Severe hypophosphatemia following ferric carboxymaltose in a patient presenting with a focal seizure: a case report

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ABSTRACT

Background: Ferric carboxymaltose (FCM) can cause fibroblast growth factor 23 (FGF23)-mediated renal phosphate wasting. Severe electrolyte disturbances may lower the seizure threshold, but causal attribution requires caution when other neurological and metabolic risk factors coexist.

Case Presentation: A 76-year-old woman presented after a 2-minute focal seizure one month after receiving a single 1 g intravenous FCM infusion for iron-deficiency anemia. Computed tomography of the head showed no acute intracranial lesion, and electroencephalography showed no epileptiform discharges. Extended testing identified severe hypophosphatemia (0.23 mmol/l) and hypomagnesemia (0.52 mmol/l), with recurrent phosphate decline despite replacement. Neurology considered the event most consistent with an acute symptomatic (provoked) seizure in the setting of metabolic disturbance, although hypomagnesemia and prior ischemic stroke were recognized as potential co-contributors. FGF23 measured on day 11 was 35 pg/ml, within the upper portion of the reporting laboratory reference interval (≤40 pg/ml). Because FGF23 would ordinarily be suppressed during severe hypophosphatemia, the non-suppressed value was considered supportive, but not confirmatory, of FCM-associated phosphate wasting. After repeated phosphate and magnesium replacement and pantoprazole discontinuation, electrolytes stabilized by day 12 and no further seizure occurred. Brivaracetam was planned for discontinuation after outpatient neurological reassessment.

Conclusion: Severe hypophosphatemia following FCM may contribute to an acute symptomatic seizure, particularly when other seizure-threshold-lowering factors coexist. Recent intravenous iron exposure and serum phosphate should be assessed in otherwise unexplained neurological events.

Keywords: Case report, seizures, hypophosphatemia, ferric carboxymaltose, fibroblast growth factor 23, iron compounds, drug-related side effects and adverse reactions.

Type of Article: CASE REPORT **Specialty:** Internal Medicine/ Endocrinology and Metabolism

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Background

Hypophosphatemia is commonly encountered in hospitalized patients, but its neurological consequences may be overlooked because early symptoms are non-specific and phosphate is not routinely measured. Severe hypophosphatemia, generally defined as phosphate below 0.32 mmol/L, may precipitate encephalopathy, respiratory failure, rhabdomyolysis, and seizures [1–4]. Ferric carboxymaltose (FCM) is associated with clinically important and sometimes prolonged hypophosphatemia, with reported incidence substantially higher than with ferric derisomaltose [2,5,6]. The proposed mechanism involves increased biologically active fibroblast growth factor 23 (FGF23), leading to renal phosphate wasting and reduced 1,25-dihydroxyvitamin D production [1,7]. We report an older woman presenting with an acute focal seizure and severe, recurrent hypophosphatemia after recent FCM administration. Neurology considered the event an acute symptomatic seizure associated with marked electrolyte disturbance; however, concurrent hypomagnesemia and a history of ischemic stroke limited certainty regarding a single causal factor.

Case Presentation

Patient information and clinical findings

A 76-year-old woman living with her family presented after witnessed involuntary jerking involving the right

hemibody and the left upper and lower limbs, with mouth deviation and tongue heaviness, lasting approximately two minutes. She remained conscious and had no incontinence, tongue biting, prolonged confusion, or post-event weakness. Her medical history included rheumatoid arthritis, hypertension, type 2 diabetes mellitus, dyslipidemia, hypothyroidism, depression, prior ischemic stroke, and osteoporosis. One month earlier, she had received a single intravenous dose of FCM 1 g during admission for melena and presumed iron-deficiency anemia. Long-term medications included pantoprazole.

Diagnostic assessment

At presentation, vital signs and capillary glucose were normal. Neurological examination showed an alert, oriented patient without new focal deficits. Non-contrast computed tomography of the head demonstrated no acute intracranial abnormality. Electroencephalography showed mild posterior background slowing without epileptiform discharges. Electrocardiography and continuous rhythm monitoring did not identify arrhythmia. Routine investigations demonstrated microcytic anemia but normal renal function, liver tests, thyroid function, standard serum electrolytes, and ammonia. Extended mineral assessment identified severe hypophosphatemia (0.23 mmol/l), hypomagnesemia (0.52 mmol/l), adjusted calcium of 2.12 mmol/l, vitamin D insufficiency, and an inappropriately normal parathyroid hormone (PTH) response (Table 2). Although phosphate initially increased to 0.91 mmol/L by day three, it fell again to 0.32 mmol/l by day five despite repletion, indicating continued phosphate loss or redistribution (Table 1).

FGF23 was measured on day 11, after several days of phosphate replacement, and was 35 pg/mL (reporting laboratory reference interval ≤40 pg/ml). The value was therefore within, but near the upper limit of, the reference interval. Because FGF23 is normally suppressed during profound hypophosphatemia, a non-suppressed upper-normal concentration was considered physiologically inappropriate and supportive of persistent FGF23 activity. However, the delayed timing of measurement and preceding phosphate replacement limit its etiological specificity; the result was considered supportive rather than diagnostic. A planned 24-hour urinary phosphate assessment could not be completed, and renal phosphate wasting was therefore not directly demonstrated.

