Case Report / *Olgu Sunumu*

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Transverse Myelitis Following Diphtheria Tetanus Toxoids (Td) Vaccination: A Case Report

Difteri Tetanoz Toksoid (Td) Aşısından Sonra Gelişen Transvers Myelit: Olgu Sunumu

Serpil SAVAŞ, Füsun Zeynep AKÇAM*, Şadiye ÇİÇEK, Ayşegül TEKDUR, Ömer YILMAZ**

Süleyman Demirel University Faculty of Medicine, Physical Medicine and Rehabilitation Department, Isparta, Turkey

**Süleyman Demirel University Faculty of Medicine, Infectious Diseases and Clinical Microbiology Department, Isparta, Turkey*

***Süleyman Demirel University Faculty of Medicine, Radiology Department, Isparta, Turkey*

Summary

Transverse myelitis (TM) has rarely been reported in association with tetanus toxoid-containing vaccines. Here, we report a 46-year-old man presented with progressive paresthesias and weakness in his arms and legs following an intramuscular injection of adult-type diphtheria and tetanus toxoids (Td). This is the sixth reported case of TM following Td vaccination. Physicians must be aware of this rare but serious side effect when prescribing Td vaccine and postvaccinial TM must be kept in mind when making a differential diagnosis of TM.

Key Words: Tetanus toxoid vaccine, transverse myelitis, immunization

Özet

Transvers myelit (TM) tetanoz toksoidi içeren aşılardan sonra gelişen çok nadir bir komplikasyon olarak bildirilmiştir. Bu olgu sunumunda, erişkin tip Difteri Tetanoz Toksoid aşısı (Td) olduktan sonra kollarında ve bacaklarında progresif parestezi ve kas güçsüzlüğü gelişen kırk altı yaşında bir erkek hasta sunulmaktadır. Bu olgu literatürde Td aşısından sonra TM gelişen altıncı olgudur. Hekimler tetanoz aşısı reçete ederken bu nadir fakat ciddi yan etki konusunda uyanık olmalı; TM'in ayırıcı tanısı yapılırken aşıya bağlı gelişen TM akılda tutulmalıdır.

Anahtar Kelimeler: Tetanoz toksoid aşısı, transvers myelit, bağışıklama

Introduction

The contributions of vaccines to global improvements in public health cannot be questioned. The mechanism of action of the vaccines is to stimulate the immune system. However this process carries the risk of developing rare neurological adverse reactions associated with vaccination (1-4).

Transverse myelitis (TM) is an inflammatory disorder affecting the spinal cord at one or more segments (5). Clinical symptoms of TM usually develop over hours or days as muscle weakness and sensory disturbance below the level of the lesion, or sphincter dysfunction (6). TM following diphtheria and tetanus toxoids (Td) vaccines is very rare and only five cases have been reported before (7-11). Here, we report a new case of TM following administration of Td vaccine.

Case Report

A 46-year-old previously healthy farmer presented with a 6-month history of progressive paresthesias and weakness in his arms and legs. Six months prior to admission, he received an intramuscular injection of adult-type Td vaccine into his left deltoid muscle, due to a knife cut, at the same day. Two hours after vaccination, he felt bilateral tingling of the fingertips and toes, which progressed to involve to his arms and up to waist line in one month. He had no history of an antecedent medical illness, any drug usage, optic neuritis, previous radiation to the spine, thoracic or lumbar pain, sweating or fever during the past 6 months before vaccination. The tetanus prophylaxis was the second he had received since his routine childhood series. The previous injections had been

Address for Correspondence/Yazışma Adresi: Serpil Savaş MD, Süleyman Demirel University Faculty of Medicine, Physical Medicine and Rehabilitation Department, Isparta, Turkey Phone: +90 246 211 92 81 E-mail: serpilsavas@yahoo.com

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well tolerated. He was admitted to a local hospital. A thoracic and lumbar spine magnetic resonance imaging (MRI) without contrast was performed and no abnormality was detected. Brucella antibody test was performed in serum by standard tube agglutination method and the result was positive at 1/10 dilution. He was prescribed oral rifampin, doxycycline and ceftriaxone combination therapy for 1 year with the suspicion of neurobrucellosis. No cerebrospinal fluid (CSF) analysis was performed. Two months after vaccination, he felt weakness in his lower extremities. He was able to walk independently. Motor system assessment showed no paresis in the upper extremities but manual muscle testing in the lower extremities revealed grade 4 muscle strength in the key muscles and clonus. Sensory system examination showed bilateral hypoesthesia below the level of Th4. Deep tendon reflexes were normal in the upper and lower extremities. Position sense was normal and vibration sense was reduced in both lower extremities. Tibial nerve somatosensory evoked potentials (SEP) showed abnormal proprioception. MRI showed a longitudinally extensive hyperintense spinal cord lesion from the Th-2 to Th-7, as well as diffuse cord swelling on T2-weighted images (Figure 1 and 2). CSF analyses showed 20 cells, normal protein level of 40 mg/dL (15-45 mg/dL), normal glucose of 63 mg/mL (40-65 mg/dL), no oligoclonal band and no brucella antigens. CSF culture was negative for Brucellosis. Hepatitis B, A, C, HIV, ANA and Brucella agglutination tests and blood cultures were negative.

