SUBCUTANEOUS FAT NECROSIS AND HYPERCALCAEMIA FOLLOWING THERAPEUTIC HYPOTHERMIA IN AN INFANT WITH BIRTH ASPHYXIA

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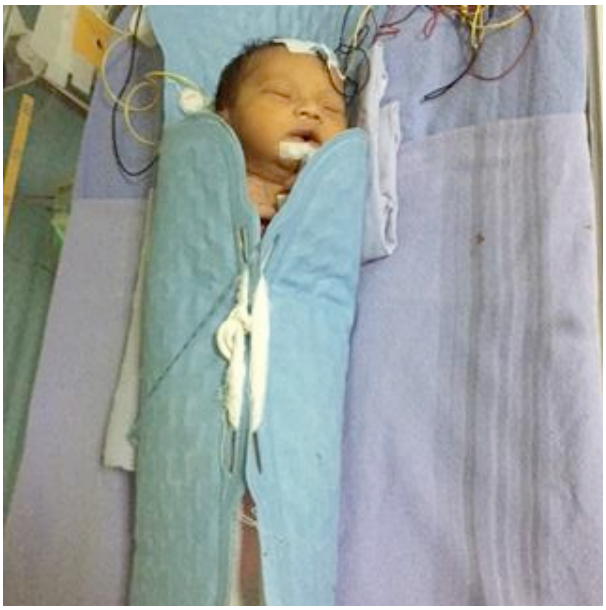
Introduction

Subcutaneous fat necrosis is a recognised complication of hypothermia. There appears to be a resurgence in this condition when therapeutic hypothermia emerges as a standard of care for asphyxiated infants. The TOBY trial reported an incidence of 0.1% for 1239 infants cooled.

We report a case of subcutaneous fat necrosis following therapeutic hypothermia which occurred in a term female infant with birth weight of 3.2kg who was born via emergency caesarean section because of abruptio placentae on 15th March 2016@1331H. Therapeutic hypothermia was started at 2 hours of life postnatally because of hypoxic ischaemic encephalopathy Sarnat Stage II. A cooling blanket (Tecotherm Neo®, model TSMed 200N, Inspiration Healthcare, Albourne, UK) was used for total body hypothermia over 72 hours therapy. Her body temperature was closely monitored via oesophageal thermometer maintaining temperature between 33.0 -34.0^{0}C.

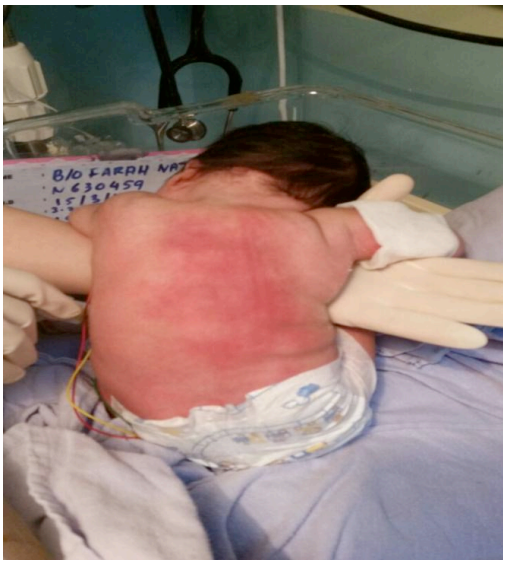
Figure 1. Cooling blanket (Tecotherm Neo®, model TSMed 200N, Inspiration Healthcare, Albourne, UK)



No other complications were noted until postnatal day 6 when examination showed red patches of indurated skin over almost her entire back, buttock and right arm. It was exquisitely tender, requiring gentle handling during cares, prone positioning to alleviate pressure from the back and regular analgesic. She was discharged well at day 13 of life with regular analgesic and breastfeeding.

Figure 2 (i, ii, iii). Day 6 of life Serum calcium: 2.45mmol/L(ionized 1.34)

i)



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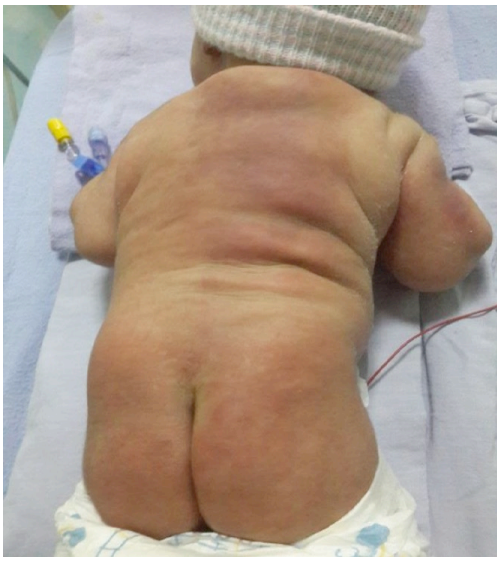

