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DIFFICULTIES OF CASE MANAGEMENT: GIANT PARATHYROID ADENOMA WITH CYSTIC APPEARANCE AND PRESENTATION AMID COVID-19 PANDEMIC

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Primary hyperparathyroidism (PH) – related parathyroid tumours, usually adenomas (regardless typical or atypical, solid or with cystic transformation) with a good outcome after surgical removal, might embrace the entire area of complications due to high parathormone (PTH) – related hypercalcemia, and rarely local compressive complications, since adenomas are usually of small dimensions. We introduce a challenging adult male case with a large parathyroid tumour who was admitted during the first year of COVID-19 pandemic. A 58-year old, non-smoking male patient was admitted as an emergency for a large anterior cervical mass in July 2020. Despite local compressive symptoms, he delayed the presentation due to pandemic circumstances. Blood tests revealed normal renal and liver function and high calcium. Bone metabolism exploration confirmed PH and high turnover status. Anterior cervical ultrasound revealed a posterior hypoechoic mass to the right thyroid lobe of very large dimensions (by 10/8.54/4.85 cm), with inhomogeneous consistence (both solid and cystic pattern with a cystic predominance), a tumour that is well shaped and has mass effect (left tracheal deviation). After fluid replacement and 5 mg zolendronic acid to correct hypercalcemia, upper right parathyroidectomy was done. The confirmation of a giant parathyroid adenoma (40 g) with cystic transformation (a total of 170 g) was done. The patient had a good clinical evolution for the following year when he was re-assessed; normal calcium levels were maintained as well as an improvement of bone mineral density parameters according to central DXA (Dual -Energy X-Ray Absorptiometry). Challenges of the case management include late presentation, most probably amid pandemic burst, the fact that a giant parathyroid tumour is expected to be a carcinoma or have some atypia (which were not confirmed), the cystic transformation that contributed to increased size and more difficult surgery, and the question if such an impressive parathyroid tumour is actually on the ground of a genetic anomaly as seen in familial PH.

Keywords: *parathyroid, adenoma, tumour, endocrine, giant, calcium, parathormone, parathyroidectomy, bone turnover marker, osteoporosis*

INTRODUCTION

Primary hyperparathyroidism (PH) related parathyroid tumours, usually adenomas (regardless typical or atypical, solid or with cystic transformation) with a good outcome after surgical removal, might embrace the entire area of complications due to high parathormone (PTH) related hypercalcemia, and rarely local compressive complications, since adenomas are usually of small dimensions (1-10). Tumours arising from parathyroid glands are either sporadic or hereditary in familial syndromes that include isolated PH or multiple endocrine neoplasia, also associating thyroid carcinomas, adrenal or pituitary tumours and neuroendocrine neoplasia (11-20).

AIM

We introduce a challenging adult male case with a large parathyroid tumour who was admitted during the first year of COVID-19 pandemic.

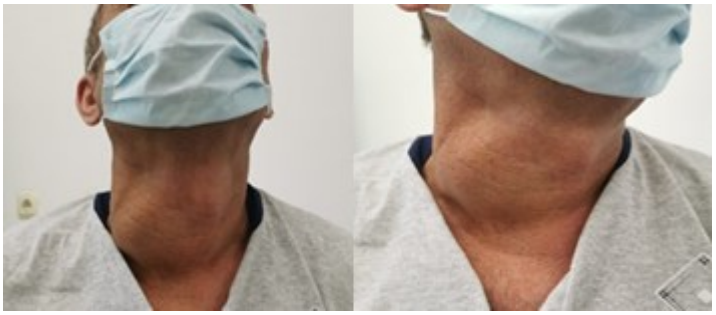
METHOD

This is a case report. The patient agreed for the use of his medical records including photos.

