

Case 3

Interhospital Endocrine
Conference
24 Mar 23



PROTOCOL



ผู้ป่วยหญิงไทยคู่ อายุ 73 ปี
ไม่ได้ประกอบอาชีพ

Consult endocrine for
glycemic control

อาการสำคัญ: ปวดหลัง 2 สัปดาห์

ประวัติปัจจุบัน:

Underlying diseases: HT, DM, MAFLD

6 เดือนก่อน - น้ำหนักลด 10 กิโลกรัมใน 4 เดือน รู้สึกมีต้น
แขนต้นขาอ่อนแรง ไม่มีไข้ ไม่มีคลื่นไส้ก่อนผดผื่น

2 สัปดาห์ก่อน - ผู้ป่วยมีอาการปวดหลัง ปฏิเสธประวัติได้รับ
อุบัติเหตุรุนแรง ไปตรวจที่ รพ. พบ Fracture at T7 vertebra



Mild thoracic scoliosis with kyphosis
Compression fracture of T7 vertebra



MRI T SPINE WITH GD

- **Acute-subacute fracture or old fracture with acute on top of T7 body about 70%**
- No definite evidence of spinal cord or nerve root compression
- No abnormal signal intensity of bony destruction
- Old compression fracture of T11 body about 10%



PROTOCOL

- Diagnosis: Compression fracture at T7 vertebra
- S/P Vertebroplasty with biopsy



PROTOCOL

Past and personal history:

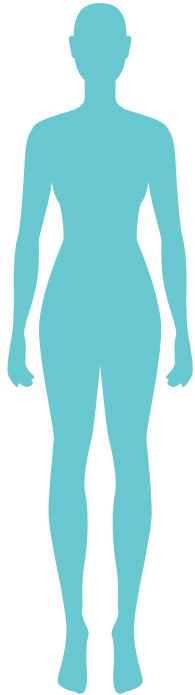
- Myoma uteri S/P TAH with BSO 30 ปีก่อน
- ปฏิเสธประวัติแพ้ยาและแพ้อาหาร
- ไม่ดื่มสุราและไม่สูบบุหรี่ ไม่มีประวัติไข้ยาสมุนไพร/อาหารเสริม

Family history: ปฏิเสธประวัติโรคเมร็งในครอบครัว ไม่มีประวัติกระดูกหักในครอบครัว





PHYSICAL EXAMINATION

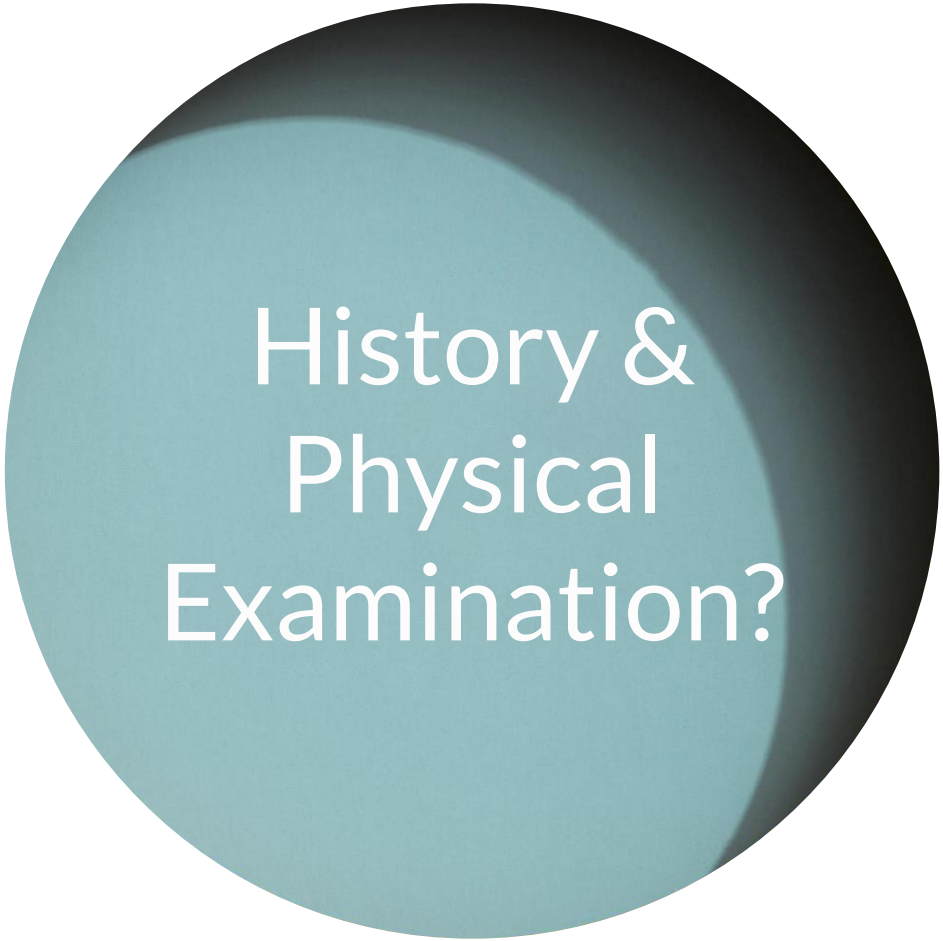


- V/S - BT 36.4 °C, PR 66 bpm, RR 20 breaths/min, **BP 147/78 mmHg**
 - BW 50 kg, HT 155 cm, BMI 20.8 kg/m²
 - HEENT - Not pale conjunctivae, anicteric sclerae
 - CVS - Normal S1S2, no murmur
 - RS - Normal breath sound, no adventitious sound
 - Abdomen - Normoactive bowel sound, soft, no tenderness, no hepatosplenomegaly
 - MSK - **Mild scoliosis and kyphosis**
 - NS - Alert, pupil 2 mm BRTL, CN intact, motor power grade V all
 - Lymph node: No superficial lymphadenopathy
- 

PROTOCOL

- CBC: Hb 10.8 g/dl, Hct 31.7%, MCV 95.2 fl
WBC 11,530 /uL (PMN 90.7%, L 4.9%, M 4.1%, E 0.1%)
Plt 128,000/uL
- BUN 17.5 mg/dL, Cr 0.43 mg/dL
- Ca 8.6 mg/dl, Alb 3.2 g/dL, ALP 90 U/L
- HbA1c 7.2%





History &
Physical
Examination?

PRESENT ILLNESS

- Underlying diseases:
 1. Hypertension: วินิจฉัย 5 ปีก่อน
 2. Diabetes mellitus: วินิจฉัย 1 ปีก่อน รักษาด้วย OHA ควบคุมระดับน้ำตาลได้ดี
 3. MAFLD



PRESENT ILLNESS

6 เดือนก่อน - ผู้ป่วยมีน้ำหนักลด 10 กิโลกรัมใน 4 เดือน สังเกตมีหน้าบวมมากขึ้น มีอ่อนแรงบริเวณต้นแขนต้นขา ไม่มีไข้ ไม่มีคลื่นไส้ก่อนผื่นปกติ ไปพบแพทย์ขณะนั้น แจ้งว่าควบคุมระดับน้ำตาลไม่ได้ จึงได้เริ่มยาฉีด insulin ร่วมกับตรวจพบมีโพแทสเซียมในเลือดต่ำ

2 สัปดาห์ก่อน - ผู้ป่วยมีอาการปวดหลัง ปฏิกิริยาประวัติได้รับอุบัติเหตุรุนแรง ไปตรวจที่ รพ.พบ Fracture at T7 vertebra



PAST & PERSONAL HISTORY

- Myoma uteri S/P TAH with BSO 30 ปีก่อน
- ปฏิเสธประวัติแพ้ยาและแพ้อาหาร
- ไม่ดื่มสุราและไม่สูบบุหรี่ ไม่มีประวัติใช้ยาสมุนไพร/อาหารเสริม
- ไม่เคยมีกระดูกหักบริเวณอื่น
- ไม่เคยมีก้อนนิ่วปนในปัสสาวะ ไม่มีท้องผูก



FAMILY HISTORY

- ปฏิเสธประวัติโรคมะเร็งในครอบครัว
- ไม่มีประวัติกระดูกหักในครอบครัว
- ไม่มีคนใกล้ชิดเป็นวัณโรค
- ปฏิเสธโรคเนื้องอกต่อมพาราไทรอยด์ / ต่อมหมวกไต / ต่อมใต้สมอง หรือแคลเซียมในเลือดสูงในครอบครัว