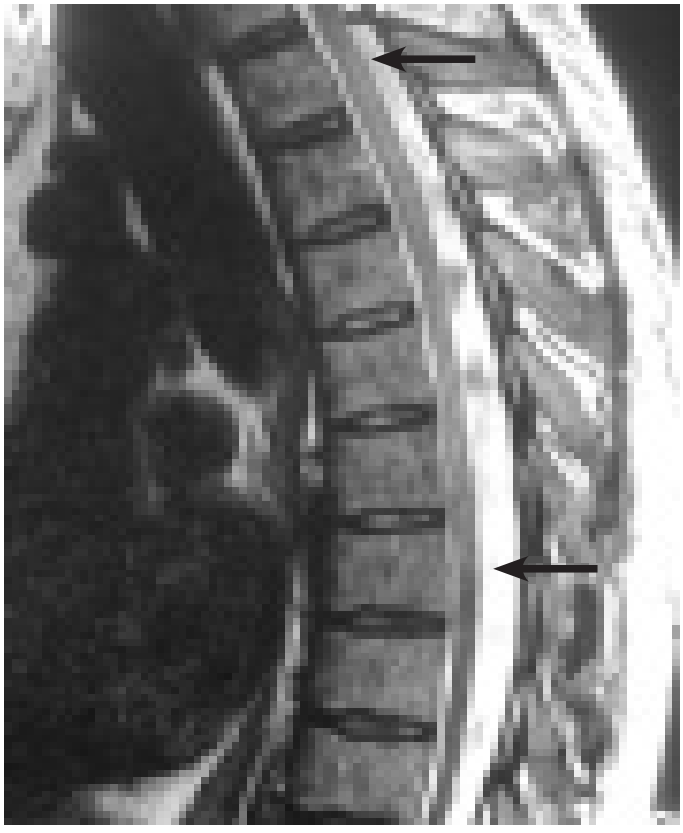

Figure 1. Sagittal T2-weighted image shows a swollen cord with hyperintense lesion beginning at the level of T-2 to T-7.

Serum B12 level was 635.7 pg/mL (191-663 pg/mL). He was diagnosed as having postvaccinial TM and was treated with intravenous methylprednisolone pulse therapy (1 g/day for 5 days). No improvement was obtained. Four months after vaccination, weakness in his lower extremities progressed and weakness appeared in his hands. He was unable to walk and sit without assistance. Manuel muscle testing in the lower extremities revealed grade 0 to grade 2 muscle strength in the key muscles. Finger abduction strength revealed grade 4 muscle strength. He had Ashworth grade 2 spasticity in his lower extremities. Urodynamic testing was normal. Repeated chest MRI showed no expansion of the lesion. Cranial MRI was normal. Intravenous methylprednisolone pulse therapy (1 g/day for 5 days) was repeated but no improvement was obtained in the patient's neurological and functional status. Our patient is now wheelchair-dependent and takes regular physical therapy.

Discussion

TM following vaccination with tetanus toxoid-containing vaccines is a very rare adverse event. Only five cases of TM following Td and diphtheria-tetanus-pertussis (DTP) as single vaccines or in various combinations have been reported before. One of those cases is TM following Td vaccination, one of them is TM following oral poliovirus-Dt-Haemophilus influenzae type b vaccination and three of them are TM following DTP vaccinations (6-10).

TM is a term used to describe inflammation of the spinal cord for a variety of causes such as demyelination (multiple sclerosis, neuromyelitis optica, acute disseminated encephalomyelitis, postvaccinial, idiopathic TM), autoimmune diseases (systemic lupus erythematosus, antiphospholipid antibody syndrome, and Sjögren's syndrome), infection (viral, bacterial, parasitic),

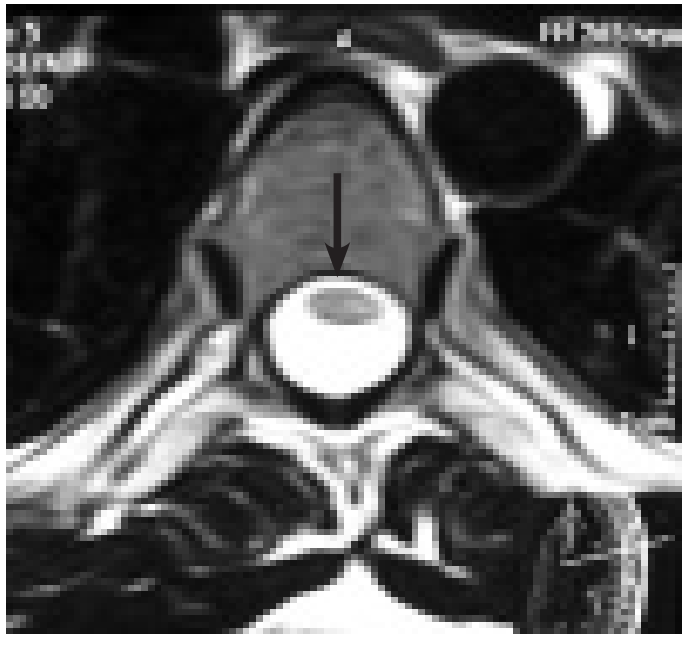

Figure 2. Axial T2-weighted image shows hyperintense lesion at the level of T-4.

intoxication (baclofen, penicillin, and lead), and vascular and neoplastic causes (2,5,12,13).

