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A Case Report Of Recurrent Multiple Myeloma Complicated With HIT On Dialysis

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Authorship Contributions

Li Bao, Kai Sun, and Yuan Chen contributed to the study design. Li Bao, Kai Sun, and Yuan Chen wrote the report. Minqiu Lu, Lijuan Fang, Shan Gao, Lei Shi, Qiuqing Xiang, Yuehua Ding, Mengzhen Wang, Xi Liu, Xin Zhao, Bin Chu, and Li Bao provided all patient data and imaging. Li Bao made critical revisions to the manuscript. All authors read and approved the final manuscript.

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1. Abstract

1.1. Backgrount:

At present, the application of heparin is becoming more and more widespread, the problems arising from the use of heparin are gradually exposed, and people are paying more and more attention to how to use heparin safely. Heparin-induced thrombocytopenia is a disease of thrombocytopenia caused by the use of heparin in the treatment process. Although this type of disease is relatively rare in clinical, it can cause dangerous situations.

1.2. Case presentation:

A 75-year-old man was admitted to the hospital due to a recurrence of multiple myeloma. He had to undergo hemodialysis due to high creatinine. During the dialysis, platelets drop to extremely low levels and iliac vein thrombosis appeared. It was found that the patient used heparin to seal the tube during dialysis, which resulted in the heparin-induced thrombocytopenia. After stopping heparin and using alternative anticoagulation, the patient's platelet count recovered gradually.

1.3. Conclusions:

HIT is a relatively hidden but very dangerous disease, which requires rapid and correct judgment and measures. When the patient has HIT and the platelet is extremely reduced, after weighing the risk of thrombosis, alternative anticoagulation can be performed. The drug, Argatroban, can still exert an anticoagulation effect even when used in low doses.

2. Key words:

Relapsed multiple myeloma; HIT; Argatroban; thrombocytopenia

3. Introduction

With the continuous progress of aging, as well as the improvement of the standardized management level of thrombotic diseases, the application of anticoagulant drugs has increased significantly. As one of the widely used anticoagulant drugs, heparin is mainly used for coronary heart disease, surgery, extracorporeal membrane oxygenator circuits, dialysis and so on1. The use of heparin is not as safe as we thought, and some patients may face the risk of heparin-induced thrombocytopenia (HIT) in clinical. HIT is an immune-mediated adverse reaction with an incidence of 0.1-5%, but in dialysis patients, the incidence is as high as 12%2, and 30% to 60% of patients develop thrombosis. Therefore, HIT needs to be taken seriously in patients undergoing hemodialysis. Many kidney failure patients have to undergo hemodialysis therapy due to high creatinine caused by multiple myeloma (MM), which increases the probability of HIT. Here, we report a case of an elderly patient who received hemodialysis due to MM recurrence and kidney failure, but thrombocytopenia was caused by using heparin during hemodialysis, in order to appeal for more arrention to the adverse effects of heparin drugs.

4. Case presentation

A 75-year-old man was diagnosed multiple myeloma 33 months ago and the patient suffered a relapse after receiving multiple treatments. When he came to hospital, hemoglobin was 81g/L, white blood cell count 8.45×109/L, platelets 233×109/L. However, his creatinine was increased to 738μmol/L and needed to have a hemodialysis, and heparin was used to seal the tube during hemodialysis. After 5 times of hemodialysis (Figure 1), his creatinine was lower than before, but his blood routine had abnormal.

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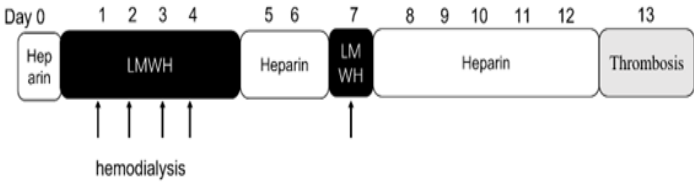

Figure 1: Heparin is used to seal the tube during hemodialysis

There was a progressive decline in platelets, from 233×109/L to 98×109/L and then to 24×109/L. The patient developed a swollen right leg after two weeks in hospital. Doppler ultrasound showed that there were multiple clots in the lower extremities, including right femoral vein thrombosis and right iliac vein thrombosis. As HIT was suspected, so the use of heparin was discontinued. We performed HIT antibody on the patient, and the result showed that the content of HIT antibody was 5.3 IU/ mL, which was significantly higher than the normal value. We used Argatroban, a direct thrombin inhibitor, to replace heparin as an anticoagulant. The initial dose of Argatroban was 0.7ug/kg·min, but the patient could not tolerate this dose and had blood in the stool, so we gradually reduced the dose, and finally 0.1ug/kg·min was used as our final therapeutic dose. Platelets were elevated after Argatroban replacement anticoagulant therapy (Figure 2), and after 10 days of treatment, doppler ultrasound showed the iliac vein thrombosis disappeared. The patient's platelets gradually recovered, and he began dialysis and chemotherapy.