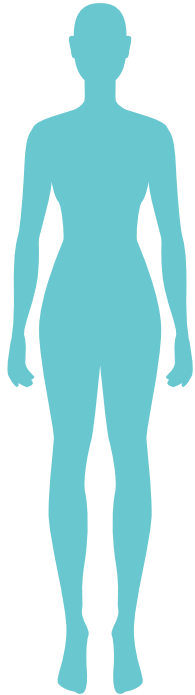
CURRENT MEDICATION:

- Doxazosin (4) 1x1
- Elixir KCL 30 ml PO bid
- Insulin lispro protamine and lispro 25
16 unit sc ac เช้า, 10 unit sc ac เย็น





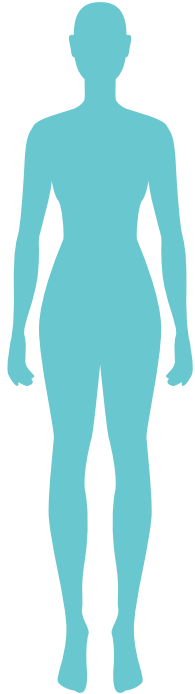
PHYSICAL EXAMINATION



- V/S: BT 36.4 °C, PR 66 bpm, RR 20 breaths/min, **BP 147/78 mmHg**
BW 50 kg, HT 155 cm, BMI 20.8 kg/m²
 - GA: An elderly woman, alert, not pale, no jaundice, **moon face, truncal obesity,**
no pitting edema
 - Skin: **Easy bruising**, no hyperpigmentation
 - HEENT: Not pale conjunctivae, anicteric sclerae, no surgical scar at neck,
no thyroid gland enlargement
 - CVS: Normal S1S2, no murmur
 - RS: Normal breath sound, no adventitious sound
- 



PHYSICAL EXAMINATION



- Abdomen: Normoactive bowel sound, soft, no tenderness, no hepatosplenomegaly, fluid thrill and shifting dullness negative
 - MSK: **Mild scoliosis and kyphosis**, no point of tenderness
 - NS: Alert, pupil 2 mm BRTL, VA LE 20/50⁻¹ / RE 20/40⁻¹, full EOM, no visual field defect
motor power grade V all
 - Lymph node: No superficial lymphadenopathy
- 

A large circle with a teal-to-black gradient background. The text "Problem list?" is centered in white.

Problem list?

PROBLEM LIST



A 73-year-old woman known case HT, DM, MAFLD presented with

1. Pathological fracture at T7 vertebra
2. Significant weight loss for 6 months
3. Worsening glycemic control for 6 months
4. Hypertension with history of spontaneous hypokalemia
5. Cushingoid appearance



Differential Diagnosis & Investigation?



INVESTIGATION





BLOOD CHEMISTRY at consultation (9/5/20)



• BUN	17.5	mg/dL
• Creatinine	0.43	mg/dL
• Sodium	141	mmol/L
• Potassium	3.5	mmol/L
• Chloride	106	mmol/L
• Bicarbonate	25	mmol/L

• FPG	167	mg/dl
• HbA1c	7.2	%





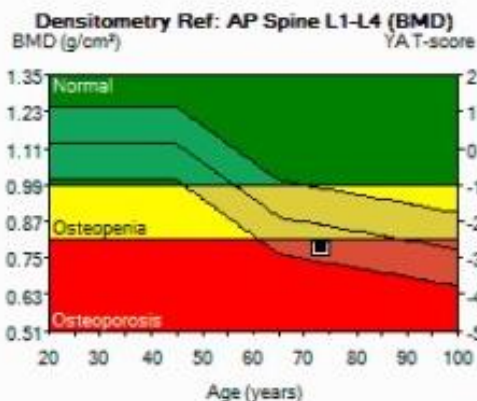
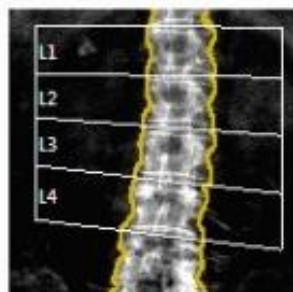
BLOOD CHEMISTRY at consultation (9/5/20)



• Calcium	8.6	mg/dl
• Phosphorus	2.8	mg/dl
• 25-OH Vitamin D	15	ng/mL
• iPTH	34.7	pg/mL

• Albumin	3.2	g/dl
• Globulin	2.6	g/dl
• Total bilirubin	0.43	mg/dl
• Direct bilirubin	0.27	mg/dl
• AST	13	U/L
• ALT	16	U/L
• ALP	90	U/L

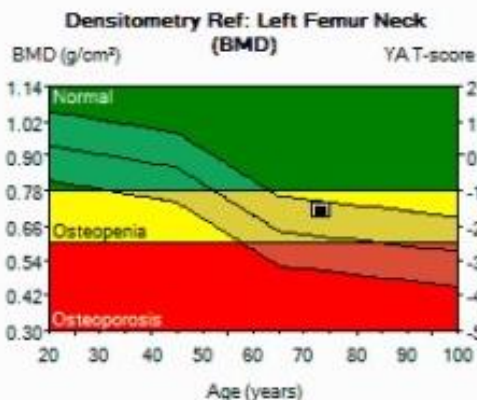




Region	BMD (g/cm ³)	Young-Adult (%)	T-score	Age-Matched (%)	Z-score
L1	0.681	64	-3.2	84	-1.1
L2	0.715	64	-3.4	82	-1.3
L3	0.796	71	-2.7	92	-0.6
L4	0.893	80	-1.9	103	0.2
L1-L2	0.699	64	-3.3	83	-1.2
L1-L3	0.735	67	-3.0	87	-0.9
L1-L4	0.778	70	-2.8	91	-0.7
L2-L3	0.758	68	-3.0	87	-0.9
L2-L4	0.806	72	-2.6	93	-0.5
L3-L4	0.845	75	-2.3	97	-0.2

Matched for Age, Weight (females 25-100 kg), Ethnic Japan (ages 20-40) AP Spine Reference Population (v110)
 Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm³ for AP Spine L1-L4)

Image not for diagnosis



Region	BMD (g/cm ³)	Young-Adult (%)	T-score	Age-Matched (%)	Z-score
Neck	0.711	79	-1.6	114	0.7
Upper Neck	0.558	-	-	-	-
Lower Neck	0.863	-	-	-	-
Wards	0.476	54	-3.1	97	-0.1
Troch	0.663	88	-0.8	112	0.7
Shaft	1.018	-	-	-	-
Total	0.832	89	-0.9	121	1.2

Standardized BMD for Neck is 645 mg/cm³.
 Matched for Age, Weight (females 25-100 kg), Ethnic



PATHOLOGY REPORT

T7 vertebra:

- Trabecular bone with trilineage marrow tissue
- No acute inflammation or granuloma
- No malignancy





SERUM CORTISOL (9/5/20)



- 14.00 Cortisol 37.3 mcg/dl
- 23.00 Cortisol 22.9 mcg/dl (Awake)





ALDOSTERONE and RENIN



- | | | |
|------------------------------------|------|----------|
| • Plasma aldosterone concentration | 4.92 | ng/dl |
| • Plasma renin activity | 0.05 | ng/ml/hr |



1 mg DEXAMETHASONE SUPPRESSION TEST (11/5/20)



- | | | |
|----------------|------|--------|
| • 8AM cortisol | 26.1 | mcg/dL |
|----------------|------|--------|



URINE FREE CORTISOL (10/5/20)



- Urine free cortisol 1,577 mcg/day [0-150 mcg/day]





LATE NIGHT SALIVARY CORTISOL (12/5/20)



- Day 1 0.208 mcg/dL [<0.274 mcg/dL]

Fluctuation of clinical and biochemical of glucocorticoid excess ?



	LNSLC (mcg/dL)	Cortisol (mcg/dL)	Others	Insulin requirement/day
9/5/20	-	(14.00) 37.3 (23.00) 22.9	POCT glucose 167-364 mg/dl	38 unit
10/5/20	-		POCT glucose 225-243 mg/dl	36 unit
12/5/20	0.208	-	POCT glucose 149-199 mg/dl	4 unit
13/5/20	-	(8.00) 6.4	POCT glucose 110-157 mg/dl, K 4.9 mmol/L	No need
14/5/20				Discharge HM Metformin 2 gm/day, Spironolactone 25 mg/day



Fluctuation of clinical and biochemical of glucocorticoid excess ?