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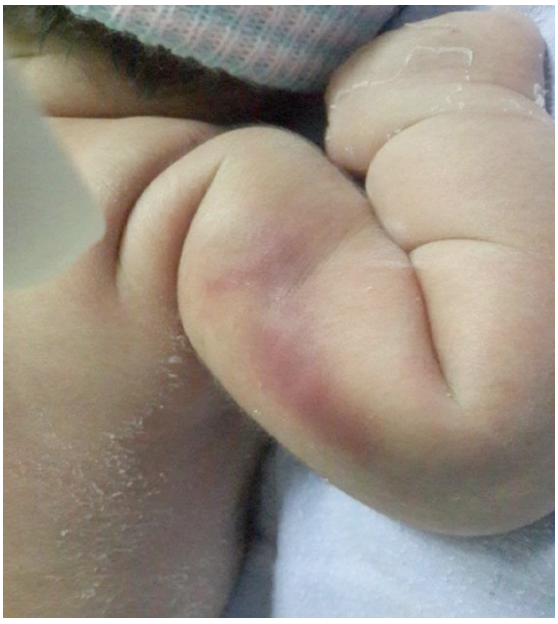
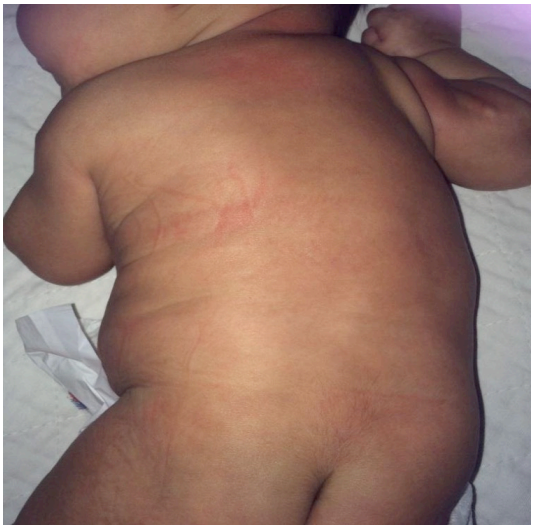


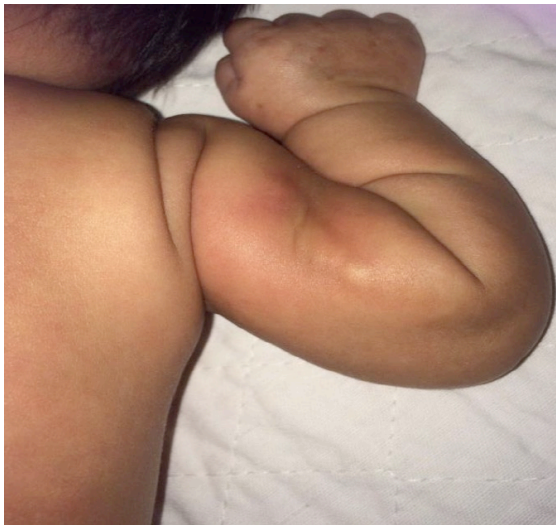
Upon review on day 29 of life at clinic, noted lumpy subcutaneous nodule over posterior aspect trunk which was non tender and asymptomatic hypercalcaemia of 3.26 mmol/L.

Figure 3 (i, ii). Day 29 of life Serum calcium: 3.26mmol/L

i)



ii)



She was admitted for intravenous hydration (full maintenance fluids with normal saline) in addition to breastfeeding on demand for calciuresis, and subsequently required additional frusemide with prednisolone because of persistent hypercalcaemia.

IVD full maintenance with breastfeeding on demand
Regular paracetamol

IVD ½ maintenance and oral frusemide 0.5mg/kg/dose BD

Oral frusemide 0.5mg/kg/dose BD with prednisolone 0.5mg/kg daily

Off both prednisolone and frusemide

Serum	13/4/ 2016	15/4/ 2016	16/4/ 2016	17/4/ 2016	18/4/ 2016	19/04/ 2016	22/4/ 2016	4/5/ 2016	26/5/ 2016 (9 weeks old)	21/6/ 2016 (follow up)
Calcium	3.08	3.06	2.94	2.65	2.55	2.86	2.95	2.52	2.68	2.57
Corrected Calcium	3.28	3.3	3.18	2.93	2.81	3.03	3.01	2.68	2.73	2.63
Phosphate	1.83									

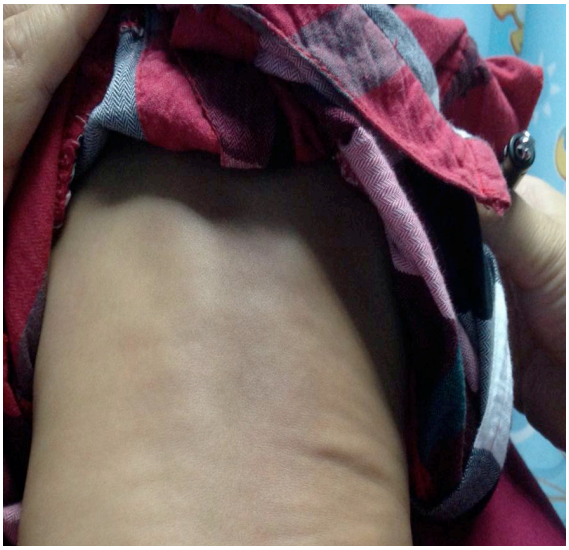
IVD full maintenance and started on IV frusemide 0.5mg/kg/dose BD

