Cutaneous complication of perinatal hypoxia

M Rato[1], A Catarino[2], C Claro[2], I Viana[2]

Affiliations: [1]Dermatology Department, Hospital de Santarém EPE, Santarém, Portugal, [2]Dermatology Department, Hospital de Egas Moniz, Centro Hospitalar Lisboa Ocidental, Portugal

Corresponding Author: Margarida Rato, Hospital de Santarém EPE, Department of Dermatology, Avenida Bernardo Santareno, 2005-177 Santarém – Portugal, Email: margaridagaiorato@gmail.com

Abstract

Subcutaneous fat necrosis of the newborn is an uncommon, transient, and self-healing panniculitis, mostly affecting term newborns with perinatal complications. The authors present a case of a female full-term neonate, born from an uncomplicated pregnancy, admitted into the neonatology unit 5 hours after delivery because of refractory multifocal seizures in the context of hypoxic-ischemic encephalopathy. Nine days after birth, indurated and erythematous nodules and plaques were noted on the left arm and back. Skin biopsy was compatible with subcutaneous fat necrosis of the newborn. Laboratory evaluation including serum calcium showed normal values. No treatment was initiated. This entity generally follows an uncomplicated course. However, there are important complications for which the patient must be regularly monitored, including thrombocytopenia, hypoglycemia, hypertriglyceridemia, and most importantly, hypercalcemia. Patients should have serial serum calcium determinations for up to 6 months after the appearance of the skin lesions. The early diagnosis and prompt treatment of hypercalcemia are essential to prevent severe complications.

Keywords: subcutaneous fat necrosis, newborn, hypercalcemia, hypoxic ischemic encephalopathy

Introduction

Subcutaneous fat necrosis of the newborn (SCFN) is a rare, self-resolving panniculitis usually found in full-post term infants within the first 6 weeks of life [1]. Although its pathogenesis remains unclear, it has been postulated that any neonatal distress may interfere with normal blood supply to the fat tissue creating an environment of hypoxia and hypothermia, which is believed to lead to inflammation and necrosis [2]. In addition, the hypodermis of the newborn has a higher proportion of saturated fats, which have a higher melting point, making them more likely to crystallize under colder conditions [2]. The prognosis is generally good and usually only symptomatic treatment is required [3]. However, there are serious complications for which the patient must be regularly monitored, especially hypercalcemia [1-7].

Case Synopsis

A female infant weighing 3985g was born at 41 weeks and 1 day by vacuum-assisted vaginal delivery, after an uncomplicated pregnancy and no evidence of maternal diabetes. Apgar scores were 7 and 9 at 1 and 5 minutes and no neonatal resuscitation was needed. Five hours after delivery a seizure was noted and the patient was admitted into the neonatology unit, where she remained until 9 days of life. Her diagnosis was refractory multifocal seizures in the context of hypoxic-ischemic encephalopathy, acute kidney injury, metabolic acidosis, and early-onset sepsis without isolated agent. The patient did not present criteria for therapeutic hypothermia. Nine days after birth, subcutaneous, erythematous, indurated nodules and plaques were noted on the left arm and on the

trunk, extending from the neck to the middle of the back (**Figure 1**).

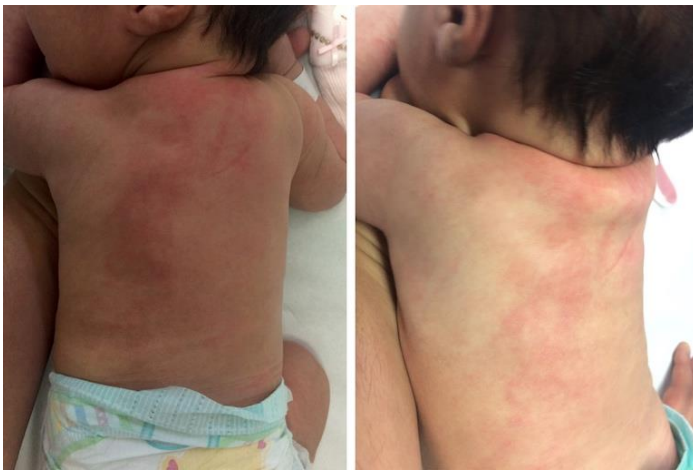

Figure 1. *Subcutaneous erythematous nodules and plaques, with ill-defined limits, distributed along the neck and back.*

A skin biopsy was performed and demonstrated a lobular panniculitis, with extensive fat necrosis, numerous radial eosinophilic crystals, and an infiltrate of lymphocytes, histiocytes, and multinucleated giant cells, consistent with SCFN (Figures 2). Laboratory evaluation, including platelets, serum glucose, and calcium levels showed normal values. The only therapeutic approach was the suspension of vitamin D supplementation. The skin lesions progressively disappeared within the first 3 months. Serum calcium levels throughout the first 6 months of life were normal.

