

Obsessive Compulsive Disorder and Multiple Sclerosis: Three Cases

Rabia Bilici¹, Nuray Türksoy Karalı², Nevin Sütlaş³, Demet Kuşçu³, Rıdvan Bilici⁴

ÖZET:

Obsesif kompulsif bozukluk ve multipl skleroz: Üç olgu

Obsesif kompulsif bozukluk (OKB) ile ilgili çok sayıda çalışma bulunmasına rağmen patogenezi ile ilgili az şey bilinmektedir. Son yıllarda immünolojik mekanizmalar ileri sürülmüştür. OKB, streptokok enfeksiyonları ile ilişkilendirilen tikler, hareket bozuklukları, emosyonel labilite ve obsesif kompulsif davranışlardan oluşan pediatrik otoimmün nöropsikiyatrik sendrom (PANDAS) kapsamında tanımlanmıştır. OKB ve otoimmün hastalıklar arasındaki ilişki yeni bir araştırma alanı oluşturacaktır. Bu nedenle, otoimmün hastalıkların bir prototipi olan multipl skleroz (MS) ile OKB birlikteliği dikkate değerdir. Bu bildiride MS ile birlikte görülen üç OKB olgusu ilgili yazın bağlamında tartışılmıştır. Tüm hastalarda OKB, MS'den önce başlamıştır. Hastalarda streptokok enfeksiyonu, tik veya hareket bozukluğu öyküsü yoktu ve immünoterapi süresince OKB belirtilerinde düzelme tanımlanmıyordu.

Anahtar sözcükler: Obsesif kompulsif bozukluk, multipl skleroz, otoimmün hastalık, PANDAS

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ABSTRACT:

Obsessive compulsive disorder and multiple sclerosis: three cases

Despite the presence of a large body of studies, little is known about the pathogenesis of obsessive compulsive disorder (OCD). Immunological mechanisms have been suggested in recent years. OCD has been described in the context of the pediatric autoimmune neuropsychiatric syndrome (PANDAS), characterized by tics, dyskinesia, emotional lability and obsessive-compulsive behaviors, associated with streptococcal infections. The association of OCD with autoimmune diseases promises to constitute a new research area. Thus, comorbidity of OCD with a prototypic autoimmune disease, multiple sclerosis (MS), would be notable. In this report we present three OCD cases with comorbid MS and discuss our cases in the light of relevant literature. Obsessive Compulsive Disorder preceded MS in all patients. The patients reported no streptococcal infection, tic disorder or movement disorder history and had no improvement of OCD during immunotherapy.

Key words: Obsessive-compulsive disorder, multiple sclerosis, autoimmune disease, PANDAS

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¹Uzm. Dr., Psikiyatri Uzmanı, Elazığ Ruh Sağlığı ve Hastalıkları Hastanesi, Elazığ-Türkiye, ²Doç. Dr., Psikiyatri Doçenti, Simurğ Psikiyatri Psikoterapi Merkezi, Nişantaşı, İstanbul-Türkiye, ³Uzm. Dr., Nöroloji Uzmanı, Bakırköy Ruh Sağlığı ve Hastalıkları Hastanesi, İstanbul-Türkiye, ⁴Uzm. Dr., Nöroloji Uzmanı, Özel Doğu Anadolu Hastanesi, Elazığ-Türkiye

Yazışma Adresi / Address reprint requests to: Uzm. Dr., Rabia Bilici, Elazığ Ruh Sağlığı ve Hastalıkları Hastanesi, Elazığ-Türkiye

Elektronik posta adresi / E-mail address: rabiabilici@hotmail.com

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INTRODUCTION

Obsessive compulsive disorder is a prevalent chronic psychiatric disorder. Although the findings as to basal ganglia, cingulate gyrus, and orbitofrontal cortex involvement have been reported in certain functional brain-imaging studies conducted for neuroanatomical localization of the disease, little is known about the pathogenesis (1). Immunological mechanisms have been suggested in recent years. Existence of antineural antibodies blocking the brain serotonin receptors in conjunction with the antibodies to somatostatin and prodynorphin that act as neuromediators in the basal ganglia indicates the autoimmune mechanisms in the etiology of the disease (2,3). Detection of monoclonal D8/17 antibodies associated with B cells in many early-onset OCD cases has increasingly drawn attention to the

immunological mechanisms (4,5).

