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Case Report

Neonatal hypercalcemia due to subcutaneous fat necrosis caused by therapeutic hypothermia in a newborn

Oznur Vermezoglu[1]*, Mustafa Celik[2], Vasfi O. Vermezoglu[1], Emine Ozbicer[1], Rıdvan Duran[3], Filiz Tutunculer Kokenli[1]

[1]Department of Pediatrics and Pediatric Endocrinology Unit-Medical School, Trakya University Hospital, Edirne, Türkiye
[2]Department of Pediatrics-Medical School, Trakya University Hospital, Edirne, Türkiye
[3]Department of Pediatrics and Neonatology Unit-Medical School, Trakya University Hospital, Edirne, Türkiye

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***Correspondence:**
Dr. Oznur Vermezoglu,
E-mail: oznur@vermezoglu.com

ABSTRACT

Subcutaneous fat necrosis (SCFN) is a rare inflammatory disorder of unknown pathogenesis of adipose tissue that occurs in the first few weeks of life, its clinical findings usually regress spontaneously, accompanied by severe systemic findings such as hypercalcemia, thrombocytopenia, and hypertriglyceridemia. It presents with painless and sharply circumscribed nodules or plaques. It is panniculitis that can be seen frequently on the face, neck, back and proximal extremities. Perinatal complications such as gestational diabetes, preeclampsia, asphyxia, meconium aspiration, birth trauma, sepsis and hypothermia are risk factors. Here, we present a newborn with a diagnosis of stage 2 hypoxic ischemic encephalopathy who was sent to our hospital due to asphyxic delivery and received cooling therapy for 72 hours with mild hypercalcemic findings and SCFN.

Keywords: Hypercalcemia, Newborn, Perinatal asphyxia, Therapeutic hypothermia, Subcutaneous fat necrosis

INTRODUCTION

Subcutaneous fat necrosis (SCFN) is an uncommon inflammatory condition of neonatal adipose tissue, predominantly observed in full-term or post-term infants who have been subjected to perinatal stressors, such as birth-related trauma, hypothermia, or oxygen deprivation.[1] Although its underlying pathophysiology has not yet been fully elucidated, SCFN is most frequently encountered in newborns receiving therapeutic whole-body hypothermia following perinatal asphyxia.[2] Several risk factors have been implicated in its development, including localized cutaneous trauma, obstetric complications, maternal conditions like preeclampsia and diabetes, neonatal sepsis, and meconium aspiration.[3] Perinatal asphyxia refers to impaired oxygen delivery or disrupted gas exchange affecting the fetus in the period immediately surrounding birth. This condition can lead to multisystem involvement, with potential injury to organs such as the brain, heart, kidneys, liver, and skin.[4] For infants with moderate to severe hypoxic-ischemic encephalopathy (HIE), whole-body cooling has become the established standard of care.

Despite its benefits, therapeutic hypothermia (TH) is associated with certain adverse effects, including bradycardia, hypotension, and coagulopathy.[5] SCFN, though rare, has been recognized as a potential complication of TH, with an incidence reported around 1%.[2,6,7] Clinically, SCFN typically presents with firm, reddish nodules or plaques located on areas such as the arms, back, buttocks, thighs, and cheeks.[2] The diagnosis is primarily clinical, and the condition often resolves spontaneously within a few weeks. Nonetheless, some

infants may develop metabolic or hematologic disturbances, including elevated calcium or triglyceride levels and thrombocytopenia. Among these, hypercalcemia is the most frequently encountered and may pose serious health risks if not identified and managed promptly.[8] Authors report the case of a male neonate who developed asymptomatic hypercalcemia as a complication of SCFN following therapeutic hypothermia administered for hypoxic-ischemic encephalopathy.

CASE REPORT

A male newborn weighing 4000 grams, born at 35 weeks of gestation to a 25-year-old mother with gestational diabetes, required advanced resuscitation due to the absence of spontaneous respiration and a heart rate below 60 beats per minute. The baby was intubated due to the failure to initiate spontaneous respiration and was transferred to our intensive care unit with a preliminary diagnosis of perinatal asphyxia. Upon admission, the infant presented in poor general condition, intubated, in a flexed posture, hypotonic, and with diminished newborn reflexes and other system findings were unremarkable.

