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# Severe Thrombocytopenia in Infective Endocarditis

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CASE REPORT

# Severe Thrombocytopenia in Infective Endocarditis

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**Abstract**

**Thrombocytopenia can be seen in about 20−25% of patients with bacterial infective endocarditis (IE). Platelets have a major role in the pathogenesis of endocarditis, and they are also sensitive monitors of systemic host response to bacteremia. Thrombocytopenia on presentation of patients with IE identifies higher risk groups and carries higher mortality risk. The presence of thrombocytopenia is an independent prognosticator of poor outcomes in IE. We present a case of a 40-year-old male with the history of injection drug use who was diagnosed with IE and was found to have severe thrombocytopenia on admission was treated with intravenous antibiotics, which dramatically improved his platelet counts as well without any need for plasmapheresis or platelet transfusions.**

*Keywords:* Thrombocytopenia, Infective endocarditis, Antibiotic therapy

## 1. Introduction

Infective endocarditis (IE) is an infection of endothelial lining of the heart with an annual incidence of 3−10/100,000 of the general population and mortality up to 30% at 30 days. It has varied clinical presentation with 90% of the patients presenting with fever, fatigue, night sweats, and weight/appetite loss.[1,2] *Staphylococcus aureus* is the most common prevalent cause of IE followed by viridians group streptococci and enterococci.[3] Older patients are more likely to have coagulase-negative staphylococcus (CoNS) IE and enterococcal IE than staph IE.

Thrombocytopenia is common in IE and more commonly associated with *S. aureus* IE, compared to other causes of IE. Patients with IE and concomitant thrombocytopenia have worse clinical outcome and higher mortality rate.[4] Thus, thrombocytopenia is considered an independent prognostic marker in IE and serial measurement of platelet count may help to monitor the evolution of disease and response to the treatment.[5] Therefore, although thrombocytopenia is a common finding in patients with IE, presentation with severe thrombocytopenia, which is defined as platelet counts <30,000 to 50,000 k/uL, is rare.

We present a case of severe thrombocytopenia in the setting of IE.

## 2. Case presentation

A 40-year-old disheveled man was brought to the emergency department after being found lethargic on the street with altered mentation of unknown duration. He also endorsed chills, night sweats and recent weight loss. Past medical history was significant for untreated hepatitis C and intravenous drug (IV) use—heroin. Vital signs revealed hypotension 85/52 mmHg without tachycardia; he was afebrile at presentation. Examination showed multiple tattoos on inspection, a dry oral mucosa and tenderness to superficial palpation of all muscle groups. His blood pressure improved with fluids. Refer to Table 1 for general serum chemistry and complete blood count lab values on presentation. Hepatitis panel was reactive for hepatitis C virus with Polymerase Chain Reaction (PCR) quantification of 19,035,502 IU/mL (reference range ≤15 IU/mL). Urine toxicology screen tested positive for cannabinoids and cocaine. The electrocardiogram (EKG) showed a normal sinus rhythm with bilateral atrial enlargement and prolonged QTc with 506 ms. Non-contrast Commuted Tomography (CT) of the head was negative for acute intracranial pathology or

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*Table 1. Serum Chemistry results and Complete blood count with differential.*

| Lab view | Results | Reference ranges |
|---|---|---|
| **General Serum Chemistry** | | |
| Sodium | 119 mmol/L | 136–145 mmol/L |
| Creatinine | 1.6 mg/dL | 0.6–1.1 mg/dL |
| Total bilirubin | 7.4 mg/dL | 0.3–1.2 mg/dL |
| Direct bilirubin | 5.8 mg/dL | 0.0–0.3 mg/dL |
| Albumin | 2.1 g/dL | 3.2–4.8 g/dL |
| Alkaline phosphatase | 340 units/L | 46–116 units/L |
| Lactic acid | 5.1 mmol/L | 0.7–2 mmol/L |
| **Complete blood count** | | |
| White Blood Cell count | 41.8 k/uL | 4–10.8 k/uL |
| Hemoglobin | 11.5 g/dL | 12.5–16.5 g/dL |
| Platelet counts | 5 k/uL | 145–400 k/uL |
| Mean Corpuscular Volume | 80 FL | 81–100 FL |

traumatic injury. He was admitted to the Intensive Care Unit (ICU) for presumed septic shock of unknown origin, at this juncture complicated by hyponatremia and severe thrombocytopenia.

As part of initial resuscitation efforts, he received IV fluids and three units of platelet transfusions prior to critical care admission, however, his platelet count plateaued at 8 k/uL. He was started on broad spectrum antibiotics (piperacillin-tazobactam, vancomycin, and doxycycline to cover for atypical infections). His lactic acidosis resolved with IV fluid resuscitation along with improvement in sodium levels and acute kidney injury. His blood cultures obtained during the admission revealed a *Streptococcus* species in 1 of 2 blood culture bottles one day following admission, which eventually speciated into alpha-hemolytic *Streptococcus mitis*. Antibiotics were then narrowed to IV ceftriaxone 1 g daily based on the sensitivity results. Ultrasound of the abdomen showed hepatic cirrhosis and splenomegaly. Thrombocytopenia workup as depicted in Table 2, was suggestive of intravascular hemolysis. Rheumatological work-up significant for a low C3 level of 59 mg/dL (reference range 90–170 mg/dL). Human Immunodeficiency Virus (HIV) screen was negative. The Echocardiogram two days following admission showed a large pedunculated unknowable vegetation on the tricuspid valve (1.6 cm × 2.0 cm).

