Y021

Water-clear cell Parathyroid adenoma: rare case report

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Objective

Water-clear cell parathyroid adenoma (WCCA) is an extremely rare cause of primary hyperparathyroidism (PHPT). Our objective was to report a patient with a WCCA that was managed by our Department and to review the relevant literature in order to further our understanding of this rare entity.

Methods

We retrospectively reviewed the case notes, histopathological records and electronic notes of a patient with WCCA that was operated in our Endocrine Surgery department. Furthermore, we reviewed the relevant literature and report our findings using Medline database to search all the relevant medical data from 1946 till present without any language restriction using the keywords: water-clear-cell, water clear cell adenoma, water clear cell parathyroid adenoma.

Results

A 73-year-old female was referred to our Department by her GP with an incidental finding of hypercalcemia. The patient was completely asymptomatic in terms of PHPT clinical features. Her biochemistry results revealed hypercalcemia (3.04 mmol/L), high parathyroid hormone (279 ng/l), Vitamin D of 73 units, eGFR of 64 and an increase in 24-hour urinary calcium extraction (9.0 mmol/D). After the diagnosis of primary hyperparathyroidism (PHPT) was established we proceeded to localisation studies. Parathyroid Ultrasonography scan showed a right 30x11mm parathyroid lesion with enlarged lymph nodes. The ^{99m}Tc scan Sestamibi scan showed increased tracer accumulation at the right lower pole of the thyroid which failed to washout while SPECT CT confirmed a posterior right thyroid location. Bone densitometry showed osteoporosis at the patient's left wrist and osteopenia in her femurs.

In view of the extremely high calcium/PTH and the size of the lesion (3 cm) there was a concern for the possibility of parathyroid carcinoma and the patient had an oncologic operation (en bloc resection of right sterno-thyroid muscle, right thyroid lobe, right lower parathyroid, right level VI lymphadenectomy) in June 2018.

Histology revealed the presence of a 3.1 cm WCAA of the right lower parathyroid gland, limited to the gland; resection margins were free of neoplasm. The neoplasm was well-circumscribed and non-encapsulated. It showed a trabecular-nested pattern with no solid/diffuse areas; the reticuline pattern was preserved with no fibre destruction, the elastic fibres were preserved with no abnormal deposition, and no

fibrosis was identified on H&E or trichrome stained sections. A rim of compressed parathyroid parenchyma was noted at the periphery of the lesion and there was no extension or thyroid invasion. No lymphovascular or perineural invasion was seen. The tumour cells revealed broad water-clear cytoplasm, low nuclear pleomorphism, inconspicuous nucleolus, and <1 mitotic figure/10 HPF (no atypical mitoses after screening 40 HPF). PTH expression was identified at the cytoplasm periphery of the tumour cells. The Ki-67 labelling index was <1%. Twelve level 6 lymph nodes were excised with no malignancy. The thyroid lobe was within the normal histological limits.

In the immediate post-operative period the PTH dropped to 68 ng/l. The patient made an uneventful post-operative recovery and was discharged home on post-op day 1 with oral Alfacalcidol 1μgr BD, Calceos 1tab TDS and Sandocal tablets PRN. Oral calcium supplementation was discontinued on the 2nd week post-op and she has been normocalcemic up to her most recent follow-up. The case had been discussed in the endocrine multidisciplinary meeting and the consensus was that there should be ongoing monitoring of her calcium/PTH.

On the literature review we performed, there are about 20 other cases reported as WCCA, all of which have been diagnosed on histopathology, 2 of the cases had been found to be intra-thyroidal and only one has been diagnosed as water-clear cell carcinoma. No change in the management or the frequency of the follow up had been suggested.

Conclusion

WCCA is a rare cause of PHPT, however the diagnosis with WCCA doesn’t change the management of the parathyroid adenoma in terms of operation and the follow up plans.

