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STEM CELL STEAL AFTER INTRAVENOUS IRON: A CASE OF TRANSIENT THROMBOCYTOPENIA IN SEVERE IRON DEFICIENCY ANAEMIA

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ABSTRACT

Background: Iron-deficiency anaemia (IDA) commonly presents with reactive thrombocytosis. A less recognized, paradoxical decline in platelets may occur shortly after iron repletion. This phenomenon is most notably seen with intravenous (IV) formulations and termed the platelet steal effect.

Case report: We describe a 68-year-old man with severe IDA (haemoglobin 6.6 g/dl; mean corpuscular volume 53.4 fl; ferritin 8.7 ng/ml; iron saturation 3.4%) who developed marked thrombocytopenia after initiation of IV iron. The platelet count trended down from 290 $\times 10^3$/µl on admission to a nadir of 39 $\times 10^3$/µl by hospital day 5 without bleeding. Other causes of thrombocytopenia were systematically excluded. Iron therapy was continued and transitioned to oral supplementation; platelets stabilized by day 10 and recovered thereafter in parallel with haemoglobin improvement.

Conclusion: Transient thrombocytopenia following iron repletion is likely under-recognized. Awareness of its timing and benign course may prevent unnecessary testing or interruption of definitive IDA therapy.

KEYWORDS

Iron deficiency anaemia, intravenous iron, thrombocytopenia, platelet steal phenomenon, stem cell steal effect

LEARNING POINTS

- Transient thrombocytopenia may occur shortly after intravenous iron repletion in severe iron deficiency anaemia, despite the usual association with thrombocytosis.
- The "stem cell steal" phenomenon reflects a temporary shift of bone marrow progenitors toward erythropoiesis once iron becomes available.
- Recognizing this benign, self-limiting response prevents unnecessary investigations or interruption of essential iron therapy.

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INTRODUCTION

Iron deficiency anaemia (IDA) is the most prevalent nutrition deficiency worldwide, affecting 2 billion people worldwide and 14% of adults in the United States[1]. It occurs due to the unmet demand for iron to form normal red blood cells. This can be caused by inadequate intake of iron, chronic blood loss or malabsorption of iron[2]. Beyond its impact on red blood cell production, iron deficiency also exerts systemic effects on haematopoiesis, including alterations in platelet count and function.

IDA is a recognized cause of reactive thrombocytosis. A proposed mechanism is that anaemia-driven increases in endogenous erythropoietin (EPO) promote thrombopoiesis in an iron-dependent fashion: when iron supply is limited the thrombopoietic effect is increased[3]. Independently of EPO, iron deficiency directly biases bipotent megakaryocytic–erythroid progenitors (MEPs). Platelet counts increase as a compensatory mechanism likely mediated by a shift in the differentiation of hematopoietic progenitor cells, specifically megakaryocytic-erythroid progenitors, toward the megakaryocytic lineage at the expense of the erythroid lineage under conditions of low iron[4,5]. Interestingly, iron repletion in patients with iron deficiency can lead to a paradoxical and transient decline in the platelet count. This effect is particularly observed when the iron is delivered intravenously and in high doses[6].

This rare response, often termed the "platelet steal phenomenon," is thought to occur due to a preferential shift in marrow activity toward erythropoiesis[7]. As iron becomes suddenly available, erythroid precursors may outcompete megakaryocytic lineages for shared resources, such as iron-dependent enzymes, growth factors, and stromal support. The resultant thrombocytopenia is typically self-limiting and benign but may raise clinical concern in the absence of awareness about this phenomenon.

Laboratory tests	Level	Reference range
Iron (ug/dl)	13	50-150
Iron saturation (%)	3.4	20-55
Total iron binding capacity (µg/dl)	378	250-400
Ferritin (ng/ml)	8.7	24-336
Folate (ng/ml)	16.2	4-20
Vitamin B-12 (ng/ml)	509	180-914
Lactate dehydrogenase (U/l)	217	122-222
Haptoglobin (mg/dl)	108	32-363
Reticulocytes (%)	3.0	≤ 2
Red cell distribution width (%)	26.5	11.8-15.6

Table 1. Baseline iron studies and haemolysis workup. Iron panel and haemolytic markers at presentation confirmed iron deficiency anaemia (low serum iron, ferritin, and transferrin saturation) without evidence of haemolysis.

