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Parathyroid Lipoadenoma: a Clinicopathological Diagnosis and Possible Trap for the Unaware Pathologist

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Abstract The authors present clinicopathological features of parathyroid lipoadenoma in a 48-year-old woman who presented with symptomatic primary hyperparathyroidism manifesting with pathological fractures and osteoporosis. Preoperative sestamibi scan failed to localize the source of her disease. Exploratory surgery identified an enlarged parathyroid gland with abundant fat tissue. The significant drop of intraoperative serum parathyroid hormone after the removal of this gland and postoperative biochemical cure justified the presence of a single gland disease presenting as parathyroid lipoadenoma. From an educational perspective, the presented case emphasizes why the historical approach to parathyroid proliferations by assessing alone the ratio of parenchymal cells to adipocytes is not a reliable method in the diagnostic evaluation of parathyroid disease. While the accurate size and weight of a parathyroid gland are defining parameters of an abnormal gland, intraoperative and postoperative biochemical workup distinguishes uniglandular disease (adenoma) from multiglandular disease (hyperplasia). The authors also provide a brief review of the previously published cases of parathyroid lipoadenomas to highlight their clinicopathological characteristics of relevance to surgical pathologists.

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Introduction

Parathyroid adenomas are the main cause of primary hyperparathyroidism, accounting for an estimated 80–85 % of cases [1]. With the exceptions of uncommon double adenomas and multiglandular multiple adenomas identified in inherited hyperparathyroidism syndromes, parathyroid adenoma is defined as a single gland parathyroid disease accompanied by an increased size and weight of the affected gland [1]. While most cases show prominent cellularity along with depletion of adipose tissue, lipoadenoma is a rare variant of parathyroid adenoma that breaks one of those rules in that it has an abundant stromal adipose tissue causing an appearance of low cellularity that mimics normal parathyroid tissue [2]. The presence of fat also changes the imaging characteristics of this type of adenoma, making them more difficult to localize [2]. We present a case report of a functional parathyroid lipoadenoma to illustrate both of these points by reviewing the literature in order to provide a brief summary of the cases published so far in English literature.

Material and Methods

Case Report

A 48-year-old female patient suffered three fractures in the span of 7 years. She was evaluated by bone densitometry and was found to have generalized low bone density affecting

the lumbar spine (0.649 g/cm^2, T-score of −3.1, Z-score of −2.3), the left femoral neck (density of 0.557 g/cm^2, T-score of −2.3, Z-score −1.8), and left forearm (UD site density of 0.299 g/cm^2, T-score of −2.5, Z-score −2.0). The patient was diagnosed with osteoporosis and the underlying causes were investigated.

The laboratory tests have shown elevated ionized calcium of 1.39 mmol/L (normal, 1.12–1.32 mmol/L), normal osteocalcin at 4.1 μg/L (normal, 2.7–11.5 μg/L), normal vitamin B12 at 271 pmol/L (normal, 222–652 pmol/L), normal ALP at 67 U/L (normal, 40–150 U/L), elevated parathyroid hormone (PTH) at 14.1 pmol/L (normal, 1.3–7.6 pmol/L), and a negative Celiac disease screen (anti-TTG, anti-gliadin, anti-endomysial antibodies). She was diagnosed with primary hyperparathyroidism and was given a subcutaneous injection of anti-RANK ligand antibody denosumab (60 mg). Repeat bloodwork has shown calcium at 2.52 mmol/L, ionized calcium at 1.37 mmol/L, PTH at 6.2 pmol/L, and fasting PTH at 10.4 pmol/L.

Neck ultrasound failed to show parathyroid adenoma but a note was made of an echogenic area immediately inferior to the right lower pole of thyroid, that was thought to represent fat-infiltrated lymph node. Subsequent technecium-99m sestamibi planar and single photon emission computed tomographic scintigraphy (T99m SPECT CT) scans also failed to localize any sestamibi-avid lesions. Upper chest and neck CT failed to show any mediastinal or ectopic neck parathyroid lesions. In light of the negative imaging studies and persisting primary hyperparathyroidism exploratory surgery was performed and identified a 1.0×0.4×0.3 cm yellow lesion posterior to the right inferior pole of the thyroid. This lesion was sent for intraoperative consultation, which was reported as "enlarged parathyroid tissue with abundant fat. No hypercellularity noted." Unfortunately, the pathologist on call did not consider weighing this enlarged gland given the gross features resembling a lipoma. A baseline intraoperative serum PTH level was 10.45 pmol/L (normal, 1.3–7.6 pmol/L). PTH levels at 15 and 20 min after resection were 1.8 and 1.74 pmol/L, respectively. Since the intraoperative serum PTH level fell over 80 % after the removal of this enlarged gland, the surgeon did not proceed with further inspection and ended the surgery.

