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Case Report

A 6 month old female patient with primary hyperparathyroidism

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Abstract

A 6 month old female patient was referred to Diabetes, Endocrine and Metabolism Pediatric Unit (DEMPU) in the Children's hospital, Cairo University because of high grade fever, dehydration, recurrent chest infection, purpuric rash over the abdomen, and failure to thrive from the first day of her life. The patient has history of multiple hospital admissions. Investigations done in the hospital revealed persistent hypercalcemia together with skeletal manifestations due to primary hyperparathyroidism. Medical treatment was initiated which proved to be unsuccessful and the calcium levels did not drop adequately until removal of the 4 parathyroid glands (total parathyroidectomy) was performed. After that, the calcium levels started to drop and replacement therapy with vitamin D and calcium was started.

Keywords: Primary hyperparathyroidism; infancy; hypercalcemia; parathyroidectomy.

Introduction

Hyperparathyroidism is a condition characterized by proliferation of the parathormone secreting cells in one or all of the parathyroid glands. It may be primary, secondary or tertiary. Primary hyperparathyroidism is a rare condition affecting infants [1]. It is usually caused by genetic mutations leading to alteration in the response of the calcium sensing receptors present on the surface of the chief cells of the parathyroid gland to the circulating ionized calcium resulting in severe hypercalcemia in addition to skeletal manifestations [2]. The mentioned genetic mutation can be inherited as an autosomal recessive [3] or autosomal dominant trait. The latter mode of inheritance results in a condition known as familial hypocalcuric hypercalcemia [4]. They may also be associated with other conditions named neonatal severe hyperparathyroidism or neonatal sporadic hyperparathyroidism which depends on whether theyoccur in the homozygous, double heterozygous, de novo heterozygous form [5].The clinical presentation of primary hyperparathyroidism may vary greatly especially during infancy. The infant with primary hyperparathyroidism may present with failure to thrive, marked osteopenia causing severe bone deformities, recurrent chest infection due to chest deformities, hepatosplenomegaly and anemia[2]. Medical treatment that may be started includes the use of isotonic saline, loop diuretics, steroids, calcitonin or bisphosphonates. [2]However, the most effective treatment is total parathyroidectomy with or without autotransplantation. [6]

Case report

A 6 months old female patient was referred to DEMPU in the Children's hospital, Cairo University with clinical presentation of high grade fever, dehydration, recurrent chest infection, purpuric rash over the abdomen, and failure to thrive.The patient was the product of non-consanguineous marriage. She was born at full term by cesarean section to a multiparous mother. Her birth weight was 2 kg. Prenatal history was insignificant except for positive maternal toxoplasma IgG antibodies. There was history of 2 sibling death of unknown cause within the first year of life.

On day 1 of life, she was admitted to the NICU for 15 days with major symptoms and signs including poor feeding, vomiting, dehydration, purpuric rash and pallor. Investigations were done and treatment was given with no available medical records.

One month later, her clinical condition deteriorated for which she had to be readmitted to another hospital for 5 days where complete blood count, KFT, LFT, electrolytes & sepsis screen were done revealing thrombocytopenia and hypercalcemia. Then, she was discharged after clinical improvement without definitive diagnosis.

After that, the patient's medical condition necessitated multiple hospital admissions.

At the age of 6 month, the patient was referred to DEMPU where she was admitted. On examination, the patient was irritable, moderately dehydrated, her temperature was 39°C, heart rate: 170 beats/min, respiratory rate: 50/minutes and blood pressure: 80/45.

All her anthropometric measures were below the 3rd percentile for age and sex. Her weight was 4.5 kg, length 54 cm and skull

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circumference 37cm.

She had a chest deformity in the form of pectus excavatum and scattered late inspiratory fine crepitation could be auscultated.

On abdominal examination, purpuric rash could be seen and hepatosplenomegaly could be palpated.

Investigations carried out at DEMPU revealed the presence of anemia Hb:8.3gm/dl (11-14), thrombocytopenia plt: $90x10^3$ (200-550), hypercalcemia Ca:17.1mg/dl (9-11) hypophosphatemia: 1.9 mg/dl (3-6.5),ALP levels:436 IU/l (up to 455). Measurement of 24 hours urinary calcium excretion was elevated (11mg/dl, reference range: 0.2-0.4) with urinary calcium/ creatinine ratio of 3.67 (0.3-0.8).The PTH level measured using immune radiometric assay was also increased: 45.5 ng/dl (1.2-7.2).The rest of the blood investigations were normal as shown in table (1).

Bone marrow aspirate was performed which revealed hypo-cellular bone marrow.

Treatment was immediately started in an attempt to decrease serum calcium levels by replenishing the intravascular volume using isotonic sodium chloride and the use of loop diuretics (furosemide) at a dose of 1mg/kg/day. A trial of steroids was also initiated at a dose of 0.5 mg/kg/day. However, serum calcium levels did not adequately drop as shown in table (2).