Our patient had no history of an antecedent medical illness, fever, rigor, sweating, diarrhea, optic neuritis, previous radiation to the spine, thoracal or lumbar pain which may be a potential cause of TM. He had a history of using antibiotics with the suspicion of neurobrucellosis just because brucellosis is endemic in our country. However, the diagnosis of neurobrucellosis requires satisfaction of the following criteria (14): 1) clinical features of the illness compatible with a known neurobrucellosis syndrome; 2) typical CSF changes (pleocytosis, elevated protein concentration); 3) positive results of either blood or bone marrow or CSF culture or appropriate serological tests (e.g., agglutination test titers of>1:160 in blood or any positive titer in CSF); 4) clinical improvement after starting an appropriate treatment; 5) inability to prove a more suitable alternative diagnosis. Our patient did not fulfill these criteria and neurobucellosis was excluded. A compressive cause of TM was excluded with thoracic and lumbar MRI and multiple sclerosis was excluded with cranial MRI and CSF analysis which revealed no abnormalities suggestive of multiple sclerosis. The lesion did not expand during the 7-month period, thus, a spinal tumor was less likely. Our case was not the classic presentation of acute idiopathic TM (ATM) either, because our patient's sensory dysfunction appeared very rapidly within 2 hours but progression of motor dysfunction continued during 7 months and this was too much longer than the progression period described in the diagnostic criteria of idiopathic ATM (6). We did not detect any other patient with slowly progressive ATM in the literature. The progression to nadir in the reported cases of TM following tetanus toxoid-containing vaccination is between 7 days and 17 days (3). The exclusion of cases from ATM diagnosis based on the interval between symptom onset and maximal deficit is arbitrary and is a limitation of the proposed criteria for acute TM (15). The clinical, laboratory and imaging results including MRI findings in our patient were consistent with the diagnosis of acute TM with mild pleocytosis (6,16).

We suspect that the tetanus portion of the vaccination produced TM in our patient because vaccination with tetanus toxoid has been mainly associated with neurological side effects such as recurrent episodes of Guillain-Barrè syndrome (GBS), brachial neuritis, peripheral neuropathy, encephalomyeloneuropathy and TM (17-22). Tetanus toxoid is generally combined with diphtheria toxoid and either whole-cell (DTP) or acellular (DTaP) pertussis vaccines. However, we cannot ignore that TM was secondary to the diphtheria portion of the vaccination.

Our patient had no improvement in his neurological function in spite of twice intravenous methylprednisolone pulse therapy. There is insufficient evidence to determine the utility of corticosteroids in alleviating TM attacks (23). Despite the lack of randomized controlled studies, administration of high-dose intravenous corticosteroid therapy (1 g daily for 3 to 7 days) should be started as early as possible in TM patients to hasten recovery and to improve the outcome (24).

Post-vaccination complications, especially neurological ones, although rare, are well described and include conditions such as autism, MS, Guillain-Barrè syndrome, giant cell arteritis, meningoencephalitis, peripheral neuropathy, isolated cranial nerve palsies, seizures, hypotonic-hyporesponsive episodes, and TM (25-28). The incidence of these neurological problems is so low, and the percentage of the people who receive common vaccinations is so high that it is very difficult to determine if vaccinations are the cause of these rare events. Up to 50% of patients with TM have a preceding infection. It is reasonable to assume that as infectious agents can induce autoimmunity, so can the recombinant or live attenuated antigens or toxins used for vaccination (3). In addition to the infectious antigen, adjuvants which vaccines contain such as aluminum salt may be responsible for the autoimmunity and neurological deficits (3,29). Td vaccine our patient received includes aluminum phosphate.

The first lumbar and thoracic MRI in our patient showed no abnormality. MRI is the modality of choice for the diagnosis of TM; it shows signal abnormalities, usually T2 hyperintensity, focal or extensive, gadolinium enhancement and sometimes cord swelling. Despite this high sensitivity, about 40% of acute TMs remain undemonstrated as in our patient (30).

In conclusion, physicians must be aware of this rare but serious side effect when prescribing Td vaccination and postvaccination TM must be kept in mind when making the differential diagnosis of TM. Although it is impossible to identify those who may eventually develop neurological complications, it is important to identify early signs of an untoward reaction for early and proper treatment. In addition, the benefit/risk relationship of anti-tetanus vaccination must be carefully evaluated.

Conflict of Interest
Authors reported no conflicts of interest.

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