BLOOD CHEMISTRY at OPD (22/5/20)



• BUN	17.5	mg/dL
• Creatinine	0.43	mg/dL
• Sodium	141	mmol/L
• Potassium	2.9	mmol/L
• Chloride	106	mmol/L
• Bicarbonate	32	mmol/L

• FPG	191	mg/dl
• Morning cortisol	58.5	mcg/dL

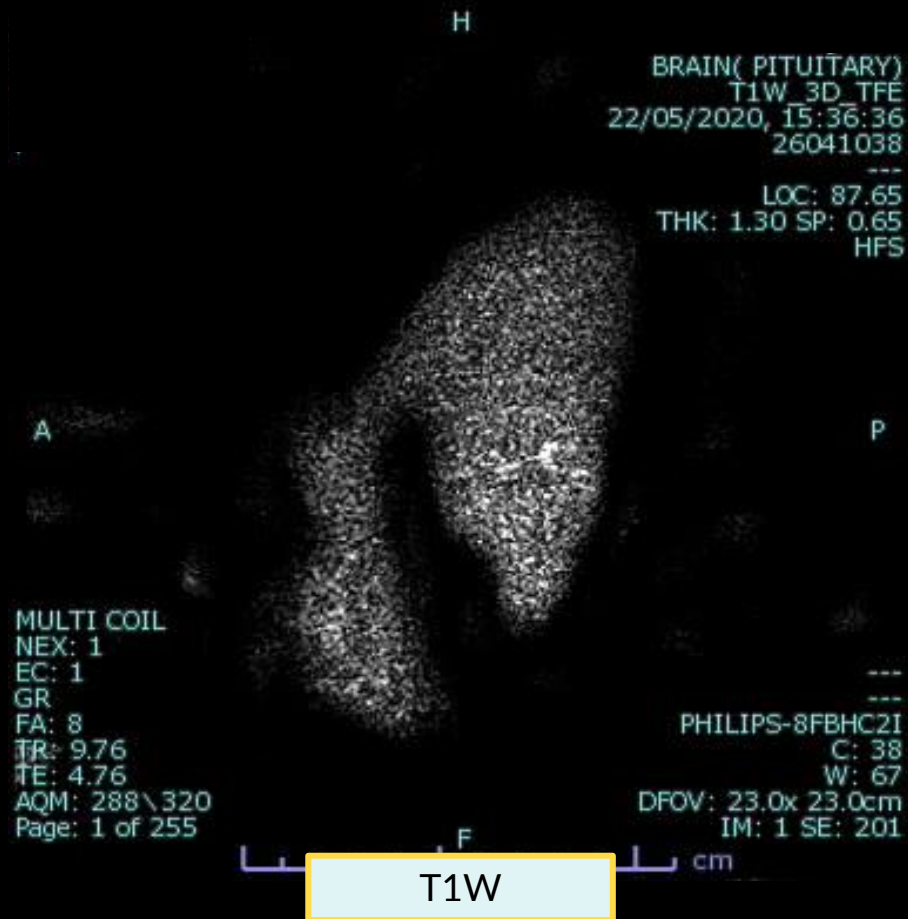


ACTH

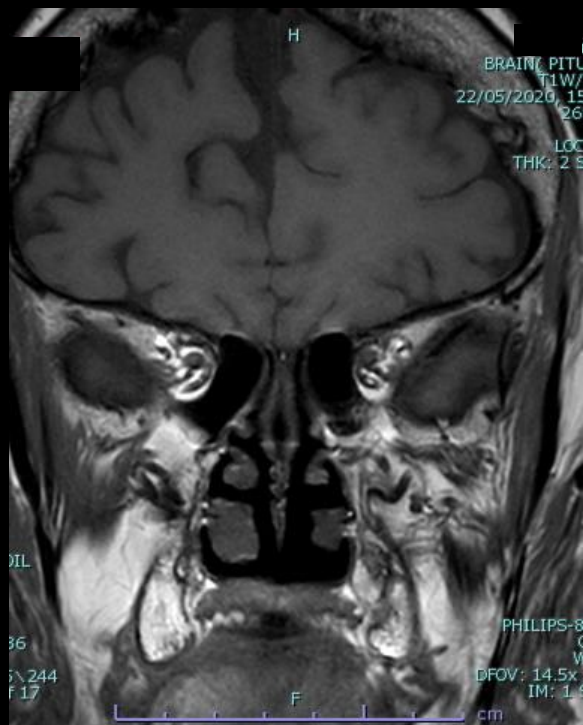


- ACTH

Day 1	107	pg/ml
Day 2	108	pg/ml







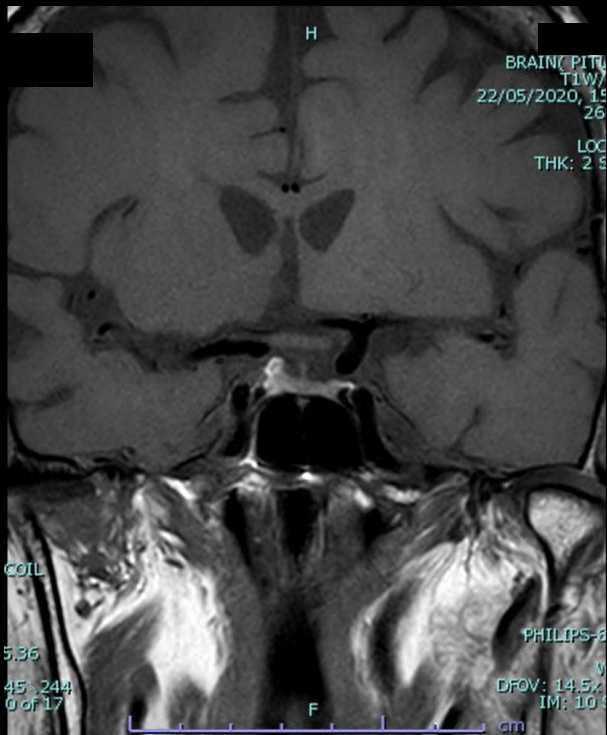
T1W



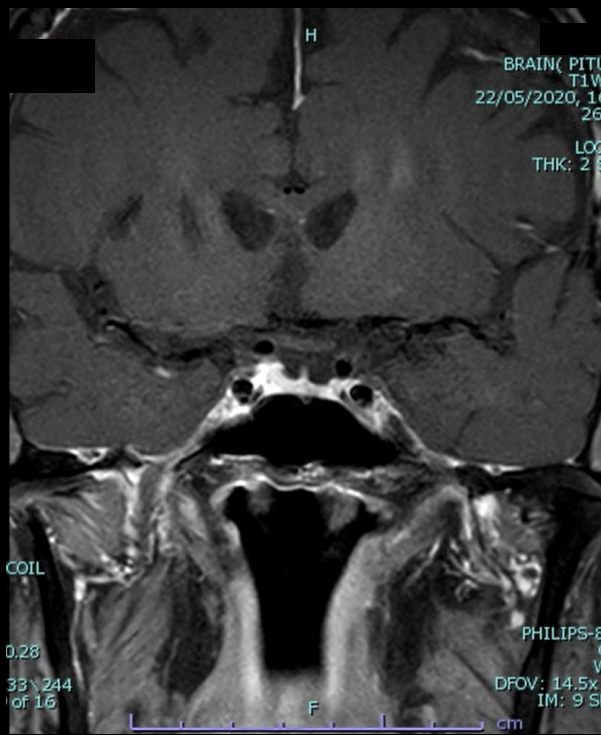
T1W with Gd



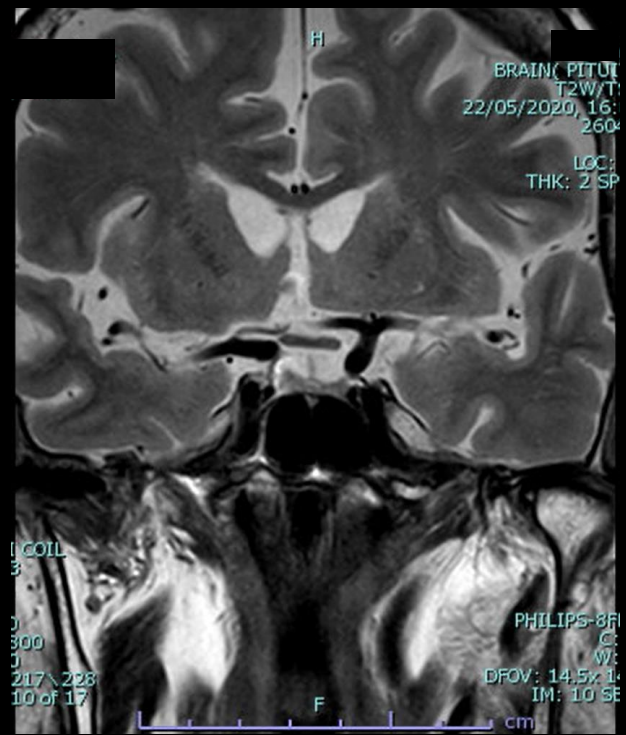
T2W



T1W



T1W with Gd



T2W

MRI Pituitary gland



- Mild asymmetrical size of pituitary gland is seen, more larger size on the right
- Posterior bright spot is noted
- No abnormal delay enhancement or focal enhancing lesion is seen
- Pituitary stalk is in midline
- A small meningioma at left frontal area, about 1.5 cm in size



8 mg DEXAMETHASONE SUPPRESSION TEST



