Cureus
Part of SPRINGER NATURE

Open Access Case Report

Hypophosphatemic Osteomalacia Associated With Long-Term Intravenous Iron Sucrose in an Anuric Hemodialysis Patient: A Case Report

Sara Tolbix [1], Manal El Morjani [1], Zineb Baba [1], Ahmed Mougui [1], Ahlam Belkhou [1]

1. Department of Rheumatology, Arrazi Hospital, Faculty of Medicine and Pharmacy of Marrakech, Mohammed VI University Hospital, Marrakech, MAR

Corresponding author: Sara Tolbix, saratolbix1995@gmail.com

Review began 11/04/2026
Review ended 11/15/2026
Published 11/16/2026

© Copyright 2026
Tolbix et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.119762

Abstract

Hypophosphatemic osteomalacia is a recognized complication of repeated intravenous iron infusions in patients with preserved kidney function. It results from an iron-induced rise in intact fibroblast growth factor 23 (FGF23), which causes renal phosphate wasting. It is rarely considered in hemodialysis patients, in whom hyperphosphatemia is the rule. We report the case of a 62-year-old anuric woman on hemodialysis for 22 years for polycystic kidney disease who had received 40 infusions of 200 mg iron sucrose (8 g in total) as maintenance therapy over 10 years, the last one two months before admission. She received no phosphate binder, vitamin D, or calcimimetic. She was referred for diffuse bone pain and proximal muscle weakness of 11 months' duration. Predialysis serum phosphate was low (0.40 and 0.52 mmol/L), alkaline phosphatase was elevated (2.35 times the upper limit of normal), and parathyroid hormone was 335 pg/mL, within the recommended dialysis target; 25-hydroxyvitamin D and serum calcium were normal. Review of her medical records revealed unexplored hypophosphatemia for at least five years. Intact FGF23 was low to low-normal (10.4 and 27.2 pg/mL), which is markedly inappropriate for a hemodialysis patient. Radiographs showed pseudofractures (Looser zones) and biconcave vertebrae. After iron withdrawal and oral phosphate supplementation, serum phosphate and alkaline phosphatase normalized, and pain decreased from 7/10 to 2/10 at eight months. The association with iron sucrose was rated as possible (Naranjo score of 3), and its mechanism remains unexplained, as the FGF23-mediated renal pathway cannot operate in anuria. Hypophosphatemia in a hemodialysis patient is never trivial and should prompt a search for osteomalacia.

Categories: Rheumatology, Nephrology, Endocrinology/Diabetes/Metabolism
Keywords: fibroblast growth factor 23, hemodialysis, hypophosphatemia, intravenous iron, iron sucrose, osteomalacia, pseudofractures

Introduction

Osteomalacia is a defect in the mineralization of the bone matrix that causes diffuse bone pain, proximal muscle weakness, and insufficiency fractures. Although vitamin D deficiency is its most common cause, it can also result from chronic hypophosphatemia of renal, tumoral, genetic, or drug-induced origin [1]. Intravenous iron-induced hypophosphatemia has mainly been described with ferric carboxymaltose (FCM) [1-4] and, less often, with saccharated ferric oxide (SFO) [5-7] or iron polymaltose [1], whereas it is uncommon with iron sucrose [8]. In published cases, it is attributed to a rise in biologically active intact fibroblast growth factor 23 (FGF23), which causes renal phosphate wasting and decreased calcitriol synthesis; with repeated exposure, it may progress to osteomalacia with pseudofractures [1,2].

In patients on maintenance hemodialysis, this diagnosis is challenging. Bone pain, fractures, and mineral abnormalities are usually attributed to chronic kidney disease-mineral and bone disorder (CKD-MBD) or osteoporosis [9], and urinary parameters cannot be assessed in anuric patients. In the absence of renal phosphate wasting, hypophosphatemia may instead reflect insufficient dietary intake, intestinal malabsorption, or excessive dialytic removal, and chronic phosphate depletion is expected to suppress FGF23 production by osteocytes. We report the case of an anuric hemodialysis patient who developed hypophosphatemic osteomalacia after repeated iron sucrose infusions. This case is of interest because of the clinical setting, the iron formulation involved, and an inappropriately low intact FGF23 level.

