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Case report

Extensive subcutaneous fat necrosis complicated by neonatal hypercalcaemia

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Summary. Subcutaneous fat necrosis (SCFN) is a benign and often self-limiting inflammatory disorder experienced by newborns who were exposed to perinatal stress in the form of asphyxia, hypothermia, cord prolapse, and/or sepsis. Lesions are usually benign and self-limiting, with complete resolution anticipated within a few weeks up to 6 months. They can be accompanied by multiple complications, of which the most significant and of life-threatening potential is neonatal hypercalcaemia. If not timely anticipated and adequately treated, the patient might deteriorate due to dehydration and acute renal failure. Symptoms of neonatal hypercalcaemia can be variable in this age group, transcending from a nonspecific presentation of irritability, poor feeding, vomiting and constipation to the well-recognised polyuria, polydipsia, and dehydration. Therapeutic options are provided through initial hyperhydration and calcium wasting diuretics, switching feeds to a low calcium and vitamin D formula milk, institution of systemic steroids and if necessary, initiating bisphosphonate therapy in hypercalcaemia that is severe, recalcitrant to the previously mentioned treatment modalities, and/or when a rapid decrease in serum calcium levels is desired. In this report we describe a case of a 10 month old female infant with moderate neonatal hypercalcaemia as a complication of extensive SCFN manifesting by the age of 10 days and persisting into a prolonged clinical course of up to 9 months until most of the lesions were resolved. (www.actabiomedica.it)

Key words: neonate, hypercalcaemia, subcutaneous, fat, necrosis

Introduction

Subcutaneous fat necrosis (SCFN) is a systemic inflammatory disorder of the subcutaneous adipose tissue and a rare form of panniculitis. It often manifests in full term or post term newborns, and rarely in those born at a gestational age earlier than 37 weeks. Those at a higher risk of developing this condition are newborns with history of exposure to perinatal stress in the form of cord prolapse, hypothermia, asphyxia, meconium aspiration, and/or sepsis (1). Prenatal history may reveal the presence of maternal diabetes, hypertension, preeclampsia, hypothyroidism, and/or placental abruption, rendering this particular population of mothers more susceptible to newborns with SCFN (2). It is hypothesised to develop secondary to a combination of local tissue hypoxia, mechanical pressure, and crystallisation of the fatty tissue when exposed to hypothermia due to the high content of stearic acids and saturated palmitic acids in neonatal adipose tissue (3). Although variable in duration, complete resolution of the lesions is expected from a couple of weeks to a reported maximum of 6 months (4). SCFN may be complicated by serious metabolic dysfunction, such as hypercalcaemia, in 36-56% of reported cases, potentially life-threatening with the development of acute renal failure if not timely and correctly addressed (5).

Presentation is usually within the first 6 weeks of life with violaceous nodules and erythematous plaques typically covering the skin of the posterior trunk and proximal limbs, with the chest and abdomen more frequently spared (6). Patients are usually irritable with persistent crying as the lesions are often swollen, inflamed and frequently tender to touch. When complicated by hypercalcaemia; polyuria, polydipsia, constipation, abdominal pain, nausea and vomiting all add to the discomfort and irritability experienced by the infant leading to poor feeding, dehydration and weight loss (7).

In this report we describe a case of a 10 month old female with moderate neonatal hypercalcaemia as a complication of extensive SCFN manifesting by the age of 10 days, persisting for a prolonged clinical course of up to 9 months duration until most of the lesions were resolved.

Case presentation

A currently 10 month old female had presented at the age of 10 days with multiple areas of purplish discolouration overlying an erythematous swollen base spreading extensively over her posterior trunk, proximal upper and proximal lower limbs. With a birth weight of 2.9 kg, she was a product of a full term unremarkable pregnancy and was delivered spontaneously through normal vaginal delivery to a healthy mother. However, her birth was complicated by hypothermia and perinatal asphyxia secondary to meconium aspiration. Her symptoms began when she was 10 days old and were associated with decreased oral intake, irritability and vomiting. Neither history of convulsions or loss of consciousness were present, nor the remaining review of her other systems remarkable for any abnormalities.