Laboratory findings were consistent with metabolic acidosis on blood gas analysis. There was a significant increase in blood lactate (187 mg/dl; normal range (NR): 5-14) and ammonia (20 ug/dl; NR: 27.2-102) levels. Serum levels of troponin (3237.4 ng/l; NR: 0-34.2), creatine kinase (1353U/l; NR: 20-200), lactate dehydrogenase (1454 U/l; NR: 135-225), and alanine aminotransferase (42 U/l; NR: 0-41) were markedly elevated. A complete blood count revealed mild leukocytosis. Based on the history, clinical, and laboratory findings, the patient was diagnosed with hypoxic-ischemic encephalopathy and underwent 72 hours of therapeutic hypothermia for treatment. The patient, diagnosed with hypoxic-ischemic encephalopathy based on clinical and laboratory findings, underwent 72 hours of therapeutic hypothermia.

During the treatment, the patient remained intubated. At the end of the therapy, the need for oxygen gradually decreased, and the patient was extubated within 24 hours and started on orogastric feeding." On the 7th day, as oral feeding was increased, the patient was started on prophylactic vitamin D supplementation at a dose of 400 units. On the 28th day postnatally, routine laboratory tests performed before discharge revealed a serum calcium level of 13.2 mg/dl, indicating hypercalcemia, and a pediatric endocrinology consultation was requested.

On the physical examination at that time, all of the patient's systemic findings were normal, except for a firm, irregularly bordered mass measuring 3×2 cm, palpated in the occipital region of the scalp (Figure 1). Further laboratory investigation revealed increased serum calcium level of 13.2 mg/dl, suppressed parathyroid hormone levels of 7.4 pg/ml, normal vitamin D level of 28.8 ng/ml. Blood gas analysis and serum albumin level were normal. The spot urine calcium-to-creatinine ratio had increased to 2.1. The ECG findings were normal. Renal ultrasonography demonstrated normal cortical and parenchymal echogenicity, with no signs of nephrocalcinosis.

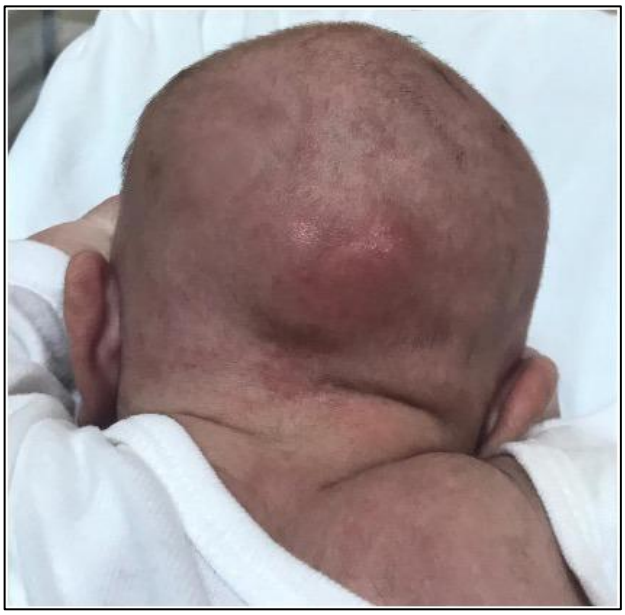

Figure 1: Red purple nodules on the back of the head.

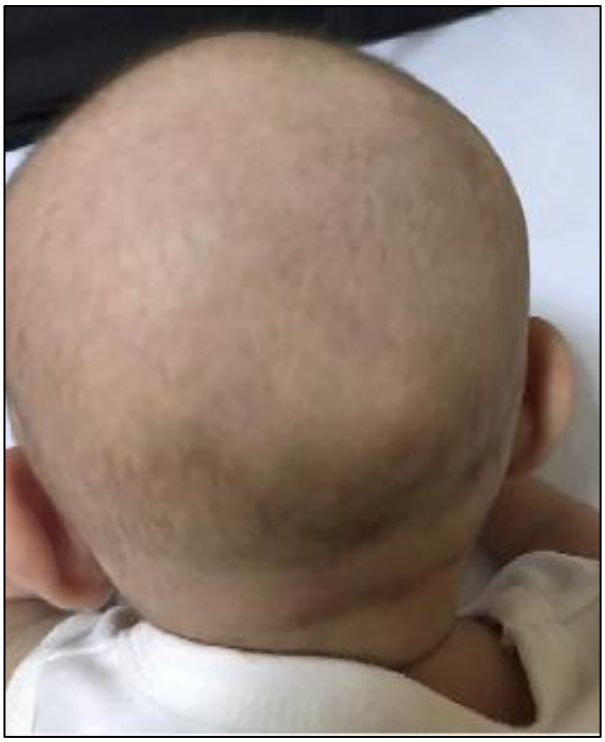

Figure 2: The appearance of the completely healed nodular lesion.

