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Monoclonal Gammopathy of Undetermined Significance Occurred after Golimumab Therapy in a Patient with Ankylosing Spondylitis

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Abstract

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease which is characterized by the involvement of the sacroiliac joint and the spine, the main therapy includes biological agents, which may increase the risk of tumor and infection in long term application. **Case Presentation:** A fifty-year-old man was diagnosed of AS. He received the therapy of golimumab 50 mg once every one month subcutaneously. After receiving this treatment for two years and eight months, the patient had an elevated level of IgA. The monoclonal protein was finally identified as the type of IgA-kappa from the immunofixation study. Bone marrow aspirate smear revealed infiltration by plasma cells (5%) and immunophenotyping was positive for CD27, CD28, CD38, CD45, CD138 and cKappa, which was finally diagnosed of MGUS. **Conclusion:** This case demonstrates that golimumab may increase the risk of premalignant disease in patients with AS. With our case report, we also like to highlight that patients with AS may have increased risk of plasma cell malignancies.

Keywords

Ankylosing Spondylitis, Golimumab, Monoclonal Gammopathy of Undetermined Significance

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease which is charac-

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terized by the involvement of the sacroiliac joint and the spine, and can cause chronic back pain and functional impairment. Monoclonal gammopathy of undetermined significance (MGUS) is a premalignant plasma cell dyscrasia that consistently precedes multiple myeloma (MM) with a 1% risk of progression per year. The association of MGUS with AS has been rarely described. Herein we report a patient with AS who presented with MGUS after the use of golimumab.

2. Case Presentation

A fifty-year-old man presented with a five-year history of inflammatory low back pain associated with morning stiffness and limited spinal mobility. But he never paid attention and received any treatment. There was no history suggestive of gastrointestinal symptoms, pheripheral arthritis, psoriasis or other infectious diseases. Physical examination revealed tenderness of the sacroiliac joints and reduced chest expansion (2 cm). Laboratory investigation demonstrated that blood routine, homologous leucocytic antigen-B27 and immunofixation study were all negative. The levels of immunoglobulin A (IgA), IgM and IgG were all in the normal range. Erythrocyte sedimentation rate was 61 mm in the first hour (normal range: 0 - 20 mm/H) and C-reactive protein level was 11.26 mg/L (normal range: 0.068 - 8.2 mg/L). X-ray showed bone fusion on the right sacroiliac joint. Narrow joint gap and bone marrow edema could be detected on the sacroiliac joints from MRI. Thus, a diagnosis of AS was established. He received the therapy of golimumab 50 mg once every one month subcutaneously. After receiving this treament for two years and eight months, the patient had an elevated level of IgA (24.25 g/L, normal range: 0.72 - 4.29 g/L). Serum protein electrophoresis revealed that the ratio of monoclonal spike in the gamma region was 13.11%. The monoclonal protein was finally identified as the type of IgA-kappa from the immunofixation study. Erythrocyte sedimentation rate was 47.00 mm/H and C-reactive protein level was normal. Laboratory tests demonstrated no anemia, renal lesion or hypercalcemia. Bone lesion could not be detected from imaging tests. Bone marrow aspirate smear revealed infiltration by plasma cells (5%) (**Figure 1**) and immunophenotyping was positive for CD27, CD28, CD38, CD45, CD138 and cKappa (**Figure 2**). Chromosome karyotyping analysis demonstrated 46, XY. Fluorescence *in situ* hybridization analysis showed partial deletion of chromosome 13q and abmormalities in 1q21 and the diagnosis of MGUS was made.

3. Discussion

MGUS is thought to be the first pathogenetic step in the development of MM, but the mechanism for MGUS remains unknown. The autoimmune disease, ankylosing spondylitis, has been reported to be associated with the incidence of MGUS and MM, and standardized incidence ratios of multiple myeloma was also significantly increased in patients with AS [1] [2] [3]. These results indicate that AS might act as triggers for MGUS/MM development. However, an opposite

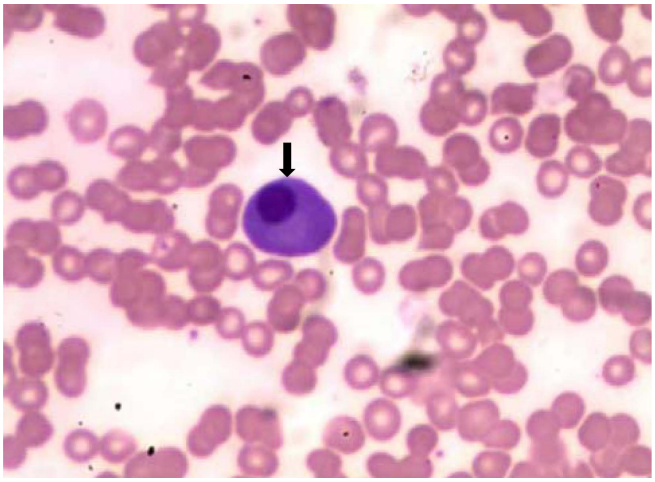

Figure 1. Bone marrow aspirate smear revealed infiltration by plasma cells (400×).

