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Subcutaneous Fat Necrosis with Hypercalcemia

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Subcutaneous fat necrosis of the newborn (SCFN) is an uncommon condition and may be complicated by hypercalcemia. A 28-day-old neonate, presenting with SCFN, hypercalcemia and nephrocalcinosis was managed with intravenous saline followed by furosemide, oral prednisolone, potassium citrate and etidronate.

Key words: *Hypercalcemia, Subcutaneous fat necrosis, Nephrocalcinosis*

Hypercalcemia in children is relatively less common when compared to hypocalcemia. Causes of hypercalcemia in infants include causes like hyperparathyroidism and vitamin D intoxication. Identification of the cause is essential for the management of

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hypercalcemia in children. Subcutaneous fat necrosis (SCFN) is a rare cause of hypercalcemia in newborns and infants. The duration of follow-up of these children and management of hypercalcemia with newer drugs are highly debatable. We report a neonate who presented with SCFN and persistent hypercalcemia.

Case report

A 28-day-old neonate, born to a primigravida mother by emergency cesarean section for fetal distress and exclusively breast-fed, was brought with swellings over right elbow, thighs, cheeks and arms of one week duration. On examination, the neonate was pink, active, normothermic with normal vital signs and had reddish purple nodular swelling over arms, thighs and cheeks. The swellings were non-tender, non-fluctuant and firm; the joints were normal. The hemoglobin level was 15 g/dL, leukocyte count 12100/cumm with 40% neutrophils, 43% lymphocytes and 15% eosinophils and platelet count of 250,000/cumm. The blood culture was sterile. Blood levels of urea 38 mg/dL, creatinine 0.7 mg/dL, sodium 136 mEq/L, potassium 3.7 mEq/L, bicarbonate 20 mEq/L, calcium 17.8 mg/dL, phosphorus 7.1 mg/dL, magnesium 2.0 mg/dL, cholesterol 100 mg/dL, total protein 6.9 g/dL, albumin 3.9 g/dL and sugar 90 mg/dL were noted. Urinalysis showed the following: pH 6.5, specific gravity 1.010, albumin 1+ and no deposits. Urine culture was sterile and the random urine sample showed calcium level of 24.4 mg/dL

and creatinine 20 mg/dL with a ratio of 1.2 (<0.4). Abdominal ultrasonogram showed medullary nephrocalcinosis; both kidneys measured 4.9 cm. A diagnosis of SCFN with hypercalcemia and nephrocalcinosis was made. Further evaluation showed elevated serum vitamin D level of 68 ng/mL (normal 9.0-37.6) and normal parathormone 42 pg/mL (normal 14-72).

The patient was treated with intravenous (IV) saline followed by IV furosemide 1 mg/kg/dose every 12 hours. The calcium level reduced to 13.6 mg/dL on the second day. Therapy was started with oral prednisolone at a dose of 2 mg/kg/day in 3 divided doses and oral sodium bicarbonate solution. The patient was discharged 10 days later with serum calcium level of 10.2 mg/dL and creatinine 0.6 mg/dL, on treatment with oral furosemide 4 mg/day, prednisolone 2 mg three times a day and potassium citrate 2.5 mL three times a day. On review, 5 days later the serum calcium level was 10.9 mg/dL and ultrasound showed worsening of nephrocalcinosis. Treatment with furosemide was stopped. The skin lesions disappeared by the third month. Prednisolone was stopped at the sixth month of follow-up when serum calcium level was 10.5 mg/dL. The serum calcium was 11.1 mg/dL at 9 months and 11.6 mg/dL at 15 months. Therapy was begun with oral etidronate at a dose of 125 mg twice a day and oral potassium citrate was continued at a dose of 5 mL three times a day. The serum calcium level dropped down to 9.1 mg/dL, with corresponding random urine Ca/Cr ratio of 0.3 and remained so for the next 3 months. Oral etidronate was stopped at the request of parents after 9 months but oral potassium citrate was continued. Two months later the serum calcium level was 11.0 mg/dL, creatinine 0.6 mg/dL and urine Ca/Cr ratio 1.0; medullary nephrocalcinosis had increased. The patient is

being treated with oral potassium citrate solution at a dose of 7.5 mL three times a day.