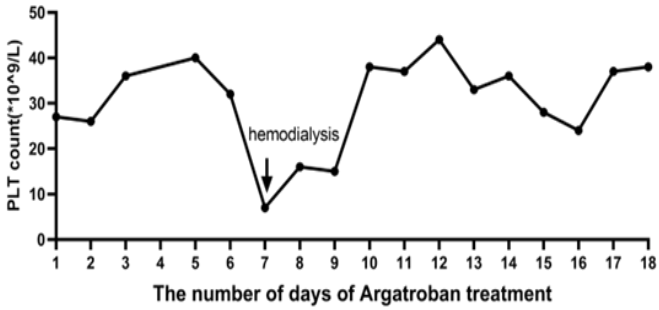

Figure 2: The course of Argatroban treatment

5. Discussion

Renal failure is a common and serious complication in patients with multiple myeloma, and it is also the main cause of death. Among newly diagnosed MM patients, 20%-50% of patients have kidney damage3,4. Increased age is related to the higher rate of kidney damage in MM patients. Therefore, approximately 10% patients with MM requiring dialysis5. In the process of hemodialysis, the incidence of HIT has increased significantly because of the use of heparin. HIT is an adverse reaction of heparin mediated by antibodies that occurs during the application of heparin drugs. Clinically, the main manifestation of HIT is the abnormal decline of platelet count, which can lead to arteriovenous thrombosis and even death in severe cases6. At present, the mainstream diagnosis of HIT in the world is based on 4T score and dynamic monitoring of platelet count, combined with HIT antibody detection and/or platelet function test for exclusion diagnosis and confirmation. The 4T score is an important criterion for determining whether a patient has HIT. It is evaluated on four aspects, including the degree of thrombocytopenia, duration of heparin use, thrombosis, and presence of other possible causes of thrombocytopenia. The patient of our reported case had a platelet decline of over 50%. Besides, the patient developed a thrombosis 8 days after heparin treatment and had no other cause of thrombocytopenia, so he was considered high clinical potential to had HIT based on the 4T score. Subsequently, we tested HIT antibody of the patient and found that it was positive, finally the patient was diagnosed as a HIT sufferer.

The presence of thrombocytopenia and/or thrombosis was determined by a 4T score7,8. To detect and diagnose HIT as quickly as possible, platelets should be measured every 2-3 days when heparin is used9. The key treatment for highly suspected or confirmed HIT patients is discontinuation of heparin and initiation of therapeutic doses of alternative anticoagulants10. The direct thrombin inhibitor Argatroban has been recommended as a drug for the treatment of HIT, and it is also the drug we used when treating this elderly relapsed MM with HIT. Argatroban is often used in critically ill patients with a relatively short half-life and is mainly metabolized in the liver, but it requires intravenous administration, affects the INR and protracts APTT. However, the hepatic clearance of the drug allows to maintain a stable therapeutic APTT during treatment, and hemodialysis does not affect its anticoagulant strength. According to a research, Argatroban is used in 6 patients with renal insufficiency requiring dialysis. It can replace the heparin without causing thrombosis during dialysis, so it is effective and safe for frail elderly patients11. Besides, Argatroban is recommended for HIT patients with renal insufficiency. Prophylactic platelet transfusions should be avoided in patients with HIT because the risk of bleeding is very low. However, such transfusions can increase the risk of thrombosis9,12.

There are many reports of HIT in patients, but there are few reports of HIT in patients with multiple myeloma. The patients we reported were not only elderly patients, but also recurrence of multiple myeloma. Previous studies have suggested that any anticoagulant drug should not be administered when platelets are below 30×109/L13 but for patients with end-stage HIT, corresponding alternative anticoagulation therapy can still be performed. During the treatment, the patient's platelets are very low, even less than 10×109/L. At this time, the patient's risk of spontaneous blood is very high and the patient also has iliac vein thrombosis, and there is a risk of pulmonary embolism at any time. After weighing the risk of blood clots and bleeding, we believe that the most important treatment at the moment is still anticoagulation therapy. Therefore, we insist on giving patients Argatroban for alternative anticoagulation therapy. In addition, the therapeutic dose of Argatroban is significantly lower than the recommended dose, but it can still exert anticoagulant effects. Facts have proved that the patient's platelet count gradually increased under the treatment of Argatroban. It shows that removing heparin and apply correct treatment, the patient can still turn from danger to safety. This case also provides a reference for the application and dosage of Argatroban in critically ill patients.

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6. Conclusions

Patients with relapsed multiple myeloma often require dialysis, but there are few reports of HIT in such patients during dialysis. We first reported the occurrence of HIT in this patient, and in the case of extremely low platelets, in the face of iliac vein thrombosis, we chose low-dose argatroban for alternative anticoagulation, and the treatment restored the patient's platelet count, proved that even low-dose alternative anticoagulation affects HIT patients.

7. Abbreviations

HIT: heparin-induced thrombocytopenia; MM: multiple myeloma; INR: international normalized ratio; APTT: activated partial thromboplastin time

8. Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki. Written informed consent for treatment and genetic testing was obtained from all patients.

9. Consent for publication
Written informed consent for publication was obtained from all patients.

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