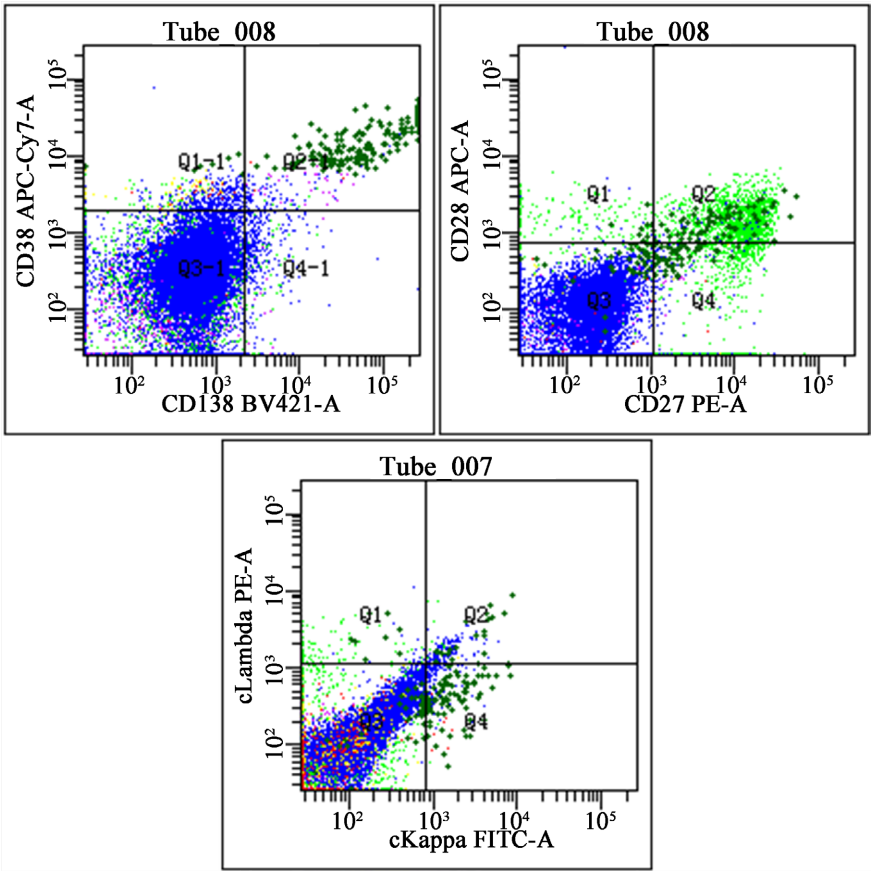

Figure 2. Immunophenotyping was positive for CD27, CD28, CD38, CD45, CD138 and cKappa.

result was reported in a systematic review which revealed that ankylosing spondylitis was not the subsequent risk of MGUS or MM [4]. Although the role of AS in the risk factor of MGUS/MM was focused on, the effect of biologic drugs on the incidence of MGUS/MM was rarely reported. It was found that no association was observed between the use of any biologic disease-modifying antirheu-

matic drug (DMARD) and risk of MM compared to never having used biologic DMARDs. However, compared to the users of conventional-synthetic DMARDs only, those receiving conventional-synthetic plus biologic DMARDs had an inverse relationship with MM. In addition, a positive association was observed with use of interleukin 6 (IL-6) antagonist tocilizumab and MM. However, there was no relationship between use of anti-tumor necrosis factor alpha (TNFα) antibody and MM [5]. In this case, this patient only received the therapy of anti-TNFα antibody golimumab, but got MGUS after two years and eight months. Since TNFα has both pro- and anti-malignancy potencies [6], we speculate that the effect of pro-malignancy predominate after use of golimumab in this patient and result in the incidence of MGUS. Finally, chromosome abnormalities could be detected and this patient may have the risk of developing into MM.

4. Conclusion

The occurence of MGUS after the use of tumor necrosis factor-α in patients with AS has rarely been reported in the literature. This case demonstrates that golimumab may increase the risk of premalignant disease in patients with AS. With our case report, we also like to highlight that patients with AS may have increased risk of plasma cell malignancies. Longitudinal cohort studies with large samples and persistent follow-up should be needed to investigate the true relationship of the use of golimumab and plasma cell diseases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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