

## Treatment of iatrogenic calcinosis cutis in neonates with topical steroids

### Yenidoğandaki iyatrojenik kalsinozis kutisin topikal steroid ile tedavisi

Muhittin Çelik<sup>1</sup> Ali Bülbül<sup>2</sup> Sinan Uslu<sup>2</sup> Merve Sanlı<sup>2</sup> Haşim Gencer<sup>2</sup>

<sup>1</sup>Diyarbakır Children's Diseases Hospital, Clinic of Neonatology, Diyarbakır, Turkey

<sup>2</sup>Şişli Hamideyi Etfal Hospital, Clinic of Neonatology, İstanbul, Turkey

#### Abstract

Calcinosis cutis, the deposition of calcium salts in the dermis, can be dystrophic, metastatic, iatrogenic, or idiopathic. Calcinosis cutis occurs through a variety of pathogenetic mechanisms. Here, we described a case of iatrogenic calcinosis cutis secondary to extravasation of an intravenous calcium-containing solution in a newborn, with topical steroid treatment. Topical steroid treatment decreased convalescence period clinically and radiologically in this disease with no current specific therapy.

**Keywords:** Calcinosis cutis, topical steroid, newborn.

#### Öz

*Kalsinosis kutis ciltte kalsiyum tuzlarının birikimi olup, distrofik, metastatik, idiyopatik ve iyatrojenik olarak ayrılmaktadır. Kalsinozis kutis çeşitli patogenetik mekanizmalar aracılığıyla meydana gelir. Bu yazıda, intravenöz kalsiyum içeren çözeltinin ekstrasvasyonu sonucu gelişen, topikal steroid ile tedavi edilen bir yenidoğan olgusu sunulmuştur. Şu anda özgül tedavisi olmayan bu durumun, topikal steroid tedavisi ile klinik ve radyolojik düzelme dönemini kısalttığı görüldü.*

**Anahtar Sözcükler:** Kalsinozis kutis, topikal steroid, yenidoğan.

#### Introduction

Calcinosis cutis is a disease characterized with accumulation of calcium salts in the skin and divided into 4 groups which are dystrophic, metastatic, idiopathic and iatrogenic (1,2). Intravenous calcium salt treatment is widely used in the management of neonatal hypocalcemia (3). Iatrogenic calcinosis cutis is defined with local swelling, induration, erythema and tissue necrosis in the skin due to extravasation of calcium salts (3). Supportive and/or symptomatic therapy is given as there is no specific treatment (4). In some cases, medical and surgical treatments could be performed in the presence of hypercalcemia, skin necrosis and secondary infections. This is the report of a case with calcinosis cutis in both upper and lower extremities due to intravenous calcium gluconate administration for hypocalcemic convulsion of a neonate and treated with topical steroid.

#### Case Report

A female neonate was born at 40 weeks of gestation via cesarean section with Apgar scores at 1 and 5 min were 8 and 9, respectively. She was child of a 60-year-old healthy father and a 40-year-old healthy mother without consanguineous marriage. She was referred to our emergency service on the postnatal ninth day with contractions in her extremities (neonatal convulsion). Her past medical history revealed neonatal intensive care unit admission with transient tachypnea of newborn and hospitalization for the first 6 days of her life. During the hospitalization, she had no mechanical respiratory support and her laboratory tests were in normal ranges. Her weight was 3840 g (75-90p), height was 51 cm (75-90 p) and her head circumference was 36 cm (75-90p) at the first physical examination. Her vital signs and systemic examination were totally normal. Laboratory analyses indicated normal complete blood count (WBC 16200/mm<sup>3</sup>, Hb 14.7 g/dL, and platelet count 180000/microL), negative CRP, 98 mg/dL of blood glucose. The cranial ultrasonography and chest x-ray examinations were normal. Her liver and kidney function tests were in normal ranges. Her total calcium level was 6.2 mg/dL, and ionized calcium was 1.1 mg/dL. She was

Corresponding Author: Muhittin Çelik  
Diyarbakır Children's Diseases Hospital, Clinic of Neonatology,  
Diyarbakır, Turkey

