A Failed Parathyroid Exploration

Or is it…?

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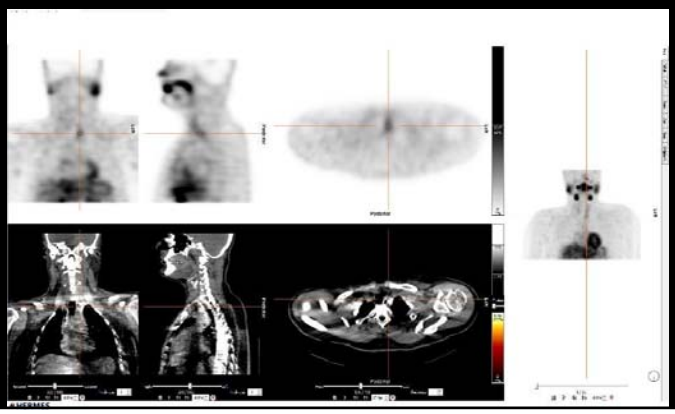
32 year old male

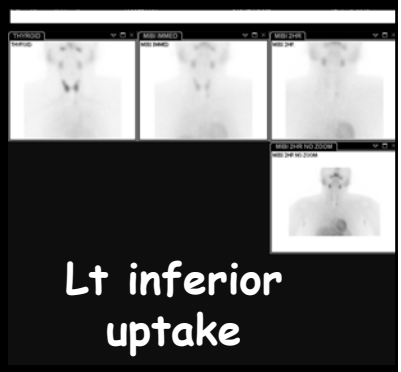
Presented with kidney stones –CaOxalate

Diagnosis of HPT

Sestamibi scan – Left inferior adenoma

Calcium	Phosphate	PTH (13-54 ng/L)	Vitamin D	uCalcium
2.96 mmol/l 11.8 mg/dL	0.87 mmol/l 2.69 mg/dl	104 ng/L	13 nmol/L 5.21 ng/ml	6.12 (0.8%)





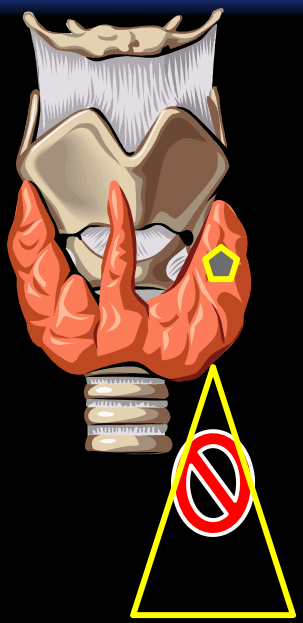
Lt inferior uptake

Intra-office US

Left inferior parathyroid

AND

A suspicious 1 cm left superior thyroid nodule



Sister in India also has kidney stones

Verbal report only from patient's sister

Feb 2012 Ca 10.9 mg/dL
Dec 2012 PTH 90 pg/ml
July 2013 Ca 9.6 mg/dL PTH 780 pg/ml
9 days later Ca 9.6mg/dL PTH 39 pg/ml

No Vitamin D

Diagnosis?

Surgical thoughts…

Thyroid nodule - ?MTC + HPT = MEN 2
FNA under US, calcitonin

Low uCalcium despite low Vit D- ? BFHH
correct Vit D and repeat Ca/PTH

Family renal stones – primary or MEN 1
genetic testing

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2.79 mmol/L 11.2 mg/dL	0.66 mmol/L 2.04 mg/dl	80 ng/L	40.2 nmol/L 16 ng/ml	

FNA – Papillary Thyroid Cancer
Calcitonin – 3 ng/L (normal <18)
Magnesium 0.79nmol/L 1.58mEq/L

