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Case Report

Biochemistry Section

A Rare Case Report of a 8-weeks-old Infant with Hypercalcaemia and Subcutaneous Fat Necrosis

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ABSTRACT

Subcutaneous Fat Necrosis (SCFN) is an uncommon transient panniculitis more commonly seen in first week of newborn life. Hypercalcaemia is tell-tale of this disorder, resulting in consequences like metabolic derangements, polyuria, seizures, vomiting, nephrocalcinosis and cardiovascular disturbances contributing to morbidity and mortality of SCFN. This is a case report of an eight-week-old male infant who presented with hypercalcaemia and multiple nodules all over the body. Histopathology is the gold standard method which helps in diagnosis and evaluation of a patient with SCFN. In this case, histopathological report revealed focal areas of fat necrosis in the fat lobules along with lobular panniculitis with infiltration of lymphocytes, histocytes, fibroblasts and multinucleated giant cells. Its granules were suggestive of SCFN. The diagnosis of SCFN was confirmed by skin biopsy and additionally supported by hypercalcaemia. This study highlights the importance of performing detailed skin examination for the evaluation of patients until the resolution of hypercalcaemia and skin lesions. In this case, hypercalcaemia resolved by the end of 12th week of life. Though, it is a benign and self-limiting condition, educating and creating awareness among the parents is of utmost importance and to prevent renal and cardiac complications associated with hypercalcaemia. Rehydration therapy, calcium and Vitamin D restricted diet are the modes of treatment for treating this condition.

Keywords: Hypertriglyceridemia, Lobular panniculitis, Neonatal sepsis, Rehydration, Thrombocytopenia

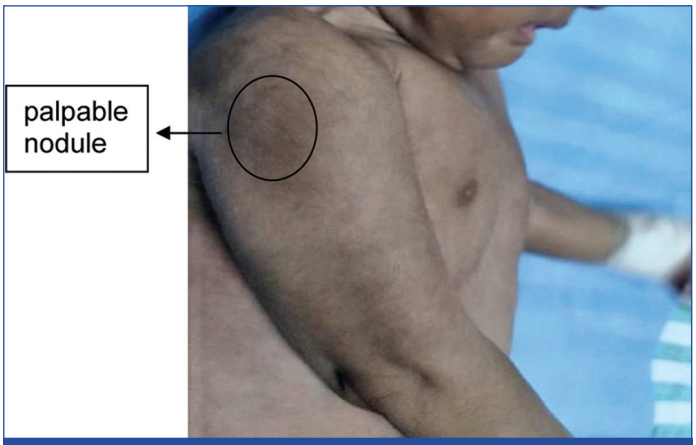
CASE REPORT

An eight-week-old male infant referred from outside clinic (suspecting neonatal sepsis for further management) was admitted to the paediatric unit. The infant presented with multiple nodules since 2nd week of life on the nape of the neck which increased all over the body in size and number. The infant had history of fever, failure to thrive and refusal of feeds since 7th week of life. Birth history revealed that he was delivered by emergency caesarean section due to foetal distress and low birth weight (1520 grams) at 37th week of gestation. Soon after birth, the baby experienced severe peripheral asphyxia secondary to meconium aspiration which required intubation and suction. Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) Score [1] was 2 and 8 at 1 and 5 minute, respectively. Positive pressure ventilation and positive end expiratory pressure were administered under intensive care for a week. The newborn did not receive body cooling therapeutic hypothermia. Mother noticed nodules over the nape of the neck during second week of life, which gradually increased in size and number, spreading all over the body in a span of four weeks, which gradually decreased over the next two weeks. There was no family history of hypertriglyceridemia.

On the day of admission the infant was febrile: temperature-99.5°F (Fahrenheit), pulse-130/minute, respiratory rate-46/minute, cardiovascular, respiratory and central nervous system examination normal, per abdomen-soft, liver palpable. Multiple well defined palpable nodules measuring about 1×1 cm to 3×3 cm were present predominantly over the upper back, cheeks, upper limbs [Table/Fig-1] and lower limbs. Lesions were non tender and not attached to the deeper structures. There was no local rise of temperature. Differential diagnoses were sepsis, SCFN or sclerema neonatorum. The clinical evaluation and skin biopsy confirmed the diagnosis of SCFN and was additionally supported by hypercalcaemia [Table/Fig-2].

Reference ranges of above parameters were extracted from Beckman Coulter kit insert (information sheet) [2,3].

The baby was admitted for 12 days. During the stay in the hospital all biochemical and haematological investigations were repeated to



[Table/Fig-1]: Well-defined palpable nodule present on right arm.