Multiple sclerosis is a disease characterized by inflammatory demyelination that affects the myelin sheath in the central nervous system due to autoimmune reactions caused by interaction of genetic and environmental factors. Evidence supports activated CD4+ myelin-reactive T cells as major mediators of the disease. In addition, a renewed interest in the possible contribution of B cells to MS immunopathology has been sparked by nonhuman primate and MS pathological studies (6). Various psychiatric manifestations accompanying MS include emotional disorders, psychotic states, personality disturbances, and cognitive disorders (7,8).

Obsessive-compulsive symptoms are more prevalent in the presence of several neurological conditions, including Tourette's syndrome, postencephalitic parkinsonism, bilateral globus pallidus necrosis,

Huntington's disease, and Sydenham's chorea (9). There are only three case reports on MS and OCD comorbidity (10,11,12). Below we present three MS cases with OCD and discuss those in accordance with the relevant literature.

METHOD

Multiple sclerosis has been diagnosed by an experienced neurologist according to McDonald criteria (13) and OCD by a psychiatrist according to DSM-IV criteria (14). All cases completed the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; 15,16) and Symptom Check-List and the Hamilton Rating Scale for Depression (HRSD; 17).

CASE 1

24 years old single male, first developed obsessive-compulsive symptoms (contamination, symmetry/exactness and sexual obsessions, cleaning/ washing, repeating and checking compulsions) at age 12. The first MS episode revealed with numbness on the right at age 16 and the course was relapsing remitting. MS episodes occurred twice a year. The patient was given pulse steroid treatments eight times. Obsessive compulsive disorder was diagnosed at age 20 when he was referred to a psychiatrist by his neurologist. The chronic, progressive OCD partly responded to serotonin reuptake inhibitors. Following MS diagnosis, aggressive and religious obsessions were added on the picture. His current obsessions are fear of speaking obscene words, causing harm to others, being responsible for things going wrong, being disrespectful to sacred things, infecting others with MS and thinking about forbidden and perverted sexual acts and that his foot might be amputated if he doesn't walk in a straight line. His current compulsions are checking doors and locks (Y-BOCS score: 27). He had a good insight for OCD and had no depressive disorder (HDRS: 13). Cranial magnetic resonance imaging (MRI) done six years ago revealed bilateral lesions compatible with MS plaques settled along the subcortical deep white matter of the frontal lobes. The patient has been receiving interferon beta 1a and serotonin reuptake inhibitor treatment for a year. There is no improvement in obsessive compulsive symptoms in the last year.

CASE 2

31 years old single female, first developed OC symptoms (contamination and symmetry/exactness obsessions, cleaning/washing, checking, counting and ordering/arranging compulsions) at age 13. The course of OCD is chronic progressive. Neurological symptoms began at age 16 with blurred sight and inability to walk and she was diagnosed with MS. In the psychiatric evaluation at the same time, euphoria and emotional lability were observed. In 12 years, eight MS episodes occurred and she was given pulse steroid (methyl prednisolone) treatment in every episode. With diagnosis of secondary progressive MS, she has been treated with interferon beta 1a for four years and MS episodes have been prevented with this treatment. Her current obsessions include concerning or being disgusted with bodily wastes/ secretions, dirt and viscid substances. She has a need for symmetry, order and exactness. She is preoccupied with unlucky numbers. Her current compulsions are excessive hand washing, ritualized tooth brushing, cleaning the house excessively, checking doors and locks, counting, excessive list making, hoarding (Y-BOCS score: 31). During interferon treatment she reported no change in OCD. She had poor insight for OCD and did not accept the treatment. She had no depressive disorder (HDRS: 0). Cranial MRI of the patient one year ago revealed bilateral lesions compatible with active MS plaques in the cerebral hemispheres' deep and subcortical white matter. These lesions, particularly the white matter, neighboring the cingulate gyrus were contrasting with the hyperintense signal pattern, in the T2-weighted sections.

CASE 3

49 years old, married male. Obsessive-compulsive symptoms began when he was 20 years old, with obsessions such as fears of speaking obscene or insulting words, being disgusted with viscid substances, and being concerned for symmetry/exactness. He expressed no compulsions. The patient's symptoms were chronic and progressive. First neurological sign was a clumsy and imbalanced right hand when he was 29. The patient has received pulse steroid (methyl prednisolone) treatments seven times with the diagnosis of relapsing remitting MS

for 20 years. There was no change in OCD during the course of pulse steroid treatment. The content and severity of his OCD symptoms have not changed until now (YBOCS:13). The patient has a perfect insight for OCD. He also has comorbid major depressive disorder (HDRS: 20). A cranial MR analysis done a year ago revealed bilateral lesions seen as multiple demyelinating plaque in the centrum semiovale deep periventricular sublenticular background.