Water-clear Cell Parathyroid Adenoma Rare Case Report

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Aim

Water-clear cell parathyroid adenoma (WCCA) is an extremely rare cause of primary hyperparathyroidism (PHPT). Our objective was to report a patient with a WCCA that was managed by our Department and to review the relevant literature in order to further our understanding of this rare entity

Case Presentation

- 73-year-old female presented with incidental finding of hypercalcemia
- Patient was completely asymptomatic
- Biochemistry results revealed:
  - Corrected serum Ca: 3.04 mmol/L (N.V:)
  - Parathyroid hormone (PTH): 279 ng/l (N.V:)
  - Vitamin D: 73 units (N.V:)
  - egfr: 64 ml/min

Localisation studies:

- Parathyroid Ultrasonography scan: right 30x11mm parathyroid lesion
- ^{99m}Tc scan Sestamibi scan: increased tracer accumulation at the right lower pole of the thyroid which failed to washout while SPECT CT confirmed a posterior right thyroid location (Fig 1,2)
- Bone densitometry: osteoporosis at the patient's left wrist and osteopenia in her femurs

Management

- Due to the presence of hypercalcemia >3 mmol/L and the large size >3 cm, the suspicion of parathyroid malignancy was raised (3+3 rule of Schulte)
- Oncologic operation (*en bloc* resection of right sterno-thyroid muscle, right thyroid lobe, right lower parathyroid, right level VI lymphadenectomy)
- Immediate post-operative period: PTH dropped to 68 ng/l
- Uneventful post-operative recovery and patient was discharged home on post-op day 1
- Oral calcium supplementation was discontinued on the 2nd week post-op and she has been normocalcemic up to her most recent follow-up
- Histopathology examination revealed the presence of a WCCA (figures 3,4)
- The case had been discussed in the endocrine multidisciplinary meeting and the consensus was that there should be ongoing monitoring of her calcium/PTH

Discussion

WCAA is a rare, benign, form of PHPT. The preoperative characteristics of WCAA (large size and significant hyperalcemia) may mimic parathyroid malignancy and clinicians need to consider it during surgical planning

Literature Review

Literature review: Medline database from 1946-present. Keywords: water-clear-cell, water clear cell adenoma, water clear cell parathyroid (Table 1).

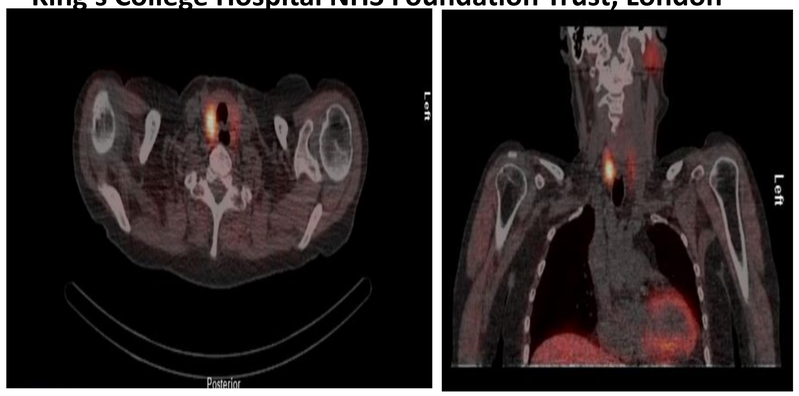

Figure 1.2 : Sestamibi scan showed increase in uptake at RT lower Lobe

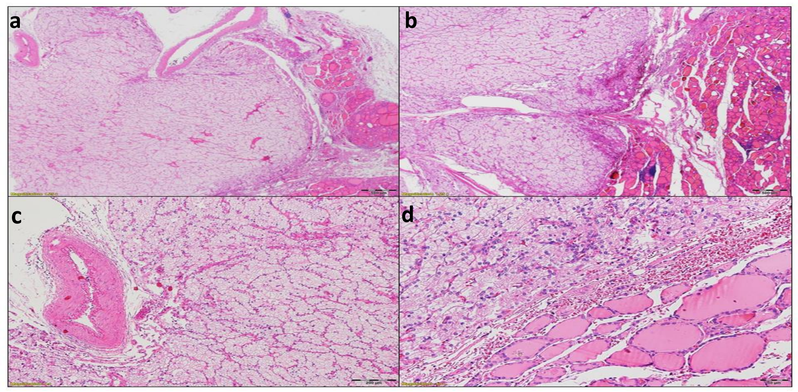

Figure 3: A,B(hematoxylin-eosin -H&E-, 12.5x) ,C (H&E, 40x) , D (H&E)