Based on the patient's history, physical examination, and laboratory findings, subcutaneous fat necrosis and the associated hypercalcemia were considered. Since there

were no signs of hypercalcemia in the patient, it was decided to continue breastfeeding while discontinuing only the vitamin D prophylaxis, with the patient being monitored clinically and through laboratory tests. On the third day of follow-up, the patient's serum calcium level was found to be 11.5 mg/dl, and the patient was discharged with instructions to return for outpatient follow-up. At the first-week follow-up after discharge, the patient's serum calcium level was measured at 10 mg/dl, and the parathyroid hormone (PTH) level was 32 pg/ml. At the one-month follow-up, the lesion on the scalp had completely healed (Figure 2) and the patient maintained normocalcemia (Ca: 10 mg/dl).

DISCUSSION

SCFN is a disease characterized by erythematous-purple subcutaneous plaques and nodules on the back, cheeks, shoulders, hips and thighs in newborns. Although its prevalence and etiopathogenesis are not known exactly. It has been reported to be associated with maternal causes such as maternal diabetes, preeclampsia, hypothyroidism, hypertension, ablatio placentae, cocaine uses during pregnancy, perinatal complications such as asphyxia, birth trauma, meconium aspiration, hypoglycemia, and therapeutic hypothermia.[9] It is thought that perinatal asphyxia and therapeutic hypothermia (33-34°C) applied in the treatment of asphyxia in newborns cause hypoxia and hypothermia in the subcutaneous tissue, initiating a granulomatous inflammation and necrosis in the adipose tissue.[9-10] In newborns, the concentration of saturated fatty acids is relatively high, and the enzyme systems responsible for the desaturation of fatty acids are immature. It has been suggested that hypoxia, hypoperfusion and hypothermia increase the storage of saturated fatty acids in subcutaneous adipose tissue by affecting the enzyme systems, causing inflammation in adipose tissue, crystallization and necrosis of adipocytes.[2]

Typical skin lesions consist of hard, erythematous or purplish hardened plaques that develop into subcutaneous hard painful nodules on the back, shoulders, upper extremities, and thighs.[2,11] Diagnosis can be made by history and typical clinical findings.[12,13] Diagnosis is mainly clinical, but skin biopsy may be helpful in case of clinical doubt. Differential diagnosis for SCFN can be difficult and includes scleroma neonatorum and cellulitis. Calcium release from necrotic fat cells, increased intestinal absorption of calcium by 1,25-(OH)2 vitamin D3, whose production is increased in macrophages, and bone resorption-enhancing effects of local prostaglandin E2 and PTH have been held responsible for hypercalcemia.[2,11]

"In our patient, the presence of perinatal risk factors including maternal diabetes, having diagnosed perinatal aphyxia and received cooling therapy and a firm and painful mass found in the occipital region in the third week postnatally, along with hypercalcemia and suppressed PTH levels, suggested a diagnosis of subcutaneous fat necrosis." Hypercalcemia usually occurs in the first month after the development of skin lesions, but can occur up to 6 months later; therefore, patients should be followed for a long time, also developed in our patient in the 3rd week. Patients with hypercalcemia may be asymptomatic or present with symptoms such as lethargy, irritability, hypotonia, vomiting, polyuria, polydipsia, dehydration, and constipation. It can lead to serious complications, both acute (cardiac arrest and kidney failure) and chronic problems (metastatic calcifications).[14] In these patients, treatment aims to lower serum calcium levels. Treatment options include restriction of calcium and vitamin D intake, intravenous fluid rehydration, and the most precise interventions. Furosemide is used to induce calciuresis and prevent calcium reabsorption. For most cases of severe hypercalcemia, glucocorticoids are recommended as they reduce intestinal calcium absorption, increase renal calcium excretion and degradation of vitamin D. The last therapeutic option should be bisphosphonates such as pamidronate or zoledronic acid that inhibit osteoclast function. In our case, it was found that PTH was suppressed due to hypercalcemia.

