


## CASE REPORT

# Hyperparathyroidism: Unusual location of brown tumors

Alia Fazaa<sup>1,2</sup> | Yasmine Makhoul<sup>1,2</sup>  | Soussen Miladi<sup>1,2</sup> | Mariem Sellami<sup>1,2</sup> |  
Kmar Ouenniche<sup>1,2</sup> | Leila Souebni<sup>1,2</sup> | Selma Kassab<sup>1,2</sup> | Selma Chekili<sup>1,2</sup> |  
Kawther Ben Abdelghani<sup>1,2</sup> | Ahmed Laatar<sup>1,2</sup>

<sup>1</sup>Department of Rheumatology, Mongi Slim Hospital, La Marsa, Tunisia

<sup>2</sup>University Tunis El Manar, Tunis, Tunisia

## Correspondence

Yasmine Makhoul, Department of Rheumatology, Mongi Slim Hospital, Sidi Daoued, La Marsa 2046, Tunisia.  
Email: yasmine.mkhoul@gmail.com

## Funding information

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

## Abstract

Brown tumors (BTs) are due to a proliferation of multinucleated giant cells in osteolytic lesions. They complicate the course of hyperparathyroidism. Thanks to an early screening of bone metabolism disorders; BTs are nowadays rare bone manifestations. We demonstrate through these two cases reports unusual locations of BTs in hyperparathyroidism.

## KEYWORDS

brown tumors, hyperparathyroidism, hyperplasia, osteoporosis

## 1 | INTRODUCTION

Hyperparathyroidism (HPT) is an endocrine disorder characterized by the secretion of the parathyroid hormone (PTH).<sup>1</sup> This systemic disease is due to lesions in the parathyroid gland, responsible for hypercalcemia and bone metabolism disorders.<sup>1</sup> Knowledge of the classic patterns of HPT can aid in distinguishing this disorder from other forms of metabolic bone diseases, but more importantly, in preventing its severe complications. Initially described in 1891 by Von Recklinghausen, brown tumors (BTs) also called osteitis fibrosa cystica, result from an increase in osteoclastic bone resorption due to a prolonged and elevated circulating PTH.<sup>2,3</sup> These lesions are particularly challenging to diagnose and to differentiate from other tumors, especially when located in the oral cavity.<sup>4</sup> Thanks to early diagnosis and more accurate control of HPT; the incidence of bone manifestations, mainly BTs, has lowered (<10%).<sup>2</sup> Herein, we report two cases of multiple

BTs complicating the course of primary and secondary hyperparathyroidism.

## 2 | CASES

### 2.1 | Case 1

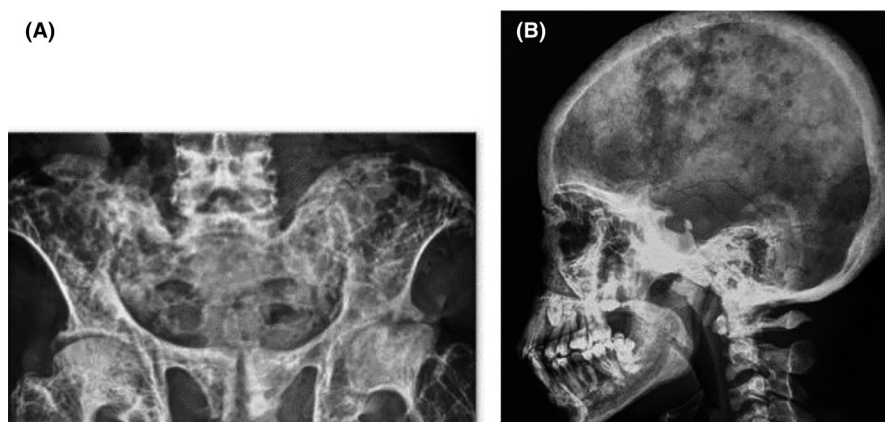
A 42-year-old woman, with no previous medical or surgical history, complained of inflammatory back pain evolving for 1 year, refractory to non-steroidal anti-inflammatory drugs. She did not experience lethargy or fatigue. Her appetite and weight were stable. Physical examination was normal except for tenderness of the lumbar spine and gingival hypertrophy (Figure 1). Moreover, the neurological examination did not show any abnormalities. She had a laboratory and spine computed tomography (CT) requested by her primary care provider. The lumbar CT showed a lytic mass of the sacrum invading

This is an open access article under the terms of the Creative Commons Attribution NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.