The final histological evaluation showed an enlarged parathyroid gland with nests of chief cells admixed with abundant adipocytes (Fig. 1). While the weight of this gland was unavailable, given the abnormal size of the gland and the significant drop of intraoperative PTH, the signing pathologist rendered the diagnosis of parathyroid lipoadenoma. Consistent with a single gland disease, biochemical cure was evidenced by postoperative PTH (1.2 pmol/L; normal, 1.3–7.6 pmol/L) and ionized calcium (1.24 mmol/L; normal, 1.12–1.32 mmol/L).

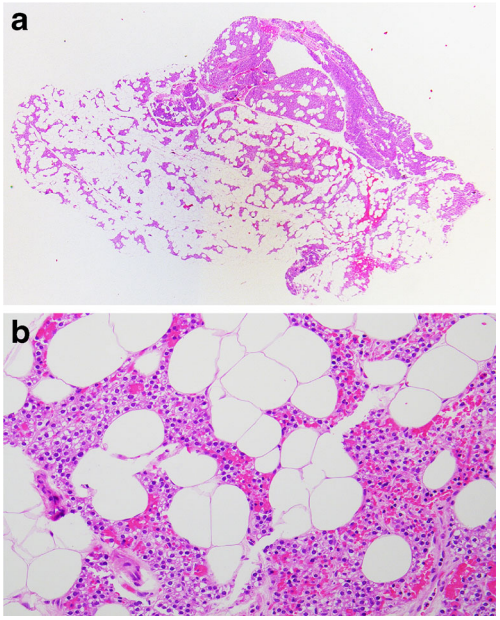

Fig. 1 Microscopic appearance of the lesion with abundant stromal adipose tissue admixed with cords and islands of chief cells (**a**, **b**)

Clinicopathological Features of Previously Reported Cases

Review of available English literature through PubMed, Summon, and web searches revealed 65 published cases of parathyroid lipoadenoma [2–43]. Several cases have been reported in more than one study and the duplicates were omitted in the summary below (Tables 1, 2, and 3).

The 66 cases (included the one presented here) occurred in 25 men and 39 women (gender unknown in two cases) resulting in M:F ratio of 1:1.5 (see Table 1). The mean age was 56 years with range of 20 to 94 years.

The median size of the lipoadenomas was 2.3 cm (mean 3.5 cm, range of 0.7 to 15 cm). Weight was recorded in 33 cases with the median weight of those cases of 1.6 g (mean 27.6 g, range 0.1 to ~420 g).

The location was not specified in 13 of the cases and specified only as neck in one case. Of the remaining cases, the tumor was left-sided in 26 cases and right-sided in 19 cases. One lesion was intrathyroidal, one occupied the thyroid bed post-total thyroidectomy, and 11 were fully or partially mediastinal, two of which were intrathymic.

Imaging modalities localized the lesion in 29 of the 66 cases (44 %) (see Table 2). Ultrasound was performed in 16 cases with the lesion seen in nine of those cases (56 %). CT was reported in nine cases with five cases in which the lesion was noted (55 %). Technicium-99m sestamibi scintigraphy (either planar or single-photon-emission computed scintigraphy, SPECT) was reported in 21 cases with 12 cases reporting detection of the lesion (57 %). X-ray was performed in two of the cases, identifying a mediastinal lesion in one case but

Table 1 The epidemiological and pathological characteristics of the 66 reported cases of parathyroid lipoadenoma (including the current case)