On examination, she was vitally stable, with multiple purple-red nodules noted bilaterally on the lateral and posterior aspects of the upper limbs extending through her back and towards the sacrum with involvement of the proximal thighs (fig. 1). On palpation, the lesions were hot and tender to touch. The clinical picture was therefore consistent with subcutaneous fat necrosis. Her metabolic profile revealed

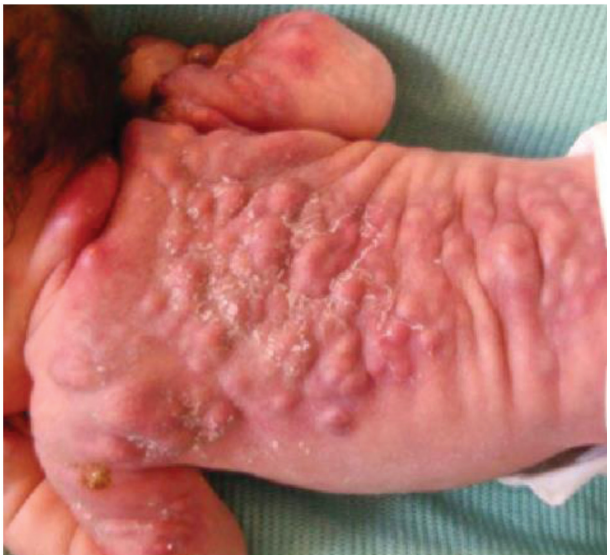

Figure 1.

hypercalcaemia with secondary hypoparathyroidism (table 1). A renal ultrasound was ordered to evaluate the renal integrity and showed no presence of hydronephrosis or parenchymal calcifications. Additional brain ultrasound came back within normal as well.

Initial protocol for the management of hypercalcaemia was instituted, with priority first allocated towards adequate patient hydration. Intravenous diuretics was initiated to achieve forced calcium diuresis but to no much improvement. Consequently, oral prednisolone was started at an initial dose of 2 mg/kg daily as indicated in the treatment of SCFN with normalisation of hypercalcaemia achieved within 2 weeks from presentation. On the other hand, her lesions took a comparatively and exceptionally prolonged clinical course, resolving after approximately 9 months of treatment. During the clinical course of the disease her steroid dosing was gradually tapered after the calcium level was restored to reference range and was continued on alternate days until the lesions were completely resolved.

Discussion

Newborns affected with SCFN are considered to suffer the complication of hypercalcaemia when serum calcium levels exceed 3 mmol/L. This is thought to oc-

Table 1

Test	Value	Reference range
Sodium (mmol/L)	137	135-145
Potassium (mmol/L)	4.10	3.5-5.0
Chloride (mmol/L)	104	98-107
Calcium (mmol/L)	3.20	2.12-2.52
Magnesium (mmol/L)	0.76	0.70-1.00
Phosphate (mmol/L)	1.51	0.81-1.58
Creatinine (umol/L)	6.44	53-115
Urea (BUN) (mmol/L)	0.40	2.5-6.4
Alkaline phosphatase (U/L)	179	134-518
Parathyroid Hormone (Pmol/L)	0.60	1.18-8.43
Vitamin D (nmol/L)	82.00	75-250
Blood culture	negative	No growth
Urine culture	negative	No growth
C reactive protein (mg/L)	19.60	0-3
Serum glucose (mmol/L)	5.10	3.6-7.8
Serum triglycerides (mg/dl)	90	< 150
Haemoglobin (g/dL)	14.00	9.6-15.6
White cell count (K/uL)	12.00	5.5-17.5
Platelet count (K/uL)	476	150-450

cur as a result of various proposed mechanisms that include osteoclast overactivation by elevated levels of prostaglandin E, increasing the rate of born turn over; overproduction of activated vitamin D by circulating macrophages leading to the increased intestinal absorption and renal reabsorption of calcium; and possible calcium release from the necrotic adipose tissue (8).

