

Cutaneous Calcinosis Caused by Parenteral Nutrition Extravasation in a Neonate Treated by Surgical Debulking: Report of a Case

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Abstract

Calcinosis cutis is an abnormal deposition of calcium compounds in the subcutaneous tissue that can result from various causes, including malignancy, metabolic diseases, and iatrogenic. In this report, we described a case of calcinosis cutis occurring in a newborn infant following extravasation of parenteral nutrition in neonatal intensive care. Due to its large size and an impending loss of the overlying skin, surgical removal of the calcinotic mass, followed by a full-thickness skin grafting. Evidence from energy-dispersive X-ray spectroscopy suggested that extravasation of the parenteral nutrition and precipitation of calcium phosphate and calcium carbonate explained the pathophysiology of calcium salt precipitation. This report addresses a potential complication from parenteral nutrition extravasation and suggests early management that might prevent the necessity for a major operation.

Keywords: Calcinosis cutis, Parenteral nutrition, Surgery

INTRODUCTION

Calcinosis cutis (or cutaneous calcinosis) is defined as the subcutaneous deposition of insoluble calcium compounds. The condition can be idiopathic or associated with various systemic diseases such as systemic sclerosis, lupus erythematosus, metastatic cancers, and chronic renal failure. Rarely were there reports of cal-

cium precipitation caused by an iatrogenic injection of calcium salts or parenteral nutrition containing calcium.^{1,2} Deposition of calcium salts is mostly asymptomatic. However, intraarterial precipitation of the crystal may block microcirculation, leading to ischemia and pain, which is known as calciphylaxis.³

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This report demonstrates a newborn patient who developed localized cutaneous calcinosis at the foot after receiving parenteral nutrition in a neonatal intensive care unit. Since the calcium-containing lump was associated with skin ischemia, surgical debridement of the deposit was performed. The specimen was sent for microscopic and chemical analysis.

CASE PRESENTATION

A 20-day-old male neonate was admitted to our neonatal intensive care unit with a problem of transient tachypnea of the newborn and hypoglycemia. The baby was born via Cesarean delivery to a 38-year-old mother at the gestational age of 37 weeks. The birth weight was 2,850 grams. Shortly after birth, the patient had tachypnea and jitteriness, which prompted admission to the NICU for intensive monitoring and ventilation therapy. With hypoglycemia during the initiation of enteral feeding, supportive parenteral nutrition was given during post-natal days 5-10. The composition of the parenteral nutrition was shown in [Supplementary Table 1](#). Intravenous lipid (4.0 grams/kg/day) was given in a separate container. All the solutions were administered via peripheral intravenous cannular size 24G. On post-natal date 14, the baby was noticed to have a swelling at the dorsum of his right foot. Initially, there was mild erythema of the overlying skin. Phlebitis was impressed, and local therapy was offered with cold compression and antibiotic (cloxacillin). After a week of conservative management, although the inflam-

mation could be improved, the lump did not disappear, and the skin became purplish; surgical consultation was decided.

On radiologic examination of the right foot, a $4.7 \times 2.1 \times 0.8 \text{ cm}^3$ well-defined elliptical heterogeneous opacities situated in the plane of subcutaneous fat along the dorsum of right foot with mild swelling of the surrounding soft tissue ([Figure 1](#)). Complete blood count showed hemoglobin 11.8 g/dL, white blood count 19,830 cells/cu.mm, platelet 612,000 cells/cu.mm. Blood chemistries were as followed: blood urea nitrogen 8.6 mg%, creatinine 0.26 mg%, Na^+ 139.5 mEq/L, K^+ 4.76 mEq/L, Cl^- 102.5 mEq/L, CO_2 23.2 mEq/L, Ca^{2+} 10.3 mmol/L and PO_4 6.0 mmol/L. There was no history of endocrine disease in the family. The mother had recent uneventful course of SARS-CoV-2 infection.

