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Case Report

Subacute thyroiditis associated with adalimumab - a case report and review of the literature

Adalimumab ilişkili subakut tiroidit - olgu sunumu ve literatür incelemesi

Şerife Mehlika Kuşkonmaz, Gönül Varan Koç, Tahsin Özenmiş, Muhammed Mustafa İnce, Mehmet Kırnap, Cavit Çulha

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ABSTRACT

Subacute thyroiditis is characterized by the painful inflammation of the thyroid and thyrotoxicosis due to thyroid destruction. A few case reports looked into the association between anti-tumor necrosis factor (anti-TNF) agents and subacute thyroiditis. A 42-year-old woman was admitted to the hospital for fever and neck pain spreading to the right ear. For the last seven years, she has been on adalimumab treatment (40 mg every 15 days) for ankylosing spondylitis. Thyroid scintigraphy showed a diffusely suppressed gland which confirmed the diagnosis of subacute thyroiditis. Adalimumab treatment was stopped, and methylprednisolone 32 mg/day was started. Adalimumab use may be associated with subacute thyroiditis.

Keywords: Adalimumab, ankylosing spondylitis, thyroid

ÖZ

Subakut tiroidit; tiroid bezinde şişlik, boyun bölgesinde dokunmayla hassasiyet ve tiroid foliküllerinin yıkımına bağlı ortaya çıkan tirotoksikoz ile karakterize bir hastalıktır. Birkaç olgu sunumunda subakut tiroidit ile anti TNF ajanların ilişkisi incelenmiştir. Kırkiki yaşında kadın hasta ateş ve sağ kulağa yayılan boyun ağrısıyla hastaneye başvurdu. Hastaya 9 yıl önce ankilozan spondilit tanısı konulduğu ve hastanın 7 yıldır adalimumab (40 mg/15gün) tedavisi aldığı öğrenildi. Hastanın tiroid sintigrafisinde tiroid bezi yaygın suprese görünümdeydi ve subakut tiroidit düşünüldü. Adalimumab tedavisi stoplandı ve metilprednizolon 32 mg/gün başlandı. Adalimumab kullanımı subakut tiroidit ile ilişkili olabilir.

Anahtar kelimeler: Adalimumab, ankilozan spondilit, tiroid

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Corresponding Author:
Ş. M. Kuşkonmaz
ORCID: 0000-0002-2602-1657
Ankara Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolic Diseases, Ankara, Turkey
✉ mehlikaisildak@gmail.com

G. Varan Koç
ORCID: 0000-0002-8512-4816
Ankara Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolic Diseases, Ankara, Turkey

T. Özenmiş
ORCID: 0000-0003-4763-5364
Dr. Ersin Arslan Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolic Diseases, Gaziantep, Turkey

M. M. İnce
ORCID: 0000-0002-4194-7810
Etimesgut Şehit Sait Ertürk State Hospital, Department of Internal Medicine, Ankara, Turkey

M. Kırnap
ORCID: 0000-0002-7472-2351
Erciyes University, Faculty of Medicine, Department of Physical Therapy and Rehabilitation, Kayseri, Turkey

C. Çulha
ORCID: 0000-0001-6563-8900
Ankara Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolic Diseases, Ankara, Turkey

INTRODUCTION

Subacute thyroiditis is characterized by painful thyroid inflammation and thyrotoxicosis due to thyroid destruction (1). Viral agents are commonly implied in the etiology of subacute thyroiditis. Adalimumab is an anti-tumor necrosis factor (anti-TNF) agent used to treat various autoimmune diseases such as psoriasis, Crohn's disease, and ankylosing spondylitis (2). Here we report a case of subacute thyroiditis associated with adalimumab treatment.

CASE

A 42-year-old female patient was admitted to the hospital for chills, fever, and neck pain spreading to the right ear. She was diagnosed with ankylosing spondylitis nine years ago and has been on adalimumab treatment for the last seven years (40 mg every 15 days). Her body temperature on physical examination was 38,2°C. The patient denied a recent history of common cold or flu, suggesting the absence of a viral infection. The thyroid gland was enlarged and tender to palpation. Laboratory evaluation results of the patient are summarized in Table 1. Thyroid scintigraphy showed a diffusely suppressed gland. Thyroid ultrasonography revealed diffuse enlargement of the gland with interspersed hypoechoic areas. The patient was diagnosed with subacute thyroiditis. Serum IgM for CMV and EBV were negative. Adalimumab was considered the reason for thyroiditis in the patient without a history of viral infection. Adalimumab treatment was stopped, and methylprednisolone 32 mg/day was started. Four weeks later, she applied to the hospital with fever and neck pain relapse due to noncompliance with the glucocorticoid treatment. She was hospitalized, and 48 mg/day of methylprednisolone was ordered. Her neck pain subsided, and her fever responded significantly to glucocorticoid treatment. She was discharged from the hospital on glucocorticoid treatment. C-reactive protein (CRP) decreased to 5.6 mg/dl six weeks later. The glucocorticoid treatment was gradually tapered.

