CASE REPORT
KAZUISTIKA

Skeletal Deformity in Children with Primary Hyperparathyroidism

Skeletální deformity u dětí s primárním hyperparatyreoidismem

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SUMMARY

Skeletal deformation like genu valgum is reported to be rare in Primary hyperparathyroidism (PHPT). The solitary adenoma or hyperplasia of the parathyroid glands are the cause in 80–85% of the cases.

We report 2 cases of girls on 12 years and 15 years of age, complaining from pain and genu valgum deformation of the lower extremities before the planned orthopaedic surgical correction. The first patient had complaints for 3 years and lost ability to walk independently, the second case lost normal gate for a period of 5 months. The paraclinical screening discovered hypercalcemia, hypophosphatemia, elevated alkaline phosphatase, normal creatinine, raised parathormone. In the first case the X-rays depicted fibrocystic osteodistrophy from a hyperparathyroid type with bone cysts, giant cell „brown tumors" and pathological bone reorganization, in the second case – coarse fibrous structure of the left knee joint with genu valgum with bone cysts in the distal metaphysis of the left femur. The ultrasound of the thyroid gland found oval hypoechoic formations with suspicious origin from the parathyroid glands. These findings were confirmed from the SPECT/CT pointing active adenomas in the parathyroid glands.

Skeletal deformation like genu valgum is the reason to search for the primary diagnosis in our 2 cases. Investigation of the serum calcium and parathormone are diagnostic in 100%. The imaging diagnosis has a critical role for indicating surgical treatment of the parathyroid gland adenoma.

Key words: genu valgum, hypercalcemia, paediatric parathyroid adenoma, ultrasound, SPECT/CT.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a rare disease in children and adolescents. It could be familial and sporadic with the most common cause in the latter form – solitary adenoma and hyperplasia of the parathyroid glands in 80–85% of the cases (13). PHPT is diagnosed in childhood when the patients are symptomatic and is usually demonstrated as skeletal pathology rather than renal (9). The clinical manifestations are atypical and the skeletal are described as bone pain and limping, growth retardation and rarely deformation of the long bones with pathological fractures. Characteristic are abnormalities in Ca-Phosphorus metabolism with hypercalcemia that guides to conducting hormonal investigations. The classical X-ray include generalized osteoporosis, osteoid cystic fibrosis, bone cysts and brown tumors of the lone bones (6, 8).

CLINICAL CASES

The first case is a 12-year-old girl with pain and deformation of the lower extremities, that progressed to inability to walk independently and is with 3-year duration. There was intensive perspiration in the last months and necessity to drink 2–3 liters fluids in the last couple of months on a daily basis without control on diuresis. The child is obese, brown skin with cervical and axillar acanthosis nigricans, with raised turgor, excessive subdermal fatty tissue, equally distributes across the whole body. The pulmonary and cardiac functions are intact. Orthopaedically the knees are with excessive valgus and was planned for orthopaedic surgical correction with hemiepiphyseodesis of the distal medial femoral physes. The child is not independent walker and uses wheelchair. On admittance in the department of paediatric orthopaedics, the para clinics demonstrate hypercalcemia Ca 3.73 mmol/l, hypophosphatemia – P 0.80 mmol/l, ALP of 4700 IU/L, creatinine of 40 μmol/l. The additional testing of parathormone counts 2238 pg/ml (x 0.106 pmol/l), 25(OH)vit.D 14 nmol/l, urine Ca – 6.16 mmol/l. The X-ray characteristics of the lower extremities are of fibrocystic osteodystrophy of hyperparathyreoid type with bone cysts, radiological opacities due to giant cell "brown tumours" and pathologic bone remodelling (Fig. 1). The ultrasonography of the thyroid gland depicts oval formation dorsal in the lower pole of the right lobe with measurements 16/18/10 mm (Fig. 2).

The conclusion of the cervical SPECT/CT is for adenoma in the parathyroid glands on the right side and for multiple lytic lesions in the scanned bones: mandible, clavicle, scapulae, sternum, spinous process of Th 1 vertebra, 3rd rib bilaterally, 6th rib on the left dorsally with characteristics of osteitis fibrosis cystica.