Investigations	Findings	Reference range
Random blood sugar (mg/dL)	57	80-140
Blood urea (mg/dL)	49	10.8-38.4
Serum creatinine (mg/dL)	0.5	0.15-0.37
Serum uric acid (mg/dL)	11	3.6-7.7
Serum total bilirubin (mg/dL)	0.5	Up to 1.2
Serum direct bilirubin (mg/dL)	0.1	Up to 0.4
Aspartate transaminase (U/L)	88	15-60
Alanine transaminase (U/L)	08	13-45
Serum alkaline phosphatase (U/L)	301	82-383
Serum total protein (gm/dL)	7.0	5.7-8.0
Serum albumin (gm/dL)	4.3	3.5-5.5
Serum globulin (gm/dL)	2.7	1.3-3.3
Total cholesterol (mg/dL)	259*	114-203
HDL cholesterol (mg/dL)	24	35-80
LDL cholesterol (mg/dL)	103	<135
Triglycerides (mg/dL)*	1969*	29-99

Serum calcium (mg/dL)*	17.5*	9-11
Serum phosphorus (mg/dL)	3.8	2.7-4.5
Serum magnesium (mg/dL)	2.7	1.8-2.6
Serum sodium (meq/L)	138	138-146
Serum potassium (meq/L)	3.9	3.5-5.5
Serum chloride (meq/L)	106	98-109
pH	7.44	7.35-7.45
Serum amylase (U/L)	0.8	25-86
Serum lipase (U/L)	94	Up to 60
Serum lactate dehydrogenase (lU/L)	448	110-295
CK MB (IU/L)	21.2	0-24
CK NAC (IU/L)	17	<175
Haemoglobin (gm%)	14.0	13-17
Total red blood cell count (mill/cumm)	4.28	4.5-5.5
Total white blood cell count (cells/cumm)	22500*	4000-11000
Platelet count (Lacs/cumm)	5.52*	1.5-4.0
Erythrocyte sedimentation rate at the end of one hour (mm)	22	0-10
Prothrombin time (second)	14.3	8-12
Partial thromboplastin time (second)	26.2	26-38
C Reactive protein (mg/L)	Negative	<6.0
Urine routine and microscopy	Motile bacteria present	
Blood culture	No growth	No growth

[Table/Fig-2]: Diagnostic evaluation on the day of admission.
*Indicates high value; HDL: High density lipoprotein; LDL: Low density lipoprotein; CK MB: Creatine kinase-MB; CK NAC: Creatine kinase N-acetyl-cystein

monitor the progress of the baby. All parameters remained normal except for few parameters which are mentioned in the [Table/Fig-3].

Histopathology report: In the upper right arm, the dermis showed normal adnexal structures. Subcutaneous fat showed focal areas of fat necrosis in the fat lobules. Lobular panniculitis with infiltration of lymphocytes, histocytes, fibroblasts and multinucleated giant cells [Table/Fig-4]. Its granules suggestive of SCFN. The diagnosis was SCFN confirmed by skin biopsy of nodule and hypercalcaemia (20 mg/dL). Blood culture and clinical stability of the infant ruled out the sepsis.

Ultrasound of abdomen and radiograph of chest reports were normal. On hospitalisation, the infant (weight-3.28 kg) was treated for urinary tract infection with appropriate antibiotics injections intravenously every 12th hourly (ceftriaxone 160 mg for seven days from day one and amikacin 25 mg for three days from day third (*Escherichia coli* susceptible to amikacin). Dehydration was corrected with intravenous fluids {DNS (Dextrose and Sodium Chloride) 6 mL per hour}. The infant was treated for fever by anamol 80 mg suppository 3/4th per rectal and dolo drops 0.4 mL (100 mg/mL) as and when required. The infant was initially started with paladai feeds and mother was encouraged to breast feed her baby. Cutaneous nodular lesions continued to regress and the infant was physically stable at the time of discharge. The mother was advised to exclusively breast feed her baby till six months and not to start complimentary feeds like ragi porridge and soup of green leafy vegetables. The serum calcium level was 20 mg/dL on the day of discharge. The baby was followed-up to six weeks periodically from day of discharge. Serum calcium level reduced to normal (10.5 mg/dL) by the end of 12th week of life without any complications.

DISCUSSION

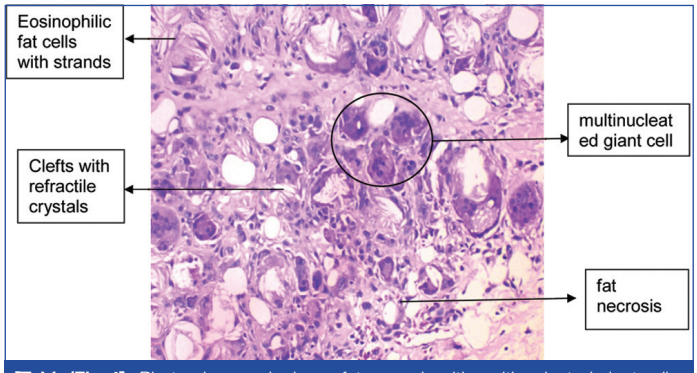
The SCFN is an uncommon, self-resolving panniculitis commonly seen in full term or post term newborns in the first few weeks of life [4]. The aetiology of the disease is unclear. It usually presents with nodules or plaques on skin of arms, cheeks, upper back, and thighs. In spite of a favourable prognosis, it may also be complicated with metabolic and haematological alterations like hypercalcaemia, hypertriglyceridemia, hypoglycaemia or thrombocytopenia [4-6] which should be managed by timely intervention [6-8].

