

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- α) antagonists. There are many complications of TNF- α 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- α antagonist.

Key words: Candida esophagitis, rheumatoid arthritis, TNF- α antagonist

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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 in women than men. Etiopathogenesis 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- α) is a proinflammatory cytokine important in

pathogenesis. Hence, TNF- α is a 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- α 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 of the TNF- α 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, and 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 has 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 was 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

typical for candida infection, was observed.

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

References

1. Khurana R, Berney SM. Clinical aspects of rheumatoid arthritis. *Pathophysiology*. 2005;12(3):153-165.
2. Aarvak T, Chabaud M, Thoen J, Miossec P, Natvig JB. Changes in the Th1 or Th2 cytokine dominance in the synovium of rheumatoid arthritis (RA): a kinetic study of the Th subsets in one unusual RA patient. *Rheumatology (Oxford)* 2000;39(5):513-522.
3. Ma X, Xu S. TNF inhibitor therapy for rheumatoid arthritis. *Biomed Rep*. 2013;1(2):177-184.
4. Kumar P, Mohan S, Verma A, Baijal SS. Candida esophagitis in achalasia cardia: case report and review of literature. *Saudi J Gastroenterol*. 2007;13(2):88-90.
5. Baehr PH, McDonald GB. Esophageal infections: risk factors, presentation, diagnosis, and treatment. *Gastroenterology*. 1994; 06(2):509-532.
6. Emmungil H, Aksu K, İnflamatuar Romatizmal Hastalıklarda Aşılama. *RAED dergisi*. 2009;1:42-47.
7. Ramanathan J, Rammouni M, Baran J Jr, Khatib R. Herpes simplex virus esophagitis in the immunocompetent host: an overview. *Am J Gastroenterol*. 2000;95(9):2171-2176.
8. Chocarro Martínez A, Galindo Tobal F, Ruiz- Irastorza G et al. Risk factors for esophageal candidiasis. *Eur J Clin Microbiol Infect Dis*. 2000;19(2):96-100.
9. Vermeersch B, Rysselaere M, Dekeyser K et al. Fungal colonization of the esophagus. *Am J Gastroenterol*. 1989;84(9):1079-1083.
10. Greenspoon JS, Kivnick S. Candida esophagitis in an immunocompetent pregnant woman. *Infect Dis Obstet Gynecol*. 1993;1(3):149-152
11. Sangeorzan JA, Bradley SF, He X et al. Epidemiology of oral candidiasis in HIV-infected patients: colonization, infection, treatment, and emergence of fluconazole resistance. *Am J Med*. 1994;97(4):339-346.
12. Pfaller MA, Diekema DJ. Twelve years of fluconazole in clinical practice: global trends in species distribution and fluconazole susceptibility of bloodstream isolates of Candida. *Clin Microbiol Infect*. 2004;10(1):11-23.
13. Pfaller MA, Diekema DJ, Gibbs DL et al. Results from the ARTEMIS DISK Global Antifungal Surveillance Study, 1997-2005: an 8.5-year analysis of susceptibilities of candida and other yeast species to fluconazole and voriconazole by CLSI standardized disk diffusion testing. *J Clin Microbiol*. 2007;45:1735-1745.