CASE PRESENTATION

A 58-year old, non-smoking male patient was admitted as an emergency for a large anterior cervical mass in July 2020. Despite local compressive symptoms, he delayed the presentation due to pandemic circumstances. On admission, clinical presentation was irrelevant, except for the large neck tumour **(Figure 1).**

Figure 1. Large anterior neck tumour on a 58-year old male admitted during the first year of COVID-19 pandemic



The patient had a visible right-sided neck mass with gradual increase in volume within the last 2 years, with compression phenomena like dysphagia, dyspnoea on decubitus (accentuated within the last 3 months). Blood tests revealed normal renal and liver function and high calcium **(Tables 1,2).** Bone metabolism exploration confirmed PH and high turnover status **(Table 2).** Normal thyroid and adrenal profile is confirmed.

Anterior cervical ultrasound revealed a posterior mass to the right thyroid lobe of very large dimensions (by

Table 1. Biochemistry panel on a 58-year old male who was admitted with a large anterior cervical mass amid first year of COVID-19 pandemic

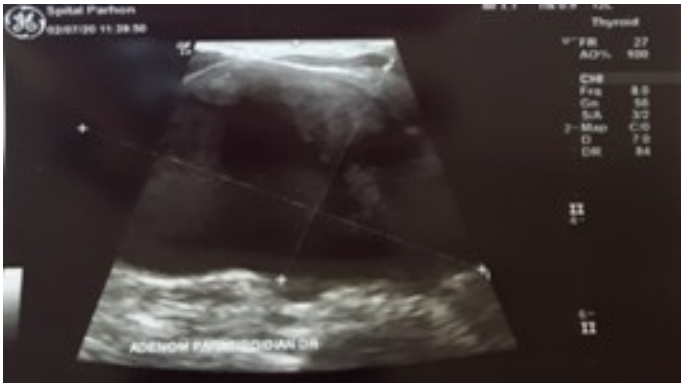
Parameter	Value July 2020	Value July 2021	Normal ranges	Units
ALT (aminotransferase)	21.5	37	0-41	U/L
AST (alanine aminotransferase)	21.1	28	0-38	U/L
Fasting glycaemia	95.7	99.4	70-110	mg/dL
Total cholesterol	**226.2**	**236.5**	0-200	mg/dL
HDL-cholesterol	55.7	52.1	35-55	mg/dL
LDL-cholesterol	148	161	60-160	mg/dL
Triglycerides	113	117.8	113.6	mg/dl
Potassium	4.8	5.06	3.5-5.1	mmol/L
Sodium	142	144	136-145	mmol/L
Total proteins	7	6.6	6.5-8.7	g/dL
Uric acid	**7.6**	**9.5**	3.5-7	mg/dL
Urea	39.1	37.3	15-50	mg/dL
Creatinine	1.25	1.22	0.5-1.2	mg/dL

Table 2. Bone metabolism evaluation on a 58-year old male admitted for a large parathyroid tumour, consistent with primary hyperparathyroidism status

Parameter	Value July 2020	Value July 2021	Normal ranges	Units
Ionic serum calcium	**5.3**	4.01	3.9-4.9	mg/dL
Total serum calcium	**12.1**	8.8	8.4-10.2	mg/dL
Serum phosphorus	**1.9**	2.3	2.3-4.7	mg/dL
24-hour urinary calcium	**0.46**	0.17	0.07-0.3	g/ 24-h
Serum magnesium	2.15	2.11	1.6-2.6	mg/dL
25OHD (25-hydroxyvitamin D)	**17.2**	26.4	30-100	ng/mL
ALP (alkaline phosphatase)	**209**	**21.14**	38-129	U/L
P1NP	NA	21.14	20.25-76.31	ng/mL
Osteocalcin	**253.9**	16.60	14-46	ng/mL
CrossLaps	**2.81**	0.120	0.104-0.504	ng/mL
PTH (parathormone)	**548.2**	62.09	15-65	pg/mL

NA=not available

Figure 2. Anterior cervical ultrasound on a 58-year old male revealing a large parathyroid tumour (hypoechoic pattern with solid and cystic components at right superior parathyroid gland)



