The Use of Steroids in the Treatment of Severe Hypercalcemia Complication in Newborn with Subcutaneous Fat Necrosis: A Case Report

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ABSTRACT:

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Subcutaneous fat necrosis (SCFN) is usually a benign disorder, which occurs within the six weeks of life in term and post-term infants and is resolved spontaneously. However, some patients may develop a rare complication of hypercalcemia due to SCFN, which requires prompt treatment. The exact pathophysiology of this condition is still unknown. Currently, there is no consensus on the treatment guidelines of hypercalcemia in newborns with SCFN. Other studies have found that intravenous fluid

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hydration, calcium-wasting diuretics, dietary calcium restriction and use of corticosteroids and bisphosphonates are all effective treatments. However, details regarding the dosage and duration of steroid treatment have not been thoroughly investigated. This study reports a case of 1-month-old newborn presented with severe hypercalcemia complication secondary to SCFN.

Our goal is to provide a detailed treatment outline of severe hypercalcemia as a complication of SCFN in similar healthcare facilities with limited resources.

Key words: hypercalcemia, subcutaneous fat necrosis, neonate, infant

Introduction

Subcutaneous fat necrosis (SCFN) is a benign and a self-limiting disorder that primarily affects infants and usually develops within the first week of life and may develop until six weeks after birth. The current pathophysiology of SCFN is still unknown but is found to be associated with both neonatal and maternal risk factors such as maternal preeclampsia, birth trauma, asphyxia and prolonged hypothermia[1]. Although SCFN is resolved spontaneously in most cases, some patients may develop severe hypercalcemia as a potentially fatal complication. Currently, guidelines for steroid treatment of hypercalcemia in patients with SCFN have not been established. According to the literature, conventional treatments involve intravenous fluid hydration, calcium-wasting diuretics, dietary calcium restriction, use of corticosteroids and bisphosphonates[2]. This case report aims to propose a steroid treatment guideline for severe hypercalcemia secondary to SCFN, which may be beneficial as future treatment reference for clinicians, particularly in countries with limited resources.

Case Report

The female infant was delivered full term by cesarean section due to fetal heart rate findings indicative of non-reassuring fetal status. Maternal risk during pregnancy involved poorly controlled gestational diabetes mellitus. The birth weight was 4,470 grams, APGAR scores were 8, 9, and 9 at one, five and ten minutes, respectively. Thirty minutes after birth, the patient developed respiratory distress syndrome. The patient was given surfactant therapy via endotracheal tube, and remained intubated for 10 days.

Dermatologic findings were first recognized at 7 days of age and were described as erythematous induration along the back and extending to both arms and thighs. The lesions were initially diagnosed as cellulitis and were treated with antibiotics for 14 days. She was then transferred to Naresuan University Hospital to receive specialized medical care.

At one month old, the patient was admitted with asymptomatic, indurated, purplish, erythematous and sharply demarcated plaques. The lesions were prominent along the back, shoulders, both upper arms and thighs, and were consistent with lesions of subcutaneous fat necrosis. (Figure 1)

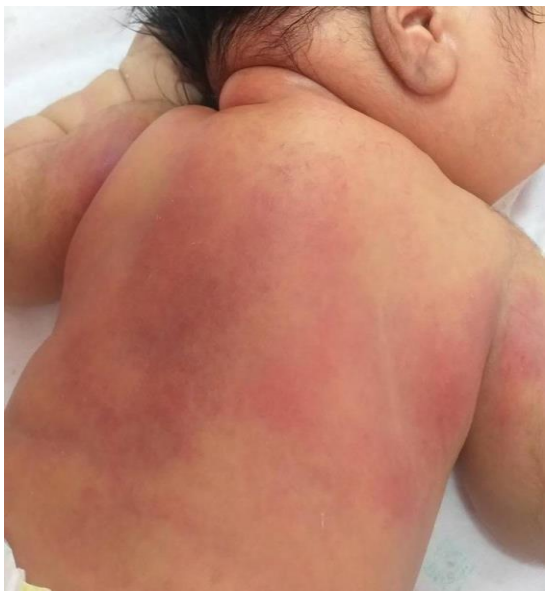

Figure 1 Skin lesion from subcutaneous fat necrosis involving the back, shoulder and upper arm areas before treatment

Laboratory results showed serum calcium level (represented as calcium corrected for albumin level) of 14.1 mg/dL (normal values for age: 8.5-11.0 mg/dL) with normal platelet count, blood glucose and triglyceride. Renal ultrasound revealed bilateral medullary nephrocalcinosis, which may be caused by hypercalcemia. Other causes of hypercalcemia were ruled out due to normal parathyroid hormone, phosphate, alkaline phosphatase, and vitamin D (25-OHD) levels.

