CASE REPORT

Life-threatening haematuria caused by vancomycin-induced thrombocytopenia

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SUMMARY

Thrombocytopenia is a rare side effect of vancomycin, an antibiotic that is often used to treat Gram-positive bacterial infections. A 67-year-old man developed bilateral pulmonary emboli and hospital-acquired pneumonia following left ureteric reimplantation. He was anticoagulated with rivaroxaban and started on intravenous vancomycin and gentamicin for treatment of pneumonia. After five doses of vancomycin, his platelet count dropped to a nadir of $0 \times 10^9/L$ (baseline: $314 \times 10^9/L$) manifesting as visible heavy haematuria and haemodynamic instability due to excessive blood loss. Reversal of the thrombocytopenia was achieved with intravenous immunoglobulin, methylprednisolone and continuous platelet transfusions.

BACKGROUND

Vancomycin is a glycopeptide antibiotic that is often used in the treatment of Gram-positive bacterial infections. Thrombocytopenia is a rare adverse effect of vancomycin, with fewer than 15 reported cases.^{1–12} Manifestations of thrombocytopenia range from no symptoms to severe bleeding in the form of lower gastrointestinal or intrapulmonary haemorrhages.¹

Drops in the platelet count of up to 93% have been reported in the literature.¹ To the best of our knowledge, this is the first case to describe complete destruction of platelets by vancomycin and should alert clinicians to this unusual and potentially life-threatening adverse effect.

CASE PRESENTATION

We report a case of a 67-year-old man who presented for an elective left ureteric reimplantation to treat an iatrogenic injury sustained during an anterior resection for sigmoid adenocarcinoma. His medical history was significant for a postoperative left leg deep vein thrombosis (DVT) and bilateral PEs, which had been treated with a 6-month course of low-molecular-weight heparin (LMWH). He reported allergies to penicillin and codeine.

The procedure was completed with no immediate postoperative complications and the patient was started on a prophylactic dose of LMWH on day 1. On day 2, he developed tachycardia (110 bpm) and hypoxia with oxygen saturations of 70% on room air. He remained normotensive and afebrile. Examination of the chest revealed reduced air entry at the right base and crepitations in the lower zones. Given his previous history, a Computed Tomography Pulmonary Angiography (CTPA) was obtained which demonstrated bilateral pulmonary

emboli, and right middle and lower lobe collapse with consolidation. He was started on rivaroxaban 15 mg twice daily, intravenous vancomycin 500 mg twice daily and gentamicin 300 mg once daily according to the trust protocol for the treatment of penicillin allergic hospital-acquired pneumonia. Sputum culture grew *Pseudomonas aeruginosa* sensitive to gentamicin.

The patient improved following antibiotic therapy. Prior to starting antibiotics, the platelet count was $314 \times 10^9/L$ and haemoglobin 114 g/L. After five doses of antibiotic therapy, the patient developed heavy visible haematuria with a platelet count of $261 \times 10^9/L$. Rivaroxaban was withheld and a three-way catheter was inserted for the purpose of bladder washout and irrigation. The following day, the haematuria worsened and the patient became haemodynamically unstable (blood pressure 80/50 mm Hg, heart rate 120 bpm, saturations 97% but remained afebrile) with a platelet count of $2 \times 10^9/L$. There was no petechial or purpuric rash or evidence of bleeding from buccal or nasal mucosa at this stage. Full blood count at this time showed haemoglobin of 66 g/L (mean cell volume 89), white cell count 9.6, international normalised ratio 1.2, activated partial thromboplastin time (APTT) 1.1, fibrinogen 3.9 g/L and U&Es normal. Blood film showed marked thrombocytopenia. He was resuscitated with 2 units of blood and 2 pools of platelets, and transferred to intensive therapy unit for stabilisation. Repeat platelet count after 2 pools of platelets was $0 \times 10^9/L$.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses considered were heparin-induced thrombocytopenia (HIT), primary immune thrombocytopenia (ITP) and vancomycin-induced thrombocytopenia (VIT). Disseminated intravascular coagulopathy was excluded as a differential diagnosis because the prothrombin time, APTT and fibrinogen were within the normal range. Rivaroxaban was also ruled out as it is not known to cause thrombocytopenia. Finally, a negative HIT screen excluded heparin as the cause of the patient's symptoms.

At present, detection of specific vancomycin-induced IgG and IgM antiplatelet antibodies is limited to a few centres, but these tests are neither validated nor standardised.¹³ However, platelet-reactive IgG and IgM antibodies were detected in the patient's serum through platelet immunofluorescence testing (PIFT), thus supporting a diagnosis of immune-mediated thrombocytopenia. The diagnosis of VIT was further strengthened by the use of the Naranjo

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Adverse Drug Reaction Probability Scale which demonstrated a probable relationship between the thrombocytopenia and vancomycin.¹⁴

TREATMENT

Despite multiple pools of platelet transfusion, the patient's platelet count remained low, suggesting an immune-mediated platelet destruction process. He was started on pulsed intravenous methylprednisolone and immunoglobulin, and required a total of 13 units of packed red cells, 13 pools of platelets and 4 units of fresh frozen plasma to correct his thrombocytopenia and anaemia. Platelet counts increased gradually, reaching normal levels after 3 days of treatment.

OUTCOME AND FOLLOW-UP

At discharge, patient's platelet count was $196 \times 10^9/L$.

DISCUSSION

The mechanism of VIT is considered to be immunologically mediated, as suggested by the presence of specific drug-dependent IgG and IgM antiplatelet antibodies in patients exposed to vancomycin.¹ These antibodies bind to the platelet glycoprotein forming a complex that is then engulfed and cleared by macrophages in the phagocytic system.¹⁵

Thrombocytopenia is typically observed after 7–10 days of vancomycin treatment and commonly manifests as petechial bleeding.¹ Another feature of VIT is refractoriness to platelet transfusions,^{1 10 12} as seen in our patient who required multiple platelet pools to correct the thrombocytopenia. An exposure–response relationship has been demonstrated between vancomycin trough levels and thrombocytopenia severity.¹⁶ In this case, however, the patient received only five doses of vancomycin before his platelet count fell and interestingly, all doses were subtherapeutic.

Vancomycin-induced antibodies may exist for months after cessation of vancomycin therapy and several cases of recurrent thrombocytopenia following vancomycin rechallenge have been reported.^{4 6 10} Treatment primarily consists of stopping vancomycin, with gradual resolution of thrombocytopenia occurring over a period of approximately a week (or longer in patients with renal failure).¹ Other treatment options include platelet transfusions, steroids, immunoglobulins and plasma exchange.¹

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Learning points

- ▶ Life-threatening bleeding may occur in patients with vancomycin-induced immune thrombocytopenia.
- ▶ Clinicians should be aware of this adverse effect and closely monitor platelet counts in patients receiving vancomycin.
- ▶ Treatment includes the discontinuation of vancomycin therapy, platelet transfusions, steroids and immunoglobulins.

Competing interests None.

Patient consent Obtained.

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