**FIGURE 1** A clinical picture showing (A): mandibular deformity, (B): a gingival hypertrophy



**FIGURE 2** (A): X-ray of the hip showing lytic lesions, (B): X-ray of the head showing salt and pepper appearance

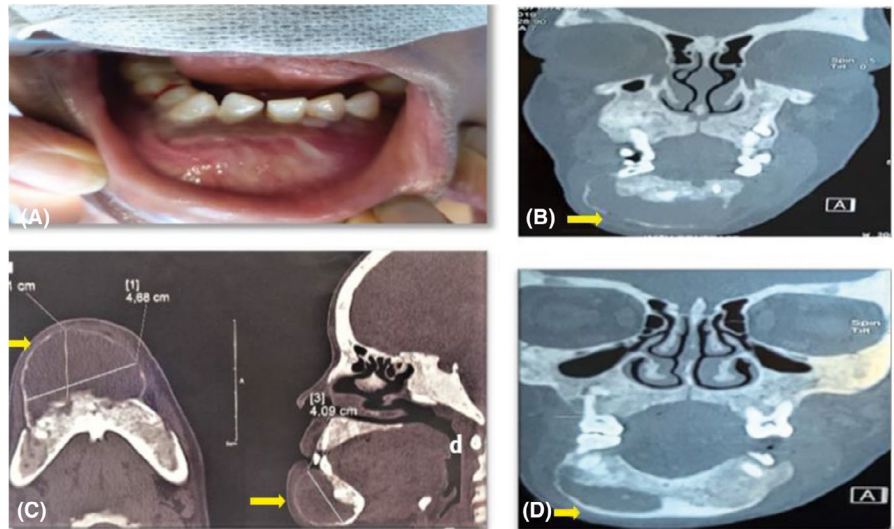
the lumbar canal and pushing back the dural sheath with multiple lesions of the pelvis. The serum calcium level (adjusted for albumin) was 3.08 mmol/L. She had neither clinical symptoms of hypercalcemia nor abnormalities on the electrocardiogram. She was admitted urgently for the management of her hypercalcemia as well as the investigation of bone metastasis of unknown primary origin. A whole-body CT was performed and revealed in addition to the lesions of the sacrum, lytic lesions of the ramus of the right mandible, as well as a left inferior cervical mass consistent with a parathyroid adenoma. Initial blood workup revealed normal acute phase reactants and serum electrophoresis. The serum calcium and phosphorus concentrations were 2.91 mmol/L and 0.77 mmol/L, respectively. The serum PTH concentration was 585 pg/ml (reference range: 14–65 pg/ml) and the phosphatase alkaline level was estimated at 790 UI/L (reference range: 40–129 UI/L). After ruling out the causes of malignancy, the patient was finally diagnosed with primary hyperparathyroidism (PHPT); with multiple brown tumors in the mandible and sacrum. A full workup was carried out which included a sestaMIBI imaging with technetium 99m, a neck ultrasound, that confirmed the parathyroid adenoma. The bone mineral density revealed osteoporosis with a T-score of  $-3.3$  at the femoral site and  $-2.4$  at the vertebral site. X-ray investigations showed acroosteolysis, salt, and pepper appearance (Figure 2B) and the dental panoramic showed

alveolysis. The patient underwent parathyroidectomy. The abnormal parathyroid gland was excised. Parathyroid adenoma was diagnosed by intraoperative frozen section pathological examination and confirmed by postoperative pathology. At follow-up, the patient did not complain of low back pain. In biology, the serum calcium concentration decreased to 2.10 mmol/L.

## 2.2 | Case 2

We report the case of a 35-year-old woman with end-stage renal disease due to chronic tubulointerstitial nephropathy. She presented with myalgia, diffuse bone pain, as well as an increasing swelling of the jaw that has worsened in the past few months. On examination, her gait was impaired. She had a mandibular deformity at chin level measuring  $5 \times 6$  cm and was hard on palpation, fixed to the tissues underneath, and free from overlying skin. Intraoral examination showed a rounded mass at the level of the anteroinferior gingivolabial sulcus. Subsequent blood analysis demonstrated the PTH level to be 2200 pg/ml (normal range: 11–69 pg/ml). Serum calcium was 2.20 mmol/L and serum phosphate was 1.85 mmol/l (0.7–1.8 mmol/L). Head CT showed cystic expansive lesions in the mandible symphysis (Figure 3). Ultrasonography and sestaMIBI scintigraphy with Technetium-99m confirmed