DISCUSSION

In the late 1980s Murphy and colleagues reported an increase of OCD symptoms in patients with Sydenham chorea (18). Later on, a subset of OCD has been proposed in the form of pediatric autoimmune neuropsychiatric syndrome (PANDAS) that is characterized by the tics, dyskinesia, emotional lability and obsessive-compulsive behaviors associated with streptococcal infections (19). There are many publications reporting that OCD symptoms appeared following the streptococcal infection in childhood (19,20,21,22). Studies suggest that antineuronal antibodies created following group A beta hemolytic streptococcal (GABHS) infection cross-react with basal ganglia neurons (23,24). This autoimmune reaction may disrupt the basal ganglia-thalamocortical circuit and generate obsessive-compulsive symptoms (23).

Poststreptococcal OCD similar to the syndrome previously identified in children may also occur in adults. There are two case reports about the adult onset poststreptococcal OCD (25,26). These cases also have tic disorder and/or choreiform movements. In our cases there is no streptococcal infection and movement disorder history prior to OCD and OCD symptoms in all of them occurred prior to MS (3-14 years). Cases 1 and 2 have early-onset OCD (ages 12 and 13, respectively) while the disorder is adult-onset (age 20) in case 3. It has been reported that some of the patients with early-onset, streptococcal related OCD may improve through plasmapheresis and immunotherapy, which may be associated with the decrease in antineuronal antibody titers. Though this may be a placebo effect (2). In our cases, however, OCD symptoms remained unchanged during the immuno-suppressive therapy (interferon Ia, methylprednisolone). Hanna et al. (1996) argued that in early-onset OCD, brain serotonin receptor antibodies

played an active role in the pathogenesis. It is postulated that they may induce an immune assault to serotonergic neurons in basal ganglia, the most consistently affected brain region in OCD (27). In this double-blind study, no serotonin receptor antibodies were found in the patients treated with serotonergic antidepressants, while in the patients with no treatment the antibody levels were high. Serotonergic antidepressants commonly used to treat OCD may suppress the autoimmune reaction (27).

Somatostatin and opioid peptides have regulatory influence on serotonergic nuclei of the median raphe (28,29) that send inhibitory projections to basal ganglia (30,31,32). In a study about autoimmune pathogenesis, the antibodies developed against somatostatin and opioid peptides were found in high amounts in OCD and it was suggested that these peptides, which were decreased in the striatum, might increase the disposition to OCD and dyskinesia (3). Genes involved in immune response therefore represent possible candidate genes for OCD, including the myelin oligodendrocyte glycoprotein (MOG) gene, which plays an important role in mediating the complement cascade in the immune system. A study by Zai et al (2004) showed an association between markers in myelin oligodendrocyte glycoprotein (MOG) gene and OCD. The authors found significant association between Y-BOCS severity score and MOG4 polymorphism. It is interesting that although limited, there is some data about the involvement of MOG gene in the pathology of MS (33,34,35).

Another contribution to the immunopathological mechanisms in OCD was made by Hansen and Bershow (1997) who found isolated immunoglobulin A deficiency in a sample of pediatric OCD patients (36). In a recent study by Dinn et al (2001) it was noted that there were more clinical symptoms of Ig A deficiency in adult OCD patients compared to other anxiety disorders and dysthymic patient groups (23).

Multiple sclerosis and OCD could co-exist coincidentally, but the possibility of coincidence should be rare due to the fact that the OCD prevalence is 2 to 3%, while the MS prevalence is 30 to 80 in 100000 (11). In three cases reported in 1995, Miguel et al argued that the coincidence might be explained with the possible demyelinating plaque sequelae in the critical locations (orbitofrontal cortex, striatum, thalamus and anterior cingulate cortex) in the central nervous system. On the

cranial MR images of two of our cases, the demyelinating plaques are compatible with the above mentioned localizations (case 2?: white substance neighboring gyrus cingulatum; case 2?: sublenticular white substance). Similar to the previously reported patients (10,11) OCD symptoms in all our cases have occurred prior to MS (3-14 years). Given the prevalences of OCD and MS, those three cases may be coincidental. However, regardless of

this possibility, we feel that cases having both OCD and MS may contribute further understanding of OCD.

To date, we are not aware of any studies investigating the relationship between OCD and MS, which may make a significant contribution in terms of both providing insight to the etiopathogenesis of the disorder and paving the way for new therapeutic approaches to the cases refractory to conventional treatments.

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