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### Candida Esophagitis Induced by TNF Antagonist in a Patient with Rheumatoid Arthritis

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#### **Abstract**

Candida esophagitis is a common disease with increasing frequency in immunosuppressive patients. There are multiple factors in etiology and one of these reasons is using immunosuppressive drugs. Various drugs are used to suppress the immune system in patients with rheumatoid arthritis (RA) and one of those is tumor necrosis factor alpha (TNF- $\alpha$ ) antagonists. There are many complications of TNF- $\alpha$  antagonist drugs. One of these complications is candida esophagitis. In this case report we aimed to present the candida esophagitis in a 42 year old female patient with RA using TNF- $\alpha$  antagonist.

**Key words**: Candida esophagitis, Rheumatoid arthritis, TNF-α antagonist,

#### Introduction

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune, inflammatory disease with joint deformations. The incidence is 1-1.5%. RA may be seen in all age groups but it is most common between the ages of 40-60 and 2-4 times more common women than in Ethiopathogenesis of RA is not clear. It is thought to be multifactorial as other autoimmune diseases. T lymphocytes are mainly responsible for RA and tumor necrosis factor-α  $(TNF-\alpha)$ proinflammatory cytokine important in pathogenesis. Hence, TNF-α destination for treatment of RA (1,2).

As well as the main drug is methotrexate for RA, combination therapies are also used in treatment. In recent years, more remission of disease has been achieved with biological agents such as TNF- $\alpha$  antagonists. But the incidence of infections increases with immunosuppressive effects of these drugs (3). Esophageal candidiasis is one of the most common opportunistic infections in immunosuppressed patients. The etiology of esophageal candidiasis was as follows; immunosuppressive states such as AIDS and malignancies, treatment with radiation, chemotherapy, steroids or other cytotoxic agents (4).

In this study, we aimed to report a case of a patient with RA receiving etanercept, one

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of the TNF- $\alpha$  antagonists, who was detected candida esophagitis.

### **Case Report**

A 44-years old woman presented to our clinic with a burning sensation in the lower part of the chest, odynophagia and recurrent bitter water come back to mouth. In her history, it was learned that she was followed with the diagnosis of RA for three 3 years. After the initial diagnosis, the patient received methotrexate (MTX) 10 mg/week, sulfasalazine 2000 mg/day, hydroxychloroquine sulfate 400mg/day for 1.5 years. During the follow-up, etanercept 50 mg/week was given to the patient due to common joint tenderness and swelling in his right elbow and both metatarsophalangeal. The patient hyperlipidemia, diabetes mellitus. asthma and hypertension. There was no abnormality in her family history. No abnormal finding was detected in the physical examination regarding systems other than locomotor system. On the examination of locomotor system, there tenderness in the proximal interphalangeal joint of right and left 2, 3, 4 fingers but there was no swelling, heat. and deformity. The complete blood count and biochemical parameters were within normal range. The erythrocyte sedimentation rate was detected as 33 mm/h, while CRP as 3.3 mg/l.

With the present complaints upper gastrointestinal endoscopy was done by gastroenterologist and reported as candida esophagitis. Therefore, etanercept was cut off and ketoconazole treatment was initiated by gastroenterologist for three weeks.

#### **Discussion**

Candida esophagitis occurs due to impaired cellular immunity and esophageal colonization or both of them. Esophageal colonization occurs in esophageal stasis. Impaired cellular immunity happens with immunosuppressive therapy, AIDS or malignancy (5). Candida esophagitis usually develops secondary to suppression of the immune system (4).

The risk of infection increased in patients with inflammatory rheumatic disease than healthy population. Immunosuppressive therapy and underlying disease is responsible for that risk (6). In our patient, mentioned two factors as risk factors for candida infection are available.

Candida esophagitis is usually acute onset of symptoms. The most common symptoms are odynophagia, nausea, dysphagia, fever and retrosternal chest pain. clinical manifestations are ranging from odynophagia to unable to eat (7,8). Similar complaints have been seen in our patient.

The coexistence of pregnancy, diabetes and H2 blockers are thought to increase the risk of candidal esophagitis. A significant relationship between fungal esophagitis and H2 blocker therapy has been found (9). The prevalence of candida esophagitis was determined as 16.7% in patients who has taken H2 blocker and in no drug group was as 3.5% (10). In our case, there was a presence of diabetes mellitus but no H2 blocker using.

White mucosal plaques are usually sufficient to diagnose the candida esophagitis with endoscopy. For definitive diagnosis, fungus and pseudo hyphae which was invasived to mucosal cells in biopsy with candida species in culture are isolated (11). In our case, culture was not made because mucosal plaques which is tvpical for candida infection. observed.



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Ketoconazole, fluconazole or amphotericin B are used for candida esophagitis due to candida albicans which required systemic therapy for long time (12,13). Ketoconazole was suggested to patient by gastroenterology clinic.

In conclusion, it should be considered that different etiological agents might cause to infection in patients with usage of anti TNF drugs for RA and patients should be informed before treatment

### Conflict of Interest: None

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