*Table 2. Thrombocytopenia workup results.*

| Tests | Results | Reference ranges |
|---|---|---|
| International normalized ratio | 1.6 | 0.8–1.2 |
| Prothrombin time | 19 s | 11.8–14.6 s |
| Reticulocyte count | 0.8% | 0.5–2.0% |
| Absolute reticulocytes count | 0.025 millions/uL | 0.020–0.1 millions/uL |
| ADAMTS13 | 29% | ≥61 |
| Fibrinogen | 117 mg/dL | 195–505 mg/dL |
| D-dimer | 2.86 mcg/mL | ≤0.5 mcg/mL |
| Lactate dehydrogenase | 252 units/L | 120–146 units/L |
| Haptoglobin | <8 mg/dL | 40–280 mg/dL |

He received IV ceftriaxone for four weeks as he was deemed a poor surgical candidate considering his other comorbidities such as thrombocytopenia, liver cirrhosis and history of IV drug use. His platelet counts improved following appropriate management of the underlying medical condition and therefore no further platelet transfusion was given. He was then transferred to the general medical floor for further treatment and appropriate disposition.

## 3. Discussion

Our patient presented with severe thrombocytopenia, secondary to IE. Moreover, his platelet counts improved with the management of IE itself with IV antibiotics. Platelet transfusion was unsuccessful in improving his platelet counts.

Platelets have a major role in the pathogenesis of endocarditis, and they are also sensitive monitors of systemic host response to bacteremia.[6] The ability of bacteria to induce platelet aggregation is conferred by two surface expressed androgens–class I antigen which promotes streptococcal addition to platelets and class II antigens that trigger platelet aggregation. This platelet aggregation–associated protein (PAAP) contains a collagen-like platelet–interacting domain. This way of platelet activation was demonstrated by streptococcus sanguis. Additional ways of streptococcal platelet binding interaction were further demonstrated by *Streptococcus mitis* which mediated binding by three surface structures that act as adhesins. Staph aureus on the other hand triggers platelet aggregation by way of bridging with fibrinogen. Platelets therefore contribute to the formation of vegetation and contribute to anti-infective host defenses by releasing inflammatory mediators and microbial peptides called platelet-derived microparticles (PMPs) or thrombocidin. They prevent and mitigate infection through three types of granules (α, δ and λ) that release a variety of mediators involved in adhesion and coagulation, vascular tone and thrombosis dissociation. However, bacteria can be either susceptible or resistant to PMPs released by platelets. PMP-susceptible organisms were rapidly eradicated from the vegetation within 24–48 h, however, PMP- resistant strains persisted into the site causing progressive infection therefore, bacteria may utilize platelets for the development of vegetation only if they escape the microbicidal actions of PMPs.[6] Complete pathophysiology is

complex; however, it does demonstrate the pathophysiology of thrombocytopenia in patients with infective endocarditis. Although our patient had multiple etiologies of thrombocytopenia, such as ongoing sepsis, infection-associated autoimmune thrombocytopenia, consumptive thrombocytopenia and liver cirrhosis; the fact that his platelet counts improved with antibiotic treatment and given low C3 levels renders an immune mediated destruction leading to consumptive thrombocytopenia as the most likely cause.

A retrospective case control trial involving 192 patients demonstrated that thrombocytopenia is an independent predictor of mortality in IE. 45.1% of patients had thrombocytopenia on presentation ($138.3 \pm 86.8 \times 10^3/\mu l$ at day 1), which increased the odds of mortality by 2.5-fold at 6 months (95% confidence interval 1.3−4.6; $P = 0.004$).[5] Another prospective cohort study involving 698 patients revealed much higher mortality in patients with thrombocytopenia as compared to patients with normal platelet counts (40.4% versus 25.3%; $P < 0.001$).[7] Therefore, thrombocytopenia on presentation of patients with IE identifies higher risk groups and carries higher mortality risk. The management of thrombocytopenia in such instances would be to treat the underlying cause as depicted in our case. Platelet transfusion alone will not correct thrombocytopenia considering the consumptive pathophysiology of low platelets.

As platelets are involved in the pathogenesis of IE, development of PMP or thrombocidin analogs for therapy may be envisioned. There have been clinical observations that have suggested that antiplatelet therapy might prevent vegetation growth and may decrease cerebral septic emboli. Experiments in rabbits that have studied the role of aspirin and ticlopidine suggested that they synergistically decrease the vegetation size and bacterial titers.[6] Aspirin was further studied using the same model of staphylococcus aureus IE in rabbits, which revealed that aspirin significantly decreased vegetation weight, vegetation bacterial titers and renal septic emboli in vivo. Moreover, pre-exposure of platelets to aspirin in vitro decreased platelet adherence and aggregation to the bacteria.[8] Despite the dual beneficial impact of antiplatelet therapy, it carries a risk of bleeding; therefore, these experimental results extrapolation onto humans must consider the risk of hemorrhage during acute IE and thus requires a formal clinical evaluation The use of antiplatelet in IE induced thrombocytopenia lacks human trial and therefore opens a wide range of opportunities for further research.

## 4. Conclusion

Thrombocytopenia in IE carries a higher mortality risk and is an independent prognosticator of poor outcomes. Treatment of IE is the best modality to improve the platelet count, however, the impact on the mortality benefit is lacking. This demands further studies to evaluate the overall patient outcome and the role of antiplatelets to improve thrombocytopenia in IE.

## Conflict of interest

The authors have no conflicts to disclose.

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