After discontinuation of vitamin D treatment, no symptoms developed in the follow-up and serum Ca value was found to be normal. Therefore, we didn't give treatment. While the calcium/creatinine ratio in the spot urine was high at the beginning, it returned to normal after vitamin D treatment was stopped; Renal ultrasonography did not reveal any signs of nephrocalcinosis. Patients with diffuse SCFN and hypercalcemia should be closely followed up for months, and the family should be informed about symptoms such as restlessness, anorexia, vomiting, constipation, and growth retardation.

CONCLUSION

Newborns with a history of perinatal asphyxia or those treated with therapeutic hypothermia should be closely monitored during the first month of life for potential complications such as SCFN and hypercalcemia. Because SCFN may initially be asymptomatic or subtle in appearance, early recognition requires a high index of clinical suspicion. In cases where hypercalcemia is detected-whether symptomatic or not-alongside suppressed parathyroid hormone (PTH) levels, a thorough skin examination is essential. Identifying SCFN promptly is critical, as untreated hypercalcemia may result in serious consequences such as nephrocalcinosis, cardiac arrhythmias, or neurodevelopmental delay. Therefore, in any neonate presenting with unexplained hypercalcemia and low PTH, SCFN should be considered, even in the absence of visible skin findings. Regular follow-up and biochemical monitoring are key to early diagnosis and effective management, helping prevent long-term complications.

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REFERENCES

1. Woods AG, Cederholm CK. Subcutaneous fat necrosis and whole-body cooling therapy for neonatal encephalopathy. Adv Neonatal Care 2012;12(6):345-8.
2. Martinelli S, Pitea M, Gatelli IF, Raouf T, Barera G, Vitelli O. Safety and efficacy of pamidronate in neonatal hypercalcemia caused by subcutaneous fat necrosis: a case report. Front Pediatr. 2022;10:845424.
3. Shumer DE, Thaker V, Taylor GA, Wassner AJ. Severe hypercalcaemia due to subcutaneous fat necrosis: presentation, management and complications. Arch Dis Child Fetal and Neonatal. 2014;99(5):419-21.
4. Improda N, Capalbo D, Poloniato A, Garbetta G, Dituri F, Penta L, et al. Perinatal asphyxia and hypothermic treatment from the endocrine perspective. Front Endocrinol. 2023;14:1249700.
5. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, et al. Whole-body hypothermia for neonates with hypoxic–ischemic encephalopathy. N Engl J Med. 2005;353(15):1574-84.
6. Grass B, Weibel L, Hagmann C, Brotschi B, Asphyxia N, Group CR. Subcutaneous fat necrosis in neonates with hypoxic ischaemic encephalopathy registered in the Swiss National Asphyxia and Cooling Register. BMC Pediatr. 2015;15:1-7.
7. Lara LG, Villa AV, Rivas MMO, Capella MS, Prada F, Enseñat MAG. Subcutaneous fat necrosis of the newborn: report of five cases. Pediatr Neonatol. 2017;58(1):85-8.
8. Lorenzo C, Romana A, Matias J, Calhau P. Subcutaneous fat necrosis of the newborn–An atypical case with typical complications. Clin Case Rep. 2021;9(4):2069-73.
9. Hogeling M, Meddles K, Berk DR, Bruckner AL, Shimotake TK, Cohen RS, et al. Extensive subcutaneous fat necrosis of the newborn associated with therapeutic hypothermia. Pediatr dermatol 2012;29(1):59-63.
10. Oza V, Treat J, Cook N, Tetzlaff MT, Yan A. Subcutaneous fat necrosis as a complication of whole-body cooling for birth asphyxia. Arch Dermatol. 2010;146(8):882-5.
11. Stefanko NS, Drolet BA. Subcutaneous fat necrosis of the newborn and associated hypercalcemia: A systematic review of the literature. Pediatr Dermatol. 2019;36(1):24-30.
12. Vasireddy S, Long SD, Sacheti B, Mayforth RD. MRI and US findings of subcutaneous fat necrosis of the newborn. Pediatr Radiol. 2009;39:73-6.
13. Pai SA, Nagesh K, Radhakrishnan CN. Subcutaneous fat necrosis of the newborn mimicking generalized lymphadenopathy. Indian J Dermatol Venereol Leprol. 2007;73:357-8.
14. Akın MA, Akın L, Sarıcı D, Yılmaz İ, Balkanlı S, Kurtoğlu S. Follow-up during early infancy of newborns diagnosed with subcutaneous fat necrosis. J Clin Res Pediatr Endocrinol. 2011;3(4):216.

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