Received: 15.09.2015

Accepted: 25.12.2015

diagnosed as hypocalcemic convulsion and treated with intravenous 75 mg/kg/day calcium gluconate and oral 400 IU/day D<sub>3</sub>-vitamin as well. In order to define the etiology of hypocalcemia, laboratory investigations were performed and D<sub>3</sub>-vitamin level of the baby was found low as 8.3 ng/mL (normal range 25-80 ng/mL). The mother's serum Ca and D<sub>3</sub>-vitamin levels were found as normal. After 2 days of intravenous Ca-gluconate treatment, the calcium level became normal and her treatment was changed as oral calcium-lactate and 400 units/day of oral D<sub>3</sub>-vitamin. On the 7th day of her hospitalization swelling and induration were observed on the right forearm and the left foreleg at the IV insertion sites. Antibiotic treatment (ampicillin-aminoglycoside) was started for the soft tissue infection that was supported by elevation of infection markers after sepsis evaluation. On the third day of the treatment, as blood culture was still negative and infection markers became negative, antibiotherapy was stopped. After excluding the soft tissue infection, for differential diagnosis of the calcifications, roentgenograms were obtained and calcifications of the left foreleg and also right forearm were detected. Therefore, it was diagnosed as iatrogenic calcinosis cutis (Figure-1). Afterwards circulatory failure in distal ends of extremities appeared and Doppler USG was performed and found as normal. Topical steroid (0.125% prednisolone) treatment was started for the lesions. Circulatory failure resolved after the second day of the treatment. She was discharged from the hospital on the 14th day of daily single dose of topical steroid treatment. After additional 2 weeks of treatment, her physical examination, radiologic and laboratory findings were totally normal and treatment was stopped. The patient was well at her follow-up visits and 10 months old at the last time.

Written informed consent was obtained from her parents for publishing the individual medical records.



**Figure-1.** Roentgenogram: Calcifications of the left foreleg.

## Discussion

Calcinosis cutis is a poorly understood situation characterized by abnormal deposits of calcium salts in the dermis and/or hypodermis. It is categorized into four types: metastatic, dystrophic, idiopathic and iatrogenic (2). Dystrophic calcinosis cutis is the most common type and occurs in damaged and traumatized tissues without abnormal serum calcium and phosphorus levels (5). Metastatic calcinosis cutis occurs in tissues in the presence of abnormal serum calcium and phosphorus levels usually due to a systemic disease. Idiopathic calcinosis cutis has undetermined origin with no systemic or biochemical abnormality. Iatrogenic calcinosis cutis is caused by extravasation of calcium salts with the usage of calcium containing drugs intramuscularly and after performing electromyography (5,6).

Although there are many theories to explain pathogenesis of calcification, the main reason could not be described. Due to the local tissue damage and transient elevation of local calcium concentration, cell membrane permeability increases and allows cytosolic influx of calcium that exceeds the capacity of mitochondria to sequester calcium and phosphate. This condition leads to the precipitation of calcium phosphate in the cytoplasm. Mast cells might play a significant role because histamine and serotonin have been found to induce local calcification (1).

The differential diagnosis of calcinosis cutis should be made with osteomyelitis, periostitis and soft tissue infection (4). Radiological findings play an important role in diagnosis, especially in uncertain cases. The local lesions appear within 2 hours to 24 days of calcium infusion, with an average of 2 weeks (3). In our case; lesions were observed at the end of the first week. Radiological changes could not be seen initially and appeared obviously within 1-3 weeks. Calcium deposition in the skin was seen radiologically at the end of the first week in the present case.

Tissue necrosis and secondary infections are the most important complications, and in severe cases drainage, debridement and tissue graft could be needed (3). Calcinosis cutis lead to compartment syndrome in neonatal period was reported (7). There are several recommendations for reducing the risk of iatrogenic calcinosis cutis. In hypocalcemia, the first choice of calcium supplementation route should be orally. The intramuscular and subcutaneous routes should be avoided because of the risk of tissue necrosis. Gluconate is preferred to chloride because the calcium is less likely to precipitate. If IV route is required, then the administration rate should be a maximum of 2 ml/min, and administration with anions such as bicarbonate, phosphates and sulfates should be avoided. Cannulation

sites should be changed regularly, and each cannula should be checked for a backflow of blood before the infusion of calcium (1,7).