Case Presentation

A 62-year-old woman had been on conventional hemodialysis for 22 years for polycystic kidney disease, with three four-hour sessions per week and no residual urine output. She received iron sucrose (Venofer) at a rate of four 200 mg infusions per year, for a total of 40 infusions (8 g) over 10 years, according to the maintenance protocol of the dialysis center and independently of hemoglobin levels, which ranged from 12.5 to 14.2 g/dL without an erythropoiesis-stimulating agent (Table *1*). The only iron indices available during these 10 years were serum ferritin values of 38 µg/L five years before admission and 99.2 µg/L at admission; transferrin saturation was not available. The last infusion was given two months before admission. She received no phosphate binder, calcimimetic, or native or active vitamin D, and she had not

undergone parathyroidectomy. She had no chronic diarrhea and no history of gastrointestinal disease or surgery. Two years earlier, she had sustained a fracture of the right distal tibia after a fall from standing height, which was managed conservatively.

Parameter	Eight years before admission	Five years before admission	Admission	Four months	Eight months
Serum phosphate (mmol/L)	1.81	0.56	0.40	0.81	1.19
Alkaline phosphatase (IU/L)	135	335	353	190	130
Parathyroid hormone (pg/mL)	125	NA	335	161	132
Ferritin (µg/L)	NA	38	99.2	NA	50
Hemoglobin (g/dL)	NA	12.5	14.2	NA	13.2
Pain (VAS)	NA	NA	7/10	4/10	2/10
Muscle strength	NA	NA	Proximal weakness	Improved	Improved

TABLE 1: Course before admission and after iron withdrawal and phosphate supplementation

Iron sucrose was started 10 years before admission; the last infusion was given two months before admission, and iron was not reintroduced. Phosphate supplementation was started at admission. The admission value of serum phosphate is the lower of two predialysis measurements (see Table 2).

NA: not available; VAS: visual analog scale

Parameter	Result	Reference range
Predialysis serum phosphate, first measurement (mmol/L)	0.40	0.81-1.45
Predialysis serum phosphate, second measurement (mmol/L)	0.52	0.81-1.45
Alkaline phosphatase (IU/L)	353	40-150
Intact FGF23, predialysis, one month before admission (pg/mL)	10.4	23.2-95.4
Intact FGF23, postdialysis, at admission (pg/mL)	27.2	23.2-95.4
Parathyroid hormone (pg/mL)	335	130-585
Corrected calcium (mmol/L)	2.46	2.12-2.62
25-Hydroxyvitamin D (ng/mL)	39	>30
Gamma-glutamyl transferase (IU/L)	34	9-36
Albumin (g/L)	40	32-45
Uric acid (mg/dL)	6.2	3.4-7.0
Bicarbonate (mmol/L)	23	22-29
Serum protein electrophoresis	Normal	Normal
Hemoglobin (g/dL)	14.2	12-16
Ferritin (µg/L)	99.2	30-300
C-reactive protein (mg/L)	3.1	<5
Erythrocyte sedimentation rate (mm/h)	22	<36

TABLE 2: Laboratory findings at admission and in the preceding month

The two serum phosphate measurements were taken five days apart. The reference range for intact FGF23 is that of the general population. The reference range for parathyroid hormone is the recommended target for dialysis patients (2-9 times the upper limit of normal of the laboratory range, 15-65 pg/mL).

FGF23: fibroblast growth factor 23

She was referred for diffuse mechanical bone pain, rated 7/10 on a visual analog scale (VAS), and proximal muscle weakness of 11 months' duration, without anorexia (body mass index 22.4 kg/m^2). Physical examination revealed diffuse bone tenderness on palpation, without deformity or neurological deficit.