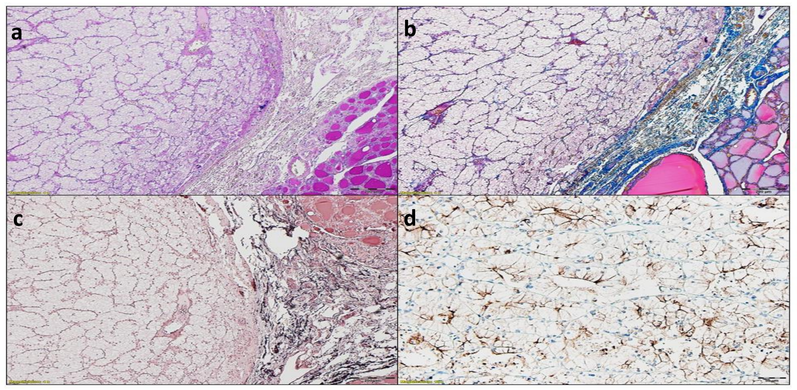

Figure 4: A(Periodic acid Schiff after diastase digestion, 40x),B (Masson trichrome, 40x) ,C (orcein, 40x) , D (PTH immunostaining, 200x)

The neoplasm is well-circumscribed and non-encapsulated. It shows a trabecular-nested pattern with no solid/diffuse areas, the elastic fibers are preserved with no abnormal deposition, and no fibrosis is identified on H&E or trichrome stained sections. A rim of compressed parathyroid parenchyma is noted at the periphery of the lesion and there is no extension thyroid invasion. No lympho-vascular or perineural invasion seen. The tumor cells reveal broad water-clear cytoplasm, low nuclear pleomorphism, inconspicuous nucleolus, and <1 mitotic figure/10 HPF (no atypical mitoses after screening 40 HPF).

