



A rare association of hyperparathyroidism and Turner's Syndrome — a case report

Rzadki przypadek współwystępowania nadczynności przytarczyc i zespołu Turnera — opis przypadku

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Abstract

We present the clinical, laboratory, radiological and pathological findings in the case and review the literature. Our patient, a 37-year-old woman of short stature, was referred because of musculoskeletal pain. After primary evaluation, she underwent treatment with calcium and vitamin D supplement with the diagnosis of osteomalacia in Turner's syndrome. The rise of serum calcium during medical therapy, which was an unusual finding, attracted the clinician's attention to another underlying disorder. Further evaluation revealed primary hyperparathyroidism due to an adenoma of the parathyroid gland. Even though this is a rare diagnosis, its presence should be considered in any patient with Turner's syndrome presenting with severe osteoporosis and a rise in serum calcium during treatment.

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Key words: primary hyperparathyroidism, Turner's syndrome, bone disease

Streszczenie

Przedstawiony przez autorów opis przypadku zawiera ocenę kliniczną, wyniki badań laboratoryjnych, radiologicznych, patomorfologicznych 37-letniej kobiety, u której początkowo rozpoznano osteomalację przebiegu zespołu Turnera i zastosowano suplementację wapnia i witaminy D. Ze względu na szybką progresję Ca we krwi rozszerzono diagnostykę, rozpoznając dodatkowo nadczynność przytarczyc spowodowaną gruczolakami tego narządu.

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Słowa kluczowe: pierwotna nadczynność przytarczyc, zespół Turnera, choroba kości

Case Presentation

A 37-year-old woman was referred to an endocrinologist because of low bone density in radiography. She had a long history of musculoskeletal pain, without fractures or nephrolithiasis. She had polyuria, polydipsia and non-significant weight loss (2–3 kg over two years). For six years she has experienced secondary amenorrhea, addressed by hormone therapy.

In physical examination, blood pressure was 90/60 mm Hg, pulse rate = 80/min, height = 131 cm, weight = 36 kg. She had no obvious neck mass or goitre and examination of her chest and abdomen showed normal findings. The proximal muscular force of the legs was 4/5.

The primary laboratory profile included a complete blood count (CBC), fasting blood sugar (FBS), blood urea nitrogen (BUN) and creatinine, liver function test and lipid profile, and was normal. Serum calcium (Ca), phosphorus (P) and alkaline phosphatase (Alk. Ph) contents were as follows; Ca = 10 mg/dl (8.6–10.3), Pi = 2.7 mg/dl (2.5–5), Alk Ph. = 1010 IU/L (70–310), FSH = 118 IU/L (follicular phase = 3.5–9.7), LH = 65 IU/L (follicular phase = 1.7–8.9).

A bone mineral density scan was performed. Spinal measurements showed an adult T-score of –4.5, which was in the osteoporotic range, and an age-matched Z-score of –3.5. Hip measurement results indicated a T-score of –3.3, in the osteoporotic range, and an age-matched Z-score of –2.5.



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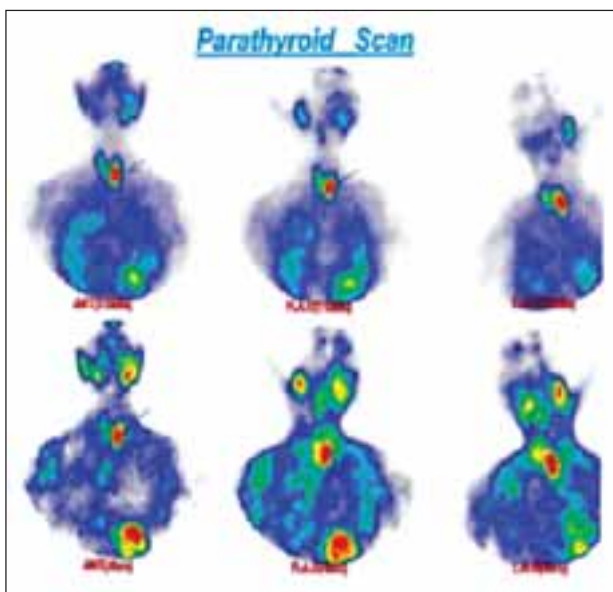