Predialysis serum phosphate was low on two measurements taken five days apart, alkaline phosphatase (ALP) was 2.35 times the upper limit of normal (ULN), and parathyroid hormone (PTH) was within the recommended dialysis target (Table *2*). Gamma-glutamyl transferase (GGT), corrected calcium, 25-hydroxyvitamin D, albumin, bicarbonate, serum protein electrophoresis, and liver ultrasound were normal. Intact FGF23 was measured on ethylenediaminetetraacetic acid (EDTA) plasma by chemiluminescence (LIAISON FGF23, DiaSorin). It was 10.4 pg/mL, below the normal range, on a predialysis sample drawn one month before admission and one month after the last iron infusion, and 27.2 pg/mL, at the lower limit of normal, on a postdialysis sample drawn at admission. Both samples were obtained before any phosphate supplementation and analyzed with the same assay. Urinary studies could not be performed because of anuria. Review of her medical records showed a predialysis serum phosphate of 1.81 mmol/L with normal ALP eight years before admission, and of 0.56 mmol/L with ALP of 335 IU/L (2.2 times the ULN) five years before admission; these abnormalities had not been investigated (Table *1*). Serum ferritin and transferrin saturation before the initiation of iron therapy were not available.

Radiographs showed diffuse demineralization; nonunion of the old right tibial fracture, which remained unhealed two years after the injury (Figure *1*); pseudofractures (Looser zones) in the left leg and left forearm (Figure *2*); a pelvic deformity with a "card-heart" appearance (Figure *3*); and biconcave thoracolumbar vertebrae, known as "fish vertebrae" (Figure *4*). Dual-energy X-ray absorptiometry showed a T-score of -2.3 at the lumbar spine and -3.0 at the total hip (Figure *5*). A diagnosis of hypophosphatemic osteomalacia was made; bone biopsy was not performed.

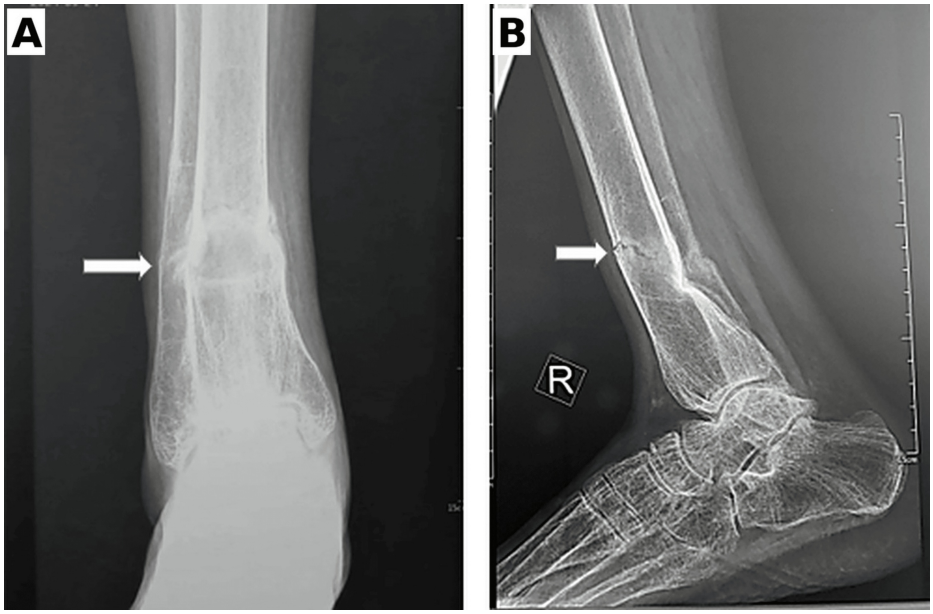


FIGURE 1: Nonunion of the right distal tibia

Anteroposterior (A) and lateral (B) radiographs of the right ankle showing nonunion of the distal tibial fracture sustained two years earlier (arrows).

