Journal of Movement Disorders 2013;6:21-22 **CASE REPORT**
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Thrombocytopenia Associated with Levodopa Treatment

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There were few cases of thrombocytopenia associated with levodopa. Herein, we report a patient with Parkinson's disease, who suffered thrombocytopenia related to long-term use of levodopa.

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Key Words: Thrombocytopenia, Levodopa, Parkinson's disease.

Levodopa is a well-known drug that is used to treat Parkinson's disease (PD). Its most common adverse effects are orthostatic hypotension, nausea, vomiting, sedation, daytime somnolence, hallucination, delusion and psychosis.

Although rare, thrombocytopenia was reported in the patients with PD with uncertain pathomechanism. Herein, we report a PD patient with thrombocytopenia in the middle of long-term use of levodopa.

Case

In 2009, a 77-year-old woman first noticed rigidity and resting tremor in her left hand and was diagnosed with PD. Treatment with the combination drug levodopa-carbidopa (200 mg/d plus 50 mg/d, respectively) was started in another hospital. In March 2010, she visited our hospital and received the same medication under the diagnosis of PD. A complete blood cell count at 6 months after the use of levodopa was normal. With the progress of the patient's symptoms, the amount of the levodopa-carbidopa combination drug was increased up to 600 mg/d plus 150 mg/d, respectively, and a dopamine agonist was added. In January 2012, the patient was admitted because of general weakness. Her medication was levodopa (600 mg/d) and ropinirole (0.75 mg/d) at the time of admission. She experienced an episode of gross hematuria 1 week before admission. Upon admission, the initial blood analysis showed a hemoglobin value of 12.1 g/dL, a leukocyte count of $7.6\times10^3/mm^3$, and a platelet count of $27\times10^3/mm^3$. The erythrocyte sedimentation rate was 27 mm.

We performed diagnostic work-ups for her thrombocytopenia. The peripheral blood smear revealed a normocytic normochromic red blood cells. Chest radiography and abdominal computed tomography was normal. The results from serologic tests for human Immunodeficiency virus and hepatitis B virus were negative. The reactions for Coombs test and antinuclear antibody (ANA) test were negative. Platelet-associated IgG was detected with the use of indirect fluorescent technique.

Three days after admission, eight platelet concentrates were transfused. After the transfusion, the patient's hematuria had resolved. As there was no laboratory abnormalities except platelet-associated IgG antibody, we suspected the possible role of levodopa.

Levodopa was stopped while ropinirole was increased up to 2.25 mg/d. Her parkinsonism was not aggravated after the drug adjustment. Her platelet count was normalized nine days after the discontinuation of levodopa. Her platelet count remained normal ($164\times10^3/mm^3$) at the follow-up after one month.

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Discussion

There have been several case reports of thrombocytopenia associated with levodopa therapy. Wanamaker et al.[1] and Henry et al.[2] have reported a positive reaction for the Coombs test in patients taking levodopa for three or more months. Henry et al.[2] have also reported an 11% incidence of positive reaction for the ANA test in the same patient population. Giner et al.[3] have reported a case of thrombocytopenia associated with levodopa therapy. In their study, severe thrombocytopenia appeared after the long-term levodopa treatment with positive antiplatelet autoantibodies. Platelet count recovered after the withdrawal of levodopa. Similar to the previous report, thrombocytopenia developed more than two years after the introduction of levodopa and recovered after the discontinuation of levodopa in our case. It may be possible that her thrombocytopenia could be related to levodopa based on the level of evidence criteria of George et al.[4]

Platelet dysfunction and destruction can be induced by different drug-related mechanisms. Drug-induced 'dysthrombopoiesis' can occur in isolation or within the context of a broader pancytopenia and bone marrow suppression which often occurs after treatment with chemotherapeutic and immunosuppressive often in proportion to the dosage.[5]

Although drug-related antiplatelet antibodies can be detected after the exposure to a new drug during within 1 or 2 weeks, a long-term use of specific drug could be complicated with thrombocytopenia.[3] For unknown reasons, platelets are the targets of drug-dependent antibodies much more often than neutrophils or red cells.[6]

Because we did not reintroduce levodopa concerning the return of thrombocytopenia, the cause-and-effect relationship between the long-term use of levodopa and the occurrence of thrombocytopenia could not be firmly established. It also remained undetermined whether platelet-associated antibody could be the possible mechanism of her thrombocytopenia.

Although limited, our case along with the previously reported cases suggest a possible development of thrombocytopenia as a side effect of levodopa, especially after long-term usage. Platelet and related antibodies should be noticed in case of unexplained hemorrhage in PD patients with levodopa. Further studies are needed to understand the mechanism of levodopa-related thrombocytopenia.

REFERENCES

1. Wanamaker WM, Wanamaker SJ, Celesia GG, Koeller AA. Thrombocytopenia associated with long-term levodopa therapy. JAMA 1976;235:2217-2219.
2. Henry RE, Goldberg LS, Sturgeon P, Ansel RD. Serologic abnormalities associated with L-dopa therapy. Vox Sang 1971;20:306-316.
3. Giner V, Rueda D, Salvador A, Hernàndez JC, Esteban MJ, Redón J. Thrombocytopenia associated with levodopa treatment. Arch Intern Med 2003;163:735-736.
4. George JN, Raskob GE, Shah SR, Rizvi MA, Hamilton SA, Osborne S, et al. Drug-induced thrombocytopenia: a systematic review of published case reports. Ann Intern Med 1998;129:886-890.
5. Kinsella F. Drug-induced platelet disorder. Adv Drug Reac Bulletin 2012;272:1047-1050.
6. George JN, Aster RH. Drug-induced thrombocytopenia: pathogenesis, evaluation, and management. Hematology Am Soc Hematol Educ Program 2009:153-158.