On surgical exploration with a circumferential incision made over the ischemic skin area, there were stony hard gritty materials underneath the non-viable skin at the dorsum of his right foot. The foreign body and the covering skin were removed with wound bed left open and cared with negative pressure dressing. The initial defect area was $4.5 \times 4 \text{ cm}^2$, which contracted to $3 \times 4 \text{ cm}^2$ in one week. The negative pressure of 80-100 mmHg was applied over a polystyrene foam for 7 days until the wound began to have granulation tissue and was covered with a full-thickness skin graft. Histopathology revealed necrosis of the skin and subcutaneous adipose tissue with inflammatory cell deposition ([Figure 2](#)).

Supplementary Table 1 Composition of the parenteral nutrition given to the child

Composition	Amount given in 24 hours (per Kg body weight)
Volume	120 ml
Dextrose	12 grams (10% weight/volume solution)
Amino acid	3 grams
NaCl	1.0 mM
Na acetate	1.0 mM
K acetate	0.5 mM
K_2HPO_3	1.0 mM
Ca (gluconate)	1.0 mM
Mg	0.2 mM
Others: Vitamin mixture 2 ml, Heparin, Zn 300.0 micrograms	

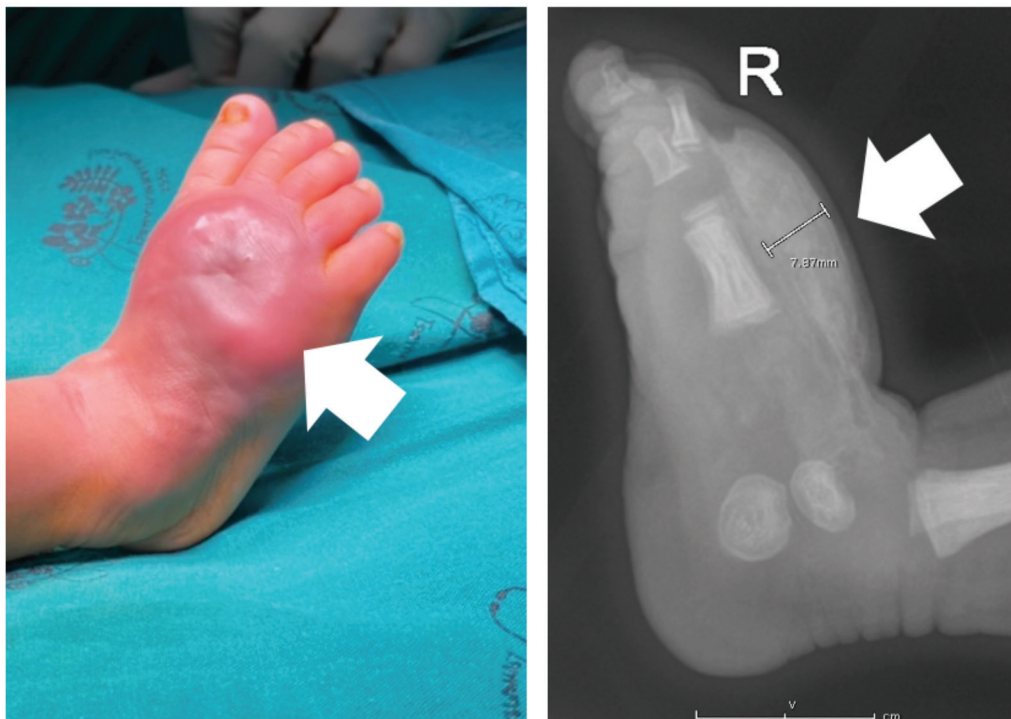


Figure 1 Clinical and radiological picture of calcinosis cutis in this case. Note the swollen skin that was detaching from the underlying tissue because of this mass.

