Case Report

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Neonatal Severe Hyperparathyroidism: A Case Report

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Abstract

Background: Neonatal severe hyperparathyroidism is an extremely rare condition that presents in the first few months of life. Recognition at the early stage followed by prompt surgical intervention are of vital importance for survival. Hypotonia, respiratory distress, lethargy and delay in growth and development occur in association with the elevated serum parathormone levels and hypercalcemia. Definitive therapy involves total parathyroidectomy.

Case Description: We are presenting a case with Neonatal severe hyperparathyroidism, who underwent total parathyroidectomy. The patient had been followed up with medical therapy until. Parathormone levels rapidly declined following total parathyroidectomy and the patient was discharged with full recovery.

Literature Review: Sestamibi scintigraphy might fail to show an ectopic parathyroid gland. In such conditions, on table confirmation of parathyroid glands by frozen section and Intra-operative parathormone monitoring is vital at this point. Persistently elevated parathormone levels might suggest a remnant parathyroid tissue at the surgical site or an ectopic parathyroid gland that should be excised.

Clinical Relavance: Neonatal severe hyperparathyroidism is a life-threatening disease. In the present case surgery performed at the early is life-saving due to the failure of medical therapy to control the disease.

Keywords: Severe Hyperparathyroidism; Hypercalcemia; Cinacalcet; Sestamibi scintigraphy; CaSR Gene**.**

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INTRODUCTION

Neonatal severe hyperparathyroidism is an extremely rare condition that manifests with severe hypercalcemia and metabolic bone disease within the first few weeks in the postnatal period. The calcium set point is elevated which lead to parathormone (PTH) secretion as well as renal absorption of calcium. Therefore the child affected with this disorder have elevated PTH, severe

hypercalcemia and wide range of manifestations such as delay in growth and development, hypotonia, dehydration, gastrointestinal dysmotility, polyuria, poor feeding, and respiratory distress. When this disorder is controlled with longterm medical treatment can have an imminent crisis. Emergency surgery must be performed if medical therapy fails to stabilize the clinical condition of the patient.[1] The current report presents an infant boy with neonatal hyperparathyroidism and discusses the approach to diagnosis and treatment. The consent was obtained from the father of the patient for publication of this case report.

CASE PRESENTATION

A 3-month-old male infant was admitted with complaints of failure to thrive, decreased activity, weight loss, loose stools and weak cry. Child was 2nd born, full-term to a 38 year-old mother with a birth weight of 3.4kg. Child was lethargic, dull, weight on admission was 2.4kg. He had severe respiratory distress and subcostal retractions. Child was in intensive care unit and on mechanical ventilation. S, Calcium - 28.6mg/dl, S. phosphate - 1.4mg/dl, S. parathormone - 269.4 pg/ml. Other blood investigations were normal. USG neck and abdomen were normal.

The whole body x-ray revealed osteopenia. Tc99 sestamibi scan revealed no evidence of parathyroid adenoma or hyperplasia. Child was treated with saline diuresis, cinacalcet and zoledronic acid for 15 days. Calcium level fell to 20mg/dl beyond which there was no response. Child was planned for surgery after resuscitaton. Total parathyroidectomy + transcervical thymectomy + b/l carotid exploration was performed. All 4 parathyroid glands were excised and confirmed by frozen section. No ectopic or supernumerary parathyroids were found. Intra-operative parathormone monitoring is not available in our hospital. No intra operative complications were encountered. Post-operative period was uneventful. Child was started on calcium and calcitriol and discharged in good general condition. Genetic analysis showed homozygous loss of function mutation of CaSR gene mutation. Postoperative weight was 4 kg, S. calcium – 10.5 mg/dl, S. phosphate – 4.6mg/dl, S. parathormone – 20 pg/ml. Child is on continuous follow up.