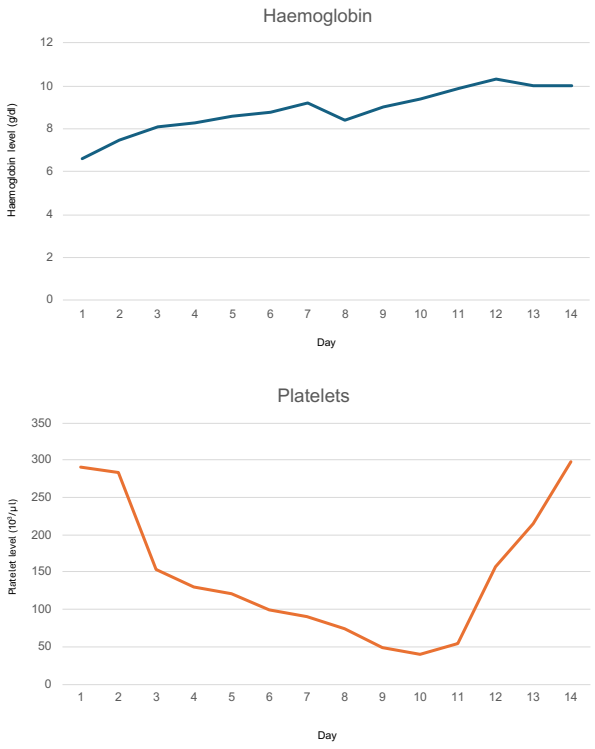


Figure 1. Timeline of hematologic parameters during hospitalization. Trend of haemoglobin (g/dl) and platelet count (×10³/µl) from hospital admission through day 10. Following initiation of intravenous iron therapy (iron sucrose 200 mg), the platelet count declined from 290 ×10³/µl to a nadir of 39 ×10³/µl by hospital day 5 without bleeding manifestations, then gradually recovered in parallel with haemoglobin improvement. The transient thrombocytopenia resolved spontaneously, consistent with the "stem cell steal" phenomenon.

In this report, we present the case of a 68-year-old male with severe iron deficiency anaemia who developed significant thrombocytopenia shortly after receiving treatment with intravenous iron. The case illustrates the temporal association between iron repletion and platelet decline. It also highlights the importance of recognizing this under-reported phenomenon to prevent unnecessary diagnostic workup or interruption of appropriate therapy.

CASE DESCRIPTION

A 68-year-old man with seizure disorder, hypertension, hyperlipidaemia, coronary artery disease, and a history of chronic lower gastrointestinal bleeding presented to the emergency department with involuntary mouth twitching and generalized shaking concerning for seizure activity. Eight months earlier, he had been admitted for a lower gastrointestinal bleed resolved after stool disimpaction via flexible sigmoidoscopy.

On arrival, he was hemodynamically stable. Physical examination was nonfocal; there were no mucocutaneous signs of bleeding such as petechiae, purpura, ecchymoses. Neurologic exam revealed no focal deficits.

Initial laboratory testing showed severe microcytic anaemia



Figure 2. Diagnostic evaluation of thrombocytopenia after iron repletion. Systematic exclusion of alternative aetiologies for thrombocytopenia in this patient. Heparin-induced thrombocytopenia was ruled out due to no heparin exposure; disseminated intravascular coagulation and thrombotic microangiopathy were excluded by normal coagulation profile and peripheral smear findings. No new medications were introduced, and infection markers remained normal. The temporal relationship to intravenous iron initiation and spontaneous platelet recovery without specific therapy supported a benign "platelet steal" (stem cell steal) mechanism.

with haemoglobin 6.6 g/dl, mean corpuscular volume 53.4 fl, platelet count 290 ×10^3/µl, reticulocyte percentage 3%, and red cell distribution width 26.5%. Iron studies confirmed iron deficiency: serum iron 13 µg/dl, total iron-binding capacity 378 µg/dl, transferrin saturation 3.4%, and ferritin 8.7 ng/ml. Vitamin B12 and folate levels were normal. The levels of lactate dehydrogenase 217 U/l and haptoglobin 108 mg/dl did not suggest haemolysis. Coagulation studies were within normal limits, and the peripheral smear showed no schistocytes.

Iron panel, ferritin levels and haemolytic workup was done to understand the underlying reason of the anaemia and are shown in *Table 1*. Iron panel demonstrated decreased serum iron level and iron saturation, along with severely low ferritin level. The findings were consistent with iron deficiency anaemia.

The patient received one unit of packed red blood cells and was started on intravenous (IV) iron therapy (iron sucrose 200 mg in sodium chloride 0.9% 100 ml). No new medications were introduced during the hospitalization, there was no heparin exposure, and the patient did not experience any infectious or inflammatory complications.

The platelet count began to decline on hospital day (HD) 2, reaching a nadir of 39 ×10^3/µl by HD 5 without clinical bleeding. Iron therapy was continued and transitioned to oral supplementation by HD 5. Platelets stabilized by HD 10 and recovered thereafter without specific intervention, paralleling a steady rise in haemoglobin *(Fig. 1)*. The patient was discharged in stable condition on oral iron with haematology follow-up. The seizure concern was attributed to prior anticonvulsant nonadherence; no further events occurred during hospitalization while on therapy.