**FIGURE 3** (A): clinical picture: right jaw swelling with dental malalignment, (B–D): enhanced computer tomography scan of the brown tumor within the mandible (yellow arrows): (B, D) Coronal and (C) axial



the existence of hyperplastic parathyroid glands. X-ray investigations showed multifocal well-defined soap-bubbly appearing lytic lesions in the iliac crest as well as “rugger jersey spine” (Figure 4). The diagnosis of secondary hyperparathyroidism (SHPT) with brown tumors in the mandible and the iliac crest was made. In peroperative, we noticed hypertrophy of the four glands. The patient underwent a 7/8 parathyroidectomy. The intraoperative PTH dropped from the initial pre-excision level to 400 ng/ml 10 min after their removal. The patient recovered well and was discharged after 1 week. Regarding the mandibular lesion, a follow-up was planned and surgery will be considered if there is no improvement in the size of the BT.

### 3 | DISCUSSION

We reported two cases of HPT caused by a parathyroid adenoma (case 1) and hyperplasia in the context of renal dystrophy (case 2), respectively. PHPT is an endocrine disorder due to an excessive synthesis and secretion of PTH by one or more of the four parathyroid glands.<sup>5</sup> Parathyroid adenoma accounts for approximately 80% of cases of PHPT, while gland parathyroid hyperplasia is seen in 15–20% of cases. Rarely (<1%), PHPT can be caused by parathyroid carcinoma.<sup>6</sup> In contrast, secondary HPT complicates the course of Vitamin D deficiency or chronic renal failure. The incidence rate of PHPT varies from 34 to 120 cases per 100,000 individuals and is more frequent among early postmenopausal women, coincident with the loss of estrogen.<sup>7</sup> The increasing incidence is thought to be due to earlier diagnosis and regular evaluations of calcium; thus, most of the patients are asymptomatic.<sup>8</sup> However, in developing countries where screening of this condition is less frequent, the clinical profile of PHPT is highly symptomatic with skeletal and renal manifestations.<sup>5</sup> In the literature, bone manifestations rarely reveal

the disease since they appear at a later stage. The most frequent features are diffuse osteopenia, subperiosteal bone resorption, fractures, or multiple circumscribed lytic lesions also called BTs.<sup>9</sup>

In our cases, the predominant bone manifestation was the BT. The latter constitutes a vascularized tissue repair replacement of the resorbed bone.<sup>2</sup> The reported incidence of BTs was 1.6% and 3% in SHPT and PHPT, respectively.<sup>2</sup> Their topography can be mono or polyostotic as in our two patients. BTs frequently affect the facial bones, pelvis, ribs, femurs, and other long bones with a lesser extent the axial skeleton.<sup>10</sup> In our case, the mandibular location was reported in both patients. A recent systematic review by Lajolo et al. identified 167 cases of oral BTs of the mandible, accounting for 70.1% of the cases.<sup>4</sup> Another important finding is that when BTs are located in the maxilla, there is a high probability of multiple, extraoral maxillofacial BTs.<sup>4</sup>

On imaging, BTs are described as geographically contoured lytic lesions, usually well limited, eccentric, or cortical, without sclerosis with occasional thinning, blowing, and rupture of the cortex.<sup>9</sup> This pseudometastatic appearance can be misleading, especially when it is the first manifestation of the disease. This atypical presentation with an appearance mimicking secondary lesions was encountered in our first patient. Another differential diagnosis to consider is other giant cell lesions central giant-cell granuloma (CGCG), peripheral giant-cell granuloma (PGCG), Langerhans cell histiocytosis, and initial stages of cherubism.<sup>5,11–14</sup> As the management of these conditions is different, it is important to distinguish between them. Laboratory results differ between the different types of HPT. PHPT has usually high serum calcium levels with low or normal phosphorus. In the second case, calcemia was within the lower range concordant with a SHPT profile. Regarding bone imaging findings, PHPT and SHPT may overlap; however, the osteosclerotic effect on the axial



**FIGURE 4** X-ray of the lumbar spine showing a rugger jersey spine

skeleton also known as “rugger-jersey spine” is specific to the SHPT.<sup>9</sup> Regarding treatment management, the definitive cure of PHPT is the surgical removal of the hyperfunctioning parathyroid tissue. Surgery usually reverses clinical symptoms, biochemical abnormalities, as well as bone mineral density.<sup>2</sup> The treatment of BTs is based on the management of the underlying etiology. However, in some cases, the curettage of the lesion is necessary.<sup>15</sup> Indeed, spontaneous regression may occur in smaller lesions as well as in young patients.<sup>4</sup>

## 4 | CONCLUSION

We report unusual locations of BTs revealing HPT. Through these two observations, we highlight the importance of early diagnosis in order to prevent severe bone disease.

