Clarithromycin induced psychotic disorder with catatonic-like features in an adolescent girl: Case report

Bir kız ergende Klaritromisin kullanımında katatoni-benzeri belirtiler ile kendini gösteren psikotik bozukluk: Olgu sunumu

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SUMMARY

Delusions and/or hallucinations developed during exposure to a medication are diagnosed medication induced psychotic disorder. Antibiotic-induced psychotic disorder have been well documented among adults. The etiology is not clear, clinical presentation is variable and catatonia-like symptoms can be seen. The prognosis is good, the symptoms decrease with the discontination of the drug, and long-term treatment is often not required. In this case, 16-year-old girl who presented with acute catatonia-like symptoms will be described. Family history of clarithromycin-induced behaviour changes accelerated the diagnosis process. Medication induced psychotic disorder should be thought in differential diagnosis of young people with acute psyhotic symptoms.

Keywords: Psychosis, clarithromycin, catatonia, adolescent

ÖZET

Sanrı ve/veya varsanılar ilaç kullanımı sırasında ortaya çıktığında ilaçla indüklenen psikotik bozukluk tanısı konulmaktadır. Antibiyotik kullanımı sırasında psikotik belirtilerin görülebileceği erişkinlerde bilinmektedir. Bu durumun etiyolojisi belli değildir; klinik görünümü değişkendir, katatoni benzeri belirtiler de olabilir. Uzun süreli tedavi çoğu zaman gerekmez, belirtiler ilaç kesilince ortadan kalkar. Bu olgu sunumunda klaritromisin kullanımı sırasında katatoni benzeri akut psikotik belirtilerle başvuran kız ergen tartışılacaktır. Olgunun kuzeninde klaritromisin kullanımı sırasında benzer belirtiler olduğunun öğrenilmesi tanı koyma sürecini hızlandırmıştır. Gençlerde katatoni dahil her türlü akut psikotik belirtide ayırıcı tanıda ilaçla indüklenen psikotik bozukluk düşünülerek kullanılan ilaçlar sorgulanmalıdır.

Anahtar Kelimeler: Psikoz, klaritromisin, katatoni, ergen

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INTRODUCTION

Clarithromycin is a semi-synthetic macrolide that used frequently in the treatment of bacterial infection. Although, gastrointestinal system adverse effects are common, neuropsychiatric adverse effects can not be ignored, especially among adults (1). Here we described acute psychotic symptoms with catatonic-like features attributed to medication in an adolescent girl.

CASE

A 16-years-old girl was brought to Emergency Department at night because of intense fear from being taken by devils. She was using 1000 mg/day oral clarithromycin for 5 days because of tonsillitis. That day, she also took another medicine that contained 60 mg pseudoephedrine and 2.5 mg desloratadine because of common cold and itchy rashes on her legs. No other behavioral changes were mentioned by the family, except sleeping less since the beginning of clarithromycin treatment. The mother told that nearly two hours after the night dose, the girl was staring in her room for nearly one and a half hours without talking or moving, then suddenly started to run to a woodland 200 m away from the house. The family said that she refused to come back because of her belief that her father was a devil. Police was called and an ambulance brought her to the hospital.

During the examination, she was very agitated, not compatible, refused to talk and consistently saying "Go away devils. I will not give you my soul." She seemed disoriented to time, place and person. Neurological examination was normal, vital signs and laboratory tests were within normal range. Neither her nor any family member had a psychiatric history. However, the family blamed clarithromycin because some behavior changes were seen in one of her cousin due to clarithromycin in the past. Haloperidol 5 mg im was given. Her symptoms were gradually improved, and approximately half an hour later she was normal except not recalling what had happened and how she arrived at hospital. She remained eight hours in emergency department. Clarithromycin was stopped, and no other medication was given. After a week from discharge, the family said that she was completely normal during the whole week but she refused to come to hospital because of Covid-19 pandemic and her prejudice towards psychiatry. So she was talked via telephone. Her orientation, speech, thought process and content seemed normal. It has been nearly one and a half year, and she still has no any psychiatric symptoms. Informed consent was obtained from the patient and the patient's parents.

DISCUSSION

In DSM-5, diagnostic criteria of substance/medication-induced psychotic disorder are delusions and/or hallucinations developed during or soon after exposure to a medication. Delirium, withdrawal or intoxication should be excluded (2). Hoigne syndrome is firstly referred to pseudo-anaphylactic reactions characterised by acute psychological and neurological manifestations after procaine penicillin injection (3). This phenomenon has also been named as antibiomania (4). However, these features may occur after some other medications (3). Neuropsychological side effects seem mostly during clarithromycin treatment, though it is considered as safe and effective (5). Albeit the etiology has not been detected, direct effect of antibiotics on neurotransmitters or indirect effect via cytokines are some hypothesis. For clarithromycin, GABA-A antagonism and drug interactions via CYP3A4 inhibition have been proposed (1).

