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Case Report

Vancomycin-induced severe thrombocytopenia in a young infant

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Abstract

Vancomycin is a first-line drug for treating methicillin-resistant *Staphylococcus aureus*. Thrombocytopenia is a rare adverse reaction to vancomycin treatment, and there are no reports of vancomycin-induced thrombocytopenia (VIT) in infants. We describe the case of a 3-month-old girl who was diagnosed with purulent meningitis. After 13 days of treatment with vancomycin, her platelet count reduced to 8×10^9/L. Vancomycin was discontinued, and intravenous methylprednisolone was administered. The platelet count returned to normal after 4 days. Patients, especially young children, receiving vancomycin for a long clinical course should undergo careful monitoring of laboratory indicators and blood tests.

Keywords: Vancomycin. Infants. Thrombocytopenia.

INTRODUCTION

Vancomycin is a glycopeptide antibiotic mainly used to treat serious gram-positive bacterial infections and bacterial infectious diseases that are resistant to other antibiotics, especially methicillin-resistant *Staphylococcus aureus* and coagulase-negative *Staphylococcus*. The most common adverse reactions to vancomycin are ototoxicity, nephrotoxicity, and erythrocyte syndrome. Vancomycin-induced thrombocytopenia (VIT) is a rare adverse reaction.

Although isolated cases of VIT have been reported in adults and few cases of VIT in children, to our knowledge, there have been no reports of VIT in infants, and only 2 cases[1,2] documented in neonates and 1 case[3] in a young child (2 years). However, this does not mean that the incidence of VIT in infants is low. There are many factors that can contribute to thrombocytopenia in infants and can lead to VIT, which are being ignored by physicians or pharmacists.

Here, we report a case of severe thrombocytopenia after the administration of intravenous vancomycin in a 3-month-old girl.

CASE REPORT

A 3-month-old girl was admitted to our hospital with a fever of 39.9°C and elevated white blood cell (WBC) count and C-reactive protein (CRP) level. Routine blood testing revealed the following: WBC, 24.1×10^9/L; platelet, 380×10^9/L, and CRP, 51.5 mg/L. The biochemical findings in the cerebrospinal fluid (CSF) are shown in **Table 1**. The patient was diagnosed with purulent meningitis and sepsis and was started on intravenous cefotaxime (0.47 g four times daily) and intravenous vancomycin (95 mg four times daily). In addition, dexamethasone was administered to reduce edema. On day 3, blood and CSF cultures were positive for *Streptococcus pneumoniae* (penicillin minimum inhibitory concentration (MIC) = 2). The drug sensitivity tests, using blood cultures, indicated a sensitivity to vancomycin, penicillin, cefotaxime, moxifloxacin, and chloramphenicol. CSF findings showed the same except that intermediate resistance to cefotaxime and resistance to penicillin were ascertained. On day 5, the plasma trough concentration of vancomycin was 10.8 mg/L, and the concentration in the CSF was 1.5 mg/L. As the patient's temperature returned to normal, her condition was upgraded to stable, and she was discharged from the Pediatric Intensive Care Unit.

After 13 days of vancomycin treatment, the patient's platelet count sharply reduced, reaching a nadir of 8×10^9/L (**Figure 1**). A few needle-point bleeding points associated with vancomycin were observed in both lower extremities. Vancomycin was discontinued, although cefotaxime administration continued. Methylprednisolone was administered to improve the platelet count, which was constantly monitored. Within 3 days of discontinuing vancomycin, her platelet count increased to 88×10^9/L, with a further increase to 166×10^9/L by day 17. The bleeding points in both lower extremities disappeared, and the patient was switched to oral methylprednisolone. The patient was discharged on day 21 in good condition.

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Table 1: Exams of cerebrospinal fluid during hospitalization.

Day	Chlorine (mmol/L)	Glucose (mmol/L)	Protein (mg/L)
1	115.9	3.68	634
3	116.6	4.99	1,481
12	121.0	3.02	2,979