10/8.54/4.85 cm), with hypoechoic, inhomogeneous consistence (both solid and cystic pattern with a cystic predominance), a tumour that is well shaped and has mass effect (left tracheal deviation) **(Figure 2).**

Computed tomography (CT) scan of the neck confirmed the presence of a large tumour of the right superior parathyroid (para-traheal and para-oesophageal region), with extension to the superior mediastinum, with predominantly cystic structure, of (overall) 9.18/4.68/7.64 cm **(Figure 3).**

CASE MANAGEMENT

Hypercalcemia, as a medical emergency, was treated with intravenous fluids and 5 mg intravenous zolendronic acid with a reduction of calcium levels within days, thus the patient underwent parathyroidectomy with focused exploration and excision of the superior right parathyroid adenoma under general anaesthesia. The surgery was challenging due to the gigantic tumour volume and its posterior position, and the tumour' adhesion to the oesophageal serosa (and associated risk of oesophageal perforation during surgical manipulation). The right thyroid lobe was also compressed while the location of the recurrent nerve was difficult. During the operation, the giant parathyroid tumour with mixed content cervico-mediastinal was identified and excised **(Figure 4).**

Figure 3. Computer tomography scan of the neck and mediastinum with intravenous contrast showing a large right upper parathyroid tumour of 9.18/4.68/7.64 cm on a 58-year old male admitted for local compressive symptoms due to recent tumour growth

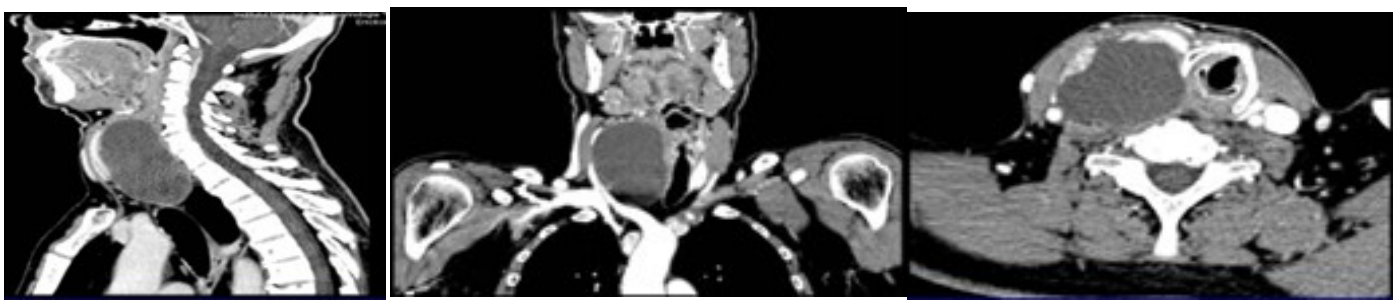


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Figure 4. Giant parathyroid adenoma identified intraoperatively

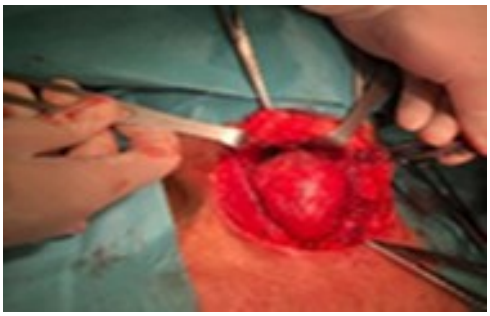
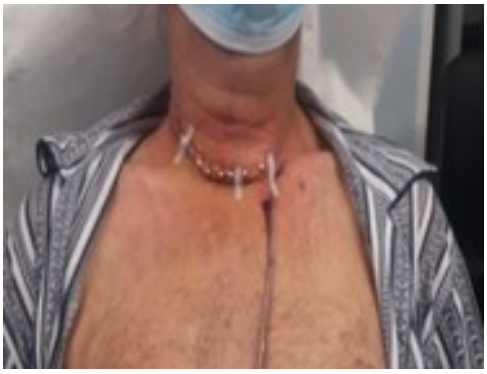


