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CASE REPORT

Dopa-Responsive Dystonia subsequent to Lamotrigine Administration: Case Reports

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ABSTRACT

Epilepsy is a common neurologic disorder affecting approximately 1% of the population. The prevalence of active epilepsy in Kerman,Iran is 7.87/1000 individuals. The past decade has brought many advances to the treatment of epilepsy, including many new pharmacological agents. Lamotrigine is one of the new antiepileptic drugs. Lamotrigine has many side effects; the most important of which are allergic reactions. In this article, the author reports two cases of dopa- responsive dystonia (DRD) after few months administration of lamotrigine for epilepsy. The cases are two girls (4 and 5 years old) who had seizures and received lamotrigine 50 mg/day. They have been free of seizure after treatment but after some time the dystonic attacks developed. Lamotrigine administration discontinued, but dystonic attacks didn't disappear. Levodopa /carbidopa was started. After a few days, the dystonic pastures disappeared. In conclusion, lamotrigine may introduce dystonia in susceptible patients. These dystonic attacks might beresponsive to levodopa.

Keywords: ????

Epilepsy is a common neurologic disorder affecting about 1% of the population [1]. The prevalence of active epilepsy in Kerman,Iran is 7.87/1000 individuals [2]. Pharmacotherapy with antiepileptic drugs remains the major treatment modality for epilepsy. This could occur as a result of decreased excitation concurrent with increased inhibition [3]. Management of epilepsy differs from the treatment of other chronic diseases in that a single breakthrough event has a major negative effect on quality of life. Complete control of seizures is necessary as a single seizure impacts negatively on patient quality of life and independence [4].

The past decade has brought many advances to the treatment of epilepsy, including many new pharmacological agents. Lamotrigine is one of the new antiepileptic drugs; it's been used more than two decades [5-7]. Lamotrigine is a broad-spectrum antiepileptic drug of the phenyltriazine class chemically unrelated to other anticonvulsants [8]. Lamotrigine has an average elimination half-life of 33 hours, although this can be influenced by concomitant therapy with other medications such as valproic acid. It's predominantly metabolized in the liver by glucuronidation [9]. Lamotrigine has many side effects, most importantly allergic reactions. Gradual introducing lamotrigine is one of the keys to reduce the frequency and severity of allergic reactions [5]. Although the overall incidence of cutaneous reactions to lamotrigine is high, the incidence of serious eruptions such as erythema multiform, Stevens-Johnson syndrome, and toxic epidermal necrolysis is low [10,11]. The revision of La Roche and Helmers demonstrated that side-effects led to drug withdrawal in 10.2% of all patients under lamotrigine therapy. Rash was the main reason for treatment discontinuation. It has been postulated that side-effects may be lessened by slow introduction and titration [12,13].

The present study reports two cases of dopa-responsive dystonia (DRD) after lamotrigine administration for a few months due to epilepsy. DRD is a broad term used to described forms of dystonia characterized by the onset dystonia in early childhood

with dramatic and sustained response to treatment with levodopa. This disorder was first described by Segawa [14]. The most common form of DRD is an autosomal-dominant condition (DYST5) caused by mutation of the gene for guanosine triphosphate cyclohydolase [15].

CASE REPORTS

Case 1

A 5 years old girl who used lamotrigine 50 mg per day due to tonic-clonic seizure and had her first attack of seizure two months before her first visit. After starting lamotrigine, the patient was free from seizure for one year. Dystonic pasture was developed in lower limb and after a time spread to lumbar spine, and then to the cervical area. Dystonic attacks worsened later in the day. Results of physical examinations, brain's MRI scans and hematologic and serologic laboratory tests were normal. Dystonic pasture did not disappear after lamotrigine was discontinued. The dystonic attacks disappear after two days, when 50 mg per day levodopa/carbidopa wasstarted.

Case 2

A 4 years old girl used lamotrigine 50 mg per day due to complex partial seizure. She had had her first attack of seizure a few months before her first visit. After receiving lamotrigine for two months, dystonic pasture developed in lower limb and then spread to lumbar spine. Dystonic pasture worsened later in the day. Physical examinations, brain's MRI scans, hematologic and serologic laboratory tests were normal. Dystonic pasture did not disappear after lamotrigine discontinued. The dystonic attacks disappear after three days, when 50 mg per day levodopa/carbidopa was started.

DISCUSSION

DRDs are a group of disorders that show a good response to levodopa. The causes of these disorders are unknown, but the mutation of a gene is recognized in some studies. Onset of this disease usually happens in the first decade of life starting with foot dystonia, which progress to involve other body parts, but typically remains more sever in the lower extremities. The severity increases progressively over the first two decades of life, but plateaus with relatively few side effects and no long-term complication [16]. Untreated individuals developed diurnal fluctuations with marked improvement in the morning and worsening in the evening. DRDs are more frequent in female than in males, with a ratio varying from 1 to 4.3:1. Diagnosis of DRD can often be made on clinical grounds [17].

There are reports about DRD induction by diazepam [18], bupropion [19], cetirizine [20], riluzole [21], and tetrabenazine [22]. The authors, however, didn't find any reports about post-lamotrigine conditions. Lamotrigine is a new antiepileptic agent that is frequently used in epileptic patients with a good tolerability and efficacy. Lamotrigine has side effects, the most important of which is exfoliative dermatitis and rashes [23]. A study showed dizziness in 11%, and ataxia in 12% of cases, but if treatment begins with low doses, these events decreases [24]. Other side effects were also reported such as sudden death due to cardiac dysrhythmia in two cases [25], psychosis as one of the rare side effects of lamotrigine [13], oral ulcers [26], chorea [27], leucopenia and thrombocytopenia [28], anticonvulsant hypersensitivity syndrome [29], abnormal eye movements and hyper-sexuality [30]. This dystonic effect may be due to the lack of selectivity of lamotrigine to block glutamate release in susceptible individuals. In dystonic mutant hamsters when subsided, dystonia can be re-invoked when these animals receive sodium channel blockers such as lamotrigine [31- 34]. The patients under discussion are two girls (4 and 5 years old) who had seizure and received lamotrigine for a time and were free of seizure attacks. Dystonic attacks disappeared after receiving 50 mg/per levodopa/ carbidopa. In conclusion, lamotrigine may introduce dystonia in susceptible patients. The dystonic attacks are responsive to levodopa.

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