Incisional skin and subcutaneous tissue biopsies were performed. Histopathological examination of the subcutaneous tissue revealed fat lobules with fat necrosis and foreign body type, multinucleated, histiocyte giant cells and granulomatous inflammatory infiltration and needle-shaped fat crystals in the cytoplasm of adipocytes. The skin tissue was unremarkable and there was no evidence of granuloma or malignancy. Biopsy result confirms the diagnosis of SCFN in this patient. (Figure 2)

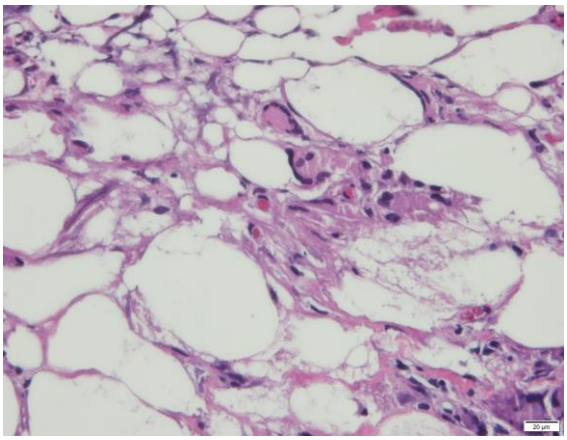

Figure 2 Histopathology of the subcutaneous tissue biopsy from skin at cervical area showing fat necrosis with multinucleated giant cells, granulomatous inflammatory infiltrate and needle-shaped fat crystals in the cytoplasm of adipocytes (H&E stain. X40 magnification)

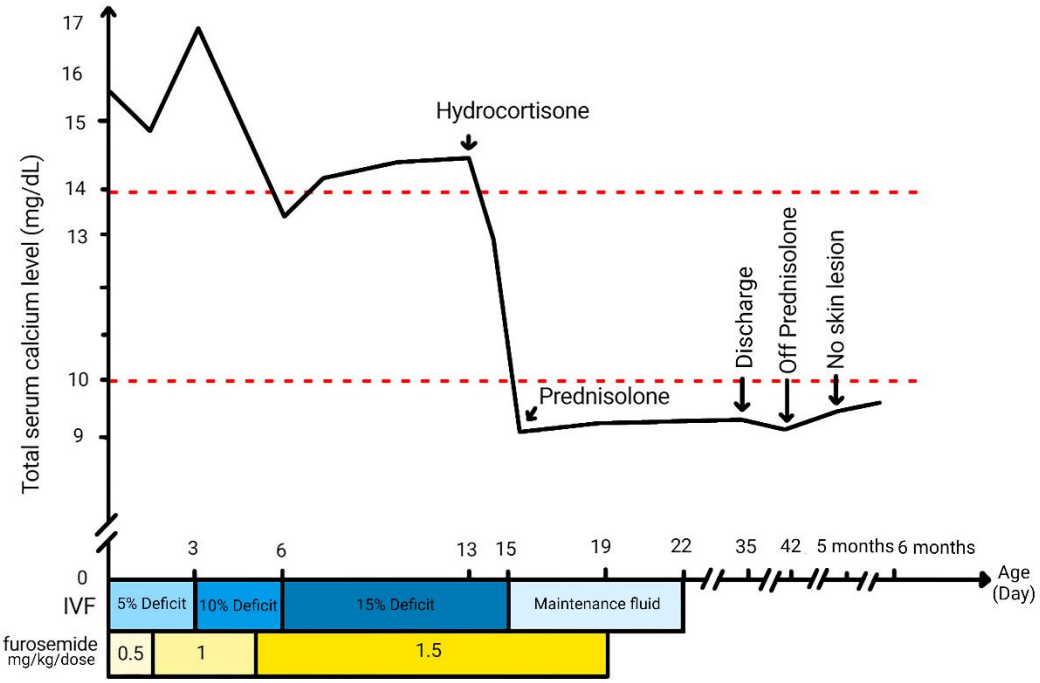

Figure 3 Response of serum calcium level to intravenous fluid (IVF) hydration, furosemide and steroid treatment

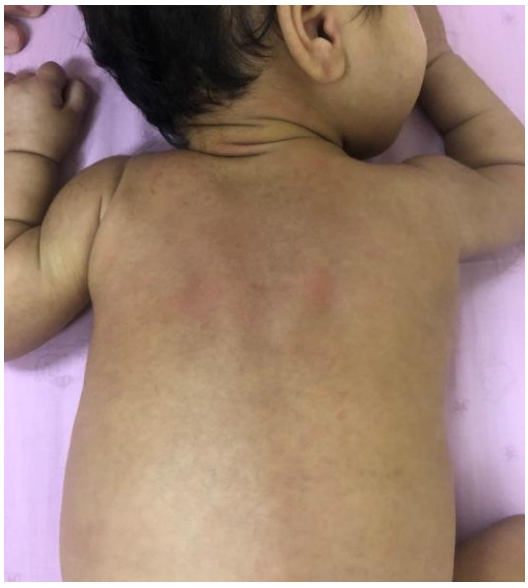

Figure 4 Resolution of subcutaneous fat necrosis at 5 months of age

Patient's serum calcium level was 15.6 mg/dL before treatment. Hypercalcemia was treated with intravenous fluid infusion with volume calculations based on the Holliday-Segar method, starting at maintenance volume plus 5% deficit fluid replacement combined with intravenous furosemide starting at 0.5-1 mg/kg/dose administered every 6 hours on the first 3 days of treatment. She later developed hypokalemia and hypomagnesemia as adverse effects of furosemide. Following intravenous fluid and furosemide therapy, a series of tests revealed that her serum calcium level remained elevated at 16.7 mg/dL (14.9-16.7 mg/dL). Intravenous fluid

