PRIMARY HYPERPARATHYROIDISM IN AN INFANT: CASE REPORT WITH REVIEW OF THE LITERATURE

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Primary hyperparathyroidism is rare in children under the age of 16 and uncommon in adolescents.[1] While most cases of primary hyperparathyroidism in neonates and infants are caused by parathyroid hyperplasia, the majority of cases appearing during childhood and adolescence are caused by a parathyroid adenoma.[2] A female Sudanese infant who has primary hyperparathyroidism due to parathyroid hyperplasia is presented. Results of workup, possible etiologies and review of the literature on primary hyperparathyroidism are presented. To our knowledge, this is the first case reported at this age in the Arab world.

Case Report

A 16-month-old Sudanese female was assessed at the age of two months and six months of age for generalized floppiness. She was the product of a full term pregnancy complicated by gestational diabetes managed by insulin, which ended by induced vaginal delivery with birth weight of 2.5 kg. At two months of age, she was noticed by her mother to be floppy. She had recurrent oral thrush and napkin rash and urine output was noticed by the mother to be high compared to her siblings. Bowel habits were normal. She was on breast feeding with a good appetite. Her developmental milestones were lagging behind (she smiled at four months and rolled over from side to side at 13 months and at 16 months she was able to sit). Her family consisted of unrelated healthy parents with two healthy sisters and three healthy brothers. There was one neonatal death. There was no history of endocrinopathy in the family. General examination showed small body build with growth parameters (weight 5.5 kg, length 67.5 cm and head circumference 40 cm) all below the 5th percentile. Blood pressure was 100/60 and remained normal. She had an open anterior fontanel measuring 1x1 cm. She had 10 teeth with no erosions. There was no corneal opacity or cataract. Neurological examination showed generalized hypotonia with exaggerated tendon reflexes. Cranial nerves and sensation were normal.

Laboratory investigations showed calcium level of 6 mmol/L (N = 2.1 to 2.6), phosphate 2.2 mmol/L (N = 0.8 to 1.4), magnesium 1.8 mmol/L, alkaline phosphatase 670, albumin 47 g/L, urine Ca/urine creatinine ratio 9.6 (N = 0.7), vitamin D level 43 (N = 20 to 120), serum parathyroid hormone (PTH) 285 (N = 5 to 45) with calcium level of 4.22, urine homovanillic acid (HVA) 0.3 mg/24 hours (N = up to 4.1). Vitamin D, PHT and HVA were done by Bioscientia Laboratories in Germany. The patient's father, mother and uncle had normal calcium levels. Electrocardiogram showed sinus tachycardia. Echocardiogram showed normal aortic arch. Abdominal and neck ultrasound, x-ray of both hands, and brain and neck computed tomography (CT) scans were also normal. Parathyroid scan (thallium scan) showed a hot area in the right lower parathyroid gland with suspicion of parathyroid adenoma.

Surgical exploration was performed after failure of medical therapy, namely good hydration and hydrocortisone. All four parathyroid glands were found hypertrophied; therefore, three-and-one-half glands were removed. Histopathology findings were consistent with parathyroid hyperplasia.

The patient was followed up over the following two years with no medications. Her calcium level remained in the range of 1.88 to 2.68 mmol/L with some improvement in her developmental milestones in the sense that she started to walk with support and had a vocabulary of a few words. Screening for multiple endocrine neoplasia (MEN) showed prolactin 16 (N = 1.3 to 20.8), FSH 4.6 (N = 2.3 to 17), LH 1.1 (N = 3 to 50), $FT3_3$ 7.9 (N = 4 to 8), $FT4_4$ 16.1 (N = 10 to 25).

Discussion

Childhood hypercalcemia, although an uncommon problem, may lead to bad sequelae. It may also be life-threatening. It has nonspecific symptoms and signs such as lethargy, hypotonia, poor feeding and subsequent failure to thrive, dehydration, constipation and respiratory distress.

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These symptoms may be apparent as early as the first few weeks of life. This nonspecificity of symptoms often leads to delay in the diagnosis. Once the diagnosis is established, the etiology has to be defined.[3] Vitamin D intoxication is an important phenomenon which always needs to be ruled out.[4] Our patient denies vitamin D intake. This was also confirmed by the normal levels of vitamin D in the blood. Familial hypocalciuric hypercalcemia, an autosomal dominant condition, is another important etiology. This was unlikely in our patient due to the lack of similar family history and the obvious hypercalciuria.[5] Contrary to the experience in the adult population, malignancy of childhood is rarely associated with hypercalcemia.[6] Our patient had neither the evidence of this possibility nor the evidence of hyperthyroidism or cortisol deficiency which very rarely can be associated with hypercalcemia in childhood. The symptomatology of this patient, strengthened by the simultaneous elevated level of parathyroid hormone and serum calcium level, made the diagnosis of hyperparathyroidism obvious. Serum calcium levels are always extremely high and most infants have serum calcium levels greater than 3.7 mmol/L or even above 5 mmol/L, as in our patient.[2] Primary hyperparathyroidism in children is a rare disease. Prevalence in the general population ranges from 25 to 28 per 100,000. The incidence in children is unknown. In 1986 Ross et al. reported 86 cases in infancy of those with what has been reported in the literature, i.e. parathyroid hyperplasia. Treatment of hyperparathyroidism with total parathyroidectomy and autotransplantation of a portion of the parathyroid gland to the surface of a skeletal muscle has proven successful.[9,10] Total removal of the glandular tissue from the neck prevents further surgery in this area. Rapid and reliable assay of intact PTH provides the means of following the functional status of the parathyroid gland intraoperatively to confirm the successful removal of the tissue and postoperatively to assess the function of transplanted tissue.[9,10] This was not feasible in our patient. Primary parathyroid hyperplasia may be part of the multiple endocrine neoplasia. Therefore, this patient was screened for the other component of this syndrome. No evidence of this was demonstrated. Parathyroid hyperplasia has also been reported in association with the familial hypocalciuric hypercalcemia.[5,11]

In conclusion, hypercalcemia is an important phenomenon to be recognized and extensively worked up in childhood. Primary hyperparathyroidism is a rare cause. Surgical treatment is almost always indicated. Other associations and etiologies of this phenomenon should always be sought.

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