- | | | |
|----------------------------|------|--------|
| • Baseline 8AM cortisol | 58.5 | mcg/dL |
| • 8AM cortisol after HDDST | 58.7 | mcg/dL |



	LNSLC (mcg/dL)	8AM cortisol (mcg/dL)	Others
25/5/20	0.6470	-	-
26/5/20	1.690	-	-
27/5/20	5.240	-	-
28/5/20	1.770	-	-
29/5/20	1.440	20.2	-
2/6/20	4.740	-	-
3/6/20	1.820	-	-
10/6/20	-	46.6	ACTH 83.51 pg/ml
13/6/20	1.660	-	-
14/6/60	7.300	37.8	-



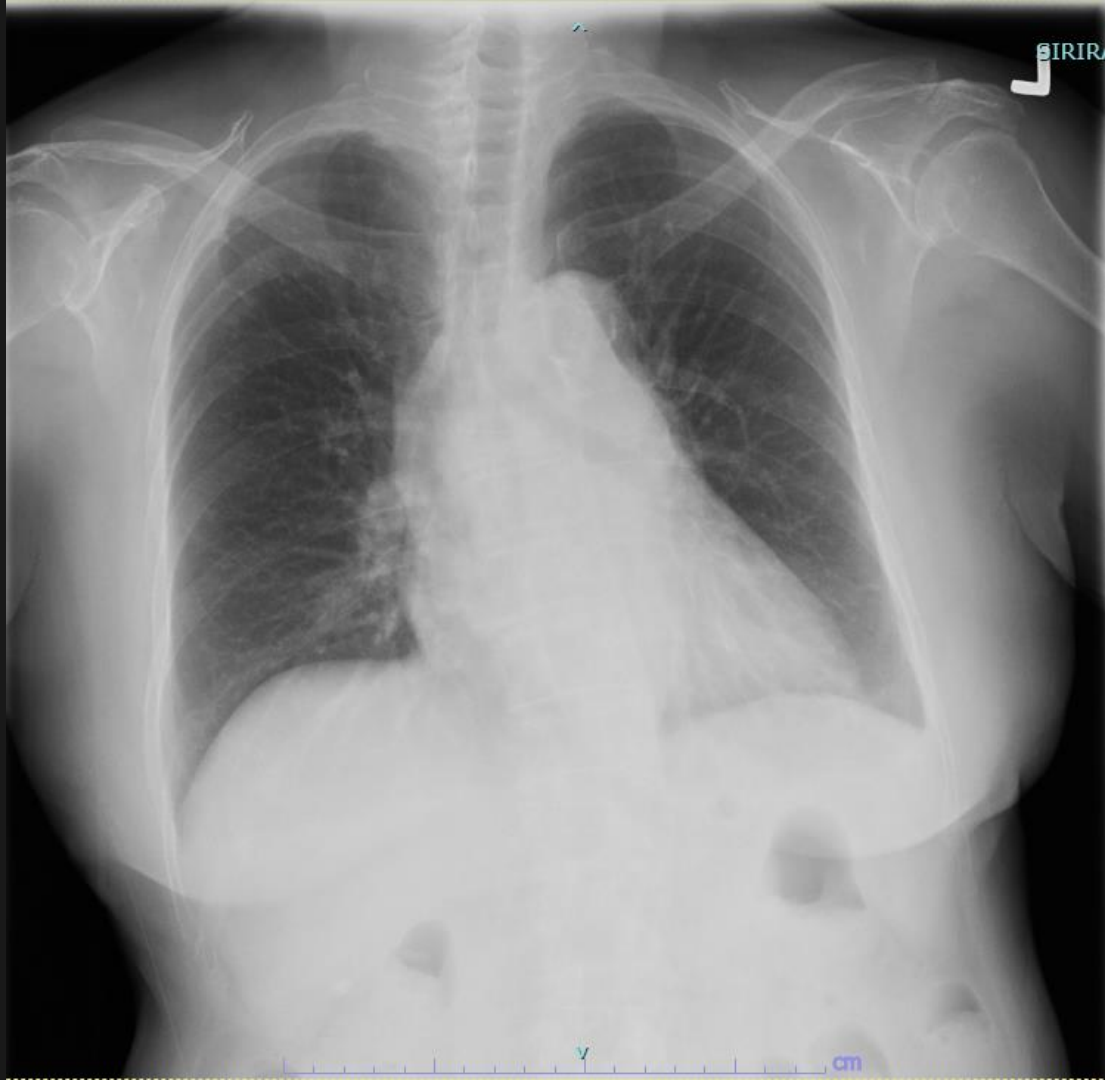
Time (min)	ACTH (pg/ml)			ACTH ratio		Prolactin (ng/ml)			Prolactin ratio	
	Rt.IPS	Lt.IPS	P	Rt.IPS/P	Lt.IPS/P	Rt.IPS	Lt.IPS	P	Rt.IPS/P	Lt.IPS/P
-5	61.19	59.32	55.55	1.10	1.07	36	20.8	19	1.89	2.28
-2	62.68	58.27	56.82	1.10	1.03	39.7	21.9	18.7	2.12	1.17
2	63.85	57.28	51.83	1.23	1.11	36.1	22.1	18.6	1.94	1.19
5	65.7	59.12	54.68	1.20	1.08	40.8	23.4	18.3	2.23	1.28
10	63.86	58.26	53.76	1.19	1.08	33.2	22.3	18.5	1.79	1.21