Ref	Age	M/F	Location	Function	Max size (cm)	Weight (g)	Cell types	Stroma
3	43	M	R neck and mediastinal	No	15.0	~420	Chief and oxyphil	Myxoid
4	41	M	R neck and mediastinal	Yes	5.0	19	Chief	Adipose and myxoid
5	24	F	L intrathyroidal	No	5.0	15	Clear	Myxoid
7	35	F	L upper neck	Yes	1.6	0.72	Most chief, some oxyphil	Myxoid
8	46	M	L inferior	Yes	0.7	NR	Chief and clear	Myxoid and adipose
	88	M	Not specified	Possibly	2.0	NR	Chief and oxyphil	Adipose
9	64	M	L superior	Yes	1.5	NR	Chief and oxyphil	Adipose
10	53	M	L superior	Yes	5.5	10	Chief and oxyphil	Adipose
10	54	F	R superior	Yes	1.0	0.54	Chief and oxyphil	Adipose
10	47	M	L neck	–	1.5	NR	Chief and oxyphil	Adipose
10	77	F	Not specified	–	1.5	NR	Chief and oxyphil	Adipose
11	55	F	R superior	Yes	1.5	NR	Chief	Adipose
12	55	F	Mediastinal (intrathymic)	Yes	1.2	NR	Chief	Adipose
13	47	M	R inferior	Yes	1.5	NR	Chief	Adipose
14	66	F	R posterior mediastinal	Yes	14.0	190	Chief	Adipose
15	64	M	R superior	Yes	10.5	17.5	Chief	Adipose
15	62	F	R inferior	Yes	1.5	NR	Chief	Adipose
15	42	F	Not specified	Yes	NR	NR	Chief	Adipose
16	72	F	Not specified	–	NR	NR	–	–
17	72	F	L inferior	Yes	2.5	0.5	Chief	Adipose and myxoid
17	58	M	R inferior	Yes	3.0	0.7	Chief	Adipose
18	61	M	R inferior	Yes	3.0	3.9	Chief	Adipose
19	94	F	R inferior & mediastinal	–	7.0	NR	Chief	Adipose
19	72	F	L superior	Yes	2.0	NR	Chief	Adipose
19	54	F	L superior	Yes	2.0	0.3	Chief	Adipose
20	87	M	Neck	–	1.5	NR	Chief	Adipose
21	48	F	R inferior	Yes	4.0	3	Chief	Adipose
21	63	F	L superior	Yes	0.8	0.3	Chief	Myxoid
21	53	M	R inferior	Yes	0.7	0.45	Chief	Myxoid
21	49	M	L inferior	–	NR	1	Chief	Adipose
22	60	F	L neck	Yes	2.6	NR	Chief	Adipose and myxoid
23	59	F	L inferior	Yes	1.2	1	Chief	Adipose
24	54	F	L inferior	Yes	2.0	NR	Chief	Adipose
25	44	F	Anterior mediastinum	Yes	7.0	17	Clear	Adipose and thymic
26	71	F	L neck	Yes	7.0	40	Chief	Adipose
27	57	M	Not specified	–	6.5	NR	Chief and oxyphil	Adipose
27	45	F	Not specified	–	3.2	NR	Chief and oxyphil	Adipose
27	70	F	Not specified	–	5.0	NR	Chief and oxyphil	Adipose
28	40	M	L neck	Yes	3.0	NR	Chief and oxyphil	Myxoid and adipose
29	54	3 F 2 M	Not specified	Yes	NR	0.405 to 10	Chief	Adipose
29	54		Not specified	Yes	NR		Chief	Adipose
29	67		Not specified	Yes	NR		Chief	Adipose
29	51		Not specified	Yes	NR		Chief	Adipose
29	83		Not specified	Yes	NR		Oxyphil	Adipose
30	41	F	Mediastinum	Yes	NR	NR	Chief	Adipose
31	64	M	L inferior	Yes	4.5	NR	Chief and oxyphil	Myxoid only
32	77	F	L inferior	Yes	3.0	3.154	Chief cell 100 %	Adipose
32	59	M	L superior	Yes	2.0	0.829	Chief 20 %, oxyphil 80 %	Adipose

Table 1 (continued)

Ref	Age	M/F	Location	Function	Max size (cm)	Weight (g)	Cell types	Stroma
32	50	M	R superior	Yes	2.3	0.957	Chief 80 %, clear 20 %	Adipose
32	65	F	R inferior	Yes	5.0	4.587	Chief 90 %, clear 10 %	Adipose
32	57	F	L inferior	Yes	1.9	0.615	Chief 60 %, clear 30 %, oxyphil 10 %	Adipose and myxoid
32	52	F	L inferior	Yes	1.2	0.367	Chief 100 %	Adipose
32	58	F	L superior	No	1.9	0.173	Chief 90 %, oxyphil 10 %	Adipose
32	62	M	L inferior	Yes	2.4	1.738	Chief 80 %, oxyphil 20 %	Adipose and myxoid
33	27	M	R inferior	Yes	1.5	NR	Chief	Adipose
34	20	U	Not specified	–	NR	0.392	–	–
35	62	F	R inferior	Yes	0.7	0.1	Chief	Adipose
36	35	F	R inferior	Yes	1.5	2.8	Chief	Adipose
37	58	F	Mediastinal	No	6.0	NR	Chief	Myxoid
38	56	F	L inferior and R inferior	Yes	2.3	2.130 and 1.510	Mostly chief, some oxyphil	Adipose and fibrous
39	63	F	R inferior and ant mediastinal	Yes	5.1	30.1	Mostly chief, some oxyphil	Adipose and fibrous
40	U	U	Mediastinal	–	NR	NR	–	–
41	37	M	Thyroid bed and mediastinal	Yes	10.3	147	Chief	Adipose
42	65	M	L inferior	Yes	5.0	NR	Chief	Adipose
43	40	F	L inferior	Yes	3.0	NR	Chief	Adipose
43	48	F	R inferior	Yes	1.0	NR	Chief cell 100 %	Adipose

U unknown, *NR* not recorded, *R* right, *L* left, *ant* anterior, *M* male, *F* female

missing a neck lesion in the second case. Positron emission tomography (PET) scan was reported in one case in which it failed to detect the lesion [40].