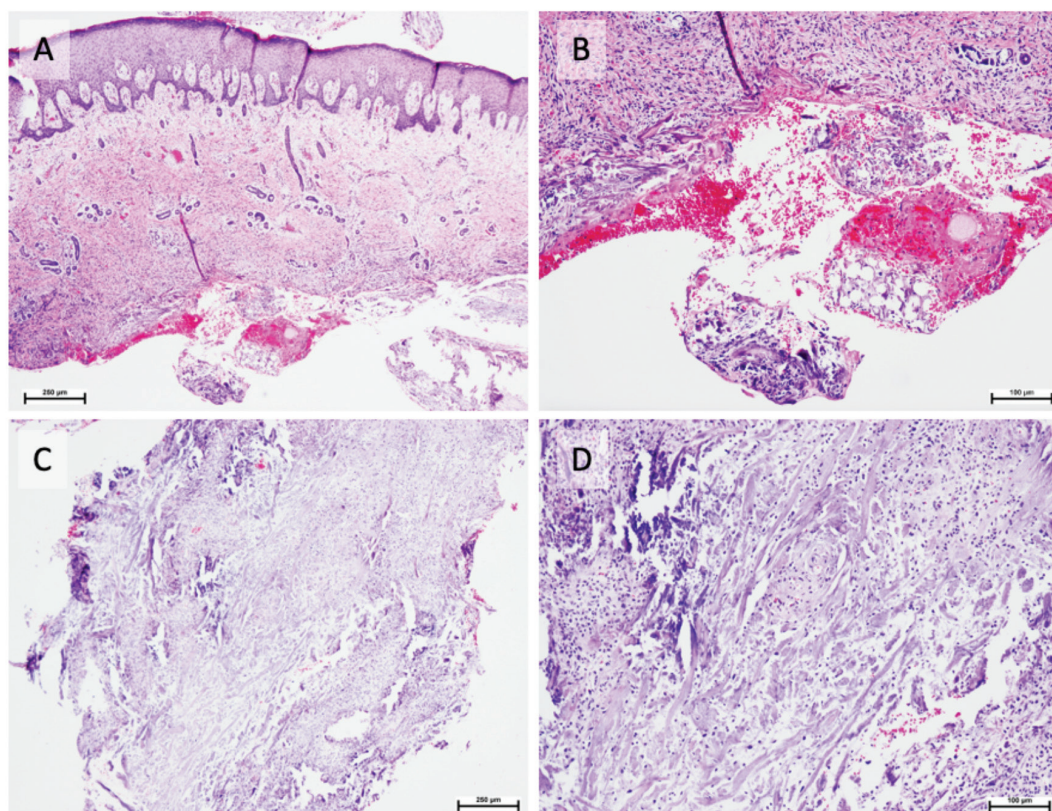


Figure 2 Histopathology of calcinosis cutis in this case. A-B: Deposition of amorphous calcium crystal in the subcutaneous fat C-D: ischemic necrosis of the surrounding tissue

Scanning electron microscopy of the surgical specimen revealed amorphous solid materials situating within adipose tissue (Figure 3). Quantitative compositional analysis using energy-dispersive X-ray spectroscopy (Hitachi SU3900, Japan) reported weight percentage of components as C 53.5%, O 32.1%, Ca 8.1%, P 4.3%, Na 0.8%, Cl 0.5%, S 0.3%, Mg 0.2% and K 0.2% (Figure 4). Fourier Transform Infrared Spectrometer

(FTIR) (Bruker Vertex70, Germany) gave an interferogram compatible with a mixture of calcium carbonate and calcium phosphate compound (Figure 4).

On follow-up visit at 6 months following the operation, the wound nicely healed and there was no scar contracture. The patient never developed a cutaneous nodule anywhere else. At the age of 12 months, the patient began to walk in accordance with the developmental milestone.