The prognosis of SCFN is relatively benign, with spontaneous resolution often encountered in most cases with no residual sequalae, while progression to ulceration and evolution of liquid filled bullae requiring local skin care being rarely seen (9). Metabolic complications include thrombocytopaenia, hypertriglyceridaemia, and hypoglycaemia, with hypercalcaemia being of the most serious consequence. Anticipation of hypercalcaemia in children affected with SCFN should be approached with mandatory screening; it can present as a biochemical finding with nonspecific lethargy, irritability, and persistent crying or run a more symptomatic course of hypotonia, constipation, polydipsia, polyuria, and a short period of retained haemodynamic stability before deteriorating into severe dehydration and acute renal failure. Differential diagnosis of SCFN to consider include cold panniculitis, scleroderma, and sclerema neonatorum which was ruled out in this case before confirming the diagnosis of SCFN.

Initial approach to hypercalcaemia consists of prompt hydration in order to treat dehydration and prevent acute renal injury, analgesia, institution of calcium wasting diuretics with the added benefit of preventing fluid overload, and changing feeds to a low calcium and vitamin D formula milk in attempt to lower

serum calcium levels (3, 10). If the aforementioned measures fail, prednisone is recommended as second line therapy for SCFN; aside from the anti-inflammatory properties of glucocorticoids, they also interfere with Vitamin D metabolism through inhibiting the activation of 25 hydroxycholecalciferol by circulating inflammatory macrophages. This avoids calcium build up and subsequent calcifications of the renal parenchyma leading to nephrocalcinosis and/or nephrolithiasis as well as other internal organ calcifications (11).

This is precisely as described by one case report of a female neonate who had developed internal organ calcifications following the manifestation of subcutaneous fat necrosis complicated by biochemical thrombocytopaenia and hypercalcaemia at 3 days of age (8). Another case report outlined the development of SCFN complicated by both hypercalcaemia and hypoglycaemia on the 11th day of life of a full term neonate following exposure to neonatal asphyxia at birth, with normalisation of serum calcium being spontaneous and within the duration of approximately one month (12). In contrast to our patient, no further complications of SCFN were observed aside from the hypercalcaemia, however, hypercalcaemia required treatment and the SCFN did not resolve neither spontaneously nor within the short span of a month, as the patient described in our report had exhibited clinically more extensive lesions covering a larger surface area and demonstrating a slower path of regression.

In theory, the clinical lesions of SCFN usually regress within weeks of instituting therapy but may take up to an utmost of 6 months to completely resolve, leaving no scarring sequelae behind (4). Although no local complications were experienced by our patients, her symptoms only approached complete resolution around 9 months of age, despite the early institution of daily prednisone and the continued therapy past normalisation of serum calcium. Her steroid dosing was gradually tapered after the calcium level was restored to reference range but was continued on alternate days until the lesions regressed to a satisfactory degree. This was preferred as hypercalcaemia was more likely to recur if treatment was stopped as her lesions were grossly extensive, covering a significant surface area, slowly regressing, and therefore could have continued to release calcium ions into the circulation from the persistent necrotic adipose tissue. It is noteworthy to mention that despite the prolonged course of steroids that was necessary to control this case, with competent dosing and regular close follow up, the patient did not develop any of the complications associated with prolonged systemic steroid therapy, such as cushings, hyperglycaemia, osteoporosis, etc.

Although hypercalcaemia was simultaneous with the manifestation of SCFN in this case, late-onset hypercalcaemia more often develops weeks after the appearance of the skin lesions, which was the case in one report where the infant developed severe hypercalcaemia of 4.15 mmol/L two weeks after development of lesions characteristic of SCFN, and had required the administration of pamidronate, a systemic bisphosphonate, in order to effectively lower serum calcium levels (13). Bisphosphonates work to lower serum calcium by directly inhibiting the activity of osteoclasts and prevent the dissolution of hydroxyapatite crystals containing calcium phosphate. Fortunately, this resort was unnecessary in our case as the patient had a moderate hypercalcaemia of 3.2 mmol/L that was responsive to prednisone with serum calcium levels normalising within 2 weeks from presentation.

In conclusion, although SCFN is a benign, sometimes self-limiting condition, it still should be recognised as a complication in newborns and infants exposed to perinatal stress, particularly birth asphyxia, as it is a predisposing factor to the more serious development of neonatal hypercalcaemia. Due to the possibility of a delayed presentation, we recommend that serial monitoring of serum calcium be continued for a minimum of 6 months after the onset of SCFN. Furthermore, we recommend continued therapy for as long as the lesions are clinically persistent to avoid the possibility of hypercalcaemia relapse.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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