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CASE REPORT

Combined Leucopenia and Thrombocytopenia Are Possibly Adverse Events of Lamotrigine

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ABSTRACT

Hematological side effects are rare with lamotrigine. We report two cases (two men; 46 years old and 65 years old) with epilepsy that developed combined leucopenia and thrombocytopenia after receiving low dose lamotrigine for a time. Three weeks after discontinuing lamotrigine, all of the hematological abnormalities disappeared. We suggest that combined leucopenia and thrombocytopenia is one of the side effects of lamotrigine that must be considered.

Keywords: *Lamotrigine, Epilepsy, Hematological side effects, Leucopenia, Thrombocytopenia, Combined leucopenia and thrombocytopenia*

Lamotrigine is one of the new anti-epileptic drugs, and it is derived from the dihydrofolate reductase inhibitor. Mechanism of action is thought to be mainly through blocking the influx of sodium ions, thereby reducing excess glutamate release and stabilizing neuronal membranes [1]. Lamotrigine is effective as monotherapy in epilepsy for adult and children [2]. Lamotrigine is also effective as an adjunctive treatment of refractory partial seizures and idiopathic generalized epilepsy [3]. It is eliminated mainly by hepatic metabolism and changes to glucuronide conjugate [4]. Lamotrigine is well tolerated in children and adults [5]. The most adverse events include headache [6], somnolences, rash and episodes of transitory diplopia. Very occasionally, lamotrigine can produce minimal hematological side effects; including agranulocytosis, neutropenia, thrombocytopenia and asymptomatic disseminated intravascular coagulopathy [7-10]. Here, we report two cases of thrombocytopenia combined with neutropenia developed after taking lamotrigine for epilepsy treatment.

CASE 1

A 46 years old man has had tonic-clonic epilepsy for 25 years with no controled epileptic attacks. We started lamotrigine 50 mg per day at first, and increased it to 100 mg per day after two weeks. In the past, this patient had been received phenytoin for a long time, and due to periodontal hyperplasia, phenytoin had been discontinued. After phenytoin discontinuation, he had received sodium valproate 1000 mg per day for a while. After a few months use of sodium valproate, hepatic enzymes increased (serum glutamic oxaloacetic transaminase (SGOT) = 260 IU/L, serum glutamic pyruvic transaminase (SGPT) = 400 IU/L, Billirubin = normal), so sodium valproate was gradually tapered and lamotrigine started. After one year follow up, all of liver function tests were normal, but platelet and WBC counts decreased to 83000/ml and 3800/ml respectively (neutrophiles = 48%, lymphocyte = 52%). Other laboratory tests were in the normal ranges. Physical examinations were normal. Brain MRI scans was normal and electroencephalogram showed generalized paroxysmal discharges. Lamotrigine discontinued immediately. After one week follow up, laboratory studies revealed platelet count of 139000/ml, WBC count of 6200 /ml. After two weeks, platelet count of 185000/ml, and WBC count of 5200/ml were detected. To control epileptic attacks, phenytoin 200 mg/day started again.

CASE 2

A 65 years old man has had tonic-clonic epilepsy for 10 years. Due to poor control by sodium valproate, lamotrigine 50 mg per day started, and it was increased to 100 mg per day after two weeks. The patient became seizures-free after two months, but follow up laboratory tests revealed platelet count of 70000/ml, WBC count of 2000/ml (neutrophiles = 40%, lymphocytes = 40%). The other laboratory tests (liver function tests, thyroid

function tests) were normal. Physical exams were normal. In past history, he has been alcoholic for a long time, but from one year ago he hasn't drink. Brain MRI scans has done and the report was normal. Electroencephalogram showed generalized abnormal discharges. Lamotrigine was discontinued immediately, after one week follow up laboratory studies revealed platelet count 129000/ml, WBC count 3200/ml, and after two weeks, platelet count was 245000/ml and WBC count was 5300/ml. For this patient, phenytoin 200 mg per day was started again.

DISCUSSION

Existing anti-epileptic drugs have considerable potential for concentration-dependent and idiosyncratic toxicity [11]. Lamotrigine is a novel anticonvulsant drug that exerts its anti-epileptic effect by decreasing glutamate release through blockade of voltage-sensitive sodium channels [12]. The clinical side effects of lamotrigine are significantly rare [4, 13]. The most adverse reactions occur during the early stage of treatment, between first and fourth month [14, 15]. There are multiple side effects; some of these side effects are common such as dizziness, somnolence, nausea and headache [6, 16-21]. Some of the side effects are not common, but well known; the most important one is Stevens-Johnson syndrome [15, 16, 19]. The rare of side effects that reported are: hyper sexuality [12], sudden death [17], purpura [18], QRS prolongation [20], oral ulcers [22] and psychosis [23]. Hematological side effects are extremely rare. In a study, it has been reported four cases of neutropenia, three cases of thrombocytopenia, and two cases of disseminated intravasculare coagulopathy (DIC) [7]. In another report, one case developed neutropenia with thrombocytopenia [24]. A few cases of sever leucopenia have been reported [8-10, 25, 26]. In the present report, combined leucopenia and thrombocytopenia developed in case 1; nearly 1 year after starting lamotrigine and in case 2; after two months without any other active diseases. Mechanisms responsible for lamotrigine-related hematological complication are unknown. In conclusion, combined neutropenia and thrombocytopenia are possible adverse effects of lamotrigine.

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