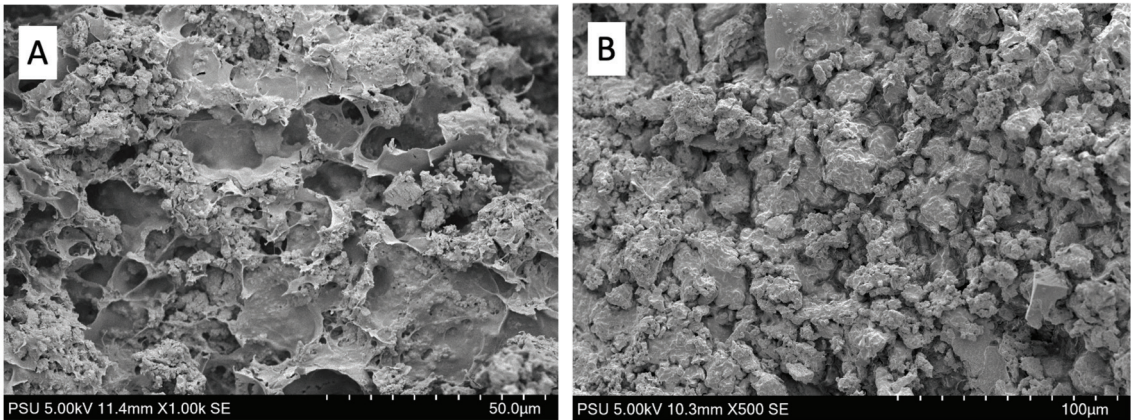


Figure 3 Scanning electron micrograph of the pathological tissue derived from surgical debridement. A:1000X magnification showing precipitation of inorganic crystal within the adipose tissue B:500X magnification

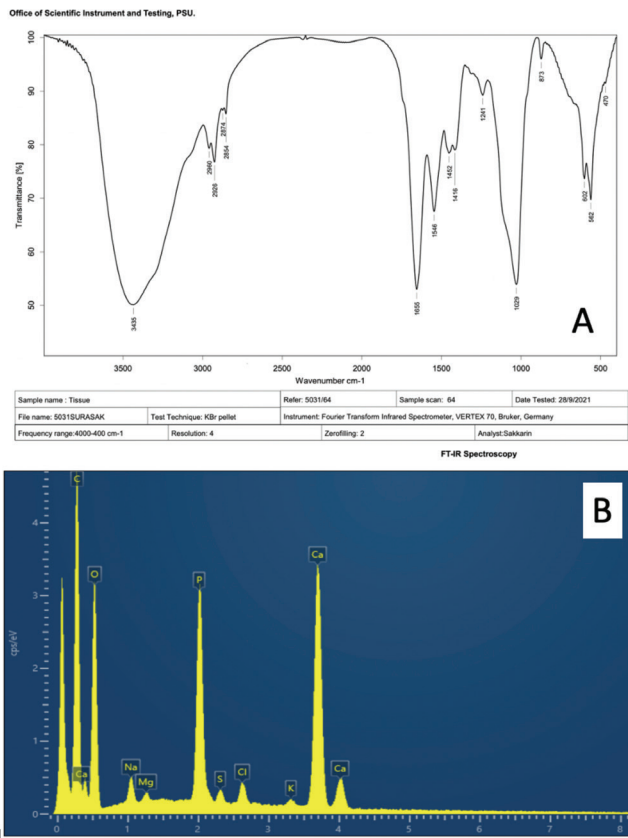


Figure 4 A: Interferogram from a Fourier Transform Infrared Spectrometer which was compatible with mixture of calcium phosphate and calcium carbonate compound B: energy-dispersive X-ray spectroscopy

DISCUSSION

There are at least five types of calcinosis cutis reported in humans which include 1. dystrophic calcinosis, 2. metastatic calcification, 3. idiopathic calcification⁴, 4. iatrogenic calcification, and calciphylaxis. Patients with dystrophic calcinosis usually have underlying inflammation that leads to microtrauma of the soft tissue. Such calcification occurs despite normal serum calcium and phosphorus. In metastatic calcification, diffuse calcification develops secondary to hypercalcemia and hyperphosphatemia. The pathology in our case belongs to iatrogenic calcification, and the most likely cause of abnormal calcification was the precipitation of calcium salt from the parenteral nutrition. Although the composition of calcium in the parenteral solution was not abnormally high, hyperphosphatemia, in this case, may predispose the leaked calcium to precipitation in the subcutaneous tissue. Most iatrogenic calcinosis cutis in newborn patients are caused by calcium gluconate extravasation.^{5,6} Since the year 1997, skin necrosis following parenteral nutrition as in our case, has been reported.⁷ In the report, the wrong calculation of parenteral nutrition led to hyperphosphatemia and calciphylaxis. Consistent with the report, the indication for surgery in our patient was necrosis of the overlying skin.

