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Case Report

# Drug-induced immune-mediated thrombocytopenia in the intensive care unit☆,☆☆,★

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**Abstract** A 62-year-old woman with prosthetic mitral valve was admitted for explant of an infected prosthetic knee. Perioperatively, she was bridged with heparin and started on empiric vancomycin and piperacillin-tazobactam. Platelet counts dropped precipitously within 2 days reaching a nadir of 6000/μL, without any bleeding. Decline persisted despite substituting heparin with bivalirudin. Antiplatelet factor 4 and anti-PLA1 antigen were negative. Schistocytes were absent. Antibiotics were substituted with daptomycin for suspected drug-induced thrombocytopenia. Pulse dose of intravenous immunoglobulin was initiated with rapid normalization of platelet count. She tested positive for IgG antiplatelet antibodies to vancomycin and piperacillin-tazobactam thereby confirming the diagnosis. Drug-induced immune-mediated thrombocytopenia is an underrecognized cause of thrombocytopenia in the intensive care units. Clinicians should be cognizant of this entity, and a definitive diagnosis should be sought if feasible.


## 1. Introduction

An estimated 15% to 58% of patients admitted to intensive care units (ICUs) have or develop thrombocytopenia [1]. In addition to being associated with longer ICU stay, increased bleeding, and higher transfusion requirements, patients with thrombocytopenia tend have a higher illness severity score than patients with normal platelet counts. Thrombocytopenia in the ICU is usually multifactorial and often leads to diagnostic dilemmas [2]. Drug-induced immune thrombocytopenia (DITP) is an underreported

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cause of severe thrombocytopenia primarily because of difficulties in establishing a definitive diagnosis. Although the true incidence of DITP is unknown, in critically ill patients, it is predicted to approach 25% [3]. We report a case of vancomycin-and piperacillin-mediated immune thrombocytopenia to highlight the importance of considering DITP as a plausible explanation for sudden severe thrombocytopenia.

## 2. Case report

A 62-year-old woman was admitted to the hospital for a suspected periprosthetic knee infection 28 days after an elective left total knee arthroplasty. Her medical history was significant for well-controlled hypertension, type II diabetes, hypothyroidism, chronic kidney disease, and rheumatic heart disease for which she had had a mechanical mitral valve replacement requiring lifelong anticoagulation. Upon admission, she was found to have significant parapatellar soft tissue swelling and cellulitis of her left knee. Explant of the prosthesis was planned by the orthopedic service pending medical optimization. She was started on a full-dose heparin infusion as thromboprophylaxis for her mechanical heart valve. Heparin was stopped 1 day before surgery and held briefly postoperatively because of bleeding from the surgical site. It was restarted on postoperative day 2 (hospital day 9). She required 2 U of packed red blood cells during this time (see Fig. 1). She was started on broad-spectrum antibiotic coverage with vancomycin and piperacillin-tazobactam on day 1 of her hospitalization for suspected polymicrobial wound infection. She underwent extensive soft tissue debridement and explant of her prosthesis with placement of a vancomycin-containing spacer on hospital day 7. Intraoperative cultures from the knee were positive for coagulase-negative *Staphylococcus* and *Staphylococcus aureus*. She was maintained on vancomycin for the prosthetic joint infection, and piperacillin-tazobactam was continued for gram-negative coverage of adjacent parapatellar soft tissue infection. Platelet counts were normal at this time.

She was transferred to the surgical ICU on hospital day 11 in the setting of an acute upper gastrointestinal bleeding with a precipitous drop in her hemoglobin from 8.8 to 6.5 g/dL and platelet count from 200,000 to 98,000/μL. An upper gastrointestinal endoscopy revealed trauma, possibly related to nasogastric tube placement. The bleeding resolved following endoscopic clipping of a vessel. Her platelet count, however, continued to fall from 98,000/μL on day 11 to 35,000/μL on day 12. Heparin was discontinued and bivalirudin was started because of the clinical suspicion of heparin-induced thrombocytopenia (HIT). Ultrasound of all 4 extremities was negative for deep venous thrombosis. During this episode, she did not appear to be clinically septic nor did she have any symptoms suggestive of arterial thrombosis. Platelet counts continued to drop further and reached a nadir of 6000/μL on hospital day 14 (Fig. 1) despite stopping heparin and substituting bivalirudin. Laboratory testing revealed probable disseminated intravascular coagulation (DIC), which was attributed to ongoing infection. A peripheral blood smear did not reveal schistocytes, and there were no clinical features of thrombotic thrombocytopenic purpura other than thrombocytopenia. Molecular testing found her to be heterozygous for platelet antigen 1/2 (PLA1/A2), essentially ruling out posttransfusion purpura (PTP).

Given the time frame and the rate of drop, a provisional diagnosis of DITP was made. Daptomycin was substituted for vancomycin and piperacillin-tazobactam, and blood samples

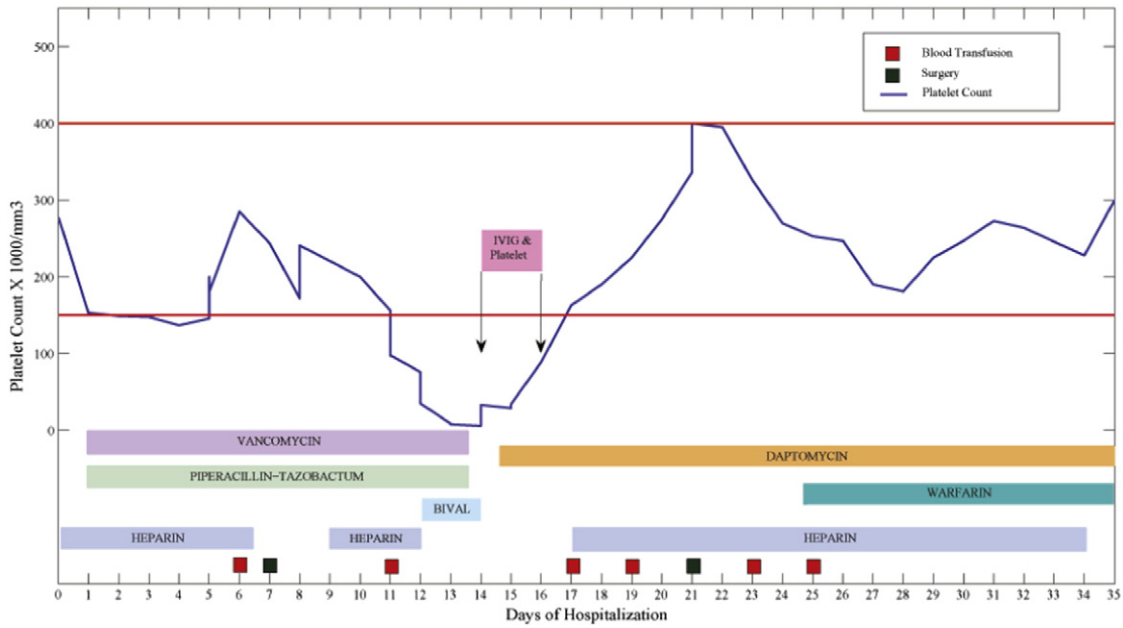


**Fig. 1** Temporal profile of platelet count.