DISCUSSION

As anti-TNF agents are being used more commonly for autoimmune diseases, data about their secondary effects on organs emerge. Some studies showed that anti-TNF agents are associated with improved autoimmune thyroid diseases and reduced thyroglobulin and thyroid peroxidase antibody concentrations (3). Data on the association between anti-TNF agents and subacute thyroiditis is scarce as case reports (4-12). A summary of the reported cases is given in Table 2.

Adalimumab is a human monoclonal anti-TNF antibody commonly used to treat some autoimmune diseases (2). Kawashima et al. (8) reported a case of painful thyroiditis on etanercept therapy for Crohn's disease, which resolved with the withdrawal of the drug but recurred with the initiation of adalimumab treatment. The authors suggested that the underlying amyloid goiter might have contributed to developing signs and symptoms. Two more cases of subacute thyroiditis were reported with adalimumab therapy for psoriasis and psoriatic arthritis (10,11).

Table 1. Laboratory values of the patient at diagnosis.

C reactive protein	132 mg/L	(<5)
ESR	56 mm/h	(0-15)
WBC	15700/mm3	(4-10.5)
PMNL	13000/mm3	(2-7.15)
TSH	0,09 mIU/L	(0.49-4.33)
Free T3	3,78 ng/L	(2.5-4.4)
Free T4	1,72 ng/dL	(0.93-1.6)
Anti TPO Ab	9.0 IU/ml	(<34)
Anti TG Ab	18,14 IU/ml	(<115)
Thyroglobulin	500 ng/ml	(3.5-77)

ESR, erythrocyte sedimentation rate; WBC, white blood cell; PMNL, polymorpho nuclear leukocytes; TSH, thyroid stimulating hormone; TPO, thyroid peroxidase; Ab, antibody; TG, thyroglobulin

Table 2. Literature review for anti TNF associated cases of subacute thyroiditis.

Authors	Age of the patient	Sex	Underlying disease	Anti TNF agent used/dose	Period to development of subacute thyroiditis
Cañas CA, et al (2009)	32	male	Rheumatoid arthritis	Etanercept 25mg/ twice a week	8 months
Vassilopoulos D, et al (2010)	50	female	Rheumatoid arthritis	Etanercept 50mg/ week	4 years
Yasuji I (2013)	24	female	Juvenile idiopathic arthritis	Etanercept 25mg/ week	5 years
André R, et al (2015)	47	male	Psöriatic arthritis	Infliximab/5mg/ kg/6 weeks	4 years
Kawashima J, et al (2015)	56	male	Crohn disease	Infliximab/5mg/ kg/ 15 days-*adalimumab	4 weeks
SenlisM,et al (2016)	50	female	Psöriaticarthiritis	Adalimumab/40 mg/15 days	10 months
Hella Z, et al (2017)	65	male	Rheumatoid arthritis	Etanercept/50mg/ week	5 years
Chiriac A, et al (2017)	54	female	Psöriasis	Adalimumab/40 mg/15 days	Not given
Present case	42	female	Ankylosing spondylitis	Adalimumab/40 mg/15 days	7 years

** adalimumab dose in not given but subacute thyroiditis is reported to recur after 3 injections*

The typical laboratory findings of subacute thyroiditis are suppressed thyroid-stimulating hormone (TSH), elevated CRP, and erythrocyte sedimentation rate (ESR). Our patient had similar laboratory findings (Table 1). Subacute thyroiditis is histopathologically characterized by granuloma formation, a T helper 1 mediated reaction (12). TNF-α plays an important role in granuloma formation and regulation of T cell functions. The net effect of anti-TNF agents on granulomatous processes is poorly defined and conflicting. With a favorable response, Infliximab had been tried in a granulomatous disease, sarcoidosis (13). On the contrary, etanercept induces granulomatous reactions in different tissues (14-16). Adalimumab is efficient in treating granulomatous diseases (17). However, this anti-TNF antibody is also implied in the paradoxical development of pulmonary sarcoidosis (18). Adalimumab is also associated with the development of granulomatous reaction in the skin in a patient with psoriatic arthritis and another with rheumatoid arthritis (19,20). The mechanism underlying the association between adalimumab and the onset of subacute thyroiditis remains unclear. Therefore, further studies are needed to elucidate the pathogenesis of subacute thyroiditis in anti-TNF treatment. Subacute thyroiditis may be associated with TNF inhibitors, and the physician might be aware of this condition.

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