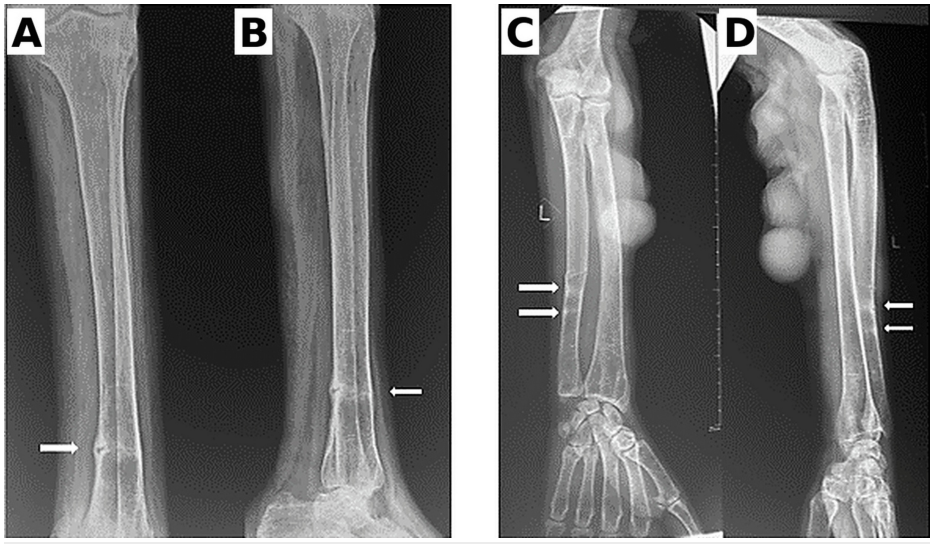


FIGURE 2: Pseudofractures in the left leg and left forearm

Radiographs of the left leg (A, B) and left forearm (C, D) showing pseudofractures (Looser zones) (arrows).

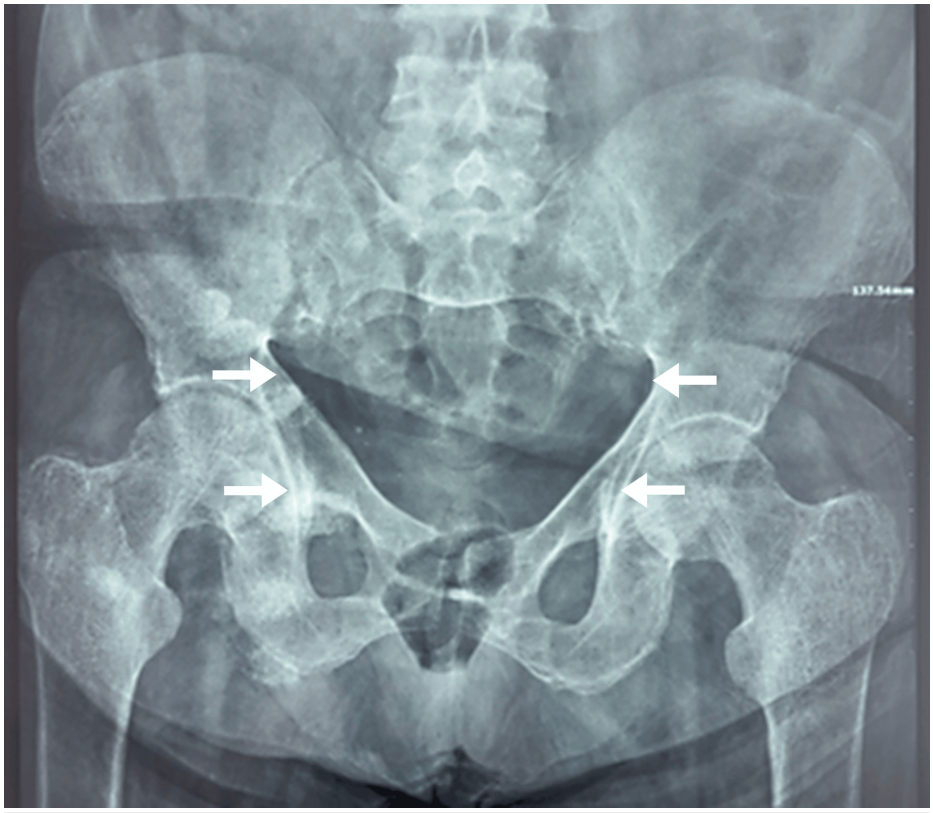


FIGURE 3: Card-heart pelvic deformity

Anteroposterior radiograph of the pelvis showing inward bowing of the lateral pelvic walls, producing a card-heart deformity (arrows).