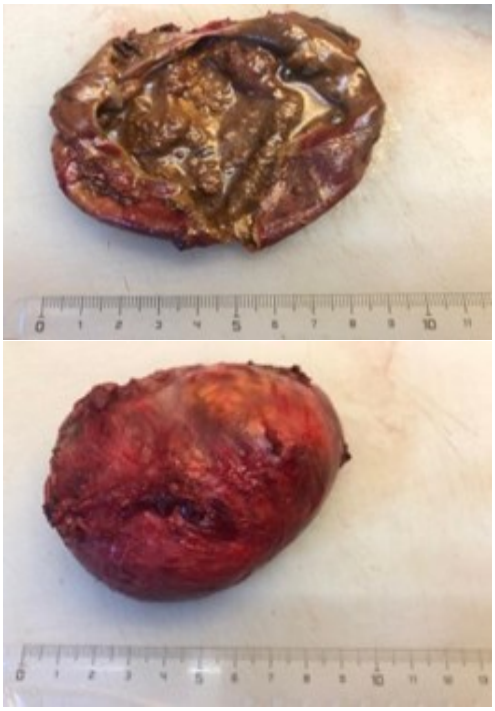
Figure 5. Post-operatory aspect of the 58-year old patient who suffered an upper right parathyroidectomy



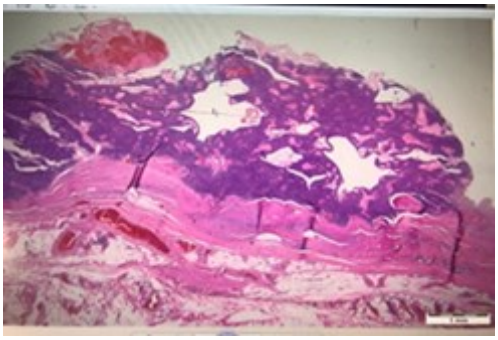
The patient was discharged few days later under good clinical condition, with normocalcemia and normal PTH under calcium and vitamin D supplementation **(Figure 5).**

Histological report confirmed a parathyroid adenoma without atypical aspects (or elements of parathyroid carcinoma). Macroscopic features are solitary, oval-shaped, brown tumour with a thin, slightly irregular capsule, a weight of 170 grams (40 grams consistent with the solid mass and 130 grams of liquid) **(Figure 6).**

Figure 6. Giant right superior parathyroid adenoma with cystic transformation A. Macroscopic aspect



B. Microscopic aspect showing proliferation of main cells and cystic (post-haemorrhagic) transformation



The patient had a good clinical evolution for the following year when he was re-assessed; normal calcium levels were maintained as well as an improvement of bone mineral density parameters according to central DXA (dual-energy X-ray absorptiometry); no vertebral fractures were identified at profile X-Ray of the lumbar spine **(Table 3).**

DISCUSSION

Challenges of the case management include late presentation, most probably amid pandemic burst, the fact that a giant parathyroid tumour is expected to be a carcinoma or have some atypia (aspects that were not confirmed), the cystic transformation that contributed to increased size and more difficult surgery, and the question if such an impressive parathyroid tumour is actually on the ground of a genetic anomaly **(Figure 7).**

