Case Report

Ceftriaxone-Induced Thrombocytopenia in a Patient with Bacterial Meningoencephalitis

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Abstract

Drug-induced thrombocytopenia is a rare and life-threatening condition. It is mainly caused by the initiation of drug-dependent platelet reactive antibodies that leads to the accelerated platelet destruction. Ceftriaxone is a third-generation cephalosporin, which has rarely reported cases of drug-induced immune thrombocytopenia. Here, we report a case of ceftriaxone-induced thrombocytopenia after the initiation of antibiotic therapy for bacterial meningoencephalitis based on the laboratory findings with the initiation and discontinuation of ceftriaxone.

Keywords: Ceftriaxone, drug-induced immune thrombocytopenia, meningoencephalitis, thrombocytopenia

Introduction

In an inpatient setting, thrombocytopenia is a common abnormal hematological result, but drug-induced immune thrombocytopenia (DITP) is an unfamiliar condition.[1] This condition is severe, and occasionally it may be a life-threatening complication.[2] Some epidemiological studies had been conducted in the Europe and United States which reported that the annual minimum incidence is approximately ten persons per million.[3]

DITP is mainly caused by the initiation of drug-dependent platelet reactive antibodies that leads to the accelerated platelet destruction. The etiology should be considered different from other causes of isolated thrombocytopenia, usually, it is <20,000/μL on the platelet nadir in DITP.[4] On the preliminary exposure of the drug, the patient will be sensitized then on reexposure or by the prolonged administration of the drug for at least 1 week which may causes acute cell destruction.[1] In some occasions, the drug metabolites are also responsible for the patient's immune response.[2]

Ceftriaxone is a third-generation cephalosporin, which has rarely reported cases of DITP. The most commonly reported cases with cephalosporins are severe drug-induced hemolytic anemia (DIHA). Usually, the second and third-generation cephalosporins such as cefotetan and ceftriaxone are involved in causing DIHA and other related events.[4]

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Hereby, we report a case of a 74-year-old female who had type 2 diabetes mellitus, systemic hypertension, dyslipidemia, and who developed ceftriaxone-induced thrombocytopenia during antibiotic therapy for bacterial meningoencephalitis with ventriculitis.

Case Report

A 74-year-old female patient with a past medical history of bacterial meningoencephalitis with ventriculitis, seizure disorder, systemic hypertension, Type 2 diabetes mellitus, and dyslipidemia came to the emergency department with complaints of reduced response since morning and she also had reduced food intake along with reduced urine output. She also had history of 5–6 episodes of vomiting containing food particles. On examination, she was drowsy and found to have hypotension. In view of hypotension, she was started on intravenous (IV) fluids and antihypertensives were withheld. Laboratory studies showed white blood cell of 9.29 K/μL, Hgb of 13 g/dl and platelets 361 K/μL.

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Table 1: Trend of platelet count during the course in hospital

Platelet count (normal range: 150-450 K/μL)				
On admission	**After initiating the therapy with ceftriaxone**			**Ceftriaxone discontinued on May 17, 2021**
May 9, 2021	May 13, 2021	May 15, 2021	May 17, 2021	May 19, 2021
361	67	26	22	185

In view of the paucity of movements on the left side with exaggerated reflex, neurological evaluation was sought which showed recurrent meningoencephalitis. Due to recurrent meningoencephalitis, imaging followed by lumbar puncture was suggested but the patient's bystander was not willing for any imaging and they opted for palliative line management. Hence, she was empirically started on IV ceftriaxone (1 g-twice a day) for 7 days in meningitis dose and fosfomycin was also started to cover for *Escherichia coli* (other antibiotics were resistant). After three days, the culture turned negative thus fosfomycin was discontinued. On the 3rd, 5th, and 7th day of therapy, the platelets dropped to 67 K/μL, 26 K/μL, and 22 K/μL, respectively. However, there were no bleeding manifestations. Hence, one unit of platelet transfusion was given, platelet level increased to 85 K/μL and thereafter it remained in stable status for a few days. However, thereafter, no significant increase in the platelet count was there. Based on the severity of thrombocytopenia, DITP was suspected. Hence, ceftriaxone was stopped and she was started on ampicillin (500 mg) for 5 days. After the cessation of ceftriaxone, the platelet count began to rise and at the time of discharge, the count was 185 K/μL [Table 1]. While discharging the patient was in a clinically stable state.

Discussion

DITP is a rare and life-threatening adverse reaction which is caused by drug-dependent antibodies (DDAbs). Thrombocytopenia is a condition which may be acquired or inherited and its etiology can be mainly classified into four categories such as platelet underproduction, splenic sequestration, pseudothrombocytopenia, and peripheral destruction.[1] The main mechanism behind DITP is destruction of platelets by the production of DDAbs.[5] Nutritional deficiencies and bone marrow diseases may also be considered in the case of destruction of platelets.[1]

In this case, ceftriaxone-induced thrombocytopenia was diagnosed based on the laboratory findings with the initiation and discontinuation of ceftriaxone. The change which occurred after the discontinuation of drug provides strong confirmation of DITP. However, in our case, due to the lack of laboratory facilities ceftriaxone-dependent antiplatelet antibodies could not be determined.

A few cases of ceftriaxone-induced thrombocytopenia were reported in some literatures.[1] A study which was conducted in Oklahoma from 1991 to 2013 showed only six reported cases of ceftriaxone-induced thrombocytopenia.[6] There were two cases reported by Grossjohann *et al*. showed that platelet reactive DDAbs were found to react with epitopes which resides on the GPIIb/IIIa subunit and complex of GPIX which results in the proliferated destruction of platelets and this may lead to severe thrombocytopenia.[2] However, the reason behind the formation of platelet reactive antibodies due to ceftriaxone or other drugs which causes DITP remains unclear.

DITP usually occurs on the preliminary exposure of the drug and the patient may be sensitized either on reexposure or by the prolonged administration of the drug for at least 1 week which causes acute cell destruction. The treatment of DITP should be the immediate discontinuation of the drug which is implicated.[5] In case of patients with bleeding or with platelet count >10,000 K/μL, platelet transfusion should be initiated. In case of severe bleeding, IV immunoglobulin may also be considered. In our case, discontinuation of the drug led to improvements in platelet count.

Moreover, in this case, the patient had bacterial meningoencephalitis, hence an alternative antibiotic therapy is very much essential for this patient. Thus, in our case, we opted for ampicillin, a broad spectrum beta-lactam penicillin antibiotic which is considered the most preferred drug for most cases of bacterial meningoencephalitis. During our literature search, there were no reported cases of ampicillin-induced thrombocytopenia; hence, these might be considered a suitable option in our case.

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Conflicts of interest

There are no conflicts of interest.

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