



Hypercalcemia and Nephrocalcinosis in an Infant with Subcutaneous Fat Necrosis: A Rare but Potential Serious Clinical Condition

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Authors' contributions

This work was carried out in collaboration among all authors. Author JNN Concept of idea, Data collection and Drafting of Manuscript. Author AC Concept of idea, Drafting and Editing of Manuscript. Author SJ Critical reviewing, Scientific facts. Author MJ Critical reviewing, Scientific facts. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Background: Subcutaneous fat necrosis of the newborn (SCFN) is a panniculitis characterized by the presence of violaceous subcutaneous nodules and indurated plaques on the back, buttocks, proximal extremities, or cheeks. It is a self-limiting benign condition sometimes associated with hypercalcemia that can lead to serious complications such as seizures, failure to thrive and renal failure. It usually develops in full term neonates who experienced some perinatal stress. The literature shows that hypercalcemia is found in nearly 51% of infants, with 95% of the infants developing it within 60 days of onset of skin lesions.

Clinical Description: In this case, we describe a full-term female infant presented to us with failure to thrive at 2 months of age with a postnatal history of meconium aspiration syndrome. On further evaluation, child was found to have hypercalcemia, anemia and bilateral nephrocalcinosis.

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Management & Outcome: The clinical findings and lab investigations were consistent with subcutaneous fat necrosis with hypercalcemia as its main complication. Child was successfully treated with oral corticosteroids.

Conclusion: Being a rare clinical condition, it is important to consider it as a differential diagnosis in infants with significant perinatal stress and hence this case report.

Keywords: Failure to thrive; hypercalcemia; nephrocalcinosis; perinatal stress; subcutaneous fat necrosis.

1. INTRODUCTION

Subcutaneous fat necrosis of newborn is an uncommon disorder primarily affecting term and post-term neonates. It usually presents within the first few weeks of life. It is characterized by firm purple subcutaneous nodules or plaques commonly on the trunk, buttocks, cheeks, and extremities [1]. The precipitating factors include asphyxia, hypothermia, meconium aspiration, hypoxemia, obstetric trauma, and maternal conditions such as preeclampsia and diabetes. Therapeutic hypothermia in neonates with birth asphyxia is an additional risk factor [2,3,4]. The pathophysiology of the disease is considered to be a combination of the higher tendency for crystallization of neonatal fat following hypoxia compared with adult fat and the presence of adipose tissue stress factors that precipitate this crystallization. Newborns have a higher ratio of saturated fat to unsaturated fatty acids in adipose tissue compared to older children and adults. A lower solidification point and a higher melting point of fat tissue in neonates result in solid nodules [5,6]. Adipose tissue of newborns is considered to be more sensitive to hypoxia and more likely to develop necrosis under stressful conditions [7].

The important complications include local tissue breakdown, hypercalcemia, hypoglycemia, anemia, thrombocytopenia, hypertriglyceridemia. Hypercalcemia associated with subcutaneous fat necrosis is usually asymptomatic [8]. However, it can lead to irritability, vomiting, polyuria, failure to thrive, seizures, hypertension, arrhythmia, renal failure, and even death. It is usually seen within 60 days of onset of skin lesions. The mechanism for hypercalcemia is unknown, but it is suspected that the granulomatous inflammatory cells in the nodules express high levels of 1-alpha-hydroxylase, convert 25-hydroxyvitamin D3 to its active form of 1, 25-dihydroxy vitamin D3. Hence, secondary hypercalcemia occurs due to overproduction of active vitamin D from the skin lesions.

2. PRESENTATION OF CASE

A full term 2.4 kg female neonate born to a prim-gravida by caesarean section with an Apgar score 6, 8, 9. Immediately after delivery child developed respiratory distress and required intensive care in NICU. Child was started on oxygen by nasal prongs at 2L/min. A Chest x-ray was done, which was suggestive of a hyperinflated lungs with asymmetrical patchy opacities. Considering child had Meconium aspiration syndrome, she was intubated and given surfactant by INSURE technique and later received positive pressure ventilation with CPAP. Child was initially given empirical antibiotics as per the NICU protocol suspecting neonatal sepsis. The antibiotics were discontinued after 72 hours after documenting sterile blood culture. Feeding was started on Day 4 of life which child tolerated and gradually full feeds were achieved by Day 8 of life. Daily hemodynamic and weight monitoring was done. Child was discharged on Day 14 of life after documenting adequate weight gain. On first follow up visit at Day 28 of life, child had inadequate weight gain and painless nodules on her cheeks, back and arms. Other systemic examinations were normal. On investigations, no abnormalities were detected. Child was kept under close follow up.

At Day 60 of life, child presented to us with a history of poor oral intake, inadequate weight gain and subcutaneous nodules on both her arms and cheeks. On admission, the child had weight of 2442g, with a heart rate of 110 beats/min, respiratory rate of 32 breathes/min and oxygen saturation of 95% on room air and blood pressure of 85/40 mm of Hg. On general examination, child had pallor and indurated subcutaneous nodules were palpable on her cheeks, arms and back. Systemic examination was normal.