The clinics, para clinics and the imaging diagnostics confirm PHPT due to adenoma of the parathyroid glands.

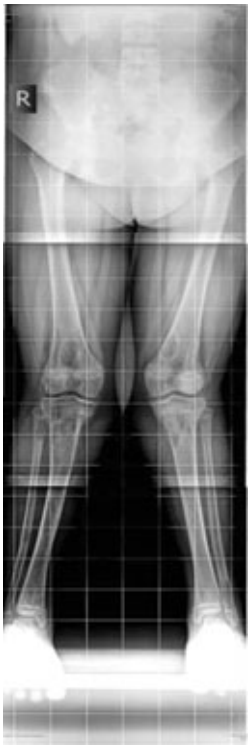

Fig. 1. Case 1. FLFS (Full Leg Full Spine) of the lower extremities.
Legend: The X-rays of the lower extremities show cystic lesions in the distal metaphysis of the right femur, the proximal tibia and fibula with rarefication of the spongiosa with osteoporosis. There is a consolidated pathological fracture of the proximal right fibular diaphysis. There are analogic morphologic manifestations on the left side. There is genu valgum with Q-angle 21° on the left and 16° on the right.

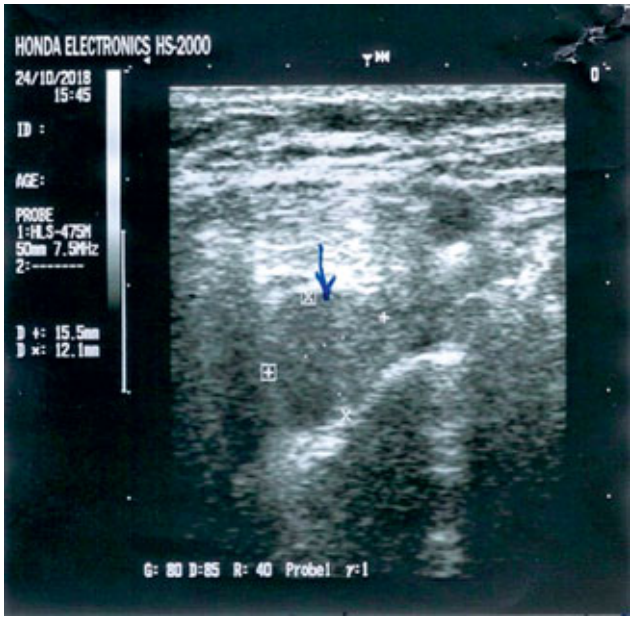

Fig. 2. Case 1. The ultrasonography of the thyroid gland.
Legend: The ultrasonography of the thyroid gland depicts oval formation dorsal in the lower pole of the right lobe with measurements 16/18/10 mm.

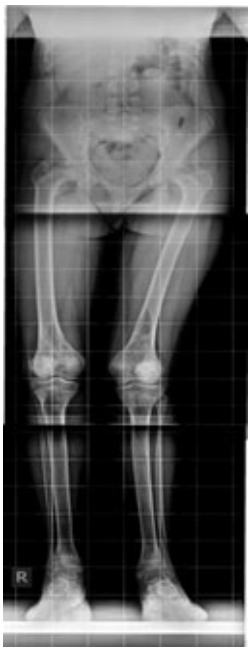

Fig 3. Case 2. FLFS (Full Leg Full Spine) lower extremities X-ray.
Legend: The lower extremities X-ray shows inactivity osteoporosis with left knee valgus, bone cysts in the distal metaphysis of the left femur, coxa vara and bilateral ankle valgus.