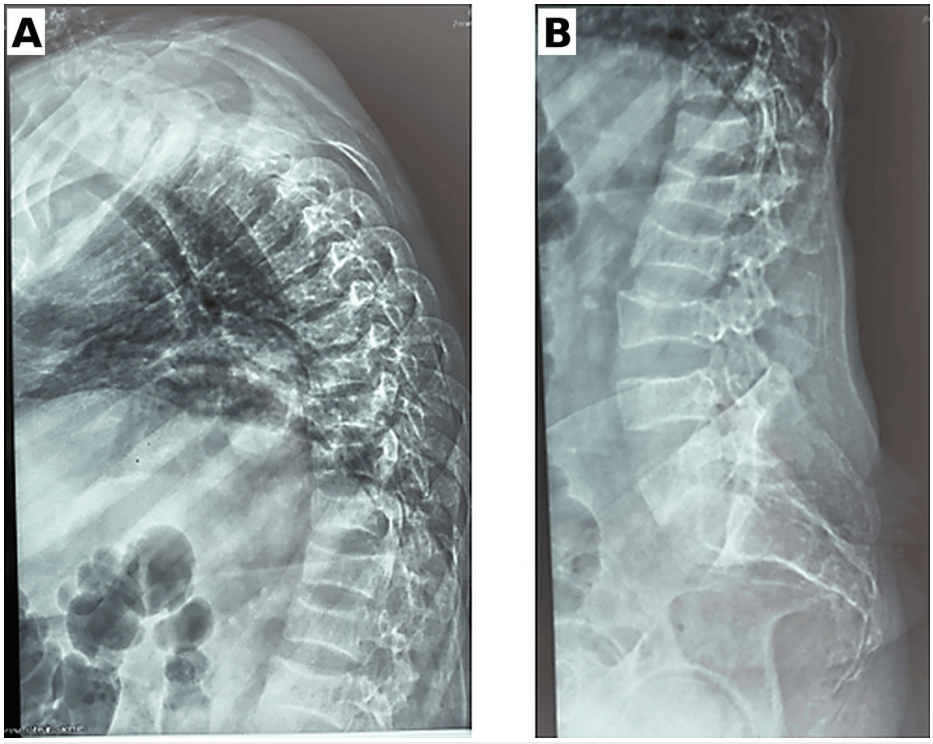


FIGURE 4: Biconcave vertebrae

Lateral radiographs of the thoracic spine (A) and lumbar spine (B) showing biconcave (fish) vertebrae.