ACTH: Adrenocorticotrophic hormone; IPS: Inferior petrosal sinus; P: Peripheral



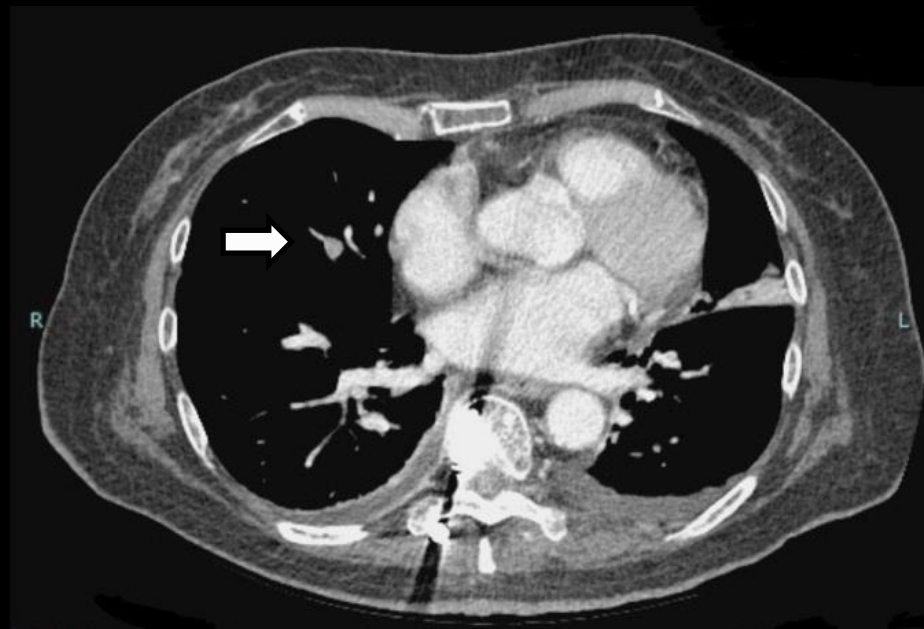
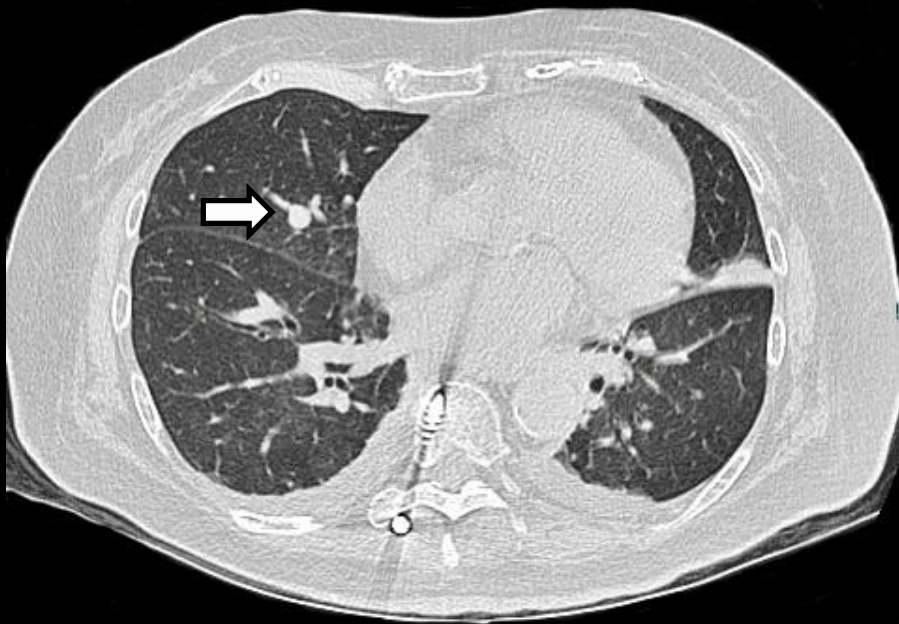
Time (min)	ACTH (pg/ml)			ACTH ratio		Prolactin (ng/ml)			Prolactin ratio		Results
	Rt.IPS	Lt.IPS	P	Rt.IPS/P	Lt.IPS/P	Rt.IPS	Lt.IPS	P	Rt.IPS/P	Lt.IPS/P	
-5	61.19	59.32	55.55	1.10	1.07	36	20.8	19	1.89	2.28	0.65
-2	62.68	58.27	56.82	1.10	1.03	39.7	21.9	18.7	2.12	1.17	
2	63.85	57.28	51.83	1.23	1.11	36.1	22.1	18.6	1.94	1.19	
5	65.7	59.12	54.68	1.20	1.08	40.8	23.4	18.3	2.23	1.28	
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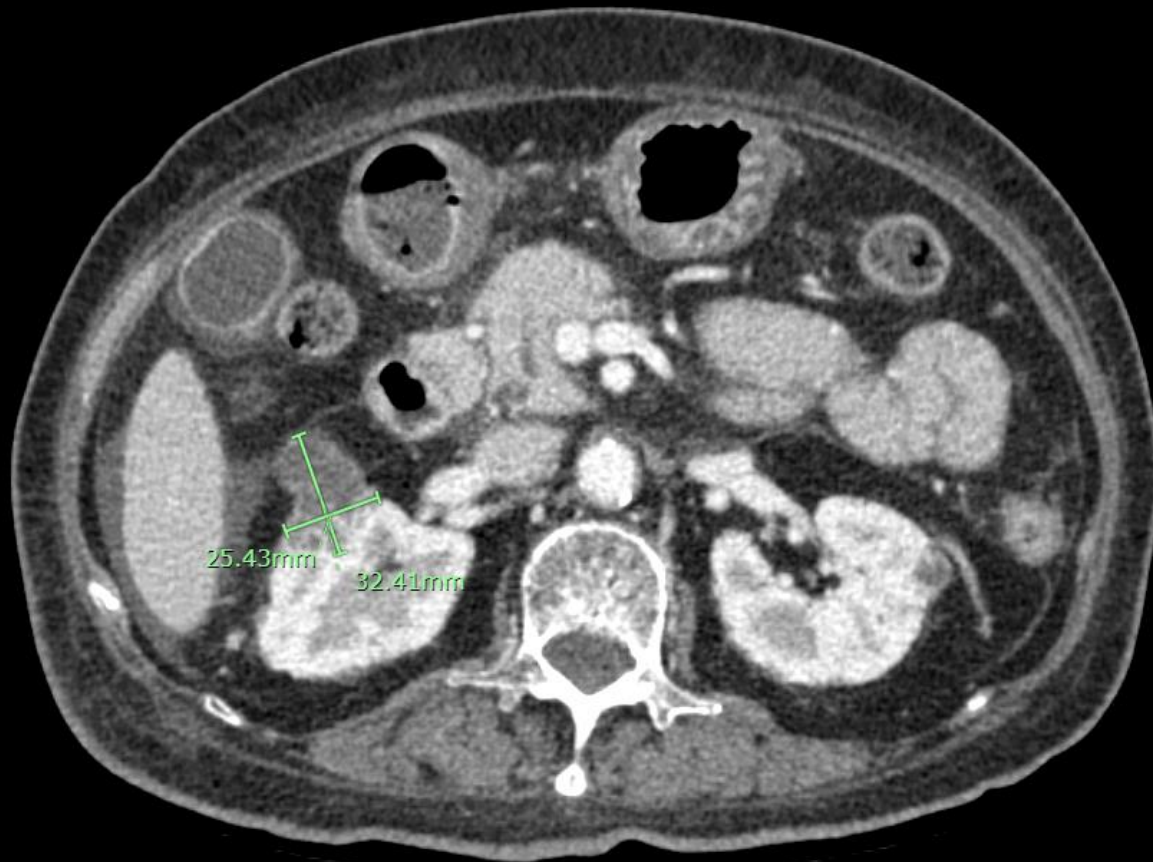
Multiple thyroid nodules