Case Discussion

Subcutaneous fat necrosis of the newborn is often seen in association with multiple neonatal and maternal risk factors. Neonatal risk factors include perinatal asphyxia, meconium aspiration, cord accidents, therapeutic hypothermia, obstetric trauma, sepsis, hypoglycemia, anemia, lactic acidosis, and localized skin trauma [1-7]. Maternal associations include preeclampsia, hypertension, gestational diabetes, cocaine or cigarette exposure, calcium blocker use during pregnancy, and materno-fetal Rh incompatibility [1-7]. In this case, since there was no history of a complicated delivery nor any kind of maternal condition, the hypoxic-ischemic encephalopathy and sepsis was presumed to be associated with hypoxia and hypoperfusion of subcutaneous tissue, predisposing to SCFN.

Clinical findings consist of indurated subcutaneous plaques and nodules with variable color change of overlying skin ranging from no change to prominent erythema or blue discoloration; these changes commonly occur on fat-bearing surfaces of the cheeks, trunk, buttocks, thighs, and arms [2-5,7]. The clinical differential diagnosis includes sclerema neonatorum, cellulitis, hemangioma, lipogranulomatosis (Farber disease), histiocytosis, and rhabdomyosarcomas [2-3].

Histopathologically, SCFN corresponds to a lobular panniculitis consisting mostly of histiocytes,

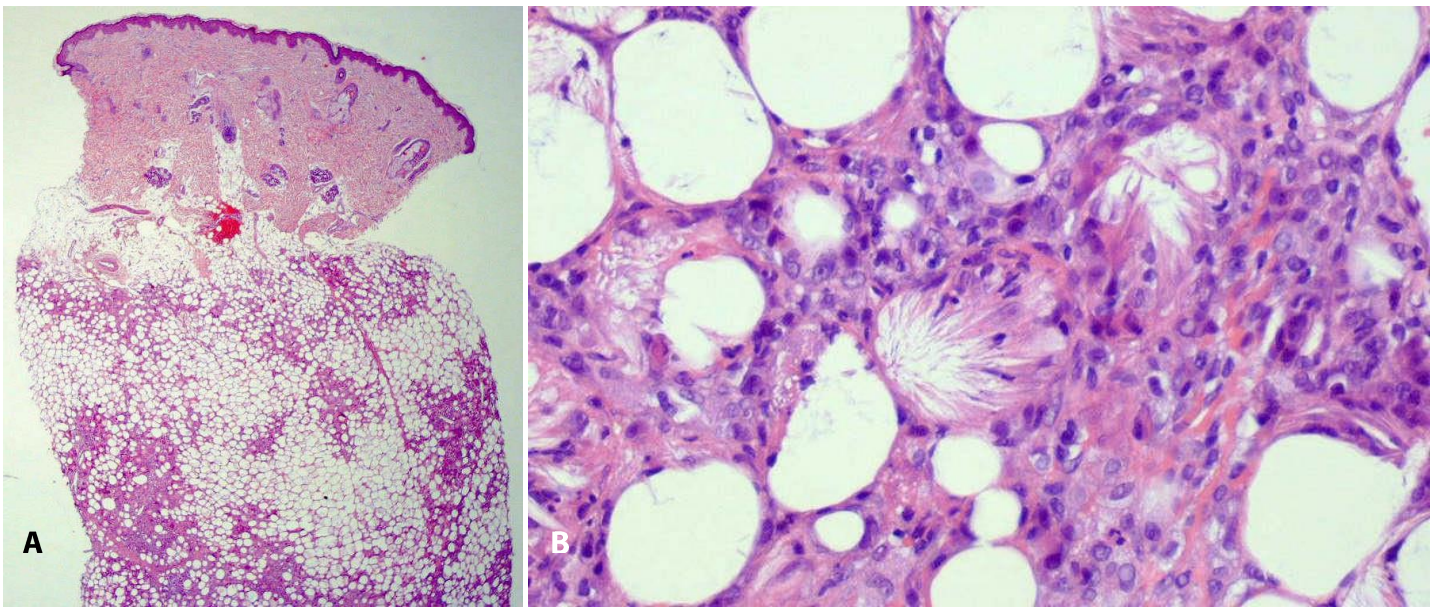

Figure 2. ***A)*** *Lobular panniculitis without involvement of the dermis or epidermis. H&E, 20×.* ***B)*** *Infiltrate composed of a mixture of histiocytes and multinucleated giant cells. Needle-shaped clefts. H&E, 200×.*

including multinucleated cells, with admixed lymphocytes and occasionally a few eosinophils, along with needle-shaped clefts and fat necrosis [8].