The SCFN is typically seen in maternal or neonatal stress, including maternal diabetes, cord prolapse, meconium aspiration, perinatal asphyxia, neonatal sepsis or therapeutic hypothermia [9-11]. The subcutaneous lesions are firm, erythematous or purplish nodules present on back, shoulders and upper limbs and thighs [4,7]. The pathogenesis of SCFN remains unclear. It has been postulated that the normal blood supply to the neonatal fat tissue is affected during neonatal distress, which results in hypoxia and hypothermia leading to inflammation and necrosis in fat tissue [9,12,13]. The newborn fat consists of more amount of saturated fatty acids compared to adult fat, because of its higher melting point associated with the tendency for solidification and crystallisation [5,9]. The histopathology contributes to diagnosis with characteristic lobular panniculitis, mixed inflammatory cell infiltrate and radially arranged crystals [4,6,12]. The skin lesion does not require any treatment as the disease is self-resolving [7,14,15].

Hypercalcaemia (Serum Ca >10.5 mg/dL) [16] was diagnosed in the present case (Serum Ca-20 mg/dL). The pathogenesis

Investigations \ Day of admission	1st day	2nd day	3rd day	6th day	12th day
Total cholesterol (mg/dL)	259*	-	-	-	156
Triglycerides (mg/dL)*	1969*	-	-	-	450
Serum calcium (mg/dL)*	17.5*	-	17.5	-	20.0
Total white blood cell count (cells/cumm)	22500*	-	16220	19800	-
Platelet count (Lacs/cumm)	5.52*		4.20	7.69	-
C- Reactive protein (mg/dL)	Negative		Positive	Positive	Negative
Urine culture		Positive; *Escherichia coli* (>10^5 CFU/mL)*		-	-
Blood culture	No growth	No growth after 5 days of intubation			
Cutaneous punch biopsy of skin (right upper arm)				Histopathology report- subcutaneous fat necrosis	

[Table/Fig-3]: Investigations done.
*Indicates high value, CFU: Colony forming unit



[Table/Fig-4]: Photomicrograph shows fat necrosis with multinucleated giant cell, fat cells with eosinophilic strands and granules, clefts containing refractile crystals. (40X H&E).

for hypercalcaemia is not clear [17] and research has shown many mechanisms which include: a) increased prostaglandin activity leading to osteoclast activation; b) calcium released from necrotic fat cells; c) increased production of activated vitamin D by macrophages which causes release of calcium from bone and increased absorption of calcium from the gut [18-20]. Farooque A et al., demonstrated the presence of extrarenal 1α-hydroxylase in immune cells associated with SCFN [21]. Hypercalcaemia can lead to gastrointestinal, neurological and cardiac life-threatening complications. Hypercalcaemia may reduce renal concentrating capacity presenting with polyuria and dehydration leading to kidney failure and metastatic calcifications [4,7,12,15]. It is vital to monitor the patient's serum calcium levels for at least six months after the diagnosis [7,12]. For this case, infant was followed-up for a period of three months until serum calcium returned to normal (10.5 mg/dL). Hypercalcaemia treatment includes aggressive hydration, drugs like furosemide and prednisolone to decrease serum calcium and low vitamin D and calcium diet [14,22]. In 76% of cases resolution of hypercalcaemia seen within 4 weeks of detection [23].

In this case, the infant's serum was turbid at eighth week. The observed hypertriglyceridemia may be due to the resolution of nodules and mobilisation of lipid from necrotic adipose tissue [4,12,24]. Thrombocytopenia is known to be associated with SCFN due to sequestration of platelets in subcutaneous tissue [12,18]. In this case, thrombocytosis was present which was similar to cases observed by Lorenzo C et al., and Sahni M et al., [10,11]. It may be attributed to the reactive inflammatory response of SCFN [10,11]. The present case showed multiple features of SCFN which is supported by a skin biopsy in the clinical diagnosis. Serum parathyroid hormone and vitamin D levels was not measured as the patient attenders could not afford the costs which would have further strengthened our laboratory diagnosis.

CONCLUSION(S)

The SCFN is a rare self-limiting condition. Early diagnosis and appropriate intervention are required to prevent the complication that arises from SCFN. Hypercalcaemia is a potentially life-threatening complication that occurs in this subset of patients. Periodic monitoring until the resolution of lesions and hypercalcaemia is required. This helps in reducing morbidity and mortality for SCFN in the newborn. Educating and reassuring the parents regarding its self-limiting nature is also an important part of the treatment protocol. This case highlights the importance of early recognition, initial management. This case presentation can be used as reference for SCFN cases at tertiary care hospital.

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