Fifty of the 66 tumors were functional causing varying degrees of hyperparathyroidism (see Table 3). Four were clearly nonfunctional and the remaining 12, the data was either missing or inconclusive. Presentations varied from nonspecific fatigue, bone and joint pain, nausea and vomiting, abdominal pain, and muscle weakness to nephrolithiasis, pathologic fractures due to underlying osteoporosis, acute pancreatitis, hypertension, chest pain (ventricular tachycardia), and mental disturbances. Occasionally, palpable neck mass was the initial presentation. In a proportion of cases, an asymptomatic elevation of serum calcium was discovered during a routine bloodwork, and only after primary hyperthyroidism was diagnosed were further mild symptoms elicited. Nephrolithiasis, pathological fractures, and asymptomatic hypercalcemia were the most common presentations.

Preoperative serum calcium was reported in 56 cases and was elevated in 51 cases (see Table 3). The reported values ranged from 8.2 to 15.0 mg/dL (mean 11.4 mg/dL). Postoperative normalization of the serum calcium was reported in 19 cases. Elevated serum parathyroid hormone was reported in 33 cases and in 10 of those cases, the levels dropped or normalized either during or after the surgery.

Among the 65 cases reviewed in this study, 14 showed variable amounts of myxoid stroma in addition to the adipose component and in four of the cases, the myxoid stroma was the primary constituent of the stromal portion of the adenoma, leading some authors to propose the use of the term parathyroid myxadenoma [31]. Even though the main component of most lipoadenomas is chief cells, careful examination of the lesion often leads to identification of other cellular (oncocytic cells, clear cells, and even water clear cells) components [2, 5]. Other rare variants reported among the 65 cases included two lesions with additional thymic component, termed lipothymoadenoma [2, 25], as well as a follicular-pattern tumor with superficial resemblance to a thyroid lesion, despite lacking a colloid component [2]. One report described a double lipoadenoma [38].

Discussion

Parathyroid lipoadenomas are rare pathological correlates of hyperparathyroidism with a reported incidence ranging from 0.5 to 1.6 % [16, 21, 44]. As summarized in this case and reported in previous publications, lipoadenomas pose a difficulty for the commonly used parathyroid imaging modalities such as ultrasound, CT, or scintigraphy [32, 40]. The lesions are frequently missed, and when they are detected,

Table 2 The imaging characteristics of 29 cases of parathyroid lipoadenomas reported in the literature (including the current case)

Authors [ref. no]	X-ray	US	CT	Tc-99m
Hargreaves & Wright [14]	+	-	-	-
Auriol et al. [17]	NI	-	-	-
Auriol et al. [17]	-	+	NI	NI
Auriol et al. [17]	-	+	-	-
Auriol et al. [17]	-	+	-	-
Bleiweiss et al. [23]	-	NI	-	NI
Frennby et al. [24]	-	NI	+	NI
Van Hoeven & Brennan [25]	-	-	+	-
Turner et al. [26]	-	NI	NI	NI
Fischer et al. [28]	-	+	-	+
Nanji & Roth [31]	-	+	-	-
Seethala et al. [32]	-	+	-	+
Seethala et al. [32]	-	-	-	NI
Seethala et al. [32]	-	-	-	+
Seethala et al. [32]	-	-	-	+
Seethala et al. [32]	-	-	-	NI
Seethala et al. [32]	-	NI	-	+
Seethala et al. [32]	-	NI	-	-
Seethala et al. [32]	-	+	-	+
Meng et al. [33]	-	-	-	+
Lee et al. [35]	-	-	-	NI
Bansal et al. [36]	-	+	-	+
Sanei et al. [37]	-	-	+	-
Ogrin [38]	-	-	-	+
Yoon et al. [39]	-	NI	-	+
Chicklore et al. [40]	-	-	+	+
Johnson et al. [41]	-	-	NI	+
Cetani et al. [42]	-	+	+	NI
Current case	-	NI	NI	NI
Seen		9	5	12
Not identified		7	4	9
Total		16	9	21

+ lesion was detected, *NI* lesion was not identified, - imaging not performed or not reported

their interpretation is that of a lymph node, lipoma, or a fat-rich lesion inconsistent with parathyroid adenoma. Occasionally, such as in this case, all three imaging modalities fail to detect the lesion. With typical parathyroid proliferations and employing the single-photon-emission computed tomographic scintigraphy (SPECT) detection, technetium 99m sestamibi modality has a reported sensitivity of 89–95 % although this drops to about 60 % in patients with repeat surgeries [45, 46]. Nevertheless, in parathyroid lipoadenomas, the sensitivity of this technique is lower with the success rate linked to the size of the lesion and the amount of the adipose stroma. Small lesions with higher adipose tissue percentage (>50 %) will likely remain difficult to detect since target-to-background signal ration of such lesions is low [45].

These tumors are common enough that a surgical pathologist is likely to encounter at least one or a few in his or her career. Yet, the lesion is rare enough to cause difficulty with its diagnosis, especially at the time of intraoperative consultation. The abundance of adipose tissue in lipoadenomas causes an appearance of normocellularity and if the pathologist relies only on cellularity of the lesion by looking for the absence of fat to diagnose an abnormal parathyroid tissue, he or she will be misled into thinking they see an apparently normal parathyroid tissue. As emphasized by many authors [1, 2], the main responsibility of practicing pathologists is limited to the identification of an abnormal gland in individuals with hyperparathyroidism during intraoperative consultation. Thus, the solution to avoiding the pitfall of lipoadenoma is also to record carefully the precise size and weight of the gland. An abnormal gland is typically enlarged (greater than 6–8 mm) and weighs greater than 40–60 mg [1].