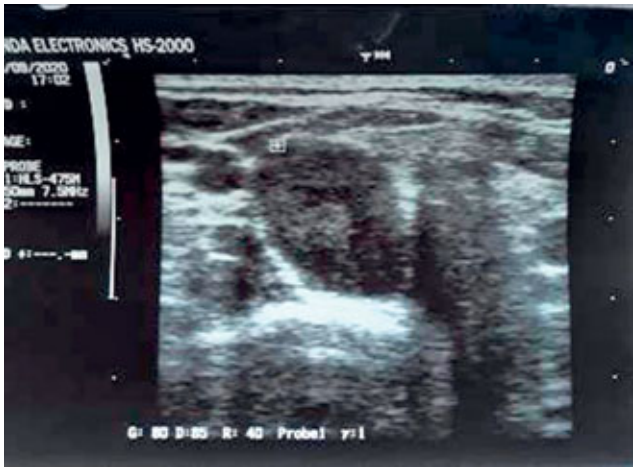

Fig. 4. Case 2. The ultrasound of the thyroid gland.
Legend: The ultrasound of the thyroid gland finds caudally on the left side of the gland hypo echoic nodule with size 24/19/17 mm.

The second clinical case is of a 15-year-old girl with genu valgum deformation of the left lower extremity, planned for orthopaedic surgical correction with distal femoral varus osteotomy with LCP plate. The girl was with waddling gait abnormality for 5 months period. The preoperative para clinical screening shows Ca 3.15 mmol/l, P 0.87 mmol/l, ALP 1973 IU/L, 25(OH)vitamin D 23.32 nmol/l, parathormone 709 pg/ml (x 0.106 pmol/l), creatinine 35.04 μmol/l. The lower extremities X-rays shows inactivity osteoporosis with left knee valgus, bone cysts in the distal metaphysis of the left femur, coxa vara and bilateral ankle valgus (Fig. 3). The ultrasound of the thyroid gland finds caudally on the left side of the gland hypoechoic nodule with size 24/19/17 mm., most probably originating from the left parathyroid glands (Fig. 4). The ultrasonography was confirmed by parathyroid SPECT/CT, depicting active adenoma of the left parathyroid gland, located in the lower pole of the left lobe of the gland (Fig. 5).

DISCUSSION

The primary hyperparathyroidism is extremely rare child disease. Several big series of paediatric cases are reported in the last 30 years, which are more than 300, describing the important characteristics of the paediatric PHPT (5, 7). The incidence of the disease is 1 per 300 000 newborns, in contrast with the incidence in adults, that is 30 per 100 000. The distribution is bimodal in children's age and these are the newborn period and the second decade of life. The pediatric cases are sporadic in 65–70% and are due to adenomas and gland hyperplasia, only 27–31% are familial. There are 13 pediatric cases described for parathyroid cancer (3). Our cases are sporadic and are investigated by multidisciplinary pediatric team.

The clinical presentation in the newborn period consists of failure to thrive, persistent constipation, lethargy or increased irritability, respiratory distress syndrome, severe skeletal demineralisation with bone deformities, pathological fractures and hypotonia. The diagnosis in older children in 80% of the cases is delayed. Our first patient had complaints for more than 3 years and falls into this group. The second patient has a short anamnesis and fast diagnosis. The latter is fulfilled when target organs are affected and there are complaints of easy fatigue, reduced physical activity, polydipsia and polyuria, arterial hypertonia, abdominal pain, nephrolithiasis and nephrocalcinosis, muscular-skeletal symptoms and depressive states. In the described cases the anamnestic data is scarce, but separate elements of the clinical picture are observed. The first patient was with delayed diagnosis and as a result she lost ability to walk independently. She had multiple bone pathologies. Bone deformities like genu valgum, as was observed in our patients, are rare in kids with PHPT. There are only 10 reported cases in the literature, 7 girls and 3 boys. The aetiology and the direct mechanism producing the bone deformities are still under research. The explanations are that hyperparathyroidism like rickets causes demineralisation and bone weakening, hence it can influence the remodelling of the long bones. There can be a direct effect of the raised parathyroid hormone on the growth zones during the pubertal spurt (1, 11). The atypical skeletal deformity in this disease and its rareness delayed the diagnosis in the first case. In both cases the diagnosis was confirmed after strict, preoperative screening from a multidisciplinary team.