0.9 cm enhance nodule at lateral segment of the right middle lung



Diffuse thickening of both adrenal glands

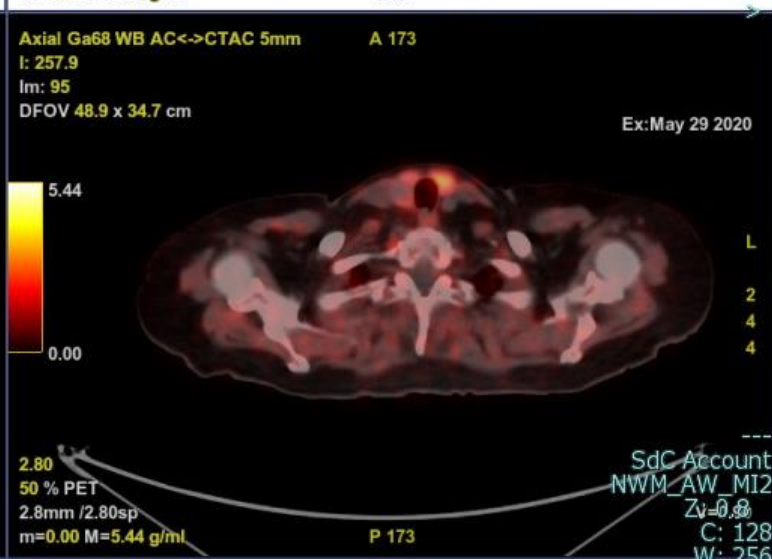
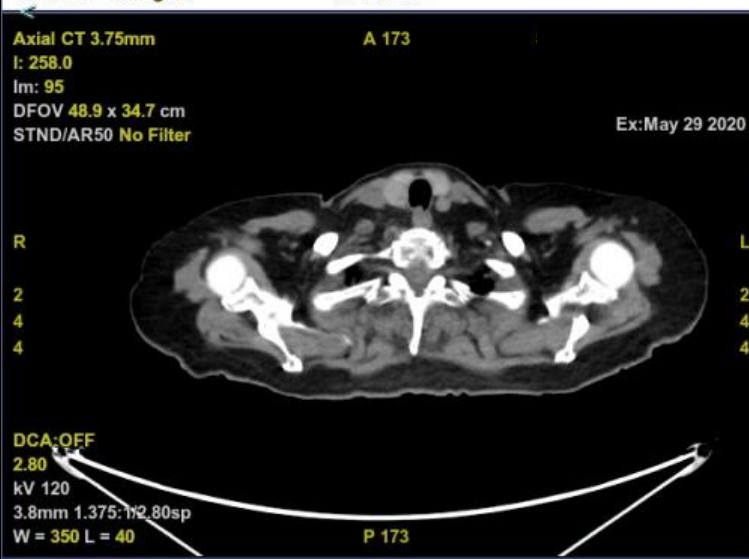
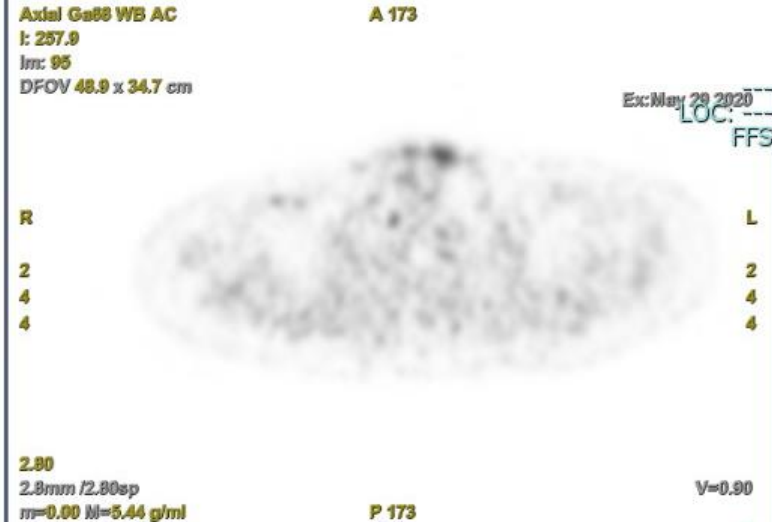


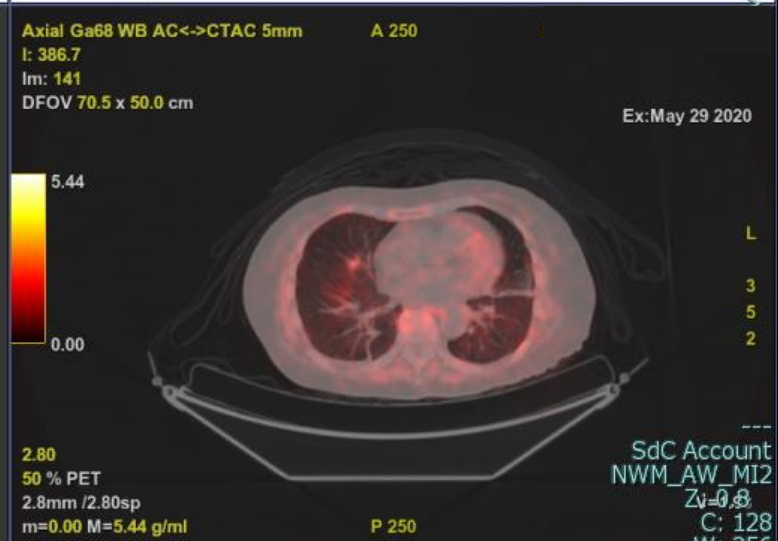
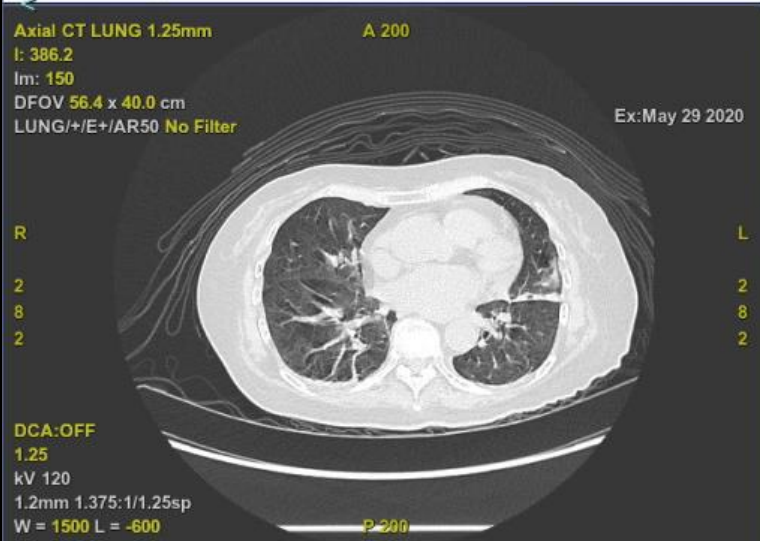
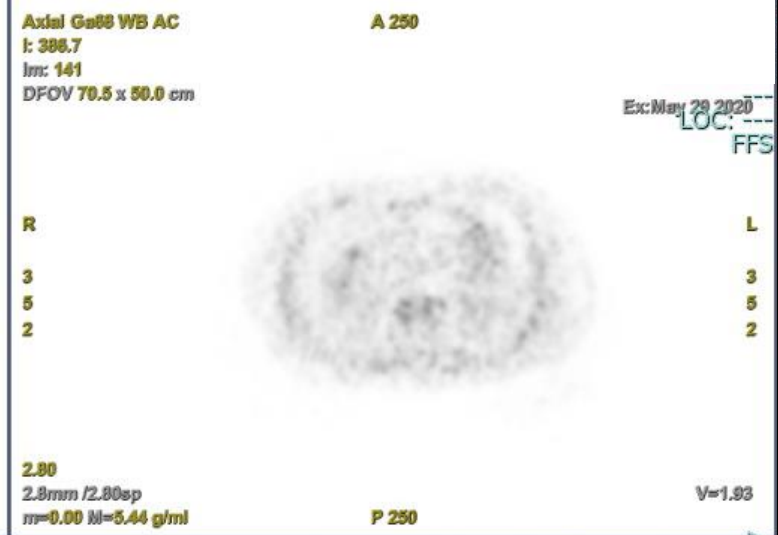
Innumerable cortical renal cysts, with some internal septa

CT Chest & Whole abdomen



- 0.9 cm enhanced nodule at lateral segment of RML
- Minimal centrilobular ground-glass nodules at anterior segment of LUL
- Minimal bilateral pleural effusion with passive atelectasis at both basal lungs
- Multiple thyroid nodules
- Gallbladder shows diffuse wall thickening with four gallstones
- Diffuse nodular thickening of both adrenal glands
- Innumerable cortical renal cysts, with some internal septa





Ga-68 DOTATATE PET/CT

Whole body (29/5/20)



- 1.8 x 1.6 cm well-defined hypodense thyroid nodule without Ga-68 DOTATATE uptake
- 1.1 x 1.0 cm endobronchial nodule at the lateral segment of RML with mildly increased uptake (SUV_{max} of 2.0)

BRONCHOSCOPY & BAL



- No endobronchial nodule was detected
- Cytology: Non-specific reactive process, negative for malignancy



THYROID FUNCTION TEST



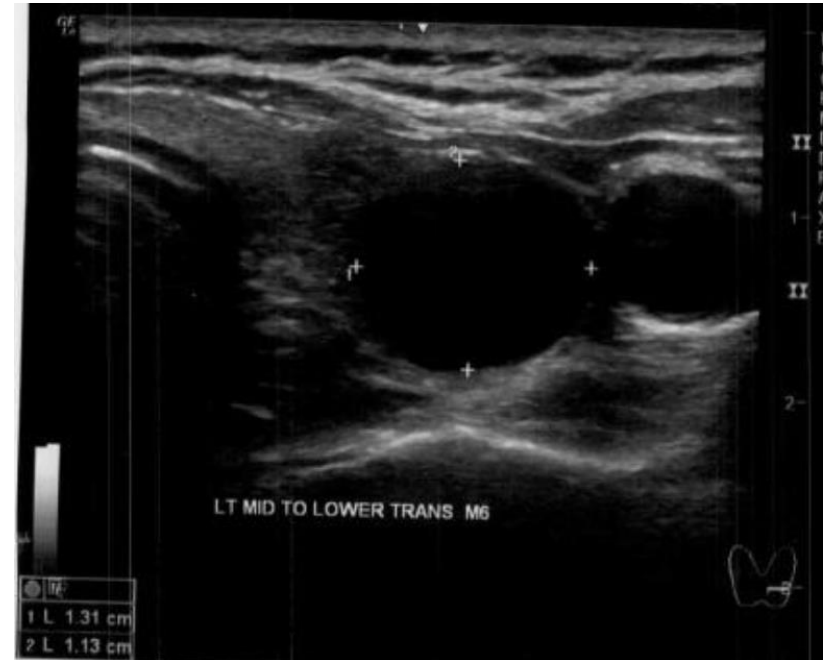
• FT3	1.55	pg/mL	[1.71-3.71]
• FT4	0.83	ng/dL	[0.70-1.48]
• TSH	1.654	uIU/mL	[0.350-4.940]