Lipohyperplasia is the main differential diagnosis of lipoadenoma. Parathyroid lipohyperplasia is a rare condition in which lipomatosis and enlargement are found in several or all parathyroids. This is equivalent to usual parathyroid hyperplasia but with the added feature of increased stromal adipose tissue comprising over 30–50 % of the gland [2, 47, 48]. Since the rapid intraoperative PTH assays have already became available in almost all centers with high parathyroidectomy volume, the fall of intraoperative PTH of more than 50 % in 10 min after the removal of an enlarged gland suggests a single gland disease and result in cessation of further surgical exploration [1].

From a morphological perspective, other parathyroid adenoma variants, adenolipoma of the thyroid, and parathyroid carcinoma can also simulate parathyroid lipoadenoma. Parathyroid adenomas may occasionally contain foci of adipose tissue; however, if the adipose tissue stroma is focal and fails to reach 30 % of the gland volume, the diagnosis is best given as a parathyroid adenoma. Similarly, parathyroid hyperplasia may focally show adipose tissue. Nevertheless, involvement of multiple glands and focality of the finding should prompt the right diagnosis. An intrathyroidal parathyroid lipoadenoma may raise a differential diagnosis of adenolipoma of the thyroid, a rare form of follicular adenoma with abundant adipose stroma [49]. The presence of thyroid follicular epithelium and colloid will usually make the distinction straightforward, however, in parathyroid proliferations with follicular (glandular) growth application of markers defining cell lineages (positivity for PTH, GATA-3, and GCM-2 for parathyroid origin; positivity for thyroglobulin, TTF-1, and PAX8 for thyroid follicular epithelial origin) may be useful.

Infiltrating parathyroid carcinoma in the adipose tissue may be mistaken for lipoadenoma. The diagnosis of parathyroid

Table 3 The presentation, functional status, and serum calcium, phosphorus and PTH levels in the 59 reported cases of parathyroid lipoadenomas (including the current case)

Ref	Presentation	Preop Ca [mg/dL]	Preop P	Preop PTH	Postop Ca	Postop P	Postop PTH
4	Nephrolithiasis	15.0	2.0 mg/dL	–	9.8 mg/dL	3.0 mg/dL	–
7	Confusion	Elevated	–	–	–	–	–
8	Joint pain, nausea, and vomiting	11.4	–	Elevated	–	–	–
8	Nephrolithiasis, abdominal pain, confusion	10.8	–	–	–	–	–
9		12.5	–	–	–	–	–
10	Fracture, nephrolithiasis, hypertension	11.0	1.5 mg/dL	Elevated	9.0 mg/dL	3.3 mg/dL	–
10	Hypertension, abdominal pain	11.2	2.4 mg/dL	–	8.9 mg/dL	–	–
10	Seizures, nephrolithiasis	–	–	–	9.9 mg/dL	3.1 mg/dL	–
11	Nephrolithiasis, muscle cramps	11.4	–	Elevated	–	–	–
12	Bone pain, duodenal ulcer	10.8	3.3 mg/dL	–	9.6 mg/dL	–	–
13	Nephrolithiasis	10.6	–	–	–	–	–
14	–	13.2	–	–	–	–	–
15	Headache	12.2	–	–	–	–	–
15	Symptomatic	14.0	–	–	–	–	–
15	–	Elevated	–	–	–	–	–
16	–	12.0	–	–	–	–	–
17	Bone pain	11.2	–	Elevated	–	–	–
17	Chronic pancreatitis	11.3	–	–	–	–	–
18	–	11.2	–	Elevated	–	–	–
19	–	8.2	–	–	–	–	–
19	Renal dysfunction	11.6	–	–	–	–	–
19	–	12.0	–	–	–	–	–
20	–	12.2	0.23 mmol/L	440 pmol/L	–	–	–
21	Nephrolithiasis	12.3	1.9 mg/dL	–	Normal	–	–
21	Asymptomatic	11.0	2.5 mg/dL	482 pg/mL	Normal	–	–
21	Hypertension	11.4	–	–	Normal	–	–
21	Hypertension, acute pancreatitis, peptic ulcer	11.6	2.0 mg/dL	–	Normal	–	–
22	Fracture	11.6	–	Elevated	–	–	–
23	Bone pain	11.4	–	Elevated	–	–	–
24	Hypertension	12.0	–	–	Normal	–	–
25	Nephrolithiasis, osteopenia	12.2	–	–	–	–	–
26	–	10.9	–	Elevated	–	–	–
28	Asymptomatic hypercalcemia	11.5	2.1 mg/dL	221 pg/mL	9.5 mg/dL	3.5 mg/dL	–
29	–	11.0	–	Elevated	–	–	–
29	–	11.8	–	Elevated	–	–	–
29	–	11.6	–	Elevated	–	–	–
29	–	11.3	–	Elevated	–	–	–
29	–	10.7	–	Elevated	–	–	–
30	–	Elevated	–	Elevated	–	–	–
31	Nephrolithiasis	11.6	0.71 mmol/L	228 pg/mL	9.6 mg/dL	3.4 mg/dL	–
32	Fatigue, polydypsia, joint and bone pain	10.8	–	173 pg/mL	–	–	22 pg/mL
32	Joint pain	10.7	–	93 pg/mL	–	–	<35 pg/mL
32	Nephrolithiasis	10.3	–	149 pg/mL	–	–	<35 pg/mL
32	Fatigue	11.2	–	165 pg/mL	–	–	<35 pg/mL
32	Joint pain, osteoporosis	10.8	–	75.6 pg/mL	–	–	47 pg/mL
32	Bone and joint pain, osteoporosis	10.6	–	85 pg/mL	–	–	14 pg/mL
32	Asymptomatic	9.5	–	–	–	–	–