The X-ray characteristics of PHPT include osteitis fibrosa cystica, bone cysts and brown tumours of the long bones. They are described in our first case with a 3-year history and these are scarce in our second patient. In the recent years authors conclude lack or reduction of these classical changes in older patients in countries, where serum calcium is investigated routinely (2).

The diagnosis is confirmed on the basis of biochemical and hormonal studies and with the aid of imaging studies. The first step includes the serum levels of Ca, Ca2+, Magnesium, and parathormone, levels of 25-OH vitamin D, renal function indicators, and calciuria. These instigations in our patients show hypercalcemia, hypophosphatemia, raised levels of parathormone, low levels of 25-OH vitamin D and normal renal function. The imaging diagnosis has a critical role for indicating surgical treatment of the parathyroid gland adenoma before the orthopaedic correction. The ultrasonography has 86% sensitivity in solitary adenoma, 67% specificity and 95% prediction in identification of solitary lesions and hyperplasia. The hybrid imaging diagnostics with SPECT/CT, contemporary nuclear medical method, has advantage in the search of ectopic adenomas, but has also the disadvantage like difficult differentiation between thyroid and parathyroid tissues (4). Our patients have SPECT/CT, confirming parathyroid gland adenoma.

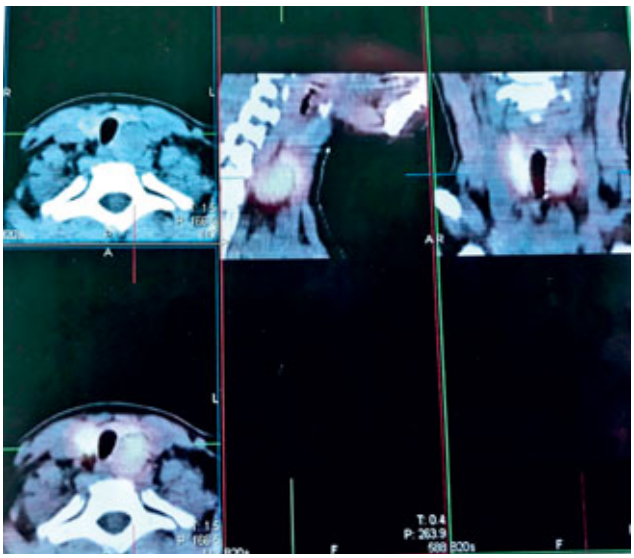

Fig. 5. Case 2. SPECT/ CT of the left parathyroid gland. Legend: SPECT/CT shows focal intensive fixation of the radio contrast agent, situated in the lower pole of the lower lobe of the thyroid gland. On the CT is visualized huge oval structure, located behind the lower pole of the thyroid gland with size 19/24 mm.

The differential diagnosis is based on the presence of hypercalcaemia in children's age. This can be investigated in regard with the parathormone levels, being dependent or not with them, genetic and acquired. The differential diagnosis includes diseases, connected with secretion and the effect of the parathormone like generalized hyperplasia of the glands, isolated and multiple adenomas, benign familial hypercalcemia, familial primary hyperparathyroidism; vitamin D metabolism impairment; in granulomatosis diseases; syndromes; neoplastic lesions; hypophosphatemia (12).

The treatment in children with PHPT depends on the foundings and calcium levels. In symptomatic hypercalcemia or Ca over 3.0 mmol/l conservative treatment is conducted by paediatric endocrinologists. In the lack of presenting symptoms, the diagnostics are investigated with an aim to localize the adenoma for precise surgical treatment in 83–89% of the children with very good results (10).

CONCLUSIONS

Skeletal deformity like genu valgum is rare in PHPT. In our cases this deformity was the trigger for searching the diagnosis. Investigation of the serum calcium and parathormone in this children are diagnostic in 100 percent. The imaging diagnosis/ultrasonography and SPECT/CT/ has a critical role for indicating surgical treatment of the parathyroid gland adenoma before the orthopaedic correction.

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