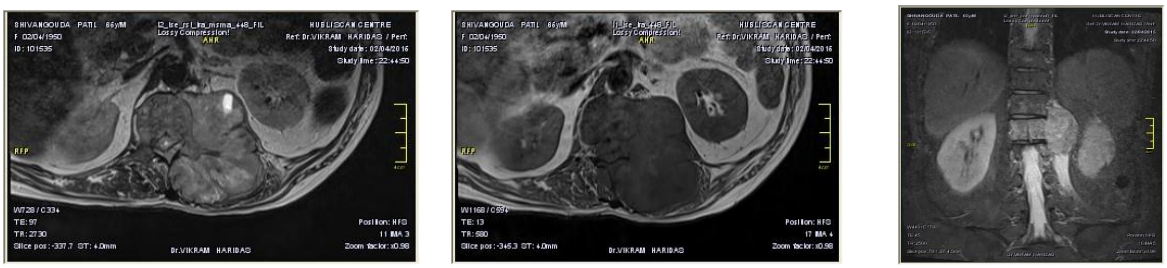
Further, Magnetic resonance imaging (MRI) of whole spine and pelvis was done. It showed a large soft tissue mass lesion in left paraspinal region at the level of L1 vertebral body, extending into left psoas and left errector spinae muscles (Figure 1 A, B). Lesion was extending into left neural foramen, anterior, left lateral and posterior epidural space at L1 level compressing thecal sac and causing narrowing of spinal canal. Marrow signal alteration was seen in body and posterior elements of L1 vertebra (Figure 2 A, B, C). MRI findings suggest presence of malignant lesion. Lesion size measured as 7.5 × 6.8 × 5.5 cm. Changes of chronic bilateral sacroiliitis were seen with multiple subarticular cysts. Fine needle aspiration cytology (FNAC) of the swelling was suggestive of undifferentiated adenocarcinoma. A

diagnosis of probable metastatic adenocarcinoma with unknown primary malignancy was made and referred to oncology center for further management. Surgical decompression was planned with chemoradiotherapy.



(A) (B)

Figure 1 (A), (B): Sagittal T1 and T2W MRI images show abnormal altered marrow signal in L1 vertebral body. Soft tissue lesion is seen in posterior epidural space at this level compressing thecal sac and nerve roots.



(A) (B) (C)

Figure 2 (A), (B), (C): Axial T1, T2W and STIR images reveal a large soft tissue mass lesion in left paraspinal region at the level of L1 vertebral body, extending into left psoas and left errector spinae muscles. Lesion is extending into left neural foramen, anterior, left lateral and posterior epidural spaces at L1 level compressing thecal sac and causing narrowing of spinal canal. Lesion is seen around the left transverse process of L1 vertebra.

DISCUSSION

Adalimumab is a vital biological agent approved by US FDA for the treatment inflammatory disorders such as rheumatoid arthritis, moderate to severe psoriasis, Crohn's disease and ankylosing spondylitis. Adalimumab treatment is associated with some adverse events. The most common side effects such as injection site reaction, infection with tuberculosis (TB), and deep fungal infections were observed in adalimumab treated patients.[5] In a double-blind,

placebo controlled study; five individual infectious adverse events (herpes simplex, influenza, pharyngitis, nasopharyngitis, and upper respiratory tract infection) were reported in adalimumab treated patients than in placebo group.[6]

In Adalimumab Trial Evaluating Long-Term Efficacy and Safety (ATLAS) trial, malignancies was reported in four patients includes single case of non-Hodgkin lymphoma, two cases of non-melanoma skin cancer and a case of malignant melanoma.[7] Recently a case of squamous cell carcinoma of the lip presented which was associated with adalimumab therapy (40 mg every other week for 2 years) for AS.[8] In present study, after treatment of 3 doses of adalimumab there was development of malignant lesion in cervical and lumbar spine detected by MRI scan. The biopsy results of the sample confirmed presence of adenocarcinoma. This is a rare case of adenocarcinoma after treatment of adalimumab in AS. Gordon et al. mentioned gastric adenocarcinoma in a patient with a history of peptic ulcer disease as a serious adverse event in the adalimumab (40 mg) weekly group at week 31.[9] In another study, a case of adenocarcinoma of colon was reported after treatment of adalimumab (80 mg) in rheumatoid arthritis patients.[10] Total 10 cases of lymphoma were reported in study of rheumatic arthritis patients treated with adalimumab. Patients had multiple risk factors such as long-standing disease, previous and/or concomitant immunosuppressive therapy, high disease activity, and older age for the development of lymphoma.[11] Lymphoma has been reported after use of anti-TNF-α therapy. Brown et al. reported 26 cases of lymphoma to FDA after treatment of etanercept (18 cases) and infliximab (8 cases) in patients for Crohn's disease and RA. Lymphoma was developed in patients on average 8 weeks after initiation of treatment.[12]

Chronic inflammation is allied to carcinogenesis. Chronic inflammation may result in chronic cellular proliferation and consequently has been associated to carcinoma development.[13] TNF-α is a vital cytokine involved in immune response, inflammation and carcinogenesis. The double nature of TNF-α activity may be responsible for its inconsistent anti- and pro-tumor activities depending on the cell, dose, environment, and other factors. [14] Currently used TNF-α inhibitors in the treatment of ankylosing spondylitis, RA, psoriasis and Crohn's disease, are all associated with inflammation and immune-mediated tissue damage and increased risk of carcinogenesis. [13]

Regulatory authority gives permission for a biosimilar product if efficacy to the original product showed in particular class of disease. For example adalimumab (TNF-α inhibitor) is

approved for rheumatoid arthritis then approval is given for psoriatic arthritis. However, there is a need of long-term safety and efficacy studies to evaluate biosimilar for each disease separately to avoid such adverse events and appropriate treatment of disease. Biosimilars are highly target specific drugs so should be used carefully.

CONCLUSION

Adenocarcinoma was developed after treatment of adalimumab in a patient with ankylosing spondylitis.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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