Started on oral prednisolone 0.5mg/kg daily
Off IVD and frusemide

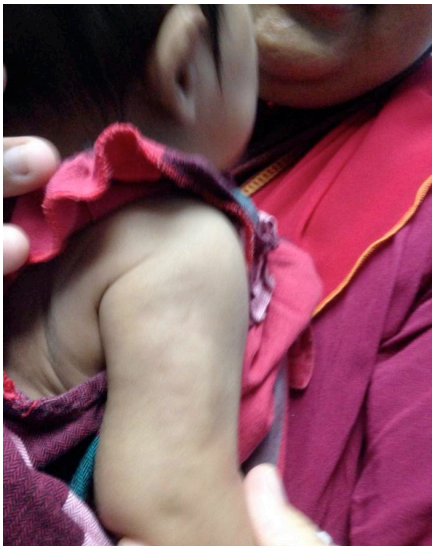
Discharged home with prednisolone and frusemide

Figure 4 (i, ii). 9 weeks old Serum calcium: 2.68mmol/L

i)



ii)



Serum calcium decreased to normal over 20 days and the subcutaneous nodules regressed entirely by 9 weeks of life. Renal function was normal and ultrasound of the kidneys did not show nephrocalcinosis.

Discussions

History

- Subcutaneous fat necrosis is a self-limiting, non-infectious panniculitis (inflammatory disorder of subcutaneous)adipocytes that occurs in term infants who experience significant distress in the 1st weeks of life [1].

Risk

- Multifactorial causes predisposes for development of subcutaneous fat necrosis i.e. traumatic delivery, perinatal asphyxia, local ischemia, hypothermia, maternal diabetes mellitus, maternal cocaine use and maternal pre eclampsia [2].

Pathology

- Subcutaneous (Brown) fat in infant contains high concentration of saturated fatty acids (stearic and palmitic acids) with a high melting point. Hence more susceptible to solidification and crystallizations after hypothermic injury [1].
- Subcutaneous fat necrosis may cause local skin ulceration, blister formation, abscess and later epidermal atrophy.
- Histologically, there will be lobular panniculitis, extensive fat necrosis, dystrophic calcification, radial eosinophilic crystals, infiltrates of lymphocytes, histiocytes and multinucleated giant cells [4].

There are various hypothesis were postulated for pathogenesis of hypercalcaemia following subcutaneous fat necrosis [4]:

- Necrosis in the damaged immature fat tissue caused by granulomatous cell and macrophages infiltration. Macrophage will later produce 1,25-dihydroxyvitamin D3 [1,25(OH)2D3] which will increased intestinal absorption of Ca2+.
- Release of calcium from necrotic fat cells.
- Increased osteoclastic activity due to elevated PTH and effect of local prostaglandins (PgE2)

Clinical course and treatment

- Common complications following subcutaneous fat necrosis are hypoglycaemia, anaemia, thrombocytopaenia, hypertriglyceridaemia and the hypercalcaemia that may lead to nephrocalcinosis, liver and cardiac calcification and arrythymia [4].

- Neonatal hypercalcaemia, defined as total calcium >2.70 mmol/L or ionised calcium >1.35 mmol/L, is rare but a carries risk of nephrocalcinosis. Typically, hypercalcaemic neonates are asymptomatic, but calcium levels (>3.2 mmol/L) can cause irritability, poor feeding, vomiting, polyuria, hypertension and seizures [4].

- Mainstay of treatment of hypercalacemia are hyperhydration, loop diuretic i.e. frusemide and low calcium milk formula [4].

- Prednisolone can be used if persistent hypercalcaemia despite hyperhydration and frusemide. Steroid interferes with the metabolism of vitamin D to its active form 1,25-hydroxyvitamin D and inhibits the production of 1,25-dihydroxyvitamin D by the macrophages involved in the inflammatory process [4]. In case of resistant hypercalcaemia, biphosphonate, eg. Palmidronate may be useful [4].

- In one of the case series involving 7 neonates who had severe hypercalacemia following subcutaneous fat necrosis published in 2014 by Daniel et al, the average age of presentation of hypercalcaemia was 3 weeks of life, and all of them were treated with intravenous hydration, furosemide (1–1.5 mg/kg/dose every 6–12 h) for a median of 5 days (range 3–18d) and glucocorticoids (prednisolone or methylprednisolone 1–2 mg/kg divided once or twice daily), median of 56 days (range 19–155d). Low-calcium formula was given to five infants and continued for 1–5 months. Pamidronate was given to one patient who failed to achieve normocalcaemia after 15 days of hydration, furosemide and glucocorticoids.Serum calcium normalised within 12 h of pamidronate infusion, and normocalcaemia was subsequently maintained with low-calcium formula alone. Two out of seven patients required readmission for recurrent hypercalcaemia [5].

Conclusions

A careful examination for subcutaneous fat necrosis potentially complicated by hypercalcaemia should be screened for infants who received total body cooling therapy.

References

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