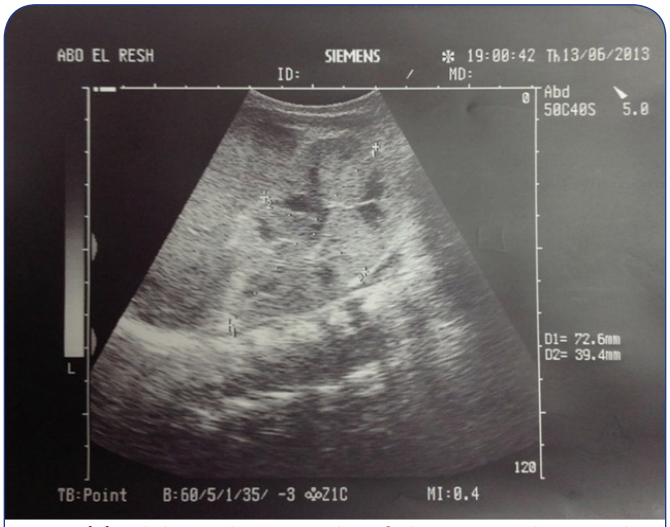

Figure (1): Abdominal sonography of the patient showing the absence of nephrocalcinosis

Abdominal ultrasound was performed revealing hepatosplenomegaly & bright echo-texture of both kidneys but there was no evidence of nephrocalcinosis or cholecystolithiasis.

Investigation	Parameter	Results	Reference range
CBC	Hb (gm/dl)	8.3	11-14
	Hct (%)	24.3	38-50
	WBC's (per mm^3)	$11.7x10^3$	6-16
	Platelets(per mm^3)	$90x10^3$	200-550
Blood chemistry	BUN (mg/dl)	13	5-23
	Creatinine (mg/dl)	0.3	0.2-0.4
	Na (mmol/L)	135	135-150
	K (mmol/L)	4	3.5-5.2
	Ca (mg/dl)	17.1	9-11
	Ionized Ca (mg/L)	9.3	4.4-6
	Phosphate (mg/dl)	1.9	3-6.5
	ALP (IU/L)	436	Up to 455
	AST (IU/L)	38	Up to 38
	ALT (IU/L)	19	Up to 40
	GGT (IU/L)	31	Up to 50
	Albumin (gm/dl)	4.2	3.5-5.3
	T. Bilirubin(mg/dl)	0.5	Up to 1
	Bl. glucose(mg/dl)	82	60-110

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Table (1): Results of laboratory investigations

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Parameter	14/5	15/6	22/6	7/7	16/7
Ca mg/dl (9-11)	17.1	16	12.2	18.7	19
Phosphate mg/dl (3-6.5)	1.9	2.7	2.9	2.4	3.1
ALP U/l (up to 455)	436	912	281	426	718

Table (2): Serial measurement of calcium profile

Additionally, skeletal survey was carried out showing osteopenic bone texture with extensive sub-periosteal bone resorption of metacarpal bones, phalanges as well as distal ulnar border. In addition, extensive bone resorption of the right femoral head was noticed causing its total vanishing with residual ill-defined proximal shaft. Mild cardiomegaly was noted and echo was done with NAD

Lung fields showed multiple consolidation patches together with extensive thickening of pulmonary interstitium for which CT chest was done.

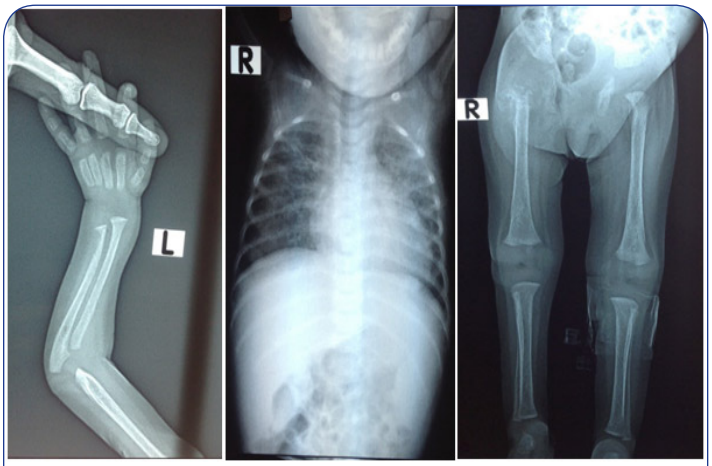

Figure (2): Multiple bone X-rays revealing marked bone osteopenia, and destruction

The CT chest with contrast revealed wide spread pulmonary areas of ground glass mosaic attenuation of both lung fields. Both lungs showed multiple patches of consolidation.

Tc99m-SestaMIBI parathyroid scintigraphy performed was negative for any sizable parathyroid gland adenoma or hyperplasia.