Authors	Year	Age Sex	Symptoms	Ca mmol/L	PTH	Imaging Method	Management	Number of Adenomas	Size (cm)	Adenoma localization
Kovasc et al.	1994	48 M	NA	2.95	435 mIU/mL	NA	Right hemi-thyroidectomy and total Parathyroidectomy	Single	NA	LI
Roth et al.	1995	48 M	NA	2.95	4.5 mIU/mL	NA	Parathyroidectomy	Single	NA	NA
Grenko et al.	1995	40 M	Fatigue, Leg cramps	2.82	945 pg/mL	USG(-) / MIBI (-)	Parathyroidectomy	Single	5	RS
Begueret et al.	1999	73 M	Nephrolithiasis	3.45	207 pg/mL		Parathyroidectomy	Single	2.8	LI
Dundar et al.	2001	43 F	Fractures, Leg cramps	3.33	1667 pg/mL	USG(+) / Scinti (-)	Near Total Thyroidectomy	Single	6	Intrathyroidal L lobe
Kuhel et al.	2001	56 F	Asymptomatic	3.50	52 ng/L	USG(+)/MIBI (-)	Parathyroidectomy + right lobectomy and isthemctomy	Double	2.8	RS/LS
Kanda et al.	2004	52 F	Gastritis, Nephrolithiasis	2.93	672 pg/mL	USG(+)/TITc(+) MR (+)	Parathyroidectomy	Single	6.8	LI
Prasad et al	2004	40 F	Weakness	3.10	346 pg/mL	NA	Parathyroidectomy	Single	3.0	LI
Kodoma et al.	2007	18 F	Nephrolithiasis	2.90	356 pg/mL	USG(+)/ TITc(+)	Parathyroidectomy	Single	5.0	RS
Liang et al.	2010	59 F	Depression	2.95	265 pg/mL	USG(-)/ MIBI(+)	Parathyroidectomy	Single	4.5	RS
Bai et al.	2012	81 M	NA	NA	22.2 pmol/L	USG (-) / MIBI(+)	Parathyroidectomy	Single	4.0	RS
Bai et al.	2012	55 M	NA	NA	15.9 pmol/L	USG(-) / MIBI (-)	Parathyroidectomy + Bilateral Thyroidectomy (Papillary ca)	Single	1.4	LS
Papanicolau-Sengos et al.	2013	64 M	Asymptomatic	NA	N/A	NA	Parathyroidectomy	Single	4.7	LI
Piggott et al.	2013	74 F	Abdominal, Pain Lethargy, constipation	3.13	488.9 ng/L	USG(+) / MIBI(+)	Parathyroidectomy	Single	5.5	LI
Ezzat et al.	2013	73 M	NA	3.24	30.8 pmol/L	USG(+) / MIBI(+)	Parathyroidectomy	Single	3.7	LI
Ezzat et al.	2013	74 F	NA	2.9	11.8 pmol/L	USG(+) / MIBI(-)	Parathyroidectomy	Single	1.6	LI
Mukrakami et al.	2014	59 F	Nephrolithiasis, bone Fractures	2.98	72.3 pg/dL	USG (+) / MIBI (-) CT(+)	Parathyroidectomy	Single	0.8	LI
Chou et al.	2014	81 F	Pancreatitis	3.00	450 pg/mL	USG(+) / MIBI(+)	Parathyroidectomy	Single	3.8	NA
Tassone et al.	2014	54 F	Depression, bone pain	3.1	130 ng/L	USG(+) / MIBI(+)	Parathyroidectomy	Single	2.8	LI
Yazar et al.	2016	47 M	Asymptomatic	4.15	744 pg/mL	USG (+) / MIBI(-)	Parathyroidectomy	Double	2.5	RI/LI
Pirela et al.	2016	34 F	Weight gain, hair loss	2.33	NA	USG (+)	Right hemithyroidectomy+ isthmusectomy	Single	NA	Intrathyroidal
Arik et al.	2017	70 M	Back Pain	NA	NA	CT	Surgical excision "	Single	6	Mediastinal
Current study	2018	73 F	Asymptomatic	3.04	279 ng/L	USG (+) / MIBI(+)	*En bloc* resection of right sterno-thyroid muscle, right thyroid lobe, right lower parathyroid, right level VI lymphadenectomy	Single	3.1	RL

Table 1: Summary of the literature review of WCCA cases

NA : not available , RS : Right superior , LS : left superior , RI : right inferior , LI : Left Inferior

Conclusion :

WCCA is a rare cause of PHPT, however the diagnosis with WCCA doesn't change the management of the parathyroid adenoma in terms of operation and the follow up plans.

Hammersmith Abstracts

Friday 7th December 2018

13th Hammersmith Multidisciplinary Endocrine Symposium 2018

Available online on http://metmed.info

Hammersmith Hospital 13th Multidisciplinary Endocrine Symposium
Provisional programme Fri 7th Dec 2018

Wolfson Conference Centre, Hammersmith Hospital, London

8.30am Registration & Coffee

8.55am Welcome and Introduction
(Fausto Palazzo, Karim Meeran & Waljit Dhillo)

Session 1: Genetics and Endocrine disease (Chair James Ahlquist)

9.00am Phaeochromocytoma – Which genetic tests & why?
Dr Scott Akker – (St Bartholomew's Hospital)

9.30am When to do genetics in Primary HPT?
Prof Jeremy Turner (Norfolk & Norwich Hospital)

10.00am Clinical case: **Y013 (OC1)**: Phaeochromocytoma Crisis: Adrenal Incidentaloma with Contralateral Renal Infarction and beta blockade administration

10.15am Coffee Break

Session 2: Metabolic Medicine & Surgery (Chair Prof Tricia Tan)

10.45am Clinical case**: Y002 (OC2):** Flash glucose monitoring for diagnosis and management of post bariatric hypoglycaemia.