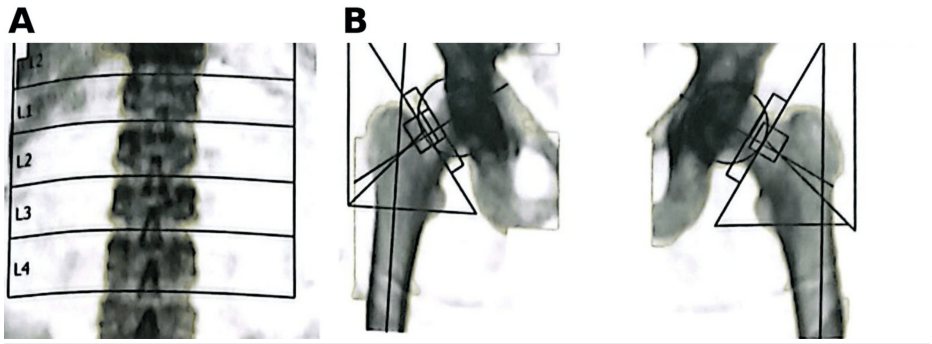


FIGURE 5: Dual-energy X-ray absorptiometry

Dual-energy X-ray absorptiometry scans (Lunar Prodigy, GE Healthcare, Chicago, IL, USA) of the lumbar spine (A) and both hips (B). Lumbar spine L2-L4: bone mineral density 864 mg/cm², T-score -2.3, Z-score -0.2 (osteopenia). Total hip: T-score -2.8 on the left and -3.2 on the right, mean T-score -3.0, Z-score -1.4 (osteoporosis according to the WHO classification).

WHO: World Health Organization

In collaboration with the nephrologists, iron therapy was discontinued, and oral phosphate supplementation was initiated (Phosphoneuros, 50 drops four times a day, equivalent to 1,576 mg of elemental phosphorus per day), with monitoring of serum calcium and serum phosphate levels. At eight months, pain was rated at 2/10, muscle strength had improved, and serum phosphate levels and ALP had normalized, without resuming iron supplementation (Table *1*).

Discussion

This case has three notable features: hypophosphatemia went unrecognized for at least five years in a hemodialysis patient, a setting in which hyperphosphatemia is the rule; anuria ruled out any renal phosphate wasting; and intact FGF23 was low to low-normal, whereas it is elevated in published cases of iron-associated osteomalacia [1]. Bone biopsy with double tetracycline labeling remains the reference

standard for osteomalacia [9]. In its absence, the diagnosis was based on a body of concordant evidence: pseudofractures, the most suggestive radiological sign [1], a nonunited low-energy fracture, persistent hypophosphatemia, and normalization of serum phosphate and ALP with phosphate supplementation. Normal GGT and liver ultrasound supported a bone origin of the elevated ALP.

Several differential diagnoses specific to dialysis patients were considered [9]. Predominant hyperparathyroid bone disease seemed unlikely, as PTH was within the recommended target. Adynamic bone disease, another form of renal osteodystrophy, was also unlikely, as it is typically associated with low PTH and normal or low ALP levels, whereas our patient had PTH within the target range and elevated ALP. Aluminum-related osteomalacia could not be formally excluded because serum aluminum was not measured, but the patient had never received phosphate binders. In all three cases, the clinical and biochemical improvement after iron withdrawal and phosphate supplementation argues against these diagnoses.

In an anuric patient, phosphate balance depends only on intestinal absorption and dialytic removal. The patient had no apparent malnutrition (body mass index 22.4 kg/m², albumin 40 g/L) and no gastrointestinal disease and was not following a phosphate-restricted diet at admission; she was treated with an unchanged schedule of conventional hemodialysis without hemodiafiltration, which had been associated with hyperphosphatemia (1.81 mmol/L) eight years earlier. However, quantitative data on dietary phosphate intake, dialysis adequacy (Kt/V), and dialyzer membrane or dialysate composition over time were not available; therefore, low phosphate intake and excessive dialytic removal cannot be excluded as contributors to hypophosphatemia. Moreover, the established mechanism of iron-induced hypophosphatemia, namely, FGF23-mediated renal phosphate wasting [2,6], cannot occur in anuria.

FGF23 also distinguishes this case. In published cases of SFO-associated osteomalacia, all of which occurred in patients not on dialysis [5-7,10,11], intact FGF23 was elevated whenever it was measured [6,7,11]. In hemodialysis patients, intact FGF23 is physiologically very high, with a median of 843 pg/mL, and iron sucrose does not change it [12]. In contrast, our patient had a low to low-normal FGF23 level (10.4 and 27.2 pg/mL), which is inappropriately low for a hemodialysis patient. This finding cannot be explained by dialytic clearance [13], as the lowest value was measured before a dialysis session. Rather, it reflects an adaptive response: in the face of prolonged phosphate depletion, FGF23 production decreases.