US Thyroid

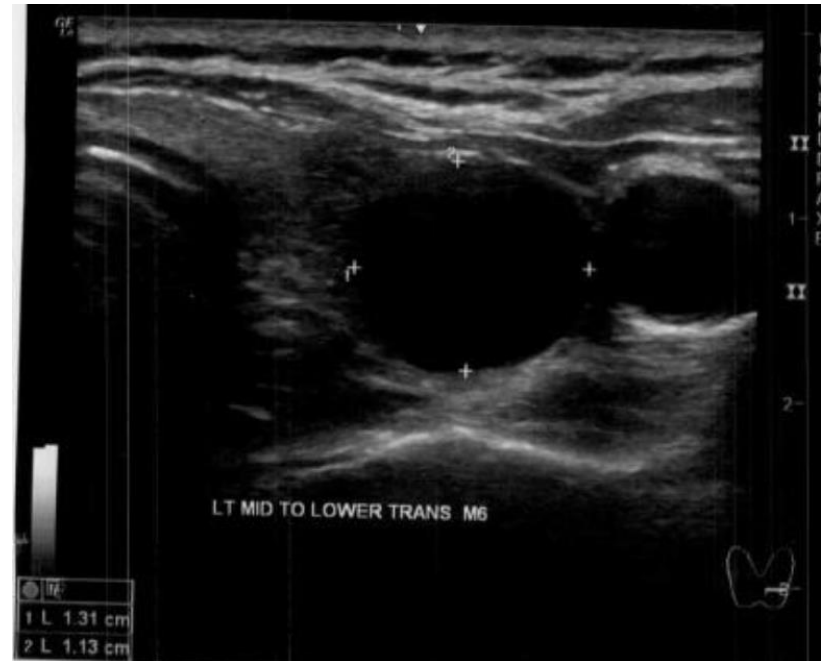


- Multiple small anechoic solid nodule, cysts, and spongiform nodule scattering in both lobes of the thyroid gland
- The largest, **anechoic solid nodule** **1.31x1.13x1.56 cm** at mid to lower pole of the left lobe of the thyroid gland



FNA

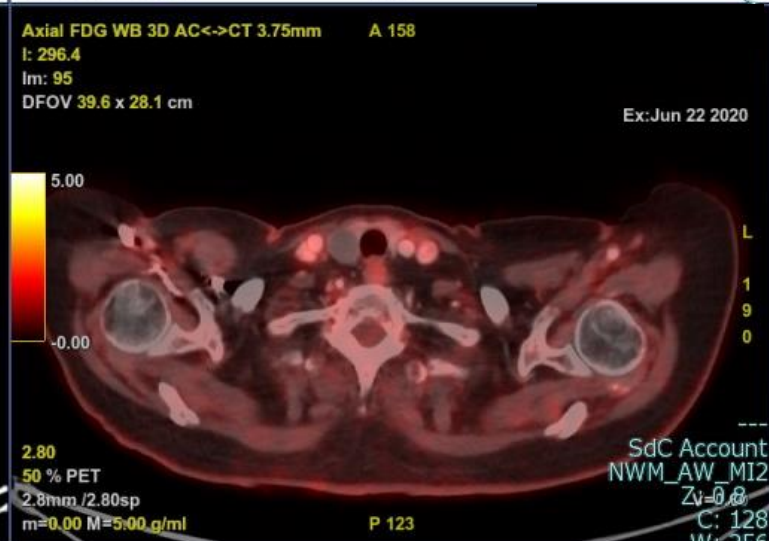
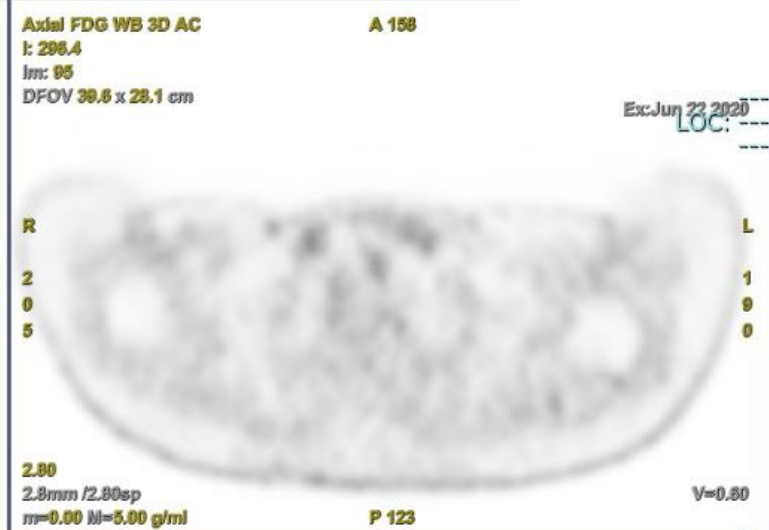
Benign follicular nodule
(The Bethesda category II)

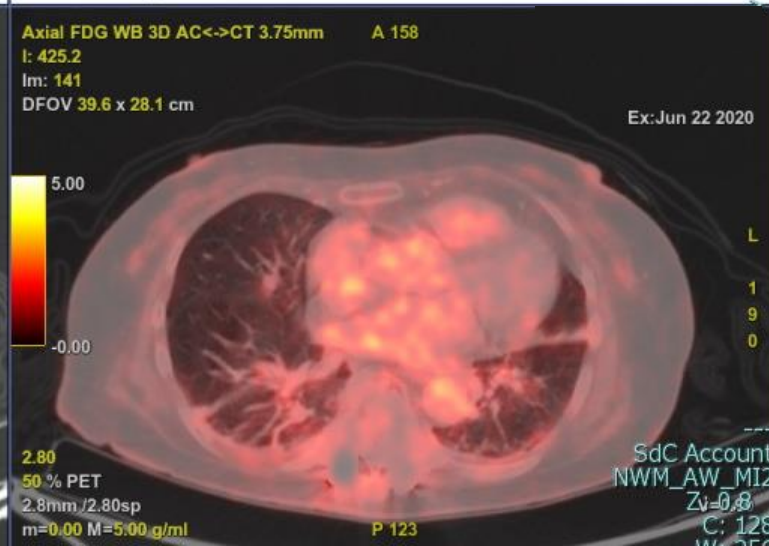
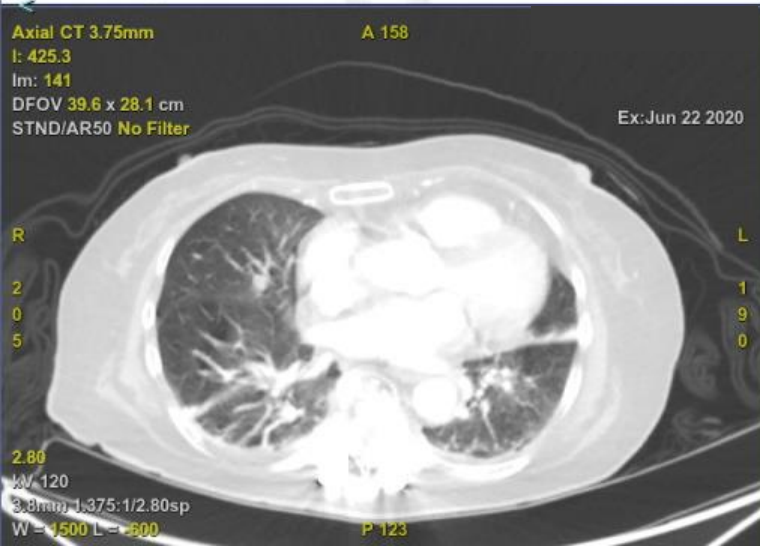
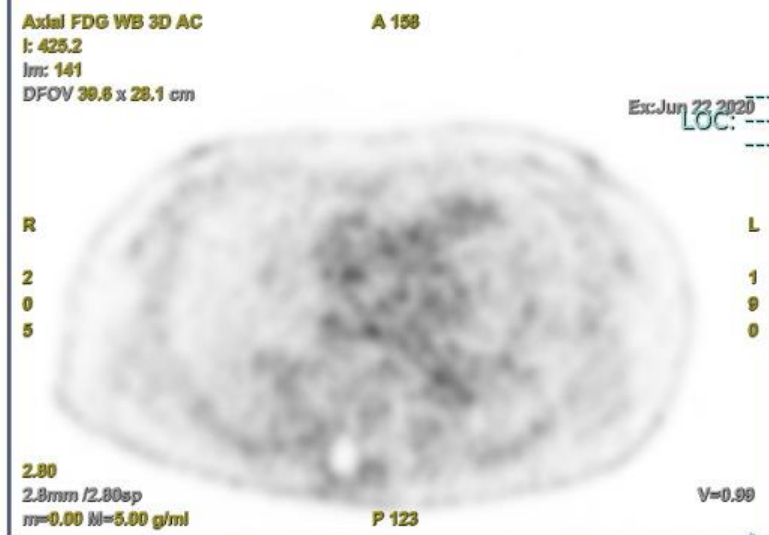