Figure 1. Parathyroid scintigraphy study of the patient, showing parathyroid adenoma

Rycina 1. Badanie scyntygraficzne przytarczyc ujawniające gruczolak przytarczycy

In view of the patient's short stature, high gonadotropin level, secondary amenorrhea and low bone density, further evaluation was performed, including a determination of karyotype. This confirmed the diagnosis of mosaic Turner's syndrome (TS) (mos 46,X,i(X)(q10)[14]/45,X[6]). The pertinent paraclinical studies, including echocardiography, ultrasonography of the urinary system and thyroid function test, were normal. An occult blood test was negative. In addition, audiometry demonstrated a sensory neural defect in the left ear.

With a diagnosis of osteomalacia she underwent medical therapy with calcium carbonate (1 g daily) and calcitriol (0.25 mcg twice daily). Total serum calcium increased during follow-up (from 10 mg/dl to 11.3 mg/dl). Three months later, in an assessment of hypercalcaemia, the results of laboratory findings were as follows: Ca = 11.4 mg/dl (8.6–10.3) P = 2.6 mg/dl (2.5–5) Alk. Ph. = 802 IU/L (70–310) Intact PTH = 188 pg/ml (10–70), and Ca (24 h urine) = 465 mg/24 h (female < 250). Hypercalcaemia persisted, despite discontinuation of the oral calcium and calcitriol.

Skull and chest radiographies were unremarkable. In radiography of both hands, there was no abnormality apart from osteopenia.

A 99m Tc-sestamibi scan on delayed imaging showed a zone of intensive increased activity in the left thyroid inferior pole, highly suggestive of parathyroid adenoma (Fig. 1).

The woman was admitted to hospital for parathyroid surgery. During exploration of the neck, an 8 mm

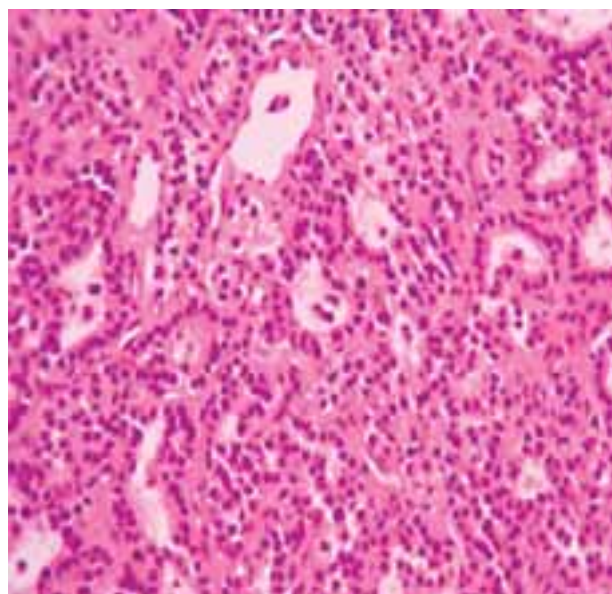


Figure 2. Microscopic appearance of the tumour, showing parathyroid tissue composed of uniform cells with eosinophilic granular cytoplasm, supported by abundant vascular stroma, scattered oxyphilic cells and foci of follicular structure containing a colloid-like material, also visible. Chief cell adenoma

Rycina 2. Mikroskopowy obraz guza przedstawiający tkankę przytarczycy złożoną z jednolitych komórek z eozynofilowymi ziarnistościami w cytoplazmie otoczonych przez podścielisko naczyniowe, rozproszone komórki oksyfilowe oraz ogniska struktur pęcherzykowych wypełnionych płynem koloidopodobnym

tumour was found in the inferior left parathyroid gland, and this was removed completely. The superior left parathyroid and both right parathyroid glands seemed to be normal. Intraoperative frozen section analysis confirmed the diagnosis of parathyroid adenoma. Final pathological diagnosis was the same (Fig. 2).