FGF23 is therefore unlikely to be the mechanism involved in our patient. If iron sucrose was involved, it may have acted through another pathway, such as a direct toxic effect on bone, as SFO inhibits bone formation in vitro [5]. This hypothesis remains to be confirmed.

Using the Naranjo scale, the association with iron sucrose was rated as possible (score of 3) [14]: previous reports of the reaction (+1), onset after drug administration (+2), confirmation by objective evidence (+1), and alternative causes not fully excluded (-1). No point was assigned for improvement after discontinuation, because iron was withdrawn at the same time as phosphate supplementation was started, so the improvement cannot be attributed to iron withdrawal. The time course was consistent: serum phosphate was high two years after iron initiation and low three years later, with a parallel rise in ALP. In the absence of iron rechallenge, this report describes an association rather than a causal relationship.

This case carries two practical messages. First, predialysis hypophosphatemia is abnormal in a hemodialysis patient and should prompt a search for osteomalacia; in our patient, it went unrecognized for at least five years. Second, bone densitometry cannot distinguish osteomalacia from osteoporosis. Our patient had a hip T-score of -3.0 and fractures, a presentation that could have led to a mistaken diagnosis of osteoporosis and the prescription of an antiresorptive agent. In dialysis patients, however, these agents, particularly denosumab, can cause severe hypocalcemia [15].

Iron withdrawal and phosphate supplementation, the latter prescribed under close monitoring because of the risk of vascular calcification [9], were followed by clinical improvement and biochemical normalization. However, no guidelines currently address the management of hypophosphatemia in patients with end-stage kidney disease, and phosphate-enriched dialysate may be an alternative in selected patients.

The main limitations of this report are the absence of transiliac bone biopsy with double tetracycline labeling, serum aluminum measurement, data on dietary intake and dialysis adequacy, and follow-up radiographs. Moreover, tubular phosphate reabsorption (TmP/GFR) could not be assessed because of anuria, and only intact FGF23 was measured, whereas C-terminal assays, which also detect inactive fragments, may yield different results. Further studies, including bone histomorphometry and bone-specific ALP, are needed to determine whether intravenous iron directly impairs bone mineralization, for example, through iron deposition in osteoblasts and osteocytes, and to clarify how FGF23 is suppressed in this setting.

Conclusions

This case describes osteomalacia associated with long-term iron sucrose in an anuric hemodialysis patient. Its occurrence without renal phosphate wasting and with an inappropriately low FGF23 level suggests that,

if iron was involved, a mechanism other than that described with other iron formulations may be implicated. Hypophosphatemia in a hemodialysis patient should not be overlooked; it should prompt a search for osteomalacia, which may improve after iron withdrawal and phosphate supplementation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Sara Tolbix, Manal El Morjani, Zineb Baba, Ahmed Mougui, Ahlam Belkhou

Acquisition, analysis, or interpretation of data: Sara Tolbix, Manal El Morjani, Zineb Baba, Ahmed Mougui, Ahlam Belkhou

Drafting of the manuscript: Sara Tolbix

Critical review of the manuscript for important intellectual content: Sara Tolbix, Manal El Morjani, Zineb Baba, Ahmed Mougui, Ahlam Belkhou

