Primary Mucinous Epithelial Ovarian Carcinoma in a Patient with Ankylosing Spondylitis Treated with Infliximab: Case Report

İnfliksimab ile Tedavi Edilen Ankilozan Spondilitli Bir Hastada Primer Müsinöz Epitelyal Over Karsinomu

Yılmaz DİKMEN,[a]
Mustafa Coşan TEREK,[a]
Cem Yaşar SANHAL,[a]
Ahmet Mete ERGENOĞLU,[a]
Ahmet Özgür YENİEL,[a]
Osman ZEKİOĞLU,[b]
Aydın ÖZSARAN[a]

Departments of
[a]Obstetrics and Gynecology,
[b]Pathology,
Ege University Faculty of Medicine, İzmir

Geliş Tarihi/*Received:* 06.03.2011
Kabul Tarihi/*Accepted:* 15.12.2011

Yazışma Adresi/*Correspondence:*
Cem Yaşar SANHAL
Ege University Faculty of Medicine,
Department of Obstetrics and Gynecology,
İzmir,
TÜRKİYE/TURKEY
cemsanhal@yahoo.com

ABSTRACT Ankylosing spondylitis (AS), the prototype of spondyloarthritis is a chronic inflammatory rheumatic disease with a prevalence of 0.5-1.9% among all types of spondyloarthritis. Inhibition of the proinflammatory cytokine tumour necrosis factor (TNF)-α has demonstrated efficacy in patients with active AS. However, de novo malignancies have been reported in some patients undergoing this therapy representing a major concern. Here, we reported a case with AS who was diagnosed with carcinoma of ovary after receiving therapy with infliximab.

Key Words: Spondylitis, ankylosing; infliximab; tumor necrosis factor alpha (36-68); ovarian neoplasms

ÖZET Spondiloartritin prototipi olan ankilozan spondilit (AS), kronik yangısal romatizmal bir hastalık olup, tüm spondiloartritler içinde %0,5-1,9 arasında bir prevalansa sahiptir. Aktif AS'li hastalarda proinflamatuar sitokin tümör nekrozis faktör (TNF)-α'nın inhibisyonunun etkin olduğu gösterilmiştir. Fakat bu tedaviyi alan hastalarda de novo maligniteler bildirilmiştir. Bu makalede, infliksimab tedavisi aldıktan sonra over kanseri tanısı alan AS'li bir hasta bildirilmiştir.

Anahtar Kelimeler: Spondilit, ankilozan; infliksimab; tümör nekroz faktörü alfa (36-68); over tümörleri

Turkiye Klinikleri J Med Sci 2013;33(1):238-40

Ankylosing spondylitis (AS), the prototype of spondyloarthritis is a chronic, progressive inflammatory rheumatic disease with a 3.4:1 male to female ratio; the mean age of diagnosis for female patients is 32.4±9 years.[1]

Inhibition of the proinflammatory cytokine tumour necrosis factor (TNF)-α has been demonstrated to show efficacy in patients with active AS, psoriasis and various other inflammatory diseases.[2] Infliximab (IFX) is a product containing monoclonal antibodies that neutralize the biological activity of TNF-α by binding with high affinity to the soluble and transmembrane forms of TNF-α and inhibits or prevents the effective binding of TNF-α to its receptors. However, *de novo* malignancies have been reported in some patients undergoing this therapy, currently representing a major concern among researchers.[3]

doi: 10.5336/medsci.2011-23682

Here, we reported a case with AS who was diagnosed with carcinoma of ovary after receiving IFX therapy.

CASE REPORT

The patient was a 20-year-old, virgin, HLA-B27-negative woman who had been diagnosed with ankylosing spondylitis (AS) at the age of seventeen. Sulfasalazine therapy in combination with nonsteroidal anti-inflammatory drugs did not relieve her intractable arthritis and enthesitis of both Achilles tendons. Due to her active, treatment-resistant disease, initiation of IFX therapy was considered by the rheumatology department. To rule out tuberculosis (TB) infection, computerized tomography (CT) of the thorax, tuberculin skin test and mycobacterium tuberculosis cultures were performed and both were negative; there were no abnormalities on CT images. Respiration function test parameters were also normal. She was informed on and was offered gynecologic consultation and examination but she refused these by denoting her virginity. She was given isoniazid before IFX therapy in order to avoid reactivation of latent tuberculosis. The first dose of IFX infusion 3 mg/kg was followed by second and third line therapies within 6 weeks. After the third dose, she continued to use IFX at two-month intervals and all of her complaints regressed. At month 20 of IFX therapy, she suffered from abnormal menstural bleeding and was referred to the gynecology department, this time accepting gynecologic examination, by her primary rheumatologist. Her gynecologic examination and history revealed that she had normal genital system findings and menstrual disorder as menorrhagia. Routine biochemical tests such as tumor markers (CA 125, CA 19-9, CA 15-3, CEA and AFP) and hormone profile were all normal except for hemoglobin level. She had hypochromic microcytic anemia with an hemoglobin level of 6 g/dL. Transvaginal sonography revealed a simple ovarian cyst 3 cm in diameter. She was prescribed combined oral contraceptive therapy comprised of drospirenon and ethinyl estradiol to suppress the ovarian cyst and to establish menstrual regulation. One month later, colored Doppler sonographic examination revealed right-sided complicated ovarian cyst 147x107x70 mm in size with 66x56 mm solid components and septations with low resistant flow (resistance index 0.40). The patient was hospitalized and during the investigation period abdominal CT examination revealed both pleural effusion and abdominal ascites and a 17x11 mm sized right ovarian cyst consisting of solid components and septations (Figure 1). She underwent immediate laparotomy due to tense abdominal ascites and respiratory distress. Abdominal inspection revealed approximately 1500 mL of mucinous ascites and an ovarian cyst 15 cm in size. The patient was operated by an oncologic surgeon for unilateral salpingo-oophorectomy in order to preserve fertility. Peritoneal frozen section biopsies obtained during the operation yielded borderline histology. The definitive pathological examination revealed mucinous adenocarcinoma of the ovary (Figure 2).