On investigation, her complete blood count showed hemoglobin level of 9.1 gm/dL, total leukocyte counts of 11,540 /mcL, platelet count of 3.13 lakhs /mcL. Her C-reactive protein was

0.2mg/dL. Her serum calcium level was 14.9mg/dL (Normal range 8.8 to 10.3mg/dL), serum phosphate was 2.41mg/dL (4.3 to 9.3mg/dL), serum alkaline phosphatase was 185 IU/L (200 to 600 IU/L) and parathyroid hormone level was 1pg/mL (15 to 87pg/mL). The liver function tests and renal function tests were normal. Her chest x-ray was normal. Her Blood and urine cultures were sterile. Her urinary calcium was 20.8 (Normal range-20-275 mg/24-hour), urine calcium creatinine ratio of 0.1 (normal range <0.14). The abdominal ultrasound was suggestive of bilateral nephrocalcinosis. The biopsy of subcutaneous nodules was not performed as parents refused for consent. As per the clinical presentation and laboratory parameters, the diagnosis of subcutaneous fat necrosis of newborn was made. The child was given intravenous normal saline with injectable furosemide at 0.5mg/kg in two divided doses for two days. Her serum calcium was normalized. On day 8 of admission, she again developed hypercalcemia with a serum calcium of 17.5 mg/dL. She was started on oral prednisolone at 2mg/kg/day in two divided doses and gradually tapered over 10 days. The serum calcium levels were monitored regularly and no hypercalcemia was documented. The child was gaining weight and hence was discharged. On regular follow ups after 15 days, 1 month following discharge, she was asymptomatic and was gaining adequate weight. Her follow up serum calcium levels were normal. An informed written consent was obtained from parents for reporting this case.

Table 1. Trend of Serum calcium level during hospital stay

Days of hospital stay	S. Calcium level (mg/dl)
1	14.9
2	13.7
4	15.10
8	17.5
9	12.9

3. DISCUSSION

Subcutaneous fat necrosis is a rare entity occurring usually in term and post term newborn. It can be precipitated by birth asphyxia, hypothermia, meconium aspiration or some obstetric condition or birth trauma. Although benign, it can sometimes present with life threatening hypercalcemia [9]. This can further lead to complications that can affect the growth

and development of the child. These complications may mimic sepsis in infants. The child may present with irritability, vomiting, polyuria, failure to thrive, neurologic symptoms/seizures, hypertension, mental retardation, renal failure, and even death. In a systemic review of the case series, the incidence of hypercalcemia was found to be 51%, with a usual presentation before 2 months of age [10]. A significant stress during perinatal period increases the risk of subcutaneous fat necrosis. The proposed pathogenesis behind subcutaneous fat necrosis is that the neonatal distress may lead to hypoperfusion and cooling of the subcutaneous fat causing necrosis and granulomatous inflammation [11]. The underlying mechanism can be compared to that of hypercalcemia of sarcoidosis where PTH-independent overproduction of 1, 25-dihydroxy vitamin D occur. This hydroxylation of vitamin D occurs in the macrophages within the granulomas rather than the kidneys [11]. It is recommended to screen children for hypercalcemia, especially those who develops signs and symptoms. Severe Hypercalcemia with serum total calcium > 16mg/dL, ion calcium level >1.mmol/L require immediate medical intervention [12]. In this report, 2 months old female child presented with subcutaneous fat necrosis and failure to thrive. The child had history of neonatal intensive care unit stay for meconium aspiration syndrome. On further evaluation, child was found to have hypercalcemia, anaemia and bilateral nephrocalcinosis. The child was initially treated with loop diuretics but was discontinued as child was having significant weight loss. The child was then successfully managed with oral prednisolone and a good response was seen. The child's serum calcium levels came down to the normal as the subcutaneous fat necrosis resolved. Child was feeding well and gaining weight. Other treatment modalities for hypercalcemia, such as the use of calcitonin and bisphosphonates could not be explored due to limited resources. On regular follow ups, child was monitored for growth and hypercalcemia. Child had two follow ups on 15 days and 1 month post discharge, and had normal serum calcium levels and had no anemia.

4. CONCLUSION

The subcutaneous fat necrosis of newborn is a rare self-limiting clinical entity, but it may present with life-threatening complications like anaemia, thrombocytopenia, hypercalcemia, arrhythmia

and nephrocalcinosis. It is important to consider SCFN as one of the differentials in infants presenting with subcutaneous nodules, anaemia, failure to thrive and thrombocytopenia as it mimics infection. The early identification and timely treatment of complications are important to reduce morbidity and mortality. Hence, infants with perinatal stress or postnatal hypothermia should be followed up closely for the development of subcutaneous fat necrosis during infancy.

CONSENT

An informed written consent was taken from parents before writing the case report.

ETHICAL APPROVAL

Ethical approval not required as per institutional ethics policy for case reports.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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