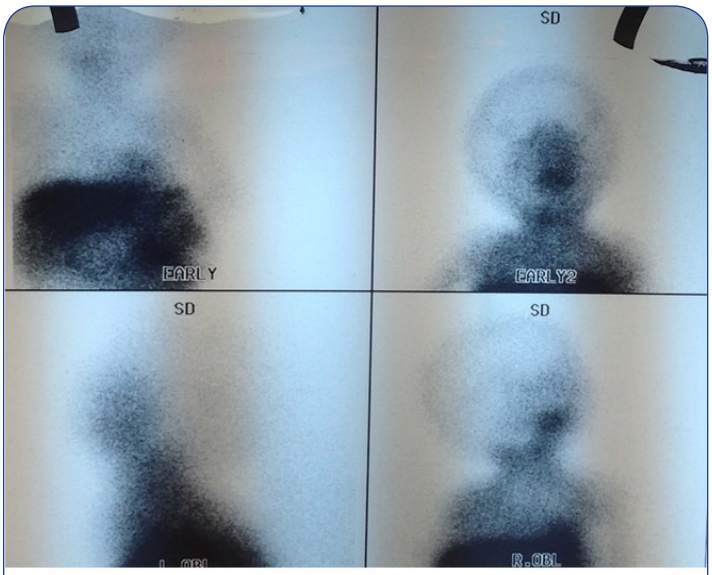

Figure (3): Parathyroid scintigraphy

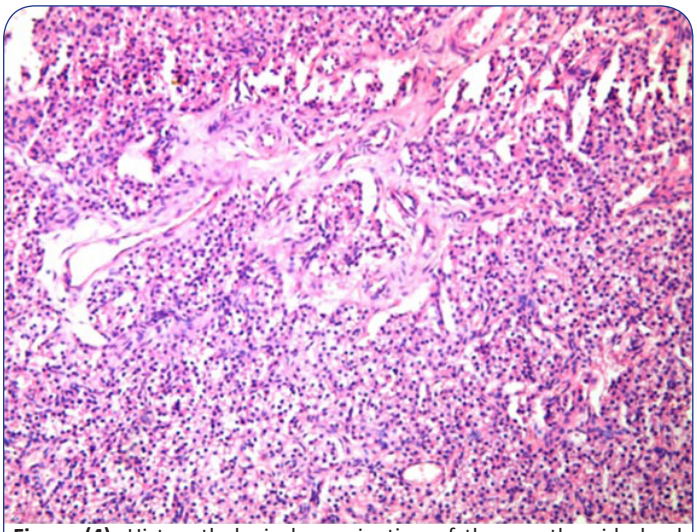

Figure (4): Histopathological examination of the parathyroid gland specimens Gross:- multiple greyish white focally brownish specimen measuring 1x1 cm. Microscopic examination of the specimen revealed (1) Pieces of parathyroid tissue, formed of chief cells with regular central nuclei, arranged in nests and trabeculae. (2) Pieces of fatty tissue entangling one lymph node were also seen. (3) No malignancy seen Diagnosis:Hyperplastic Parathyroid tissue

Analysis of the clinical data, the results of the laboratory investigations and the radiological findings were consistent with the diagnosis of primary hyperparathyroidism due to parathyroid hyperplasia most probably NSHPT despite of the negative parathyroid scintigraphy.

The patient was prepared for parathyroidectomy which was done and the 4 parathyroid glands were removed. Additionally, specimens were sent for pathological examination which revealed the presence of hyperplastic parathyroid tissue with no evidence of parathyroid adenoma or malignancy

The patient was admitted to the ICU postoperatively where her blood calcium levels were followed up. Eventually, a progressive decline was noted and the calcium level was normalized within the first 24 hours postoperatively. The decrease in calcium continued on subsequent days and supplementation with calcium at a dose of 50 mg/kg/day and activated form of Vitamin D (one alpha) at a dose of 0.05 μg/kg/ day was initiated. Unfortunately, the patient passed into postoperative chest complications most probably due to her chest deformity.

Conclusion

Primary hyperparathyroidism is a rare disorder in pediatric age group especially during infancy. The clinical presentation may vary greatly especially in this age group. The diagnosis of primary hyperparathyroidism can be done on clinical and laboratory basis in the absence of positive results of radioactive isotopic scanning. The only effective treatment is surgical removal of the gland.

Summary

A 6 month old female patient presented to the hospital with medical history of recurrent chest infection, purpuric rash on the abdomen and pallor for which she was admitted. Physical examination was remarkable for failure to thrive and hepatosplenomegaly. Laboratory findings demonstrated anemia, thrombocytopenia, hypercalcemia, hypophosphatemia, hypercalcuria and elevated parathormone levels. Bone marrow aspirate was done revealing hypo-cellularity. Skeletal survey was performed showing osteopenic bone texture, extensive sub-periosteal bone resorption of the metacarpal bones, phalanges, distal ulnar border as well as the right femoral head causing total vanishing with residual ill-defined proximal shaft. Abdominal ultrasound revealed the presence of hepatosplenomegaly. Chest CT examination showed ground glass mosaic attenuation of both lung fields. Tc99 parathyroid scintigraphy was negative for parathyroid adenoma. The patient was diagnosed to have primary hyperparathyroidism and was treated by IV fluids, diuretics (furosemide) and a trial of steroids was given. Successful Para-thyroidectomy was done and the calcium blood levels decreased postoperatively. Pathological examination of the removed parathyroid gland revealed hyperplasia. Unfortunately, the patient's passed into postoperative complications.

Acknowledgment

I would like to acknowledge the Pediatric ICU team who followed up the patient's condition postoperatively.

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