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A case report of thrombocytopenia induced by sodium valproate sustained release tablets in a schizophrenic patient

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Clinical data

The patient, a 28-year-old female, was aggravated by suspicion for more than a year, and the total course of the disease was unknown. She was sent to the outpatient clinic of our hospital by the staff of the rescue station on December 20, 2020. Outpatient clinic with "schizophrenia?" Admitted to hospital. Psychiatric examination after admission found that patients had obvious victim delusion, absurd content, the object was generalized, and the patient firmly believed it. No obvious abnormalities were found in admission physical examination. The patient denied the history of severe somatic disease, drug allergy and infection. Deny taking any drugs recently. No obvious abnormalities were found in the blood routine examination, liver and kidney function, electrolyte, blood glucose, blood lipid, thyroxine, stool routine, infectious diseases (5 markers of hepatitis B, hepatitis C, syphilis, HIV antibody), electrocardiogram, electroencephalogram, chest CT, abdominal color ultrasound and so on. PANSS score 81. According to ICD-10 diagnostic criteria, schizophrenia was diagnosed after admission, and aripiprazole was given antipsychotic treatment. The initial dose was 10 mg/day, and increased to 20 mg/day after 3 days and maintained until discharge. On January 10, 2021, the patient developed impulsive behavior and was treated with sodium valproate sustained-release tablets (VAP) 500 mg/day to stabilize emotion. The effective concentration of drug treatment was 50-100 μg/mL [1]. During the follow-up of 7 February 2021, the platelet count of the patients was decreased, and the platelet count was 82 X 10^9/L Considering the adverse drug reactions caused by VAP, VAP was stopped immediately on the same day. On February 16,2021, routine blood platelet count showed that it returned to normal. After March 10,2021, the platelet was in the normal range, and further increased compared with February 16 (See Table 1).

On April 1, 2021, the father of the patient came to the hospital to receive the patient. At discharge, the PANSS scale score was 40 points. Before and after admission, 75 % > PANSS reduction rate ≥50%, suggesting that the therapeutic effect is remarkable progress.

Table 1: Drugs and platelet count.

Date	Drug dosage	Platelets Counting X 10^9/L
2020-12-20	No medication on the day of admission	180
2020-12-20	Aripiprazole Tablets 10mg / day	180
2021-01-12	Aripiprazole Tablets 10mg / day +Sodium valproate 500 mg / day	183
2021-01-12	Aripiprazole Tablets 20mg / day	82
2021-02-10	Aripiprazole Tablets 20mg / day	85
2021-02-16	Aripiprazole Tablets 20mg / day	116
2021-03-10	Aripiprazole Tablets 20mg / day	162

Discussion

Sodium valproate is commonly used as a common antiepileptic drug in clinic, and psychiatric use of sodium valproate sustained-release tablets used as mood stabilizers or antipsychotics synergist. Its anti-epileptic and emotional stability mechanism are not entirely clear, studies have shown that VAP is obtained by changing the metabolism of GABA [2]. It has been reported that sodium valproate sustained release tablets can cause leukopenia, erythrocytopenia and thrombocytopenia, that is cachexia [3]. It has been reported that sodium valproate sustained release tablets can cause leukopenia, erythrocytopenia and thrombocytopenia, and its mechanism can be as follows: VAP metabolite 2-propyl-2-pentadienoic acid destroys liver fine cells and inhibits the synthesis of coagulation factors. And VAP can inhibit the conversion of arachidonic acid on the platelet membrane to prostaglandins and thromboxane, thus inhibiting platelet aggregation [4]. Drug-induced thrombocytopenia means that some drugs cause the platelet count in peripheral blood to be less than 100 X 10^9/L. Its clinical manifestations are skin ecchymosis, mucosal hemorrhage, gastrointestinal bleeding and even intracranial hemorrhage. If it is not found and treated in time, there is often a high fatality rate. Xing Ying and other authors believe that thrombocytopenia may be related to

1. The time of drug use is related to the cumulative dose.

2. Combined use of drugs is more likely to lead to thrombocytopenia [5]. In this case, the patient combined with antipsychotic drugs, depending on the confirmation that the combined use of drugs is more likely to lead to thrombocytopenia. But what is inconsistent is that the dose of VAP in this case is 500 mg/d for 4 weeks, which does not support this conclusion either in terms of dose or time. The reason for thrombocytopenia in patients may be related to individual differences. Limited by the unit at that time no valproate blood concentration monitoring conditions, unable to measure the blood concentration of patients at that time.

When patients have symptoms of thrombocytopenia, Xing Ying and others think that stopping the use of sodium valproate can restore platelets, but the effect of reduction is not good [5]. Looking at the drug manual, the treatment of this adverse reaction can be taken to reduce the dose of asymptomatic thrombocytopenia patients according to platelet levels and the control of epilepsy, which can usually eliminate thrombocytopenia. Pei Pei Gao et al reported a case in this way [6]. Because the dosage of sodium valproate sustained-release tablets in this case was small and it was not the main drug for treatment, the reduction scheme was not adopted, and the platelet count recovered quickly after drug withdrawal, and the effect was accurate.

Although sodium valproate sustained-release tablets drug instructions 'adverse reactions' column described thrombocytopenia as 'occasionally dose-related thrombocytopenia case reports'. However, it should be pointed out that psychiatric patients are different from ordinary patients. Affected by the disease, most of them have different degrees of cognitive impairment. They are often unable to actively provide complaints of thrombocytopenia-related discomfort, which is not conducive to the early detection of related adverse reactions. At the same time, it is necessary to improve the understanding of the clinical manifestations, diagnosis and treatment of drug-induced thrombocytopenia, so as to achieve the purpose of rational drug use [7]. The purpose of this case report is to alert the majority of psychiatric personnel to use VAP in clinical practice, especially to pay attention to its adverse reactions to thrombocytopenia. At the same time, psychiatric patients may not be able to tell their own history of adverse drug reactions in detail after discharge, laying a safe hidden danger for future doctors to use similar drugs to repeat the same adverse reactions.

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