Table 3 (continued)

Ref	Presentation	Preop Ca [mg/dL]	Preop P	Preop PTH	Postop Ca	Postop P	Postop PTH
32	Nocturia	11.4	–	115 pg/mL	–	–	–
33	Fractures, bone pain	13.8	0.60 mmol/L	158.0 pmol/L	2.86 mmol/L	–	–
34	Asymptomatic, thyroid disease	10.0	–	–	2.30 mmol/L	–	–
35	Asymptomatic hypercalcemia	11.3	–	94.7 pg/mL	10.6 mg/dL	–	41 pg/mL
36	Fractures, myalgias, nephrolithiasis	11.1	2.9 mg/dL	1114 pg/mL	–	–	–
37	Asymptomatic normocalcemic	Normal	–	–	–	–	–
38	Asymptomatic hypercalcemia	11.9	3.0 mg/dL	60 pg/mL	9.8 mg/mL	–	32 pg/mL
39	Chest pain, ventricular tachycardia, nephrolithiasis, constipation, compresion fractures	13.6	–	281.5 pg/mL	9.8 mg/dL	2.2 mg/dL	148.2 pg/mL
41	–	–	–	25.9 pmol/L	1.8 mmol/L	–	5.2 pmol/L
42	Nephrolithiasis	10.4	–	105 pg/mL	8.6 mg/dL	–	–
43	–	–	–	–	Normal	–	–
Current case	Fractures, osteoporosis	10.1	–	10.5 pmol/L	Normal	–	1.74 pmol/L

Ca calcium, *P* phosphorus, *PTH* parathyroid hormone

carcinoma rests on documentation of at least one of the following: vascular invasion, perineural invasion, invasion of neighboring organs or structures, or metastasis to lymph nodes or distant organs [1, 50].

The pathogenesis of this curious lesion has not been investigated so far. The early idea of the lesion representing a hamartoma has been largely discarded as the incidence of the lesion is mainly in the sixth and seventh decade and very few cases present before the age of 30 years. In addition, after a few initial reports of large non-functional tumors, most of the subsequent reports described hormone-producing lesions presenting with varying degrees of clinical hyperparathyroidism. Seethala et al. has suggested that obesity as measured by high body mass index (BMI) may contribute to the presence of fat in the adenomas [2]. While most patients in that series had elevated BMI, lack of comparison to parathyroid adenomas in non-obese controls prevented the authors from making conclusion that the two factors are associated. It would be interesting to speculate that some adipogenic factors may be produced by the adenoma, either in the epithelium or by the stromal cells that in turn stimulate adipocyte proliferation. It should be noted that similarly rare lesions are known to also occur in thyroid (thyroid adenolipoma) [27, 49, 51] and salivary glands (sialolipoma a.k.a. sialolipoadenoma) [52].

Conclusion

Parathyroid lipoadenoma is an uncommon clinicopathological correlate of hyperparathyroidism. Preoperative imaging is often unhelpful in localizing and identifying this lesion. During intraoperative consultations, these lesions may pose diagnostic difficulty for surgical pathologists who are not aware of this unique presentation. The evaluation of the ratio of parenchymal cells to adipocytes is not a reliable approach. While the size and weight of a parathyroid gland are defining parameters of an abnormal gland, the distinction between adenoma (uniglandular disease) and hyperplasia (multiglandular disease) should be based on intraoperative PTH along with postoperative biochemical workup.

Compliance with Ethical Standards This case report does not contain any research studies with human participants or animals performed by any of the authors. Therefore, for this type of manuscript, formal consent is not required.

Conflict of Interest The authors declare that they have no competing interests.