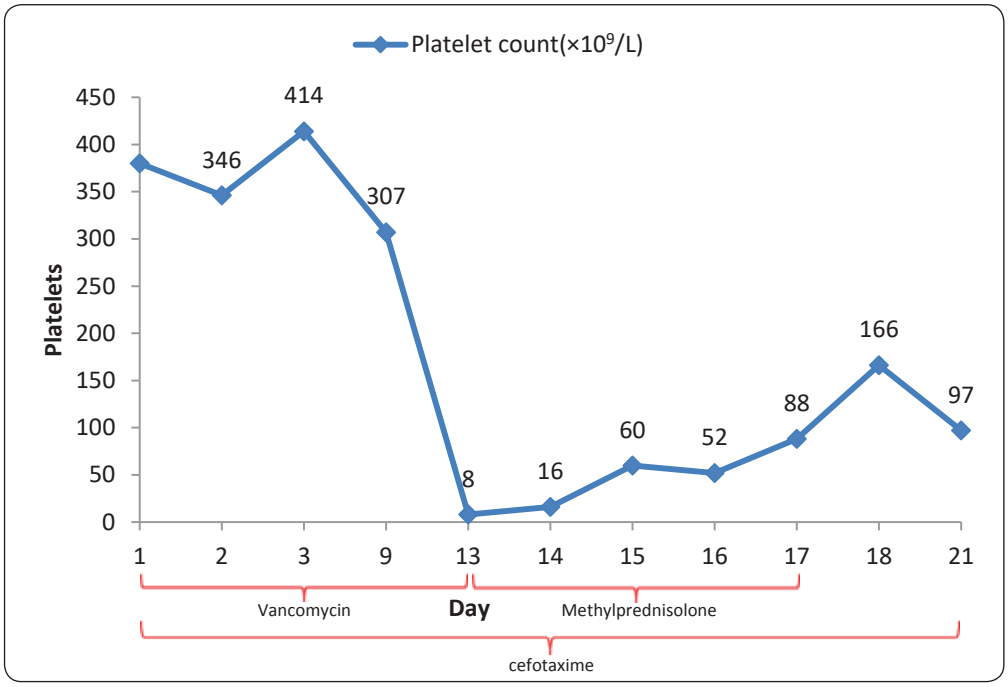

FIGURE 1: Progression of platelet count during the hospitalization.

DISCUSSION

The pathogenesis of VIT is not well understood. Although there is some evidence that supports an immune-mediated mechanism, several aspects of the molecular mechanism, such as how vancomycin causes antibody production and how antibodies precipitate the destruction of platelet structure and loss of platelet function, remain unknown.

Drygalski et al.[4] detected vancomycin-dependent platelet reactive antibodies (IgG and IgM) in patients clinically suspected of VIT. These antibodies can form complexes with platelets, causing structural damage and loss of function. Kenney et al.[5] contested that there are two immune mechanisms associated with VIT. One is the persistent presence of antibodies against vancomycin following vancomycin treatment, resulting in the rapid development of thrombocytopenia. Donnell et al.[6] reported a case of thrombocytopenia following vancomycin treatment within 4 hours. The other mechanism is the presence of an innate vancomycin-dependent antibody, resulting in a rare probability of thrombocytopenia upon the first administration of vancomycin.

Although the detection of vancomycin-dependent antibodies is beneficial for diagnosing VIT, not all hospitals have appropriate testing conditions. As reported by Drygalski et al.,[4] the patient's platelet counts reached a nadir after approximately 8 days of treatment with vancomycin, with a mean value of 13.6 × 10^9/L. Hemorrhagic patients had a platelet count of 8.4 × 10^9/L, and asymptomatic patients had a platelet count of 35 × 10^9/L. The reported nadir of patients with other bleeding disorders is 2 × 10^9/L –10 × 10^9/L, and the average restoration time of platelet counts after discontinuing vancomycin was approximately 6 days,[5, 7-10] whereas patients with renal impairment generally have severe thrombocytopenia for 7–8 days. Vandecasteele et al.[11] suggested that several weeks are needed to reach a normal platelet count owing to the low clearance rate of vancomycin. Restoration of the platelet count in patients with peritoneal dialysis requires 40 days according to the study by Pascual et al.[8] In our case, the platelet count reached a nadir of 8 × 10^9/L after 13 days of treatment with vancomycin. Vancomycin was discontinued, and the patient received intravenous methylprednisolone, following which the platelet count returned to normal after 4 days of methylprednisolone treatment. Liver and kidney functions were normal. The Naranjo adverse reaction probability score for our patient was 6, and other causes of thrombocytopenia, such as thrombosis, heparin-induced thrombocytopenia, and idiopathic thrombocytopenic purpura, were excluded. Although

tests for detecting vancomycin-dependent antibodies were not performed, the clinical manifestations and test indicators suggested that the drug caused the side effect.

Thus, it is necessary to discontinue vancomycin immediately in patients who are clinically suspected of VIT,[12] and replacement with other drugs according to the results of drug sensitivity and the risk of drugs in young children should be considered. Blood transfusions, corticosteroids, and intravenous immunoglobulin are options, and plasma exchange can also be considered if thrombocytopenia is prolonged or accompanied by hemorrhagic signs and symptoms. Closely monitoring of platelet counts (once every 3 days) is recommended. Previous reports and this case suggest that VIT can occur in patients of all ages. Therefore, physicians prescribing vancomycin as the first choice for treating purulent meningitis caused by *S. pneumoniae* infection and penicillin MIC ≥2, should be mindful of special populations, especially young children, although VIT is a rare adverse reaction. In addition, we should pay attention to previous adverse reactions and abnormal liver and kidney function. Patients with long courses should be monitored for laboratory indicators and hemorrhagic manifestations.

Conflict of Interest

All authors have no conflicts of interest directly relevant to the content of this article.

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