Therapeutic intervention

Brivaracetam 25 mg orally twice daily was started. Neurology considered the event an acute symptomatic (provoked) seizure related to metabolic disturbance, with hypomagnesemia and prior ischemic stroke as potential co-contributors. Brivaracetam was intended as temporary therapy and planned for discontinuation after outpatient reassessment. Replacement followed the institutional protocol: sodium phosphate 0.32 mmol/kg intravenously over 4–6 hours and magnesium sulfate 2 g intravenously over one hour, repeated according to serial concentrations, from days 1–12 [9]. Pantoprazole was discontinued because of its possible contribution to hypomagnesemia.

Outcome and follow-up

The working diagnosis was severe hypophosphatemia following recent FCM exposure with concurrent hypomagnesemia, associated with an acute symptomatic seizure; FCM-related phosphate wasting was considered a probable contributor rather than a proven sole cause. By day 12, phosphate was 0.82 mmol/l, magnesium 0.85 mmol/l, and adjusted calcium 2.14 mmol/l. No further seizures occurred, and the patient remained at her neurological baseline. She was discharged on oral phosphate and magnesium. Brivaracetam was planned for

Table 1. *Clinical timeline, diagnostic evolution, and treatment outcome.*

TIME	CLINICAL/LABORATORY FINDINGS	INTERVENTION/OUTCOME
1 month before admission	Melena and presumed iron-deficiency anemia.	Received ferric carboxymaltose 1 g intravenously.
Day 1	Witnessed 2-minute focal seizure; CT head negative; phosphate 0.23 mmol/l, magnesium 0.52 mmol/l.	Brivaracetam 25 mg orally twice daily commenced; protocol-guided intravenous sodium phosphate (0.32 mmol/kg over 4–6 hours) and magnesium sulfate (2 g over 1 hour) initiated.
Day 3	Phosphate 0.91 mmol/l; magnesium 0.81 mmol/l.	Initial biochemical response.
Days 4-5	Phosphate fell to 0.32 mmol/l; magnesium 0.54 mmol/L despite repletion.	Repeat protocol-guided replacement; endocrine review; pantoprazole contribution considered.
Day 8	Phosphate 0.41 mmol/l; history clarified recent FCM exposure.	Pantoprazole discontinued; renal phosphate wasting suspected.
Day 11	Phosphate 0.75 mmol/l; FGF23 35 pg/ml.	Upper-normal, non-suppressed FGF23 considered supportive but not confirmatory; delayed sampling after replacement noted.
Day 12	Phosphate 0.82 mmol/l; magnesium 0.85 mmol/L; no recurrent seizure.	Discharged on oral phosphate and magnesium; brivaracetam planned for discontinuation after neurology review. Post-discharge laboratory results were unavailable.

Table 2. *Key diagnostic investigations.*

INVESTIGATION	RESULT	REFERENCE RANGE	INTERPRETATION
Hemoglobin/MCV/RDW	100 g/l/75 fl/16%	120–160 g/l/80–96 fl/11.5%–14.5%	Microcytic anemia
Phosphate	0.23 mmol/l	0.80–1.50 mmol/l	Severe hypophosphatemia
Magnesium	0.52 mmol/l	0.70–1.00 mmol/l	Hypomagnesemia
Adjusted calcium	2.12 mmol/l	2.10–2.55 mmol/l	Low-normal
Parathyroid hormone	24.3 pg/ml	15–65 pg/ml	Inappropriately normal in context
25-hydroxyvitamin D	42 nmol/l	50–125 nmol/l	Insufficiency
Creatinine	78 micromol/l	45–90 micromol/l	Preserved renal function
FGF23 (day 11)	35 pg/ml	≤40 pg/ml*	Upper-normal and non-suppressed; supportive but not confirmatory

**Reference interval reported by the testing laboratory; FGF23 reference intervals are assay-specific.*

discontinuation after neurology follow-up. Follow-up phosphate and magnesium testing was planned, but no post-discharge results were available. A patient perspective was not recorded.

Discussion

This case is clinically important because the initial presentation directed attention to structural or epileptic causes, whereas the metabolic abnormalities were identified only after extended electrolyte testing. Neurology considered the event most consistent with an acute symptomatic (provoked) seizure in the setting of severe electrolyte disturbance. Severe phosphate depletion can impair adenosine triphosphate-dependent neuronal membrane function and reduce the seizure threshold; hypomagnesemia can further increase neuronal excitability [1,5,7]. Nevertheless, causality cannot be attributed to hypophosphatemia alone because concurrent hypomagnesemia, prior ischemic stroke, and initiation of antiseizure therapy were relevant confounders. The metabolic abnormalities were therefore regarded as plausible contributors rather than a proven sole cause.