In the follow-up period, the patient was discharged with cure at day 7 of the operation. She was administered six courses of chemotherapy (paclitaxel and carboplatin). Systemic and gynecologic examination findings through magnetic resonance imaging, transvaginal sonography and tumor markers were unremarkable. After the completion of chemotherapy with no evidence of disease, she was offered interval debulking consisting of lymphadenectomy, hysterectomy and omentectomy; however, she refused the radical operation.

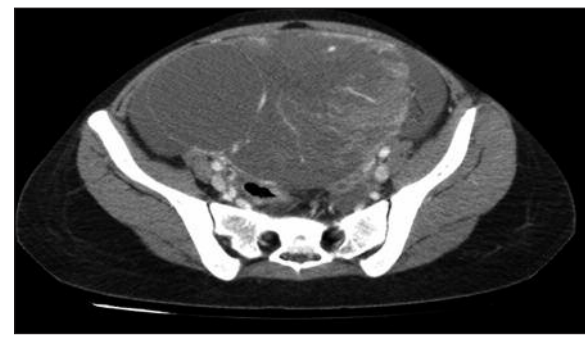

FIGURE 1: Abdominal computed tomography image of right ovarian cyts consisting of solid components and septations.

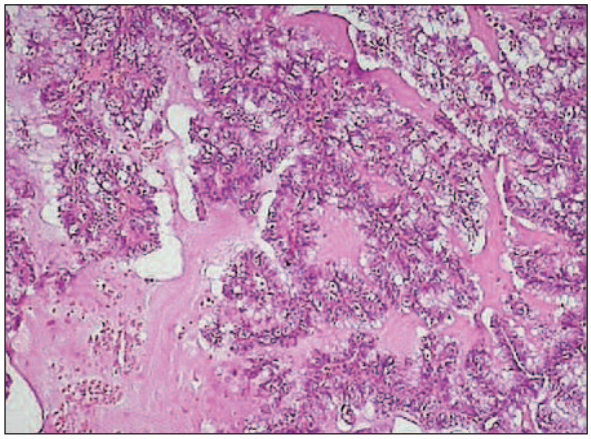

FIGURE 2: Mucinous adenocarcinoma of ovary. (hematoxylin-eosin, magnificationx20).

(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

DISCUSSION

One decade ago, the introduction of IFX, a monoclonal antibody against TNF-α, has tremendously enriched the therapy of immunologic diseases.

Primary ovarian carcinoma is rare in the case of a 20-year-old woman without a genetic predisposition (3-17%) and a possible role for TNF-α antagonist therapy should be considered. The role of TNF-α and other proinflammatory cytokines on carcinogenesis is controversial, because they have a beneficial effect on the host as they enhance the immunological responses against infectious agents and tumour cells. However, they also drive the chronic inflammation that contributes to cell transformation, the production of the vascular adhesion molecules, growth factors involved in angiogenesis and cancer growth, and the development of metastases.[4]

There are also concerns that the therapeutic use of anti-TNFα agents may also be associated with the development of cancer. So far, the concern about an increased potential for cancer among patients treated with anti-TNF agents has focused primarily on lymphomas.[5] Although the overall incidence of cancer was reported not to be increased in patients treated with these agents, small case series have described a potential link between these agents and a variety of malignancies, including leukemia, squamous cell carcinoma of the skin, and adenocarcinoma of the colon.[6]

To the best of our knowledge, this is the first description of an ovarian carcinoma in a patient with AS during infliximab therapy. With the concerns of the possible relationship between anti-TNFα exposure and carcinogenesis, the presentation of this patient's ovarian carcinoma could be one of the side effects on tumor surveillance.

REFERENCES

1. Sayıner Çağlar N, Burnaz Ö, Akın T, Özgönenel L, Çetin E, Aytekin E, et al. Demographic and clinical properties and medical treatments of patients followed as ankylosing spondylitis. Istanbul Med J 2011;12(1):19-24.
2. Bülbül Başkan E, Yazıcı Öztürk Z, Erdem H, Sarıcaoğlu H. [Our clinic experience with ınfliximab in cases with moderate-severe psoriasis: a retrospective study]. Turkderm 2009; 43(3):95-9.
3. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials. JAMA 2006;295(19):2275-85.
4. Szekanecz E, András C, Sándor Z, Antal-Szalmás P, Szántó J, Tamási L, et al. Malignancies and soluble tumor antigens in rheumatic disease. Autoimmun Rev 2006; 6(1):42-7.
5. Brown SL, Greene MH, Gershon SK, Edwards ET, Braun MM. Tumor necrosis factor antagonist therapy and lymphoma development: twenty-six cases reported to the Food and Drug Administration. Arthritis Rheum 2002; 46(12):3151-8.
6. Simsek I, Pay S, Dinc A, Erdem H, Kurt B. Atypical carcinoid tumor of the thymus with ectopic ACTH production developed during the course of etanercept treatment-case report. Clin Rheumatol 2007;26(9):1561-2.