

# A Rare Complication of a Common Problem: Thrombocytopenia Subsequent to Iron Replacement Therapy in an Adolescent Girl with Severe Iron Deficiency Anaemia

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## Abstract

Thrombocytosis may accompany iron deficiency anaemia (IDA). However, thrombocytopenia is a rare occurrence that might be associated with IDA. A 15-year-old girl presented with IDA related to menorrhagia. Erythrocyte transfusion was given, since the haemoglobin level at presentation was 4.7 g/dL and oral iron supplementation was initiated with ferrous glycine sulphate. On 12th day of iron treatment, platelet count was found to have decreased to a level of  $48 \times 10^9/L$ . Bone marrow aspiration was obtained in order to investigate the aetiology of thrombocytopenia and revealed erythroid hyperactivity, severe megaloblastic changes, binucleated normoblasts, and decreased number of megakaryocytes. Oral iron replacement therapy was continued and vitamin B12 was added to treatment in view of severe megaloblastic changes in the bone marrow examination. Platelet count normalised and haemoglobin level increased during the follow-up with the replacement of oral iron and vitamin B12.

## Key words

Iron deficiency anaemia; Thrombocytopenia; Vitamin B12

## Introduction

Iron deficiency anaemia (IDA) is still a common cause of anaemia among paediatric age group.<sup>1</sup> Thrombocytosis has not uncommonly been reported to accompany IDA, but thrombocytopenia is a rare occurrence to be associated with IDA.<sup>2</sup> Iron deficiency anaemia associated thrombocytopenia is generally detected at initial presentation and improves after iron replacement.<sup>3</sup> Thrombocytopenia may develop secondary to iron supplementation in severe IDA very rarely. There were a few cases in the literature on thrombocytopenia occurring after iron replacement therapy.<sup>4-6</sup> Herein, we presented an adolescent patient presenting with menorrhagia with severe iron deficiency

anaemia who developed thrombocytopenia subsequent to oral iron replacement therapy.

## Case

A 15-year-old girl presented with paleness and fatigue for the last two months and the history revealed menorrhagia for the last nine months. Physical examination revealed the absence of hepatosplenomegaly. Complete blood count showed haemoglobin 4.7 g/dL, haematocrit 16%, RBC  $2.5 \times 10^{12}/L$ , MCV 64.2 fL, RDW 25.2%, white blood cell count  $8.5 \times 10^9/L$ , neutrophil count  $5.5 \times 10^9/L$ , platelet count  $820 \times 10^9/L$ . On peripheral blood smear, hypochromia and microcytosis were prominent in erythrocytes. Serum ferritin level was 2.4 ng/mL, transferrin saturation 0.95%, and vitamin B12 level 530 pg/mL. A diagnosis of severe IDA was established and erythrocyte transfusion was given once. Oral iron supplementation was initiated with ferrous glycine sulphate with dose of 4 mg/kg, subsequently. On 12th day of treatment, complete blood count revealed haemoglobin 8.2 g/dL, haematocrit 26.8%, RBC  $3.7 \times 10^{12}/L$ , MCV 72 fL, RDW 31.5%, white blood cell count  $5.9 \times 10^9/L$ , platelet count  $48 \times 10^9/L$ ,

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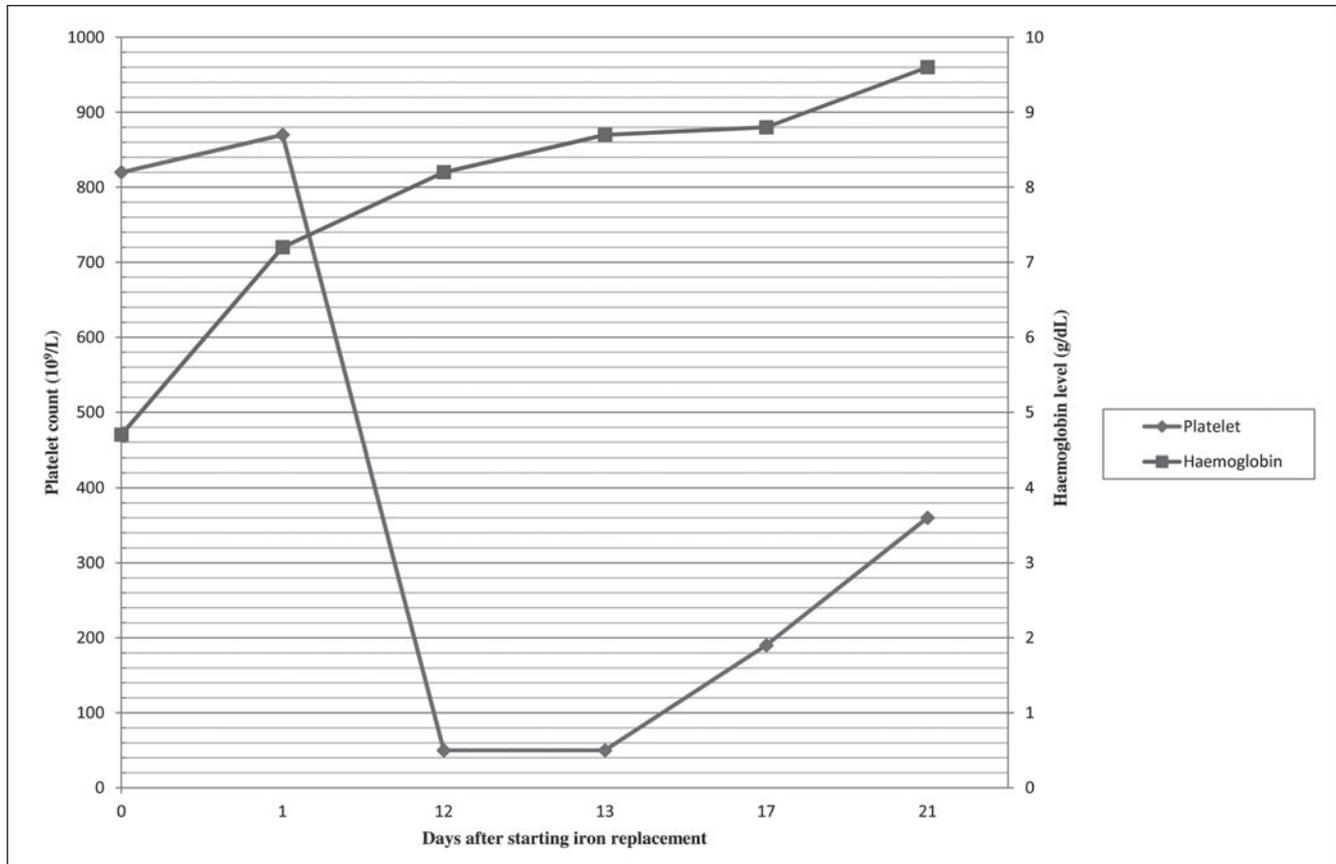
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reticulocyte 2.4% (Figure 1). Mean platelet volume was 9.4 fL. Platelet morphology was normal on peripheral blood smear. Bone marrow aspiration was performed in order to investigate the aetiology of newly developed thrombocytopenia and erythroid hyperactivity, binucleated normoblasts and severe megaloblastic changes in nuclear structure of both myeloid and erythroid lineages, in addition to decreased number of megakaryocytes were detected. She hadn't any symptom or sign of viral infections. There was no history of drug use other than iron. Vitamin B12 was initiated with dose of 10 mcg/kg and oral iron treatment was continued. After five days, haemoglobin level was 8.8 g/dL and thrombocyte count was found to be normalised to a level of  $189 \times 10^9/L$ . On 21st day of iron replacement, haemoglobin level was measured as 9.6 g/dL and thrombocyte count was  $363 \times 10^9/L$ . In order to determine the underlying condition for the menorrhagia, coagulation work-up was done and revealed von Willebrand disease of type I.