Antibiotic-induced psychiatric reactions have been well documented among adults (1), but few cases of neuropsychological side effects have been reported among children. A 18-year-old teenager was the first pediatric case of antibiotic-induced psychosis, whose acute psychosis symptoms after anesthesia were resolved with the discontinuation of clarithromycin and/or amoxicillin (6). Hypomania, mania, visual hallucinations were described among children during clarithromycin treatment. (Table 1)

In this case, the vital symptoms were within normal range, so as the neurological examination. The dose of pseudoephedrine was within normal range, as the neuropsychiatric adverse effects mostly seen in overmedication (12). There was no drug interac-

Table 1. Clarithromycin-induced psychiatric symptoms among children

Age, Gender,	Diagnosis for treatment	Dosage	Time to psychiatric symptoms	Psychiatric symptoms	Other drugs	History of any disorder	Family history of psyhiatric disorder
18 y, Boy	For H.pylori infection, started after cholecystectomi operation	1000 mg/day	Two days	Acute pyshcosis (Anxiety, insomnia, delusional thoughts, fear)	Amoxicillin	No	No
12 y, Boy	Pneumonia	500 mg/day	After first dose	Mania	No	No	No
6 y, Girl	Acute sinusitis	15mg/kg bid	After second dose	Visual hallucinations (animals)	No	No	No
7 y, Boy	Acute otitis media		After five days	Visual hallucinations (spiders)	No	No	No
3 y, Boy	Pneumonia	15 mg/kg	After second dose	Hypomania (psychomotor agitation, pressured speech, irritability, agrresive behavior, insomnia)	No	No	No
16 y, Girl	Upper respiratory tract infection	500 mg/day (for 13 days)	After 7 days	Mania	Inhaled steroid	Asthma	No
4 y, Girl	Respiratory drug infection	20 mg/kg (250 mg morning, 125 mg evening)	Shortly after the second dose	Visual hallucinations (snakes), fear	No	Multiple allergies	No

tion between pseudoephedrine and clarithromycin (13). Desloratadine is a non-sedating antihistamine which penetrates less to central nervous system and acts especially on H1-receptors. Psychosis is not expected as an adverse effect of desloratadine (14). The familial risk of clarithromycin-induced behavioral changes in this case should also be taken into consider. Therefore clarithromycin-induced psychosis is most likely.

Clarithromycin-related psychiatric symptoms are acute, while the prognosis is excellent. The symptoms seem to be age-related as fears and hallucinations, especially concerning animals, are seen among children (8,11) while psychosis and mania are seen among youths (15,16). Duration of symptoms are variable, in most cases withdrawal of clarithromycin was enough (6,8,9,11), while olanzapine was needed in one case (7) and risperidone with valproat were needed in another (10). Haloperidol had been used for acute agitation in a clarithromycin-induced psychotic state (16). Although the examination of the case was compatible only with psychosis, the sudden onset of marked agitation after unresponsiveness (might be considered as stupor and mutism) could be defined as unspecified catatonia. In DSM-5, unspecified catatonia is diagnosed when symptoms cause significant impairment even though full criteria of catatonia are not met and/or underlying medical condition is unclear. No duration has been mentioned (2). The category of unspecified catatonia is believed to increase early identification and appropriate treatment of pediatric catatonia (17). Since GABA-A agonists seem to alleviate catatonic symptoms (18), clarithromycin can cause catatonia via GABA-A antagonism.

Psychosis itself is still a mystery, that both diagnosis of substance/medication-induced psychotic disorder and unspecified catatonia in DSM-5 are open to discussion with unclear borders. Any presentation of neuropsychiatric symptoms, including catatonia, can be seen during many medications. Some of the questions that come to mind are; what are the differences between substance/medication-induced psychotic disorder and other psychotic disorders, what makes these children vulnerable to psychosis even without any family history of psychiatric disorder?, does this reaction be an indicator of an elevated risk for any psychiatric disorder during the whole life?, do all the medications lead to psychiatric symptoms via the same mechanisms? The studies that referred these questions are spare (19), because of many factors like heterogenity and short duration of clinical presentation. As the manifesta-

tion of psychiatric symptoms are different among children, it is even more difficult to identify and distinguish psychiatric symptoms during medications. Acute psychotic symptoms are not common among young children, and drugs should be thought in differential diagnosis. Since early discontinuation of clarithromycin may result in quick recovery of neuropsychiatric side effects, it is important for clinicians to be aware of them during treatment.

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