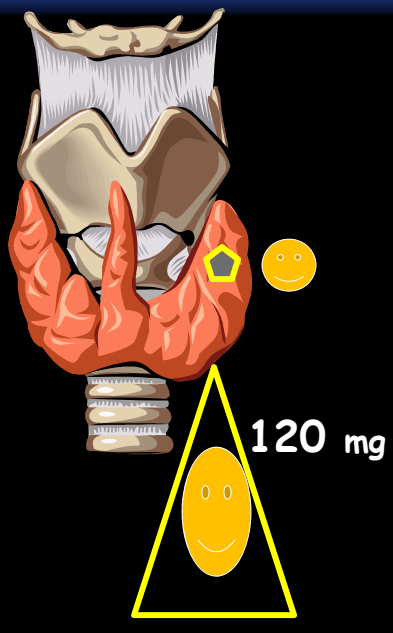
No pathological mutations in MEN 1 gene

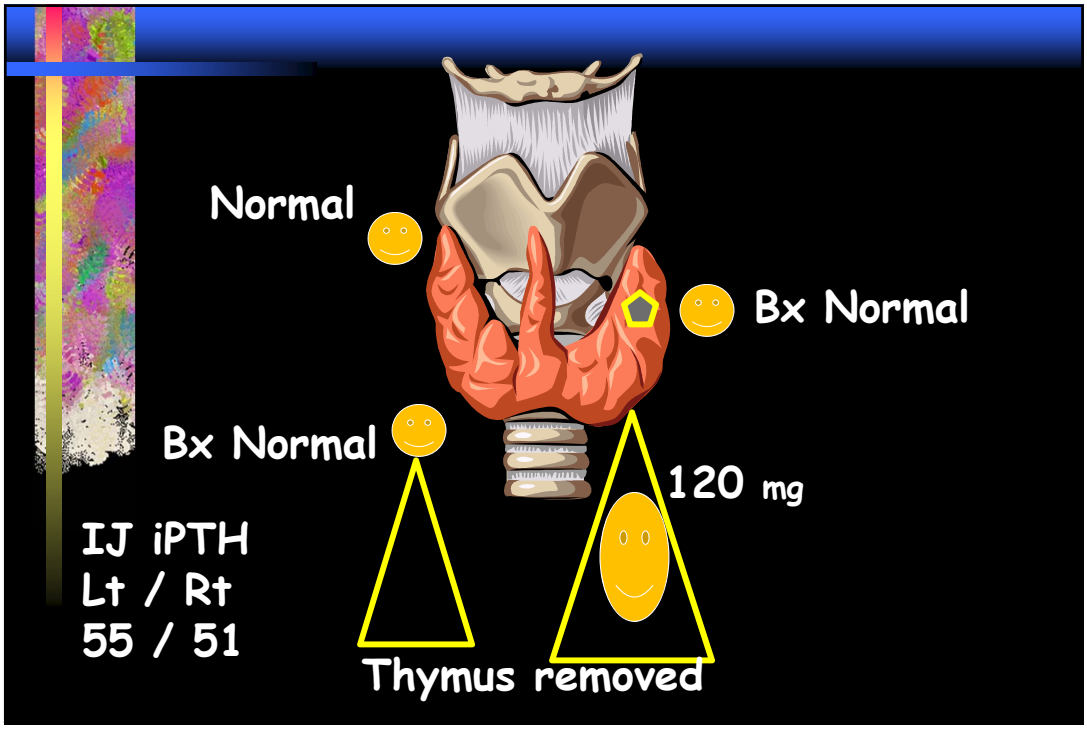
No pathological mutations in RET gene
Variant of uncertain significance
c.2393-9C>T
Not been reported
Likely benign polymorphism

