Acute Dystonic Reaction Associated with Cefuroxime Axetil in a Child
Running Title: Acute Dystonic Reaction

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Abstract
Dystonia is an extrapyramidal motor function disorder characterized by intermittent spasmic or sustained involuntary muscle contractions of the face, neck, trunk, pelvis and extremities causing repetitive movements and postural abnormalities. A 10-year-old male child was presented to the emergency department with complaint of regular rhythmic spasms on the head. He was diagnosed as dystonic reaction induced by cefuroxime axetil. After cessation of the therapy and administration of 2.5 mg of biperiden intravenously, the spasms were stopped. Our aim is to make up an awareness of this adverse drug reaction when prescribing such antibiotic in children.

Keywords: Child; Cefuroxime axetil; Dyskinesia, Drug-induced; dystonia

Introduction
Dystonia is an extrapyramidal motor function disorder characterized by intermittent spasmic or sustained involuntary muscle contractions of the face, neck, trunk, pelvis and extremities causing repetitive movements and postural abnormalities [1,2]. The abnormal posture may induce significant anxiety and distress for the patient and relatives. In adults, the head and neck muscles are the most frequently involved [3,4]. If muscles of pharynx and larynx are affected life-threatening events may also occur [5,6]. Although dystonia is mostly seen as an adverse drug reaction, risk factors include young age, male gender, history of acute dystonic reaction and cocaine use [2]. Prevalence varies according to individual tendency, type and dosage of drug and duration of exposure [3]. Herein we present a case of dystonic reaction in a child associated with the use of cefuroxime axetil and make up an awareness of this adverse drug reaction when prescribing such antibiotic in children. To our knowledge, this is the first cefuroxime axetil-related dystonic reaction in the literature.

Case Report
A 10-year-old male child was presented to the emergency department with complaint of regular rhythmic spasms on the head. He had been using N-acetyl cysteine and ibuprofen since five days for his non-productive cough. As he did not have any improvement, his family physician added cefuroxime axetil to his therapy one day ago. He had the first dose of the drug in the morning. Almost one hour later, his family observed regular rhythmic spasms on his head. At presentation, he was conscious, cooperative and oriented but anxious. His speech was normal. His pupils were isochoric (3 mm/3 mm), direct and indirect light reactions were normal but eye movements could not be evaluated due to abnormal posture. He did not have any motor function loss nor rigidity and muscle tonus was normal. Deep tendon reflexes were normoactive on four extremities. Plantar responses were bilaterally flexor. Sensory and cerebellar examinations were normal. Extrapyramidal system examination revealed torticollis and oculogyric crisis. The rest of the systemic examination was unremarkable. His laboratory findings were: WBC, 13.6 K/ul; Hemoglobin, 12.4 gr/dl; platelet, 509 K/ul; liver and renal function tests and electrolytes were normal. He was thought to have medication-induced dystonic reaction because of lack of previous history of such symptoms and acute onset of symptoms. His drugs were stopped and 2.5 mg biperiden was given intravenously over 15 minutes. His symptoms were dramatically relieved within 10 minutes. After four hours of follow-up period the patient was discharged. He was symptom free and there was no recurrence on follow-up examination after three days.

Discussion
Acute dystonic reactions are most commonly seen secondary to medications. Many drugs (antipsychotics, antidepressants, antiemetics, antihistaminics, chemotherapeutics, and antitussives) may cause dystonic reaction even in therapeutic doses [5-7,11]. Most common mechanism of dystonic reaction is alteration of dopaminergic-cholinergic balance on nigrostriatal neurons by drugs [3,12]. Many drugs block D2 receptors on basal ganglia resulting in increased cholinergic effect. Although strong D2 receptor antagonists commonly cause acute dystonic reaction, drugs that balance D2 receptor and M1 muscarinic receptor blockade less frequently cause dystonia. Paradoxically, another reason for dystonic reaction is the increased dopaminergic activity due to compensatory dopamine release from presynaptic terminals in response to blockade of postsynaptic dopamine receptors, and upregulation or increased sensitivity of postsynaptic receptors in response to diminished quantities of dopamine [2,12,13]. In the literature some drugs such as albendazole, gemifloxacin rarely cause acute dystonic reaction with an unknown mechanism [14,15].

It occurs abruptly, usually one or two days following drug ingestion. If long acting drugs are taken, onset of symptoms may delay up to 5 days [4]. In this case, although the effects of drugs on dopaminergic system are not known, they caused extrapyramidal side effects. These reactions occur at head and neck region in adults and are more severe and generalized in children [3]. In our case, involvement of head and neck region differs from classical involvement. Clinical signs and symptoms vary between patients. Different signs and symptoms may occur according to the affected site. Most commonly seen signs are oculogyric and buccolingual crisis due to muscle contractions at head, neck and face, tics, grimacing, trismus and spasm of lips. If neck muscles are affected torticollis and retrocollis may be seen. If paravertebral muscles of the back are affected postural abnormalities such as scoliosis, opisthotonus and tortipelvis may be seen. Involvement

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of pharyngeal and laryngeal muscles may cause dysphagia, speech disturbance and cyanosis. In these life-threatening conditions early management is important [5,6].

Although acutely occurring dystonic reactions are commonly seen following drug intake, they may be misdiagnosed as meningitis, encephalitis, conversion disorder, hypocalcemia, food intoxication, seizure and tetanus [10,16].

In treatment of dystonic reactions, Anticholinergic agents (diphenhydramine or biperiden and benzodiazepines (diazepam) are used [4]. Rapid onset of symptoms, absence of underlying disease, any other drug than present medication and normal laboratory findings supports that dystonia in this patient results from present medication. Rapid relief of symptoms after therapy confirmed the diagnosis in this patient. In the literature search no report of dystonic reaction related to cefuroxime axetil was found.

In conclusion, adverse events related to drugs may be seen besides beneficial effects. Although acute dystonic reaction seems to be a side effect mainly associated with antipsychotics, antidepressants and antihistaminics, it should be in concern while prescribing commonly used antibiotics such as cefuroxime axetil in children. Detailed anamnesis including medications should be obtained in patient evaluation.

References