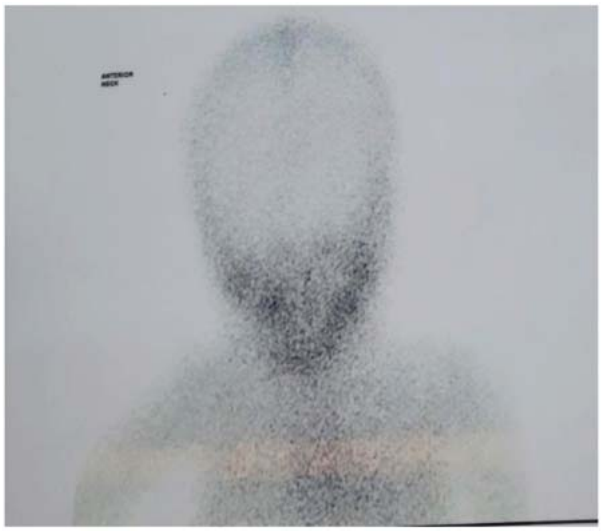

Fig. 1: Tc99 Sestamibi Scan,

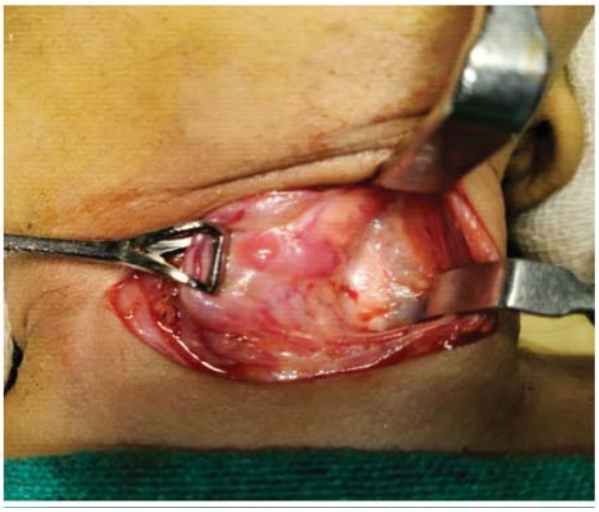

Fig. 2: Superior Parathyroid

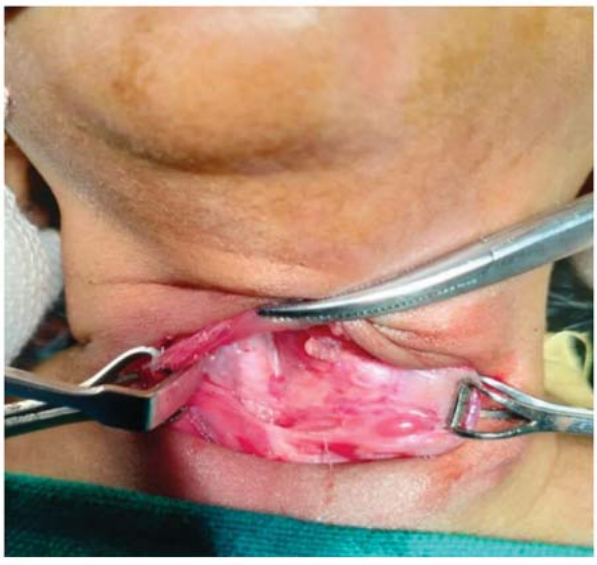

Fig. 3: Inferior Parathyroid

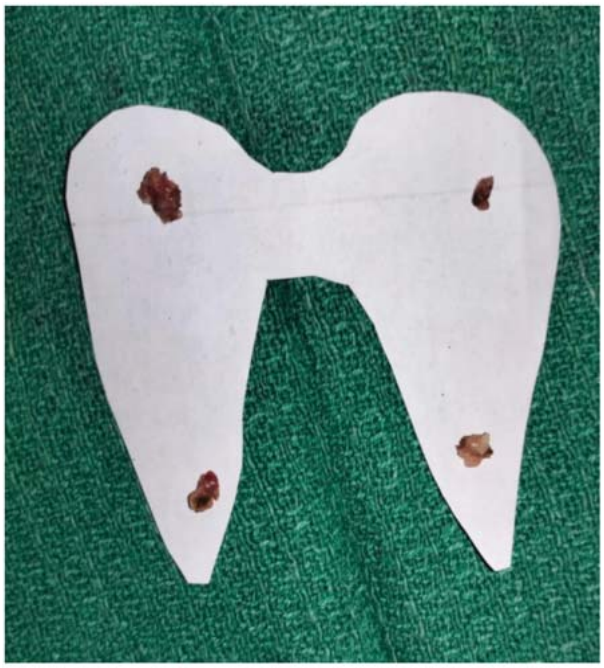

Fig. 4: Specimen

DISCUSSION

Neonatal severe hyperparathyroidism is a rare disease characterized by severe hypercalcemia and metabolic bone disease that usually manifests in the first six months of early life and more often during the first weeks of life. The delay in growth and development are often associated by hypotonia, dehydration, polyuria, Gastrointestinal dysmotility, poor feeding and respiratory distress. The radiograph shows severe bone demineralization, bellshaped deformity of chest, subperiosteal bone resorption, osteopenia and bone fractures. Laboratory findings reveal increased serum calcium and parathormone levels, hypocalciuria, hypophosphatemia. The disease shows a genetic background characterised by autosomal recessive inheritance where extracellular calcium fails to inhibit parathormone release by inactivating mutation in calcium sensing receptor (CaSR) gene. The chief function of the CaSR gene is to maintain calcium homeostasis by regulating calcium absorption from the GIT, bone formation and resorption and calcium excretion from the urinary tract. The CaSR is expressed in the thyroid and parathyroid glands which induces the release of parathormone from the parathyroid gland or calcitonin release from the C cells in the thyroid gland. The CaSR is also found in the kidney epithelium, bones and the intestine. CaSR also involved in the proliferation of fibroblast, induction of cellular differentiation in keratinocytes, inhibit apoptosis in prostate carcinoma cells and regulate the development of cataract in epithelial cells of lens.[4] The mutations in the CaSR gene can either be homozygous or heterozygous.[5] Homozygous mutations mutation result in severe hypercalcemia that manifests early in the neonatal period, whereas heterozygous mutations result in a mild disease course which shows asymptomatic hypercalcemia (Familial Hypocalciuric Hypercalcemia, FHH).[6] In the etiology of FHH, mutations in two other genes along with the CaSR gene play a main role in disease etiology.