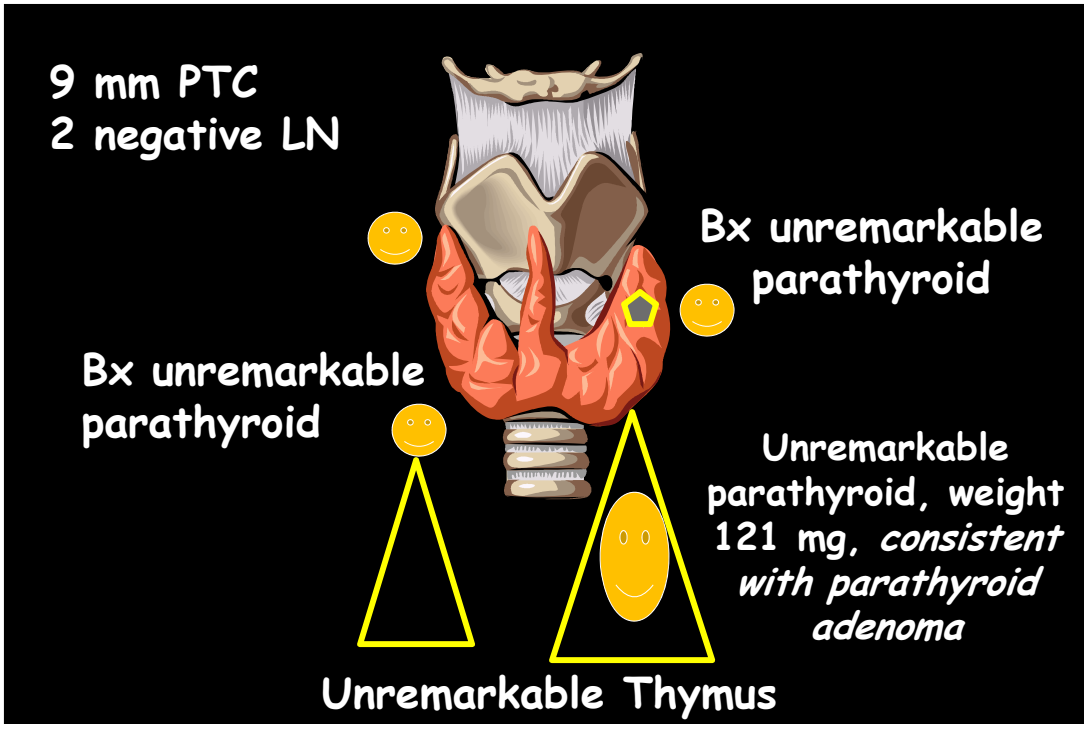
Surgical strategy ?

iPTH

Time zero	164
Pre-excision	158
5 min post	149
10 min post	143
20 min post	149




Normal
Bx Normal
Bx Normal
120 mg
IJ iPTH
Lt / Rt
55 / 51
Thymus removed


9 mm PTC
2 negative LN
Bx unremarkable parathyroid
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Unremarkable parathyroid, weight 121 mg, *consistent with parathyroid adenoma*
Unremarkable Thymus

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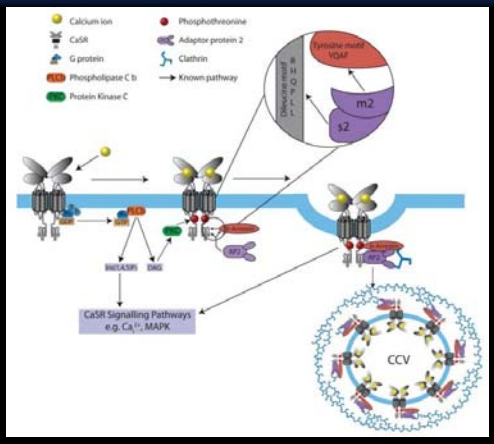
2.79 mmol/L 11.2 mg/dL	0.66 mmol/L 2.04 mg/dl	80 ng/L	40.2 nmol/L 16 ng/ml	
2.89 mmol/l 11.6 mg/dl	0.64 mmol/L 1.98 mg/dl	75 ng/L		

No mutations or variations of CaSR gene

Persistent HPT



Nesbit MA *et al* NEJM 368;2013
Nesbit Nat *et al* Nat Gnet 45;2013
Hendy GN *et al* JCEM 99;2014
Stratto P *et al* NephroDialisis Transp 29;2014

BFHH

Type 1 – loss of function *CaSR gene*
(3q13.3-21)
47-56%

Type 2 – inactivating mutations *GNA11* gene
(19p13.3)
10%

Type 3 – *AP2S1* adaptive-related protein
missense mutations (19q13.3)
15-22% of *CaSR* negative patients

AP2S1 gene testing – pathological mutation

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12/2013	2.79 mmol/L 11.2 mg/dL	0.66 mmol/L 2.04 mg/dl	80 ng/L	40.2 nmol/L 16 ng/ml	
02/2014	2.89 mmol/l 11.6 mg/dl	0.64 mmol/L 1.98 mg/dl	75 ng/L		
01/2015	2.57 mmol/L 10.3 mg/dL	0.77 mmol/L 2.38 mg/l	*53 ng/L (7 – 37 ng/L)	60.3 nmol/L 24.2 ng/ml	

Take-home points

HPT challenging Dx when VitD deficient

MIBI / US are NOT diagnostic

Surgical findings in BFHH – enlarged but not adenomatous gland(s)

Novel mutation in BFHH
Screen for *AP2S1* in clinically suspicious BFHH – *CaSR* gene negative