Subcutaneous fat necrosis resolves spontaneously within weeks to months [5]. Potential complications include local ulceration, abscess formation, and most importantly, hypercalcemia [5]. Other complications such as thrombocytopenia, hypoglycemia, and hypertriglyceridemia have also been reported in many cases. However, the association is controversial [6]. Hypercalcemia occurs in 28-69% of the cases and is one of the most dangerous complications [7]. Untreated it may lead to severe complications both acute, like cardiac arrest and renal failure, as well as chronic, such as metastatic calcifications (in kidneys, falx cerebri, skin, myocardium, liver, and inferior vena cava), [2, 6]. Its pathogenesis is not fully understood. The most widely accepted theory proposes an excessive production of 1,25 hydroxyvitamin D3 by macrophages independent of the renal absorption independent of parathormone [3]. Although hypercalcemia generally manifests with the onset of skin lesions, it has been reported to occur as late as 6 months afterwards, which is why patients with SCFN warrant long term follow-up of their serum calcium levels [2, 3, 5]. Del Pozzo-Magaña and Ho proposed guidelines for monitoring patients with SCFN [6]. They suggest that when this diagnosis is made serum levels of ionized calcium should be determined and if the patient has a normal value calcium levels should be repeated once a week until one month of age and then once a month until 6 months of age or after resolution of skin lesions. Some authors also suggest that vitamin D supplementation should be discontinued during the first six months of life, and whenever hypercalcemia or associated complications are detected owing to the iatrogenic risk of worsening hypercalcemia [7].

Conclusion

The authors highlight the importance of a uniform work-up and follow-up in SCFN cases as this will allow a better assessment of the prevalence, risk factors, and complications of this entity. Clinicians should be aware of subcutaneous fat necrosis as a possible risk factor for hypercalcemia and patients should have serial serum calcium determinations for up to 6 months after the appearance of the skin lesions.

References

1. Wiadrowski TP, Marshman G. Subcutaneous fat necrosis of the newborn following hypothermia and complicated by pain and hypercalcaemia. Australas J Dermatol 2001;42:207e10. [PMID: 11488718].
2. Lara LG, Villa AV, Rivas MM, Capella MS, Prada F, Enseñat MA. Subcutaneous Fat Necrosis of the Newborn: Report of Five Cases. Pediatr Neonatol. 2017;58(1):85-88. [PMID: 28237247].
3. Oliveira AC, Selores M, Pereira O. Fat necrosis of the newborn - report on two cases. An Bras Dermatol. 2011;86(4 Suppl 1):S114-7. [PMID: 22068788].
4. Rubin G, Spagnut G, Morandi F, Valerio E, Cutrone M. Subcutaneous fat necrosis of the newborn. Clin Case Rep. 2015 5;3(12):1017-20. [PMID: 26734138].
5. Gomes C, Lobo L, Azevedo AS, Simão C. Nephrocalcinosis and subcutaneous fat necrosis. Acta Med Port. 2015;28(1):119-22. [PMID: 25817487].
6. Hogeling M, Meddles K, Berk DR, Bruckner AL, Shimotake TK, Cohen RS, Frieden IJ. Extensive subcutaneous fat necrosis of the newborn associated with therapeutic hypothermia. Pediatr Dermatol. 2012;29(1):59-63. [PMID: 21906137].
7. Del Pozzo-Magaña BR, Ho N. Subcutaneous Fat Necrosis of the Newborn: A 20-Year Retrospective Study. Pediatr Dermatol. 2016;33(6):e353-e355. [PMID: 27574011].
8. Ricardo-Gonzalez RR, Lin JR, Mathes EF, McCalmont TH, Pincus LB. Neutrophil-rich subcutaneous fat necrosis of the newborn: A potential mimic of infection. J Am Acad Dermatol. 2016;75(1):177-185.e17. [PMID: 27157147].