FCM is distinctive among intravenous iron preparations because it may provoke marked FGF23-mediated renal phosphate wasting. In randomized studies, hypophosphatemia was more frequent with FCM than with ferric derisomaltose, and intact FGF23 rose substantially after FCM exposure [5,6,8]. In this patient, the temporal association with a 1 g FCM infusion and recurrent hypophosphatemia after initial correction supported this mechanism. FGF23 was 35 pg/ml on day 11, near the upper limit of the reporting laboratory reference interval. During profound hypophosphatemia, FGF23 would ordinarily be suppressed; therefore, the non-suppressed concentration was physiologically inappropriate. However, because the sample was obtained after repeated phosphate replacement, this finding was supportive but not confirmatory. The biochemical pattern partially overlaps with the reported "6H syndrome" of high or inappropriately active FGF23, hyperphosphaturia, hypophosphatemia, hypovitaminosis D, hypocalcemia, and secondary hyperparathyroidism [6,7].

Pantoprazole-associated hypomagnesemia was an additional confounder. Magnesium depletion may impair PTH secretion and action, contributing to the low-normal calcium and inappropriately normal PTH response [10]. Improvement in magnesium after pantoprazole withdrawal supported its contribution. Persistent phosphate decline despite magnesium replacement and the temporal relationship to FCM favored an FCM-related mechanism, although renal phosphate wasting was not directly confirmed.

The strengths of this case include serial mineral measurements demonstrating recurrent hypophosphatemia despite supplementation and identification of a temporally relevant medication exposure. Important limitations remain. First, the planned 24-hour urinary phosphate collection was not completed, and neither fractional phosphate excretion nor tubular maximum phosphate reabsorption was available; renal phosphate wasting was therefore not directly demonstrated. Second, FGF23 was measured only on day 11 after repeated phosphate replacement, limiting interpretation of the upper-normal result. Third, exact cumulative phosphate and magnesium replacement doses could not be verified from the available medication-administration record. Fourth, no post-discharge phosphate or magnesium results were available, and a patient perspective was not recorded. Finally, hypomagnesemia, prior ischemic stroke, and initiation of brivaracetam prevent definitive attribution of the seizure solely to FCM-associated hypophosphatemia. In practice, clinicians should inquire about recent intravenous iron in patients with unexplained neurological symptoms and obtain serum phosphate when FCM exposure is suspected. For patients requiring future intravenous iron, lower-risk formulations should be considered and phosphate monitoring planned, particularly after repeat dosing [2,6,7].

Conclusion

Severe hypophosphatemia following FCM may contribute to an acute symptomatic seizure and may recur after initial replacement. In this patient, the temporal association and biochemical pattern raised concern for FCM-associated phosphate wasting, but concurrent hypomagnesemia, prior ischemic stroke, delayed FGF23 testing, absence of urinary phosphate measurement, and initiation of brivaracetam precluded definitive causal attribution. Patients developing neurological symptoms after FCM administration should undergo prompt phosphate assessment, serial monitoring, and appropriate replacement, with consideration of alternative iron formulations for future treatment.

What is new

A new-onset acute symptomatic seizure may occur in association with severe hypophosphatemia after ferric carboxymaltose, particularly when other factors that lower the seizure threshold coexist. Recent intravenous iron exposure should be specifically sought when a patient has unexplained neurological symptoms or recurrent phosphate decline despite replacement. FGF23 values within the laboratory reference interval may still be physiologically inappropriate if they are not suppressed during profound hypophosphatemia, but delayed testing after replacement should be interpreted cautiously.

List of Abbreviations

CT	Computed tomography
EEG	Electroencephalography
FCM	Ferric carboxymaltose
FGF23	Fibroblast growth factor 23
PPI	Proton pump inhibitor
PTH	Parathyroid hormone

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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None.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Data availability

De-identified clinical data are available from the corresponding author upon reasonable request.

Use of Artificial Intelligence

AI-assisted wording support (Perplexity, powered by GPT-5.1) was used solely to improve language and clarity. The authors verified all clinical data, interpretations, references, and final text and take full responsibility for the manuscript.

Reporting guideline

This case report was prepared in accordance with the CARE case-report guidelines and includes patient information, clinical findings, diagnostic assessment, therapeutic intervention, a timeline, outcome and follow-up, and written patient consent.

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Summary of case

1	Patient (gender, age)	Female, 76 years
2	Final Diagnosis	Severe hypophosphatemia following ferric carboxymaltose with concurrent hypomagnesemia and an acute symptomatic (provoked) focal seizure; the ferric carboxymaltose association was considered probable but not definitive.
3	Symptoms	Witnessed focal seizure with involuntary limb jerking and post-event fatigue
4	Medications	Ferric carboxymaltose 1 g intravenously before presentation; protocol-guided intravenous and oral phosphate/magnesium replacement; temporary brivaracetam with planned discontinuation; pantoprazole discontinued.
5	Clinical Procedure	Metabolic assessment, CT head, EEG, serial electrolyte monitoring, FGF23 testing; urinary phosphate collection was planned but not completed.
6	Specialty	Internal Medicine / Endocrinology and Metabolism / Neurology