

CASE REPORT

# Tertiary Hyperparathyroidism Secondary to X-linked Hypophosphatemic Rickets

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## ABSTRACT

Tertiary hyperparathyroidism is a rare complication of X-linked hypophosphatemic rickets. The surgical treatment is already unclear.

**Keywords:** Hyperparathyroidism, Parathyroidectomy, X-linked hypophosphatemic rickets.

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## INTRODUCTION

X-linked hypophosphatemic rickets (XLHR) is the most common heritable hypophosphatemic disorder.<sup>1</sup> It results from the combination of impaired renal tubular resorption of phosphate and abnormal vitamin D regulation in the kidney.<sup>2</sup> It is associated with inactivating mutations of the Phosphate regulating endopeptidase homolog, X-linked gene, that encodes a transmembrane endopeptidase, to reduce FGF 23. An increased level of FGF 23 may be responsible for the hyperphosphaturia or low calcitriol levels and skeletal mineralization disorders.<sup>3</sup>

Medical treatment consists of large doses of oral inorganic phosphate and vitamin D supplements,<sup>4</sup> although long-term treatment may lead to nephrocalcinosis and secondary to tertiary hyperparathyroidism.

## CASE REPORT

A 24-year-old female with XLHR was diagnosed at the age of 14 and she had undergone two corrective osteotomies. She was exposed to long-term oral vitamin D and phosphate supplementation, developing nephrocalcinosis diagnosed by ultrasound without clinical disorders. She

developed a tertiary hyperparathyroidism with persistent elevation in both serum calcium and parathyroid hormone (PTH) levels at the age of 23.

Two parathyroid imaging with 99m-Tc-Sestamibi scintigraphy revealed a hyperfunctioning left side parathyroid gland.

Prior to surgical intervention, she was treated with cinacalcet and vitamin D supplements to avoid postoperative hungry bone syndrome (HBS), with PTH levels decreased 200 pg/mg and serum calcium levels <10 mg/dL.

The patient underwent bilateral cervical exploration. Intraoperative findings were not correlated with preoperative imaging, with four large orthotopic parathyroid glands, with a particularly large gland in left superior gland.

We performed a total parathyroidectomy with autotransplant in the nondominant forearm, getting a decrease in intraoperative PTH levels to 12 pg/mL.

The pathologic examination results describe all four parathyroid glands as enlarged (weight of: Left superior gland 910 mg, left inferior gland 230 mg, half right superior gland 30 mg, and right inferior gland 90 mg).

She developed clinical and analytical postoperative hypocalcemia for which she was treated with oral calcium treatment and was maintained on an IV calcium infusion.

She was discharged on postoperative day 7 asymptomatic with oral supplements.

Six months postoperatively, her PTH levels increased with normal calcium and phosphate levels and normal 99m-Tc-Sestamibi scintigraphy. She was managed increasing calcitriol doses and adding oral magnesium. At follow-up, she remained asymptomatic and PTH levels were normal 9 months later, being possible to reduce the calcium and vitamin D. After 3 years, she is still asymptomatic and controlled with small doses of vitamin D, magnesium, and phosphate.

## COMMENTARY

Tertiary hyperparathyroidism secondary to XLRH is a rare complication associated with long-term administration of calcitriol and phosphate salts.

The role of preoperative parathyroid localization including 99m-Tc-sestamibi Single photon emission computed tomography imaging and parathyroid ultrasound is unclear, and its efficacy has been questioned.

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Intraoperative PTH decreasing >50% after 10 minutes is highly predictive of successful surgical treatment.<sup>5-6</sup> In our case, the PTH level dropped from 176 pg/mL to 12 pg/mL.

The surgical treatment is already unclear, but it is the only effective treatment. The gold standard is neck exploration with identification and excision of abnormal parathyroid tissue, taking a decision with intraoperative findings.

A review of the previously reported cases (Table 1)<sup>5,7-13</sup> shows us the different treatments, the recurrence, complications, and hospital stay.

The literature presents the resection of a single or double adenoma as an effective treatment, but many authors defend that subtotal parathyroidectomy is neces-

sary for operative cure.<sup>14-19</sup> The largest series of surgical management of tertiary hyperparathyroidism associated with XLHR contains six patients: Three had total parathyroidectomy, two had three parathyroid glands resected, one of them required completion parathyroidectomy for recurrent disease, and one had two abnormal parathyroid glands resected, dying in the follow-up.<sup>13</sup>

The size of the resected parathyroid tissue maybe is a predictor of the HBS in patients with XLHR after parathyroidectomy

Surgical management of tertiary hyperparathyroidism secondary to XLHR is still unclear, but it is mandatory for a thorough neck exploration.

**Table 1:** Previous cases/series presenting tertiary hyperparathyroidism secondary to X-linked hypophosphatemic rickets

Article	Surgery/Pathologic results	Hypocalcemia	Recurrence	Complications	Hospital stay (d)
Crowley et al <sup>10</sup>	Total hyperparathyroidectomy	Yes			160
Savio et al <sup>7</sup>	+2 gland-excision (2 adenomas)	Yes	No	Died of intracranial hemorrhage 8 mo postoperatively	10
	3 gland-excision and righthemithyroidectomy (3-gland hyperplasia)	No (Yes)	Yes	No	2 (+6)
	Total parathyroidectomy with autotransplant (1 adenoma/3-gland hyperplasia)	Yes	No	No	16
	Total parathyroidectomy, thyroidectomy and thymectomy (4-gland hyperplasia)	Yes	No	No	2
	Total parathyroidectomy and left hemithyroidectomy (5-gland hyperplasia)	No	No	Wound infection	6
	3 gland parathyroidectomy and thymectomy (3-gland hyperplasia)	Yes	No	No	9
Vázquez et al <sup>8</sup>	1 gland excision previously 1 gland excision and 1 biopsy no patologic	Yes	Yes	Died of renal dysfunction 6 years postoperatively	
Moreno Molina et al <sup>9</sup>	(1 adenoma + 1-gland hyperplasia)	No			
Neal et al <sup>5</sup>	Subtotal parathyroidectomy (4-gland hyperplasia)	Yes			6
Tournis et al <sup>11</sup>	Subtotal parathyroidectomy (4-gland hyperplasia)	No			
Alon et al <sup>12</sup>	Total parathyroidectomy with autotransplant (4-gland hyperplasia)	Yes			
Mäkitie et al <sup>13</sup>	Subtotal parathyroidectomy (hyperplasia)				

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