References

1. Duan K, Gomez Hernandez K, Mete O. Clinicopathological correlates of hyperparathyroidism. J Clin Pathol 68: 771–87, 2015.
2. Seethala RR, Yim JH, Hunt JL. Pathology quiz case 2. Parathyroid lipoadenoma. Arch Otolaryngol Head Neck Surg 132: 1391–1393, 2006.
3. Ober WB, Kaiser GA. Hamartoma of the parathyroid. Cancer 1: 601–6, 1958.
4. Abul-Haj SK, Conclin H, Hewitt WC. Functioning lipoadenoma of the parathyroid gland. Report of a unique case. N Engl J Med 266: 121–3, 1962.
5. Aukee S, Meurman LO. Hormonal inactivity in a case of parathyroid tumour. Acta Chir Scand 37:478–82, 1971.
6. Heaton LD, Beisel WR, Sprinz H, Forsee JH. Parathyroid tumors with an analysis of 18 surgical cases and with special reference to diagnosis. Ann Surg 155: 90–102, 1962

7. Grimelius L, Johansson H, Lindquist B. A case of unusual stromal development in a parathyroid adenoma. Acta Chir Scand 138: 628–9, 1972.
8. Legolvan DP, Moore BP, Nishiyama RH. Parathyroid hamartoma: report of two cases and review of the literature. Am J Clin Pathol 67: 31–35, 1977.
9. Daroca PJ Jr, Landau RL, Reed RJ, et al. Functioning lipoadenoma of the parathyroid gland. Arch Pathol Lab Med 101: 28–29, 1977.
10. Weiland LH, Garrison RC, ReMine WH, et al. Lipoadenoma of the parathyroid gland. Am J Surg Pathol 2: 3–7, 1978.
11. Saik RP, Gmelich JT. Hyperparathyroidism from a hamartoma. Am Surg 45: 542–543, 1979.
12. Wolff M, Goodman EN. Functioning lipoadenoma of a supernumerary parathyroid gland in the mediastinum. Head Neck Surg 2: 302–307, 1980.
13. Gabbert H, Rothmund M, Höhn P. Myxoid lipoadenoma of the parathyroid gland. Pathol Res Pract 170: 420–5, 1980.
14. Hargreaves HK, Wright TC Jr. A large functioning parathyroid lipoadenoma found in the posterior mediastinum. Am J Clin Pathol 76: 89–93, 1981.
15. Geelhoed GW. Parathyroid adenolipoma: clinical and morphologic features. Surgery 92: 806–810, 1982.
16. Bondeson AG, Bondeson L, Ljungberg O, et al. Fat staining in parathyroid disease—diagnostic value and impact on surgical strategy: clinicopathologic analysis of 191 cases. Hum Pathol 16: 1255–1263, 1985.
17. Auriol M, Malki B, Koulibaly M, Delcourt A, Chomette G. Lipoadenome et hyperplasie lipomateuse parathyroïdiens. Trois observations. Arch Anat Cytol Pathol 33: 205–8, 1985.
18. Ducatman BS, Wilkerson SY, Brown JA. Functioning parathyroid lipoadenoma. Report of a case diagnosed by intraoperative touch preparations. Arch Pathol Lab Med 110: 645–647, 1986.
19. Úden P, Bergllund J, Zederfeldt B, Aspelin P, Ljungberg O. Parathyroid lipoadenoma: a rare cause of primary hyperparathyroidism. Case report. Acta Chir Scand 153: 635–9, 1987.
20. de Leacy EA, Axelsen RA, Kleinman DS, et al. Functioning lipoadenoma of the parathyroid gland. Pathology. 20: 377–380, 1988.
21. Obara T, Fujimoto Y, Ito Y, et al. Functioning parathyroid lipoadenoma—report of four cases: clinicopathological and ultrasonographic features. Endocrinol Jpn 36: 135–145, 1989.
22. Coen G, Bondatti F, de Matteis A, et al. Severe vitamin D deficiency in a case of primary hyperparathyroidism caused by parathyroid lipoadenoma, effect of 25OHD3 treatment. Miner Electrolyte Metab 15: 332–337, 1989.
23. Bleiweiss IJ, Harpaz N, Strauchen JA, et al. Functioning lipoadenoma of the parathyroid: case report and literature review. Mt Sinai J Med 56: 114–117, 1989.
24. Frennby B, Nyman U, Aspelin P, et al. CT of a parathyroid lipoadenoma. Case report. Acta Radiol 34: 369–371, 1993.
25. van Hoeven KH, Brennan MF. Lipothymoadenoma of the parathyroid. Arch Pathol Lab Med 117: 312–314, 1993.
26. Turner WJ, Baergen RN, Pellitteri PK, Orloff LA. Parathyroid lipoadenoma: case report and review of the literature. Otolaryngol Head Neck Surg 114: 313–6, 1996.
27. Daboin KP, Ochoa-Perez V, Luna MA. Adenolipomas of the head and neck: analysis of 6 cases. Ann Diagn Pathol 10: 72–76, 2006.