### Discussion

Iron deficiency anaemia is a public health problem in both developed and developing countries. In the paediatric population, IDA prevalence increases in adolescent period due to rapid growth in both genders and commencement of menstrual bleeding in girls.<sup>1</sup> Thrombocytosis is one of the well-known laboratory findings of IDA. Thrombocytosis associated with IDA has been explained with increased stimulation of platelet progenitors by elevated erythropoietin activity.<sup>7</sup> However, thrombocytopenia may rarely accompany IDA as well. Thrombocytopenia has been reported in patients with IDA with a prevalence of 2.3-2.4% in different studies.<sup>8,9</sup> Thrombocytopenia has been reported to develop secondary to depressed activity of iron dependent enzymes functioning in thrombopoiesis.<sup>4</sup> When transferrin saturation is  $\leq 1\%$ , maturation of three cell lineages may be inhibited.<sup>10</sup> In this situation, continuation of iron replacement may improve cytopenias. However, in



**Figure 1** Platelet count and haemoglobin levels during iron replacement.

our patient, thrombocytopenia developed after initiation of iron replacement therapy. Thrombocytopenia after iron replacement therapy is a very rare clinical condition. There are a few cases of iron replacement related thrombocytopenia in literature.<sup>4,6</sup> Thrombocytopenia has been reported after oral ferrous sulfate, ferrous gluconate, parenteral iron dextran, and parenteral iron sucrose infusions.<sup>4,6</sup> In these patients, thrombocytopenia has been reported to be detected between 2nd to 10th days of iron replacement therapy.<sup>4,6</sup>

Mechanism of thrombocytopenia after iron replacement isn't known exactly. Ganti et al explained the pathophysiology with stem cell steal phenomenon.<sup>4</sup> During severe iron deficiency, erythropoietin level and iron demand of erythrocyte precursors may increase, and after iron replacement pluripotent stem cells may lead to evolve towards erythrocyte lineage. This may result in decrease of other cell lineage precursors and subsequently, mature cells.<sup>4</sup> In our patient, bone marrow aspiration smear revealed increased erythroid activity and severe megaloblastic changes in normoblasts. Although serum vitamin B12 and folate levels were in normal range at the initiation of iron replacement therapy, elevated erythropoiesis after treatment of severe iron deficiency might have led to rapid consumption of these vitamins at cellular level related to increased erythropoiesis and it might have been another cause of the thrombocytopenia developing after iron replacement. However, megaloblastic changes in bone marrow may also be secondary to severe iron deficiency which has inhibited the consumption of folate and vitamin B12.<sup>6</sup> In our patient, we performed bone marrow aspiration at 12th day of treatment. So, association of megaloblastic changes with severe iron deficiency is a remote possibility. Unfortunately, we couldn't measure vitamin B12 level at the same time with bone marrow aspiration because of technical reasons. We added oral vitamin B12 to iron treatment and thrombocytopenia improved in five days. It is difficult to attribute the resolution of thrombocytopenia to vitamin B12 replacement in our patient, since in previously reported cases, thrombocytopenia subsided after continuation of iron replacement solely.<sup>4,6</sup>

## Conclusion

In conclusion, in patients with severe iron deficiency anaemia, temporary thrombocytopenia may occur after initiation of iron replacement therapy. In this circumstance, iron treatment should be continued and vitamin B12 treatment may fasten improvement of thrombocytopenia, in the presence of megaloblastic changes in the bone marrow precursors.

## Conflict of Interest

Authors have no conflicts of interest to disclose.

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