Potential causes of thrombocytopenia were systematically evaluated *(Fig. 2)*. Heparin-induced thrombocytopenia (HIT) was excluded given no heparin exposure; disseminated intravascular coagulation was unlikely due to normal coagulation studies and lack of schistocytes. There were no new culprit drugs, and immune thrombocytopenia was considered but unlikely given the no bleeding on presentation and spontaneous recovery by day 10 without ITP-directed therapy. Findings were most consistent with a stem cell steal (platelet "steal") effect related to IV iron.

The patient's haemoglobin improved steadily with iron therapy. Thrombocytopenia resolved without intervention. He was discharged in stable condition on oral iron supplementation with outpatient haematology follow-up. The reason for seizures was found to be medication noncompliance, and no seizure activity was observed during the hospitalization while the patient is on anticonvulsant.

DISCUSSION

Untreated IDA commonly features reactive thrombocytosis, whereas a paradoxical decline in platelets after iron repletion, particularly with intravenous IV formulations, remains less recognized. The present case demonstrates a marked yet self-limited thrombocytopenia temporally associated with IV iron initiation in a patient with severe IDA and no bleeding, infection, or new medications. Platelets reached a nadir by hospital day 5 and recovered without specific intervention while haemoglobin rose with continued iron therapy. This pattern is consistent with prior observations[6,7].

Two complementary mechanisms likely cause thrombocytosis in IDA and its reversal after iron repletion. First, anaemia-driven increases in endogenous EPO promote thrombopoiesis in an iron-dependent fashion: when iron supply is limited the thrombopoietic effect is accentuated, whereas with adequate iron availability erythropoiesis predominates and platelet counts normalize or may transiently fall[3]. Second, iron deficiency directly biases bipotent MEPs toward megakaryopoiesis, at least partly via signalling changes that favour megakaryocyte maturation; this lineage effect has been demonstrated in murine models and human cells[4,5]. Rapid restoration of iron might reverse these pressures, temporarily shifting marrow activity toward erythropoiesis at the expense of megakaryopoiesis, a phenomenon described as "stem cell steal" (also called the platelet steal effect). As a result, a short-lived platelet nadir is observed followed by recovery as iron stores and erythropoiesis stabilize[6].

In this case, potential alternative aetiologies for the thrombocytopenia were systematically evaluated and found unlikely. Heparin-induced thrombocytopenia was excluded given the absence of heparin exposure. Disseminated

intravascular coagulation or thrombotic microangiopathy was unlikely in the setting of normal coagulation studies and a peripheral smear without schistocytes. Drug-induced thrombocytopenia was not supported by the medication history, considering no new culprit agents were initiated. Immune thrombocytopenia was considered but deemed improbable given the non-bleeding presentation and spontaneous platelet recovery by approximately hospital day 10 without steroids or intravenous immunoglobulin (IVIG). Bone marrow suppression or infiltrative disease was similarly unlikely in view of isolated thrombocytopenia, normal white blood cell counts, preserved erythropoiesis with an elevated reticulocyte percentage, and subsequent normalization. Post-transfusion thrombocytopenia was considered. Dilutional thrombocytopenia typically follows massive transfusion, and this patient received only one unit of packed red blood cells. Immune-mediated post-transfusion purpura usually presents 5–10 days post-transfusion with profound thrombocytopenia (often <10 $\times 10^3$/μl) and bleeding; in this case, the 48–72-hour onset, a nadir of 39 $\times 10^3$/μl without bleeding, and spontaneous recovery without IVIG argue against this entity. Taken together with the close temporal relationship to initiation of IV iron and a benign, self-limited trajectory the findings most strongly support a stem cell steal effect.

Clinicians should anticipate that a subset of patients with severe IDA may experience a transient platelet decline. This phenomenon is seen especially in those receiving IV iron. This decline begins within 48–72 hours, with a nadir around days 3–7 and recovery by day 10 if no alternative pathology is present. Iron repletion can be safely continued for stable and asymptomatic patients without bleeding or laboratory red flags with close monitoring, while carefully watching for features that would prompt an alternative workup (e.g., exposure to heparin, haemolysis, consumptive coagulopathy, new drugs, or infection). This can reduce low-value testing and prevent premature interruption of definitive IDA therapy.

The incidence, predictors, and dose-specific risk of post-iron thrombocytopenia remain uncertain. Prospective pharmacovigilance and mechanistic studies could clarify which patients are most susceptible and whether particular IV iron regimens modulate risk.

Transient, benign thrombocytopenia following IV iron consistent with a stem cell steal effect should be considered early in the post-repletion period once alternative causes are excluded. Recognizing its timing and trajectory preserves appropriate iron therapy and focuses evaluation on true red flags, aligning care with the underlying biology.

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