Electron micrography and chemical analysis in our case by FTIR suggested that the precipitation was a mixture of 2 calcium salts, calcium carbonate and calcium phosphate. The postulation was supported by the results of energy-dispersive X-ray spectroscopy which showed high percentage of carbon, oxygen, calcium, and phosphate in the amorphous crystals laid within the subcutaneous adipose tissue. To our knowledge, this is the first report of details chemical analysis of the calcinosis cutis that occurs following iatrogenic extravasation of parenteral nutrition.

There were reports of successful treatment of iatrogenic calcinosis cutis caused by extravasation of phosphate-containing solution with topical sodium thiosulfate.⁸⁻¹⁰ The treatment might help if it could have been started early after the extravasation happened. In our case, surgical decision was made to remove the entire calcinosis because of impending necrosis of the overlying skin at the dorsum of foot, which was a result of a relatively large size of the lesion. With an awareness that residual calcification may act as a foreign body and interfere with the musculoskeletal functions of the foot, copious irrigation and gentle curettage of the subcutaneous plane was

done. Following the procedures, the wound surface can be later closed with a full-thickness skin graft, and the child could return to normal development. For discrete tiny calcinosis such as those found in rheumatoid disease, systemic pharmacologic therapies may help improving lesions.¹¹

In conclusion, we report a case of iatrogenic calcinosis cutis caused by extravasation of parenteral nutrition. Surgical treatment was given with acceptable outcome.

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CONFLICT OF INTEREST

The authors possess no competing interests to declare.

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References

1. Janigan DT, Perey B, Marrie TJ, et al. Skin necrosis: an unusual complication of hyperphosphatemia during total parenteral nutrition therapy. *JPEN J Parenter Enteral Nutr.* 1997;21(1):50-2.
2. Ahn KH, Park ES. A rare case report of neonatal calcinosis cutis induced by distant and delayed extravasation of intravenous calcium gluconate. *Arch Plast Surg.* 2021;48(6):641-5.
3. Harada K, Miyasaka E, Otsuka F. Calcinosis Cutis. *Am J Med.* 2020;133(9):e528-e9.
4. Al Hajj I, Abdelmaksoud A, Wollina U, et al. Idiopathic calcinosis cutis universalis in a female child: the first case report from Yemen. *Int J Dermatol.* 2023;62(4):579-80.
5. Ching DL, Wong KY, Milroy C. Iatrogenic calcinosis cutis following a neonatal extravasation injury. *Br J Hosp Med (Lond).* 2014;75(5):295.
6. Alghaith EA, AlQahtani GA, Omer JA. Iatrogenic calcinosis cutis in 9-month-old baby boy: a case report. *J Med Case Rep.* 2022;16(1):86.
7. Janigan DT, Perey B, Marrie TJ, et al. Skin necrosis: an unusual complication of hyperphosphatemia during total parenteral nutrition therapy. *JPEN J Parenter Enteral Nutr.* 1997;21(1):50-2.
8. Del Barrio-Diaz P, Moll-Manzur C, Alvarez-Veliz S, et al. Topical sodium metabisulfite for the treatment of calcinosis cutis: a promising new therapy. *Br J Dermatol.* 2016;175(3):608-11.
9. Garcia-Garcia E, Lopez-Lopez R, Alvarez-Del-Vayo C, et al. Iatrogenic Calcinosis Cutis Successfully Treated with Topical Sodium Thiosulfate. *Pediatr Dermatol.* 2017;34(3):356-8.

10. Xie CB, Kidacki M, Ring N, et al. Iatrogenic calcinosis cutis from extravasated phosphate-containing solution treated with topical sodium thiosulfate. *JAAD Case Rep.* 2021;17:31-3.
11. Elahmar H, Feldman BM, Johnson SR. Management of Calcinosis Cutis in Rheumatic Diseases. *J Rheumatol.* 2022;49(9):980-9.