If calcium extravasated; catheter should be kept out and cold compress should be applied for 15 minutes and 4 times a day, and affected extremity should be elevated for 48 hours (8). Resolution of radiological changes takes 2-6 months (7). There is no specific and standard treatment. The efficacy of calcinosis treatment has only been reported in single cases or small case series. Various treatments have been reported to be beneficial, including warfarin, bisphosphonates, minocycline, ceftriaxone, diltiazem, aluminum hydroxide, probenecid, intralesional corticosteroids, IV immunoglobulin, curettage, surgical excision, carbon dioxide laser, and extracorporeal shock wave lithotripsy (9).

Medical therapy for calcinosis cutis is limited and of variable benefit. However, intralesional corticosteroids may be beneficial because of their anti-inflammatory and inhibitory effects on fibroblast activity. Intralesional injection of triamcinolone acetonide (10 mg/dL, 0.5 mL, single dose) for the treatment of calcinosis cutis following extravasation of calcium gluconate has been shown to be effective in an animal model (10). In most cases, progressive clearing of calcification starts

occurring without any special treatment at about 2-6 months after the onset. At about 6 months, there is no evidence of tissue calcification (3). Mast cells might play a significant part because histamine and serotonin have been found to induce local calcification (1,3). As there was no severe necrotic skin lesion in our case, intralesional injection was not considered, and topical steroid treatment was given for anti-inflammatory effects.

In the present case, daily single dose of topical steroid treatment was started after the development of peripheral circulatory failure on the extremities. At the second day of the treatment, improvement of circulatory failure was observed and the treatment was continued for 4 weeks duration. After the treatment; physical examination and laboratory findings were found in normal ranges, and radiological changes completely resolved.

In calcinosis cutis caused by usage of calcium preparations intravenously in newborn period; topical steroid treatment decreases convalescence period clinically and radiologically. We suggest that local steroid treatment should be used in the treatment for earlier resolution of radiological changes like in the present case.

## References

1. Puvabanditsin S, Garrow E, Titapiwatanakun R, Getachew R, Patel JB. Severe calcinosis cutis in an infant. *Pediatr Radiol* 2005;35(5):539-42.
2. Walsh JS, Fairley JA. Calcifying disorders of the skin. *J Am Acad Dermatol* 1995;33(5Pt1):693-706.
3. Sonohata M, Akiyama T, Fujita I, Asami A, Mawatari M, Hotokebuchi T. Neonate with calcinosis cutis following extravasation of calcium gluconate. *J Orthop Sci* 2008;13(3):269-72.
4. Arora A, Agarwal A, Kumar S, Gupta SK. Iatrogenic calcinosis cutis--a rare differential diagnosis of soft-tissue infection in a neonate: A case report. *J Orthop Surg* 2005;13(2):195-8.
5. Domizio S, Puglielli C, Barbante E, et al. Calcinosis cutis in a newborn caused by minimal calcium gluconate extravasation. *Int J Dermatol* 2006;45(12):1439-40.
6. Giorgini S, Martinelli C, Massi D, Lumini A, Mannucci M, Giglioli L. Iatrogenic calcinosis cutis following nadroparin injection. *Int J Dermatol* 2005;44(10):855-7.
7. Chen TK, Yang CY, Chen SJ. Calcinosis cutis complicated by compartment syndrome following extravasation of calcium gluconate in a neonate: a case report. *Pediatr Neonatol* 2010;51(4):238-41.
8. Millard TP, Harris AJ, MacDonald DM. Calcinosis cutis following intravenous infusion of calcium gluconate. *Br J Dermatol* 1999;140(1):184-6.
9. Reiter N, El-Shabrawi L, Leinweber B, Berghold A, Aberer E. Calcinosis cutis: part II. Treatment options. *J Am Acad Dermatol* 2011;65(1):15-22.
10. Ahn SK, Kim KT, Lee SH, Hwang SM, Choi EH, Choi S. The efficacy of treatment with triamcinolone acetonide in calcinosis cutis following extravasation of calcium gluconate: A preliminary study. *Pediatr Dermatol* 1997;14(2):103-9.