Refractory hypophosphatemia following ferric carboxymaltose administration

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Received: 24 July 2020 / Accepted: 3 March 2021 / Published online: 14 March 2021
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Abstract

Hypophosphatemia is a rare side effect of intravenous iron replacement. Urinary phosphate wasting due to increased FGF23 is the most likely mechanism. Here, we present a case of intractable hypophosphatemia in a 32-year-old female patient with history of ulcerative colitis (UC), who was primarily hospitalized due to UC flare-up. Her urinary fractional excretion of phosphate was inappropriately elevated at 70%. A careful history revealed that she had been treated with ferric carboxymaltose 2 weeks prior to hospitalization, leading to a diagnosis of iron-induced hypophosphatemia. She was treated with 5 weeks of intravenous sodium phosphate since she did not tolerate oral supplementation. In conclusion, clinicians should be aware of iron-induced hypophosphatemia and be cautious when prescribing intravenous iron.

Keywords Hypophosphatemia · Renal phosphorus wasting · Intravenous iron · Ferric carboxymaltose

Introduction

Iron deficiency is common cause of anemia and can be due to various etiologies including inflammatory bowel disease and usually treated with intravenous iron. Most concerning side effect of intravenous iron is anaphylaxis. Hypophosphatemia is another side effect of intravenous iron treatment and can cause serious adverse effects including respiratory failure. Here, we presented a refractory case of hypophosphatemia due to intravenous iron administration and provided perspective into the management.

Case description

A 32-year-old woman with history of ulcerative colitis presented to hospital with 2 months of worsening diarrhea and hematochezia. She did not respond to outpatient prednisone treatment and continued to have 10 small bowel movements daily. In the hospital, she was treated with intravenous methylprednisolone and adalimumab with gradual improvement of diarrhea and hematochezia. Her admission laboratory testing included serum phosphorus 1.5 mg/dl (normal 2.5–4.5 mg/dl), corrected calcium 8.8 mg/dl, 25-OH vitamin D 35 ng/mL, hemoglobin 7.5 g/dl with a mean corpuscular volume (MCV) of 95 fL.

Her serum phosphorus had a nadir at 0.9 mg/dl 10 days after hospitalization despite intravenous phosphorus repletion. Serum 25-OH vitamin D and PTH were found normal at 34 mg/ml and 55 pg/ml (normal 15–65 pg/ml), respectively. Further work-up showed inappropriately normal 1,25-OH vitamin D level at 32 ng/ml (normal 18–78 ng/ml). FGF23 level was not sent. Her urinary fractional excretion of phosphate was inappropriately elevated at 70%. A careful history revealed that she had been treated with ferric carboxymaltose 2 weeks prior to hospitalization, leading to a diagnosis of iron-induced hypophosphatemia. Due to her active ulcerative colitis, the patient did not tolerate oral phosphate repletion and required 15–30 mmol of intravenous phosphate/day. Three weeks after admission, a peripherally

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inserted central catheter (PICC) was placed and she was ultimately discharged with daily home administration of 15 mmol intravenous potassium phosphate. One week later, her FGF23 level was normal at 66 RU/ml (normal ≤ 180 RU/ml). By 2 weeks after discharge, her serum phosphorus levels improved to 3 mg/dL, with successful discontinuation of intravenous phosphate supplementation. Her laboratory and treatment course is summarized in Fig. 1. Her hemoglobin level had risen to 12 g/dL as her UC flare improved. Informed consent was obtained from all individual participants included in the study.

Discussion

We present a case of refractory hypophosphatemia due to intravenous ferric carboxymaltose. Fibroblast growth factor 23 (FGF23) is secreted from bone and increases urinary phosphate excretion by inhibiting sodium–phosphate co-transporters and diminishing 1,25-dihydroxy-vitamin D synthesis [1, 3]. Ferric carboxymaltose increases serum FGF23 levels by inhibiting FGF23 cleaving enzyme, which causes urinary phosphate wasting. Only certain iron formulas such as ferric carboxymaltose have been associated with hypophosphatemia [4, 7]. Clinical trials comparing iron isomaltoside to ferric carboxymaltose and

ferumoxytol to ferric carboxymaltose have shown a higher incidence of hypophosphatemia in patients treated with ferric carboxymaltose [2, 5, 6]. Increased urinary phosphate excretion despite low serum phosphorus suggested that our patient had iron-induced hypophosphatemia.

Hypophosphatemia due to intravenous iron treatment could be easily overlooked especially in patients with diarrhea. Although iron-induced hypophosphatemia was initially missed in this patient, we eventually revealed the diagnosis with careful history taking and by measuring urinary phosphate excretion. Iron-induced hypophosphatemia typically reaches a nadir 2 weeks after the administration of ferric carboxymaltose, and the phosphate normalizes between 2 and 5 weeks [2, 5]. In our patient, hypophosphatemia recovered 5 weeks after ferric carboxymaltose infusion. Oral phosphorus treatment is usually preferred to intravenous phosphorus due to risks of hypocalcemia, cardiac arrhythmias and limb paresthesia associated with intravenous treatment. Our patient did not tolerate oral treatment due to gastrointestinal symptoms which led us to choose intravenous phosphorus treatment. Absence of longitudinal serum FGF23 and 1,25-OH vitamin D levels is a limitation of our case.

In conclusion, clinicians should be aware of iron-induced hypophosphatemia and be cautious when prescribing intravenous iron, with careful monitoring of serum phosphate

Fig. 1 Laboratory and treatment course of the patient. Hypophosphatemia was detected 2 weeks after intravenous ferric carboxymaltose treatment. Serum phosphorus decreased to a nadir of 0.9 mg/dL despite repletion; fractional phosphorus excretion zenith was 70%. Patient received total of 5 weeks intravenous sodium phosphate treatment because she did not tolerate oral phosphate repletion. Serum phosphorus improved to > 3 mg/dL 7 weeks after the intravenous iron treatment

afterward. Hypophosphatemia should be aggressively treated to avoid adverse effects.

Acknowledgements All authors had access to the data and role in writing the manuscript. Informed consent was obtained from all individual participants included in the study.

Declarations

Conflict of interest None of the authors had conflict of interests.

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