Postoperatively, investigations showed a decrease in serum calcium level to 7 mg/dl, phosphorus to 1.2 mg/dl and magnesium to 1.5 mg/dl, suggestive of hungry bone syndrome. Treatment was initiated with 4 g of calcium forte and 0.5 mcg of calcitriol daily.

The patient had an uneventful recovery and was discharged from hospital with an acceptable calcium level (8.5 mg/dl).

Discussion

Diagnosis of hyperparathyroidism is usually first suggested by the finding of an elevated serum calcium concentration, and if hypercalcaemia is confirmed by a repeated sample, all of its causes should be considered. The serum parathyroid hormone concentration should then be measured and the diagnosis of primary hyperparathyroidism (PHP) is usually made

by finding an inappropriately elevated serum parathyroid hormone (PTH) concentration associated with hypercalcaemia [1].

Turner's Syndrome is the most common cause of short stature in otherwise healthy girls other than familial short stature or constitutional delay of growth and maturity. It is unclear whether patients with TS have an increased risk of osteoporosis or fractures [2–5]. Their bones appear osteopenic on radiographic evaluation and their regional bone mass is often, but not always, below that of age-matched, but not height-matched, controls [4].

The causes of low bone mass density (BMD) in TS consist of hypogonadism-induced osteoporosis, osteomalacia (especially in countries where vitamin D deficiency is more prevalent) and rarely PHP. It seems that the presence of normocalcaemia in our patient had been related to the coincidence of osteomalacia and underlying PHP, a stage which may be referred to as *normocalcaemic hyperparathyroidism*. After initiation of calcium and vitamin D, the patient's serum calcium level increased as a result of the prominence of PHP (*hypercalcaemic hyperparathyroidism*).

A review of the literature indicates that a coincidence of PHP and TS is very rare. We searched PubMed with related key words of "primary hyperparathyroidism," "Turner syndrome" and "bone disease." In 1993 a case of PHP due to parathyroid adenocarcinoma in a patient with TS was reported by Chen JF et al. [6]. This was a 45-year-old woman who presented with primary amenorrhoea and poor development of secondary sexual characteristics and had experienced repeated bone fractures, weight loss and associated thyrotoxicosis. She underwent parathyroid surgery. In 1996 Francois et al. reported a case of TS with nephrolithiasis and hypercalcaemia [7]. In 2003, Kishida et al. reported a 46-year-old female with TS and hyperparathyroidism admitted to hospital because of severe hypercalcaemia. During medical treatment she died of acute necrotising pancreatitis [8].

The question is now raised as to whether TS with signs and symptoms of osteomalacia and normocalcaemia needs to be followed to rule out PHP. We recommend that serum calcium levels should be monitored in a patient with TS and normocalcaemia during treatment of osteoporosis or osteomalacia.

Conclusion

Our patient with a primary diagnosis of osteomalacia was initially treated by calcium and vitamin D supplements. Despite treatment, serum calcium was raised in follow-up. This is an unusual finding during the treatment of osteomalacia and its presence should signal the probability of underlying hyperparathyroidism and the need for further evaluation. The case presented here would seem to be noteworthy, not only for the rarity of the association of Turner's syndrome and hyperparathyroidism, but also for the overlap of bone disease in both disorders. It should be mentioned that during treatment for osteoporosis or osteomalacia in a patient with Turner's syndrome serum calcium levels should be detected and followed. In the event of serum calcium rising with treatment, the presence of an underlying hyperparathyroidism should always be considered, rare though this association may be.

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