Discussion

The causes of hypercalcemia in an infant are varied and severe hypercalcemia is a medical emergency associated with reduction in renal function. Nephrocalcinosis may occur following persistent hypercalcemia and results in long-term renal morbidity and mortality. Common causes of hypercalcemia include primary hyperparathyroidism, William's syndrome, idiopathic infantile hypercalcemia, malignancy and toxicity with drugs like thiazides and vitamin A. Rare causes include SCFN, granulomatous disorders, hyper-vitaminosis D and limb fracture with immobilization. In our child with the typical skin changes and hypercalcemia with hypercalciuria and nephrocalcinosis, a diagnosis of SCFN with hypercalcemia and nephrocalcinosis was made.

SCFN is seen in the first week of life, commonly affecting healthy full term babies following obstetric trauma, meconium aspiration, hypoxemia and hypothermia. The characteristic features include painful, firm, indurated, erythematous nodule or plaques, over buttocks, trunk, arms and cheeks. The pathogenesis of SCFN is unknown. One popular theory is that injury to the immature fat induced by cold stress causes necrosis of the skin and granulomatous infiltration(1). Studies have documented increased saturated fatty acids within the subcutaneous tissue due to defective neonatal fat metabolism, exacerbated by neonatal stress as well as fat necrosis caused by local trauma during delivery(2). Crystallization of neonatal fat, composed of saturated fatty acids with a relatively high melting point, occurs following hypothermia(3). Ulceration and scar formation are not common. Hypercalcemia

seen in SCFN may result in significant morbidity. The exact incidence of hypercalcemia complicating SCFN is not known(4,5). Various causes have been proposed for including osteoclast activation and increased production of 1,25 dihydroxy-vitamin D3 by macrophages resulting in increased bone turnover following increased prostaglandinE activity(6,7). Hypercalcemia is usually noticed 4-6 weeks after the documentation of skin lesions and may cause metastatic calcifications in the heart, liver and inferior vena cava(8). Nephrocalcinosis and nephrolithiasis secondary to hypercalciuria occur within 4-6 months of onset of hypercalcemia. Our child presented at 4 weeks of age with hypercalcemia, hypercalciuria and nephrocalcinosis, probably the skin lesions were not noticed earlier. Thrombocytopenia is another important complication due to sequestration within the subcutaneous tissue and elevated levels of prostaglandin E. Metastatic calcifications of the heart, liver and inferior vena cava and thrombocytopenia were not seen in the present subject.

Children with SCFN commonly present only with skin lesions with or without any other symptoms. Rarely, do they present with symptoms of hypercalcemia such as irritability, weight loss, apathy, hypotonia and dehydration. Diagnosis is essentially clinical and a skin biopsy is not needed for its diagnosis. If done, it will show fat necrosis and granulomatous infiltration with lymphocytes, macrophages, giant cells and calcium crystals with or without fibrosis.

SCFN is a self-limiting condition and needs no treatment except for regular monitoring of serum calcium levels. When it is associated with hypercalcemia, treatment involves reduction of calcium and vitamin D in the diet, adequate hydration with saline, followed by IV furosemide therapy. Oral

prednisolone may be used in subjects refractory to the above treatment(8). In our patient skin lesions disappeared within 3 months and calcium levels were well controlled with oral steroids low calcium and low vitamin D containing diet, hydration and furosemide.

Subsequent increase of serum calcium was managed with bisphosphonate (etidronate), which prevents calcium resorption from the bone. Within 2 months of stopping the drug, the calcium levels had gone up with concomitant increase in urinary calcium levels and worsening of nephrocalcinosis. The need for long-term therapy with etidronate and the problem of persistent hypercalcemia are obvious. SCFN although not a very common condition, may be complicated by hypercalcemia, which might persist long after disappearance of the skin lesions as seen in our child. These patients need long-term monitoring of their serum calcium levels and aggressive and appropriate treatment of hypercalcemia in order to prevent metastatic calcification and nephrocalcinosis.

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