11.00am Obesity Surgery vs Medical Treatment: Who gets what and what is to come?
Prof Sir Stephen Bloom (Imperial College)

11.30am Obesity surgery: the surgical options, technique and morbidity
Mr Ahmed Ahmed (St Mary's Hospital, London)

11.50am The role of T3 in The hypothyroid patient
Prof Colin Dayan (Cardiff University)

12.20pm Lunch & Poster session

Session 3: Personalised Endocrine Medicine & Surgery (Chair Mr Fausto Palazzo)

1.20pm **Hammersmith International Guest Lecture:** Endocrine Surgery in 2018: Precision Medicine **Prof Frederic Sebag (Marseille, France)**

2.00pm How to avoid morbidity in Endocrine Surgery **Mr David Scott Coombes, Cardiff**

2.20pm Clinical Cases

2.20pm **Y003 (OC3):** When not to ignore the normal results in endocrinology

2.30pm **Y015 (OC4):** False positive diagnosis of a paraganglioma of the organ of Zuckerkandl

2.40pm **Y020 (OC5)**: The Challenge of a Great mimic: Case report of Pheochromocytoma presenting as Acute Coronary Syndrome complicated by Retroperitoneal bleed and Multisystem Crisis

2.50pm Coffee break

Session 4: Endocrinology & Pregnancy revisited (Chair Dr Jeannie Todd)

3.10pm Thyroid hormone supplementation in pregnancy **Dr Sheba Jarvis**

3.30pm Hyperparathyroidism & Pregnancy **Mr Fausto Palazzo (Hammersmith Hospital)**

3.50pm Clinical cases **(Chair James Ahlquist)**

3.50pm **Y001 (OC6)**: Hypercalcemia in pregnancy in a patient with multiple previous miscarriages

4.05pm **Y016 (OC7)**: Case Report: Recurrent primary hyperparathyroidism during pregnancy in MEN4

4.20pm: **Y010 (OC8)**: Don't miss neonatal thyrotoxicosis - the importance of assessing an at risk baby at 7 days

4.35pm Close and Feedback

Y001 OC6	Hypercalcemia in pregnancy in a patient with multiple previous miscarriages
Y002 OC2	Flash glucose monitoring for diagnosis and management of post bariatric hypoglycaemia
Y003 OC3	When not to ignore the normal results in endocrinology
Y004	Hyponatraemia secondary to the deficiency of adrenocorticotropic hormone
Y005	Acromegaly with Non-PTH related Hypercalcemia
Y006	Late presentation of a GLUD-1 activating mutation: consider this rare genetic cause in adults with fasting and protein-sensitive hyperinsulinaemic hypoglycaemia
Y007	HCG and diet: The ultimate way of fat burning
Y008	Severe triglyceridaemia in PPAR-gamma mutations: uncommon cause often overlooked
Y009	Hemi-ballismus as a presentation of hyperglycaemia and the classical neuro-imaging findings
Y010 OC8	Don't miss neonatal thyrotoxicosis - the importance of assessing an at risk baby at 7 days
Y011	A case of ‘non-classic’ Non-Classic Congenital Adrenal Hyperplasia
Y012	The Natural History of Silent Corticotroph Adenomas: A Tertiary Referral Centre Experience
Y013 OC1	Phaeochromocytoma Crisis: Adrenal Incidentaloma with Contralateral Renal Infarction and beta blockade administration
Y014	A masquerading parathyroid carcinoma

Y015 OC4	False positive diagnosis of a paraganglioma of the organ of Zuckerkandl
Y016 OC7	Case Report: Recurrent primary hyperparathyroidism during pregnancy in MEN4
Y017	Screening for Graves' Orbitopathy in Endocrinology Clinic: A multi-disciplinary perspective
Y018	To treat or not to treat: An interesting case of alemtuzumab-induced thyroid disorder
Y019	Gynaecomastia - an Endocrinological or a Surgical problem?
Y020 OC5	The Challenge of a Great mimic: Case report of Pheochromocytoma presenting as Acute Coronary Syndrome complicated by Retroperitoneal bleed and Multisystem Crisis
Y021	Water-clear cell Parathyroid adenoma: rare case report
Y022	Real-world use of non-echoplanar diffusion weighted MRI imaging for detection and clinical decision-making in Graves' orbitopathy