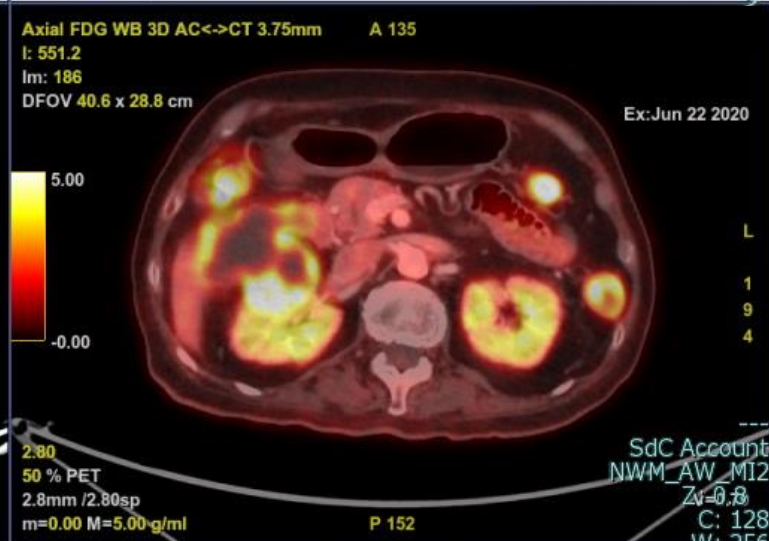
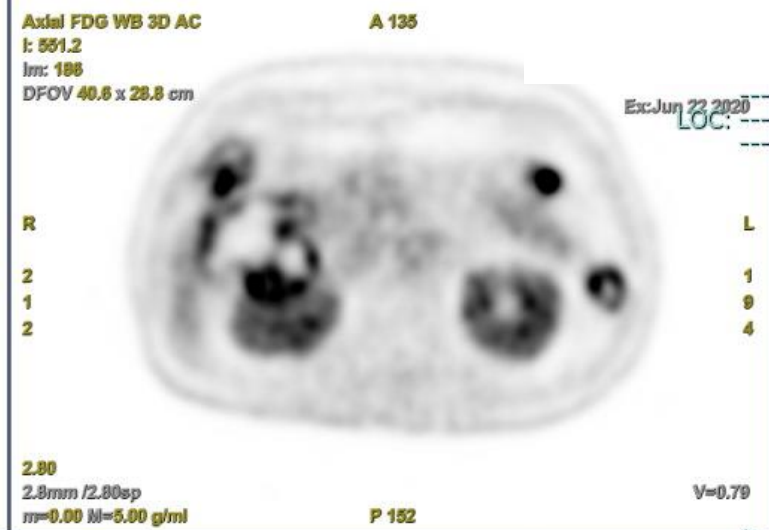
TUMOR MARKERS



- Calcitonin **17.7** pg/mL [10 – 11.5 pg/mL]
- CEA **3.78** ng/ml [0 – 3.4 ng/ml]







F-18 FDG PET/CT whole body (24/6/20)



- Multiple hypodense thyroid nodules without abnormal FDG uptake, size up to 2.1x1.6 cm
- 0.9 x 0.8 cm non-calcified solid pulmonary nodule at the lateral segment of RML without hypermetabolism
- Cystic lesion at right kidney with internal septation with focal wall thickening, 5.1x5.8 cm (prior was 3.6x2.8 cm), abutting hepatic S6 and posterior wall of gallbladder with hypermetabolism at thickening wall (SUV max 7.70)

A large circle with a teal-to-black gradient background. The word "Management?" is centered in white text.

Management?



PROGRESSION

- US and CT guidance percutaneous drainage of right renal abscess
- Procedure and finding:
 - Well-defined heterogeneous echoic lesion at upper pole of right kidney
 - The turbid pus was aspirated about 20 ml
- Pus culture: *E. Coli* (ESBL positive)
- Treatment: Meropenem IV -> Ertapenem IV -> Sitafloxacin PO (total 21 days)

	LNSLC (mcg/dL)	8AM cortisol (mcg/dL)	Management
14/6/20	7.300	37.8	-
25/6/20	Percutaneous drainage right renal abscess		
27/6/20	1.240	-	ATB / Ketoconazole (200) 1x1
1/7/20	-	43.1	ATB / Ketoconazole (200) 1x1
5/7/20	4.840	43.9	ATB / Ketoconazole (200) 1x2
12/7/20	0.086	8.4	ATB / Ketoconazole (200) 1x2
13/7/20	Off PCD / Ketoconazole		
15/7/20	1.770	-	ATB
16/7/20	-	1 mg DST = 57.7	ATB
17/7/20	-	-	ATB / Ketoconazole (200) 1x2
21/7/20	-	9.3	Off ATB / Ketoconazole

VATS Wedge resection RML

Operative finding:

- RML nodule 8 mm
- No pleural nodule
- No pleural effusion
- Complete major fissure

PATHOLOGY REPORT



Lung, right middle lobe, wedge resection (2 separate pieces):

- The larger piece (6x3x3 cm): Involve by **small round cell neoplasm** with severe crushing artifact, consistent with **ACTH-producing typical carcinoid**
 - Size: 1.2 x 0.8 x 0.3 cm
- The smaller piece (3.5x1.4x1.4 cm): Involve by **small round cell neoplasm** with severe crushing artifact, consistent with **typical carcinoid**
 - Size: 0.8 x 0.6 x 0.3 cm

PATHOLOGY REPORT



- Evaluation of the tumor morphology including histologic grade is limited by severe crushing artifact
- Mitotic rate is 0-1/2 mm²
- No necrosis is observed
- Tumor cells are **positive for AE1/AE3, synaptophysin, chromogranin A, CD56 and ACTH** but negative for CD45
- Ki-67 proliferation index is 1%
- The result support ACTH-producing typical carcinoid

	LNSLC (mcg/dL)	8AM cortisol (mcg/dL)	Others
22/7/20	-	41.8	-
23/7/20	- VATS Wedge resection RML - Pre-operative: Hydrocortisone 100 mg IV then 200 mg IV drip in 24 hr - Off Hydrocortisone		
25/7/20	-	16.8	ACTH 35.38 pg/ml
27/7/20	0.672	-	-
31/7/20	0.076	1 mg DST = 2.6	ACTH <3.8 pg/ml
17/8/20	0.071	13.70	ACTH 17.31 pg/ml
25/8/20	-	1 mg DST = 1.0	Prednisolone (5) 1x1 PO PC (due to steroid withdrawal symptom)
29/9/20	0.054	10.8	FBS 90 mg/dl, HbA1c 5.4% Off prednisolone

Diagnosis:

Ectopic ACTH syndrome
from
bronchial carcinoid tumors

