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LETTER TO THE EDITOR

Successful management of lamotrigine-associated skin rashes in an adolescent girl with autism and bipolar disorder

Otizm ve bipolar bozukluğu olan bir ergen kızda lamotrijin ilişkili deri döküntülerinin başarılı yönetimi

Zeynep Kübra Göksu[1], Ali Karayağmurlu[2]

[1]İstanbul Esnaf Hastanesi, İstanbul, Türkiye
[2]İstanbul Üniversitesi, İstanbul, Türkiye

To the Editor,

Lamotrigine is a new-generation antiepileptic drug that blocks voltage-sensitive sodium channels and inhibits the release of excitatory neurotransmitters such as glutamate and aspartate[1,2]. It is used as a mood stabilizer in the treatment of bipolar disorder, as well as in the treatment of unipolar depression, schizophrenia, substance use disorder and post-traumatic stress disorder in children and adolescents[2]. It acts by inhibiting sodium and calcium channels in the presynaptic neuron and stabilizing the neuron membrane[2]. However, side effects such as gastrointestinal symptoms, sleep disorders, thrombocytopenia, leukopenia, increased transaminase levels, interstitial nephritis, diplopia and worsening tics may be encountered during its use[2]. Skin rashes are another such side-effects. There usually present as maculopapular and erythematous rashes after dose increase and within the first six weeks. However, they improve rapidly after drug withdrawal[2]. In addition to benign rashes, severe skin rashes such as Stevens-Johnson Syndrome with high morbidity and mortality levels may also develop[2].

Autism spectrum disorder (ASD) is a childhood-onset neurodevelopmental disorder characterized by deficits in social communication and interaction, repetitive behaviors and restricted interests. Bipolar disorder (BD) is a severe affective condition characterized by recurrent-periodic mood episodes. The reported prevalence of BD in individuals with ASD may be as high as 5-7%[3]. Compared to the general pediatric population, earlier onset of BD symptoms has been reported in patients with ASD[3]. These symptoms are frequently accompanied by depressed mood, a decline in social skills and impaired functioning[4]. Additionally, it may be difficult to diagnose BD comorbidity in individuals with ASD; for example, poor verbal communication skills, hinder the recognition of intrinsic symptoms and the symptoms of one condition may overlap or overshadow the other.[4].

Lamotrigine is frequently used in the adult population. More case reports of lamotrigine-related side- effects in adults have therefore been published. Few reports have addressed the use of lamotrigine as a mood stabilizer in children and adolescents with ASD and even fewer have reported its use in co-existent ASD and BD[5]. This article describes a case of an 18-year-old girl with ASD and BD who developed skin rashes with lamotrigine therapy. This paper may make a significant contribution to the current literature due to the scarcity of studies of the association of ASD and BD, the fact that lamotrigine is rarely used for children and adolescents, and that individuals with ASD, a special population, are more sensitive to drug-related side-effects.

S.K., an 18-year-old girl, had been diagnosed with ASD according to DSM-IV TR since the age of three years. She exhibited social deficits, echolalia, stereotypical movements, insistence on sameness and

Address for Correspondence: Zeynep Kübra Göksu, İstanbul Esnaf Hastanesi Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları Anabilim Dalı, İstanbul, Turkey E-mail: zeynepbingol@istanbul.edu.tr
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sensory hypersensitivity. On the basis of her history, a hypomanic period was determined due to symptoms of decreased sleep, increased libido, irritability, psychomotor agitation, and increased speech and self-confidence commenced two months previously. Her history also revealed that she experienced two hypomanic mood episodes and two depressive mood episodes in 2011-2022, with BD type II being diagnosed. At mental state examination, her mood was irritable and affect was correlated with mood. Her Young Mania Rating Scale score was 28 and her Hamilton Depression Scale score was 10. Her olanzapine dosage was gradually increased from 15 mg/day to 30 mg/day due to the comorbidity of ASD and BD exacerbating the current situation, the persistence deterioration in functionality and the presence of intense aggression that resulted in her breaking her his mother's finger one week previously. Her Clinical Global Impressions-Severity rating score decreased from 6 to 4 following the dose increase. It was planned to add a mood stabilizer to the treatment because of the recurrent mood episodes in the patient's medical history. Valproic acid therapy was initiated. However, this was discontinued due to the development of an allergic reaction involving swelling in the head and neck region. Lithium therapy was subsequently initiated but was terminated due to significant nausea-vomiting and intolerance. It was planned to switch to lamotrigine as a mood stabilizer. Lamotrigine was gradually increased by 12.5 mg/day every three days. Erythematous-acneiform eruptions accompanied by scattered papules-pustules emerged on the patient's face on the 10th day of treatment, when the dosage was raised from 37.5 mg/day to 50 mg/day. The dermatology department was consulted, the dermatologist recommending discontinuation of lamotrigine. Regression of the skin rashes was observed one week after discontinuation. No additional dermatological treatment was required. Monthly follow-ups were planned with olanzapine therapy at 30 mg/day. Written and verbal consent to the publication of this case was recieved from the parents.

This report describes the management of an 18-year-old adolescent diagnosed with ASD and BD-II who developed erythematous-acneiform eruptions during lamotrigine therapy. Lamotrigine is used as a mood stabilizer in adult patients with BD[2]. Benign and malignant skin rashes have both been encountered during its use[2]. In the case of a 23-year-old man diagnosed with BD, lamotrigine was initiated at 25 mg/day and gradually increased to 400 mg/day during maintenance treatment. Acneiform eruptions appeared on the patient's shoulders and back, other medications being discontinued within one month. Lamotrigine therapy was terminated and the skin rashes regressed[6]. Similarly, a nine-year-old girl with focal epilepsy was started on 12.5 mg/day lamotrigine therapy. A pruritic rash appeared on her inner thigh within 10 days. This regressed following discontinuation of lamotrigine[7]. The appearance of the rash within the first days of lamotrigine therapy, the mild severity and regression following discontinuation of the treatment are similar features between these reports and the present case. However, the present case differed from those two reports in terms of, the coexistence of ASD and BD-II and the presence of rashes on the face. The side-effect that occurred in the present case was evaluated using the Naranjo Adverse Drug Reaction Probability Scale (NADRPS). The NADRPS score of 8 (probable) was determined due to the side-effect emerging after the drug dosage had been increased, its regression after the drug was discontinued, the presence of similar case reports in the literature and objective evaluation of the side-effect.

Lamotrigine is less frequently used as a mood stabilizer in the treatment of BD in children and adolescents than in adults[5]. Rashes emerging as a side-effect, are generally benign, although severe side-effects such as Stevens Johnson Syndrome may also be seen[8]. In the present case, the possibility of malignancy was considered because the rashes appeared in the head and neck region, tended to coalesce and were mildly painful. However, they were regarded as benign because of the absence of systemic symptoms, intact blood values, and the absence of additional treatment and hospitalization requirements for side-effects[9]. Since children and adolescents with ASD are more susceptible to drug side-effects when lamotrigine is used as a mood stabilizer, families should be informed prior to treatment about the emergence rashes as a potential side-effect and should be instructed to monitor patients closely. If a lamotrigine-induced skin rash is detected, clinicians should consult the dermatology department for differentiation between benign and malignant rashes and for management of the rash. Further studies regarding the use of lamotrigine as a mood stabilizer for children and adolescents are now needed.

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