was then increased to the patient's maintenance volume plus 10% deficit fluid replacement for 3 days, then a maximum 15% deficit fluid replacement for 7 days along with increased furosemide dose of 1.5 mg/kg/dose every 6 hours on day 5. At the end of the second week of treatment, her serum calcium levels ranged between 13.5-17.0 mg/dL based on repeated tests (Figure 3). Hypercalcemia was still remarkable despite aggressive intravenous fluid and furosemide intervention. She also had polyuria, showed signs of irritability. We decided to add hydrocortisone 5 mg/kg/dose every six hours to help manage the elevated serum calcium levels of the patient. Serum calcium levels decreased from 14.4 to 13.2 mg/dL after one day of intravenous hydrocortisone and from 13.2 to 9.2 mg/dL after two days. Intravenous hydrocortisone regimen was changed to oral prednisolone 1 mg/kg/day twice daily. Intravenous fluid was reduced to maintenance volume and was discontinued after 7 days of prednisolone treatment. Furosemide was then gradually tapered until it was discontinued 6 days after the steroid was started. The patient's serum calcium level stabilized (9.2- 9.5 mg/dL) after 2 days of steroid treatment as revealed in a series of tests. She was then discharged after 5 weeks of hospitalization. One week after discharge, the patient was readmitted due to secondary bacterial pneumonia. As a result, oral prednisolone was stopped abruptly. Despite its abrupt discontinuation, serum calcium level was normal (9.2-9.9 mg/dL). Follow up the calcium serum levels remained within the normal limits at age 4 and 5 months (9.4 and 9.6 mg/dL, respectively). SCFN also improved showing lightening of the skin discoloration and less pronounced induration at nine weeks of age, and resolved completely at 5 months old (Figure 4). This study was approved by the Naresuan University Institutional Review Board number P3-0134/2564. Written informed consent was obtained from the parents of the patient for the publication of this case report and any accompanying images.

Discussion

A tissue biopsy confirming the diagnosis of SCFN in our patient. According to a previous study, hypercalcemia was reported in up to 50% of those with SCFN, with the majority of patients (77%) developing hypercalcemia within 30 days of the onset of the skin lesion[3]. The first-line treatment for hypercalcemia involves (1) enhancing renal calcium excretion with fluid hydration and calcium wasting diuretics, (2) limiting dietary calcium and vitamin D intake, and (3) reducing intestinal calcium absorption and alteration of vitamin D metabolism with corticosteroids, pamidronate. Although the recommended rate of infusion is not specified in

the literature, intravenous fluid hydration is the preferred initial treatment for hypercalcemia. Furosemide is a commonly used diuretic for the treatment of hypercalcemia, with doses ranging from 1-1.5 mg/kg/dose every 6-12 hours[4-6].

In this study, maximal intravenous fluid deficit replacement of 15% along with maximal intravenous furosemide 1.5 mg/kg/dose was found to be ineffective in reducing serum calcium levels in a patient with severe hypercalcemia who later developed hypokalemia and hypomagnesemia due to furosemide side effects. Patient's urine output showed 5-8 mL/kg/hour. This confirmed that the patient received adequate hydration, with sufficient urine output needed for calcium excretion. Therefore, it was decided that the patient should begin a second-line treatment involving corticosteroids, or pamidronate. Since pamidronate was unavailable in our hospital, corticosteroid therapy was initiated in this patient, with a preliminary regimen of intravenous hydrocortisone 5 mg/kg/dose every 6 hours. Following a significant decrease in serum calcium level from 14.4 (before steroid administration) to 9.2 mg/dL (after two days of hydrocortisone), the patient was then given 1 mg/kg/day oral prednisolone. Serum calcium level normalized within 5 days after steroid initiation and the same dose of prednisolone was maintained for 21 days. Steroids have demonstrated to be effective in the treatment of severe hypercalcemia caused by SCFN in this case.

Conclusion

In hospitals where pamidronate is unavailable or clinicians have limited experience with the use of these drugs, prednisolone 1 mg/kg/day for a total course of 3 weeks is a drug of choice for the treatment of severe hypercalcemia due to SCFN in newborns. Therefore, earlier administration of steroid therapies may reduce length of hospital stay. However, close monitoring should be carried out in the event of a potential complication, such as secondary bacterial infection.

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