Supervision: Ahlam Belkhou

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **AI use statement:** The authors used Claude (Claude Opus 5.5, Anthropic, San Francisco, CA, USA); DeepL Translator (DeepL GmbH, Cologne, Germany); Grammarly (Grammarly Inc., San Francisco, CA, USA) as follows: language polishing, translation in entire manuscript (language editing and translation from French to English). The manuscript was originally written in French by the authors, who are responsible for all clinical data, interpretation, and scientific content. AI tools were used only for translation and language editing. All authors reviewed the final English text line by line against the original French version. All clinical data and laboratory values were checked against the patient's medical records, and every reference was verified against the original publication and its DOI. The authors confirm that they have reviewed and verified all AI-assisted content and take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Vilaca T, Velmurugan N, Smith C, Abrahamsen B, Eastell R: Osteomalacia as a complication of intravenous iron infusion: a systematic review of case reports. J Bone Miner Res. 2022, 37:1188-99. 10.1002/jbmr.4558
2. Wolf M, Chertow GM, Macdougall IC, Kaper R, Krop J, Strauss W: Randomized trial of intravenous iron-induced hypophosphatemia. JCI Insight. 2018, 3:e124486. 10.1172/jci.insight.124486
3. Wolf M, Rubin J, Achebe M, et al.: Effects of iron isomaltoside vs ferric carboxymaltose on hypophosphatemia in iron-deficiency anemia: two randomized clinical trials. JAMA. 2020, 323:432-43. 10.1001/jama.2019.22450
4. Schaefer B, Tobiasch M, Viveiros A, Tilg H, Kennedy NA, Wolf M, Zoller H: Hypophosphataemia after treatment of iron deficiency with intravenous ferric carboxymaltose or iron isomaltoside-a systematic review and meta-analysis. Br J Clin Pharmacol. 2021, 87:2256-73. 10.1111/bcp.14643
5. Sato K, Nohtomi K, Demura H, Takeuchi A, Kobayashi T, Kazama J, Ozawa H: Saccharated ferric oxide (SFO)-induced osteomalacia: in vitro inhibition by SFO of bone formation and 1,25-dihydroxy-vitamin D production in renal tubules. Bone. 1997, 21:57-64. 10.1016/S8756-3282(97)00084-7
6. Shimizu Y, Tada Y, Yamauchi M, et al.: Hypophosphatemia induced by intravenous administration of saccharated ferric oxide: another form of FGF23-related hypophosphatemia. Bone. 2009, 45:814-6. 10.1016/j.bone.2009.06.017
7. Yamamoto S, Okada Y, Mori H, Fukumoto S, Tanaka Y: Fibroblast growth factor 23-related osteomalacia caused by the prolonged administration of saccharated ferric oxide. Intern Med. 2012, 51:2375-8. 10.2169/internalmedicine.51.7450
8. Glaspy JA, Wolf M, Strauss WE: Intravenous iron-induced hypophosphatemia: an emerging syndrome . Adv Ther. 2021, 38:3531-49. 10.1007/s12325-021-01770-2
9. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group: KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl (2011). 2017, 7:1-59. 10.1016/j.kisu.2017.04.001
10. Ishimaru D, Sumi H: A case of an insufficiency fracture of the medial proximal tibia secondary to osteomalacia associated with long-term saccharated ferric oxide administration. Case Rep Orthop. 2017,

2017:1675654. 10.1155/2017/1675654

11. Nomoto H, Miyoshi H, Nakamura A, Nagai S, Kitao N, Shimizu C, Atsumi T: A case of osteomalacia due to deranged mineral balance caused by saccharated ferric oxide and short-bowel syndrome: a case report. Medicine (Baltimore). 2017, 96:e8147. 10.1097/MD.0000000000008147
12. Roberts MA, Huang L, Lee D, et al.: Effects of intravenous iron on fibroblast growth factor 23 (FGF23) in haemodialysis patients: a randomized controlled trial. BMC Nephrol. 2016, 17:177. 10.1186/s12882-016-0391-7
13. Carlson N, Mortensen OH, Axelsen M, Pedersen RS, Heaf JG: Clearance of sclerostin, osteocalcin, fibroblast growth factor 23, and osteoprotegerin by dialysis. Blood Purif. 2017, 44:122-8. 10.1159/000465513
14. Naranjo CA, Busto U, Sellers EM, et al.: A method for estimating the probability of adverse drug reactions . Clin Pharmacol Ther. 1981, 30:239-45. 10.1038/clpt.1981.154
15. FDA adds Boxed Warning for increased risk of severe hypocalcemia in patients with advanced chronic kidney disease taking osteoporosis medicine Prolia (denosumab). (2024). Accessed: November 3, 2026: https://www.fda.gov/drugs/drug-safety-communications/fda-adds-boxed-warning-increased-risk-severe-hypocalcemia-patien....