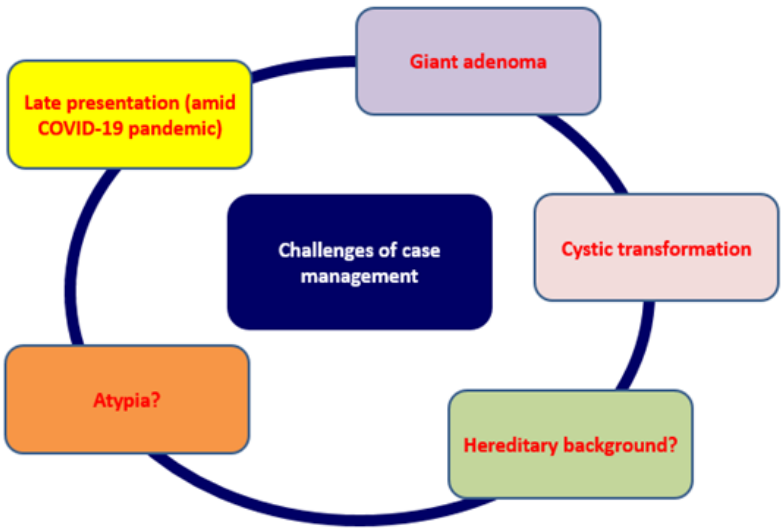
This male patient was admitted a few months after the pandemic restrictions were introduced; he was afraid to come to a hospital while his compressive symptoms were aggravating. Nevertheless, late presentation for endocrine and non-endocrine conditions was frequently registered especially during the first wave of COVID-19 pandemic and it represented a general medical and social topic of concern; also, the burden of telemedicine cannot include newly detected thyroid and parathyroid tumours with consistent mass effect (21-30). In general endocrine practice, a large anterior neck mass (for instance, a recently growing tumour) rather belongs to the thyroid (thyroid cancers, but also multinodular goitre) than to the parathyroid glands which is an exceptional presentation as here (31-40). Giant parathyroid tumour involves a more difficult procedure of parathyroidectomy than seen in cases with smaller tumours; also cystic transformation and potentially the presence of hypovitaminosis D were contributors to the challenging intervention (41-49). Interestingly, our subject did not have other typical complications of PH like kidney stones, neither high blood pressure; most data sustain the idea that the dimensions of the parathyroid tumour is a not predictor of PH-related complications; but a correlation with PTH levels is expected (50-55). Our patient had low bone mineral density for his age which was corrected under annual injection of zolendronic acid 5 mg, a drug that turned out to be useful for initial hypercalcemia which required a certain correction before surgery. Secondary osteoporosis is more frequent in menopausal females; in healthy males with PH, post-operatory normalization of PTH might be sufficient to consistently improve DXA results, making unnecessary the continuation of anti-osteoporotic therapy with bisphosphonates or denosumab (55-60). Our patient had high osteocalcin and CrossLaps at first diagnostic which decreased to normal after one year. Moreover, the fact that the patient did not actually experienced severe post-operatory hypocalcemia was an indicator of a potential hyperplasia of parathyroid glands or synchronous adenomas (which was re-named by WHO in 2022 PH-related multinodular parathyroid disease) on a genetic background, a scenario that was finally not confirmed by the assessments of the other endocrine

Table 3. DXA scan on admission and after one year since the administration of 5 mg zolendronic acid and upper right parathyroidectomy

Year	Regions	BMD (g/sqcm)	Z-score (SD)	T-score (SD)
2020 (first admission for large neck tumour)	lumbar L1-4	0.857	-2.2	-3
	femoral neck	0.791	-0.9	-2.1
	total hip	0.802	-1.3	-2.1
	1/3 distal radius*	0.444	-4.1	-4.5
2021 (after 1 year since parathyroidectomy)	lumbar L1-4	0.992	-1.2	-2.1
	femoral neck	0.860	-0.4	-1.6
	total hip	0.940	-0.4	-1.1
	1/3 distal radius*	0.475	-3.7	-4.1

**non-dominant arm*

Figure 7. Difficulties of this case management



glands and 1-year follow-up (3). As mention, normal prolactin and IGF-1 excluded a pituitary prolactin, respective growth hormone secreting adenoma, normal calcitonin excluded a medullary thyroid carcinoma while normal metanephrines and normetanephrines did not sustain the diagnostic of pheochromocytoma as seen in type 1, respective 2A multiple endocrine neoplasia (61-70). We did not test RET mutation. The patient family medical history was negative.

CONCLUSIONS

Giant parathyroid adenoma is very rare; late presentation due to pandemic circumstances might be correlated with cystic transformation and increased dimensions. Prompt surgical intervention of a skilled surgical team is required for a good outcome.

***Conflict of interest**: none*

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