## ACKNOWLEDGEMENTS

None.

## CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## AUTHOR CONTRIBUTIONS

All authors contributed toward data analysis, drafting, and critically revising the paper and agree to be accountable for all aspects of the work.

## CONSENT

Written consent was obtained from the patients.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

## ORCID

Yasmine Makhoulf  <https://orcid.org/0000-0001-8788-0626>

## REFERENCES

- Walker MD, Silverberg SJ. Primary hyperparathyroidism. *Nat Rev Endocrinol.* 2018;14:115-125.
- Dos Santos B, Koth VS, Figueiredo MA, Salum FG, Cherubini K. Brown tumor of the jaws as a manifestation of tertiary hyperparathyroidism: a literature review and case report. *Spec Care Dentist.* 2018;38(3):163-171.
- Guney E, Yigitbasi OG, Bayram F, Ozer V, Canoz Z. Brown tumor of the maxilla associated with primary hyperparathyroidism. *Auris Nasus Larynx.* 2001;28:369-372.
- Lajolo C, Patini R, Limongelli L, et al. Brown tumors of the oral cavity: presentation of 4 new cases and a systematic literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2020;129(6):575-584.e4.
- Silva BC, Cusano NE, Bilezikian JP. Primary hyperparathyroidism. *Best Pract Res Clin Endocrinol Metab.* 2018;32(5):593-607.
- Shetty AD, Namitha J, James L. Brown Tumors of mandible in association with primary hyperparathyroidism: a case report. *J Int Oral Health.* 2015;7:50-52.
- Griebeler ML, Kearns AE, Ryu E, et al. Secular trends in the incidence of primary hyperparathyroidism over five decades (1965–2010). *Bone.* 2015;73:1-7.
- Wang Y, Liu J. Severe bone disease caused by primary hyperparathyroidism: a case report and review of the literature. *J Int Med Res.* 2020;48(10):300060520966484.
- Bennett J, Suliburk JW, Morón JE. Osseous manifestations of primary hyperparathyroidism: imaging findings. *Int J Endocrinol.* 2020;10:1-10.
- Agnihotri M, Kothari K, Naik L.  $\Omega$  Brown tumor of hyperparathyroidism. *Diagn Cytopathol.* 2017;45(1):43-44.
- Duarte AP, Gomes CC, Gomez RS, Amaral FR. Increased expression of NFATc1 in giant cell lesions of the jaws, cherubism and brown tumor of hyperparathyroidism. *Oncol Lett.* 2011;2(3):571-573.
- Moskovszky L, Idowu B, Taylor R, Mertens F, Athanasou N, Flanagan A. Analysis of giant cell tumour of bone cells for Noonan syndrome/cherubism-related mutations. *J Oral Pathol Med.* 2013;42(1):95-98.
- Facciolo MT, Riva F, Gallenzi P, Patini R, Gaglioti D. A rare case of oral multisystem Langerhans cell histiocytosis. *J Clin Exp Dent.* 2017;9(6):e820-e824.

14. Lomoro P, Simonetti I, Vinci G, et al. Secondary aneurysmal bone cyst in Langerhans cell histiocytosis: case report, literature review. *Eur J Radiol Open*. 2019;6:97-100.
15. Triantafillidou K, Zouloumis L, Karakinaris G, Kalimeras E, Iordanidis F. Brown tumors of the jaws associated with primary or secondary hyperparathyroidism. A clinical study and review of the literature. *Am J Otolaryngol*. 2006;27(4):281-286.

**How to cite this article:** Fazaa A, Makhoulf Y, Miladi S, et al. Hyperparathyroidism: Unusual location of brown tumors. *Clin Case Rep*. 2022;10:e05376. doi:[10.1002/ccr3.5376](https://doi.org/10.1002/ccr3.5376)