Rarely, antibodies emerging against calcium sensing receptors may result in FHH.[6] Sestamibi scintigraphy (MIBI), ultrasound, and magnetic resonance imaging (MRI) are the imaging methods used in the diagnosis of neonatal hyperparathyroidism. Sestamibi scintigraphy is the most sensitive and specific to the parathyroid gland. Sestamibi scintigraphy is highly sensitive in demonstrating the ectopic locations of parathyroid glands. However some publications reported failure in preoperative diagnosis with diagnostic tests.[7] Treatment options include medical and surgical approach. However medical therapy might provide a complete cure in selected cases depending on the genotype of CaSR.[8] Intravenous fluids, loop diuretics, calcitonin, abundant hydration, intravenous bisphosphonates and calcimimetic agents are commonly used medication.[9] A treatment plan must be rapidly made to avoid irreversible long term complications as abnormalities[10] and emergency surgery must be performed in case of failure of medical therapy to stabilize clinical as well as laboratory parameters. Although subtotal parathyroidectomy has been considered as a valid surgical approach, total parathyroidectomy has become the main surgical option. There are studies showing the success of total thyroidectomy + auto transplantation in the treatment of neonatal hyperparathyroidism.[10] The localization of all parathyroid glands must be identified during surgery, specific attention must be shown to avoid injury to the inferior and superior thyroid arteries and recurrent laryngeal nerve. Superior parathyroid glands are located 1 cm above the intersection of the inferior thyroid artery and recurrent laryngeal nerve at the level of cricoid cartilage and inferior parathyroid glands are located below the intersection of inferior thyroid artery and recurrent laryngeal nerve posterolateral to the lower pole of the thyroid gland. Isolation of

the parathyroid glands will be difficult in case of bleeding so even mild bleeding should be avoided. Surgery is more challenging in newborns owing to small parathyroid glands, limited surgical site and high chances of lymph nodes mimicking parathyroid glands. The intravenous methylene blue injection is used in case of complication in localization of the parathyroid glans. Al-Khalaf *et al.* recorded the benefits of methylene blue injection during surgery, Janik *et al*. reported no benefits of the same.[3] Intraoperative parathormone monitoring is used in monitoring of Blood parathormone level, surgeon must be confirm about the adequacy of parathyroid gland removal.[5] The blood parathormone level must be monitored approximately 10 min after excision of the parathyroid glands as plasma half-life of parathormone is 3–5 min and the surgery must be planned accordingly. A decline in parathormone levels to the normal range shows the parathyroid glands have been removed sufficiently. The re-exploration of the surgical site in case of raised parathormone levels is essential and parathyroid glands in ectopic localizations must be reexplored. Some studies recommended bilateral jugular venous blood sampling during surgery as well as investigation of ectopic parathyroid glands at the side with elevated parathormone levels. Parathyroid glands in the ectopic localizations might undergo hyperplasia and result in further release of parathormone.[7] Ectopic parathyroid glands may be located in the neck, intrathyroidal, retroesophageal, retropharyngeal, carotid sheet and mediastinum. The intrathyroidal ectopic parathyroid gland can be visualized by ultrasound during surgery. It is important to make differentiation between intrathymic and posterior mediastinal localizations in ectopic parathyroid glands which are located in the mediastinum before surgery. A cervical incision will suit in intrathymic parathyroid glands, whereas posterior mediastinal parathyroid glands require a thoracic approach.[6] Ectopic location of parathyroid gland is the reason for failure of parathormone levels to return to normal levels even after surgery which might necessitate a second surgery.[9] The present case showed the reduction of the parathormone level after surgery which revealed the sufficient excision of the parathyroid gland so there is no need for second surgery.

CONCLUSION

Neonatal severe hyperparathyroidism is a life-threatening disease. Medical therapy should be done as early as possible and early surgery must be done in case of failure of medical therapy. The procedure should be terminated only after frozen examination of the parathyroid gland after total parathyroidectomy and intraoperative parathormone monitoring should beperformed. Sestamibi scintigraphy is sensitive in demonstrating parathyroid glands in ectopic localization[8], the reduction in parathormone level shows the complete excision of the gland. Medical therapy should be done in addition to the surgery and serial followup is essential.

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