28. Fischer I, Wieczorek R, Sidhu GS, et al. Myxoid lipoadenoma of parathyroid gland: a case report and literature review. Ann Diagn Pathol 10: 294–296, 2006.
29. Chow LS, Erickson LA, Abu-Lebdeh HS, et al. Parathyroid lipoadenomas: a rare cause of primary hyperparathyroidism. Endocr Pract 12: 131–136, 2006.
30. Rastogi A, Jain M, Agarawal T, et al. Parathyroid lipoadenoma: case report and review of the literature. Indian J Pathol Microbiol 49: 404–406, 2006.
31. Nanji SS, Roth SI. A parathyroid myxadenoma observed grossly. Endocr Pathol 18: 53–5, 2007.
32. Seethala RR, Ogilvie JB, Carty SE, Barnes EL, Yim JH. Parathyroid lipoadenomas and lipohyperplasias: clinicopathologic correlations. Am J Surg Pathol 32: 1854–67, 2008.
33. Meng Z, Zhang M, Tan J, Zhang Y, Jia Q, Zhang F. Tc-99m sestamibi parathyroid imaging in a rare case of parathyroid lipoadenoma. Ann Nucl Med 23: 317–20, 2009.
34. McMullen T, Bodie G, Gill A, Ihre-Lundgren C, Shun A, Bergin M, Stevens G, Delbridge L. Hyperparathyroidism after irradiation for childhood malignancy. Int J Radiat Oncol Biol Phys 73: 1164–1168, 2009.
35. Lee AY, Wang BY, Heller KS. Importance of intraoperative parathyroid hormone measurement in the diagnosis of parathyroid lipoadenoma. Head Neck 33: 917–9, 2011.
36. Bansal R, Trivedi P, Sarin J, Parikh B. Lipoadenoma of the parathyroid gland—a rare cause of hyperparathyroidism. Gulf J Oncol 1: 63–65, 2012.
37. Sanei MH, Naimi A, Tabatabaei SA. Ectopic lipoadenoma of parathyroid. J Res Med Sci 17: 983–4, 2012.
38. Ogrin C. A rare case of double parathyroid lipoadenoma with hyperparathyroidism. Am J Med Sci 346: 432–4, 2013.
39. Yoon V, Treat K, Maalouf NM. Ectopic atypical parathyroid lipoadenoma: a rare cause of severe primary hyperparathyroidism. J Bone Miner Metab 31: 595–6, 2013.
40. Chicklore S, Schulte KM, Talat N, Hubbard JG, O'Doherty M, Cook GJ. 18F-FDG PET rarely provides additional information to 11C-methionine PET imaging in hyperparathyroidism. Clin Nucl Med 39: 237–42, 2014.
41. Johnson N, Serpell JW, Johnson WR, Thomson K. Parathyroid lipoadenoma. ANZ J Surg 85: 489–90, 2015.
42. Cetani F, Torregrossa L, Marcocci C. A large functioning parathyroid lipoadenoma. Endocrine epub July 2015.
43. Komminoth P. Difficult/unusual diagnoses in routine endocrine pathology. Slide Seminar 7. 23rd European Congress of Pathology, Helsinki, August 30, 2011. (retrieved from the world wibe web on Aug 22, 2015 at http://demo.webmicroscope.net/Handouts/HO_88_Komminoth_Text_Helsinki_Slideseminar.pdf)
44. Attie JN, Wise L, Mir R, Ackerman LV. The rationale against routine subtotal parathyroidectomy for primary hyperparathyroidism. Am J Surg 136: 437–44, 1978.
45. Nguyen BD. Parathyroid imaging with Tc-99m sestamibi planar and SPECT scintigraphy. Radiographics 19: 601–614, 1999.
46. Kotlyarov EV. Commentary on Parathyroid imaging with Tc-99m sestamibi planar and SPECT scintigraphy. Radiographics 19: 615, 1999.
47. Carter JM, Landry A, Hinni M. Lipohyperplasia of the parathyroid glands. Ear Nose Throat J 91: 441–3, 2012.
48. Straus FH II, Kaplan EL, Nishiyama RH, Bigos ST. Five cases of parathyroid lipohyperplasia. Surgery 94: 901–5, 1983.
49. Sheikh SS, Massloom HS. Lipoadenoma: is it arising from thyroid or parathyroid? A diagnostic dilemma. ORL J Otorhinolaryngol Relat Spec 64: 448–50, 2002.
50. Duan K, Mete Ö. Parathyroid Carcinoma: Diagnosis and Clinical Implications. Turk Patoloji Derg. 31 Suppl 1: 80–97, 2015
51. Borges A, Catarino A. Case 53: adenolipoma of the thyroid gland. Radiology 225: 746–50, 2002.
52. Nagao T, Sugano I, Ishida Y, Asoh A, Munakata S, Yamazaki K, Konno A, Kondo Y, Nagao K. Sialolipoma: a report of seven cases of a new variant of salivary gland lipoma. Histopathol 38: 30–6, 2001.