In the name of God

case presentation

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12 february 2024

- Gender: woman
- Age: 53-year-old
- Source of History: Her mother, Reliable
- Single
- Born & live in Tehran
- Education: environmental health

Chief complaint:

- A 53-year-old woman with the history of Psychiatric disorders & parathyroidectomy
- Hospitalized with weakness, fatigue, imbalance, drowsy since two weeks ago

Present illness:

- A 53-year-old woman with the history Psychiatric disorders & parathyroidectomy
- Admitted in emergency room with drowsy & hypercalcemia
- Eight months ago (1402.03.15) she was hospitalized in Taleghani because of schizoaffective disorder depressive type diagnosed
- Depression mood
- Persecutory delusion
- Control delusion

Present illness:

- (1402.03.23) medical therapy + ECT with 26j
- (1402.03.25) ECT
- (1402.03.23) Endocrinology consult
- calcium = 14.2 mg/dl

Present illness:

- Hydration + diuretic therapy + calcitonin
- Lab data
- BMD
- Sonography
- MIBG

Calcium mg/dl	14.2	14.6 (1402.03.23)	13.8	12.3	11.6	10.1	9.5 4 TIR	7.8	8.5
Phosphorus mg/dl	2	2.2	1.8	1.5	1.3	1.2	1.2	1.4	1.3
Mg mg/dl	1.5						1.5		
ALB	3.8	3.9							
PTH Pg/dl		457							
25(OH)D3 ng/dl		19.4							

BONE MINERAL DENSITOMETRY

This patient attended for bone densitometry of lumbar spine and hip regions on the HOLOGIC Explorer QDR series DXA.

Risk factors of the patient for low bone density and fracture are:

Menopause

The young normal adult and age matched T and Z scores for BMD are:

Scan	BMD(g/cm2)	T-Score	Fracture Risk	Z-Score
Lumbar Spine	0.499	-4.7	High	-3.9
Total Femur	0.560	-3.1	High	-2.6
Femoral Neck	0.484	3.3	High	-2.4
Forearm	-	-	-	-

Impression: According to WHO classification, the BMD of this patient is

Osteoporosis.

Present illness: (1402.03.29)

- Thyroid sonography:
  - NL size & NL echogenicity
- Parathyroid sonography:
  - A round & isoechoic mass 13*11.5*11 mm in left parathyroid

PARATHYROID SCINTIGRAPHY BY 99m Tc-MIBI AND SPECT:

Images were obtained after IV injection of 99m Tc-MIBI in 20 minutes and 1 and 2 hours.

On MIBI scan, there are multiple focal zones of radiotracer collection in lower pole of left thyroid lobe, adjacent (or inferior) to lower pole of left thyroid lobe and the largest one in lower pole of right thyroid lobe, which are persistent in delayed images.

On thyroid scan, distribution of homogenous radiotracer uptake is seen.

IMPRESSSION:

- **Findings of scan suggest parathyroid adenoma in lower pole of left thyroid lobe, adjacent (or inferior) to lower pole of left thyroid lobe and the largest one in lower pole of right thyroid lobe.**
- Laboratory correlation (serum PTH) and sonographic evaluation are recommended for evaluation of thyroid nodules in lower pole of right and left thyroid lobes.

Present illness:

- Surgery consult
- (1402.04.04) two parathyroidectomy

(1402.04.04)

ادامه شرح عمل از صفحه قبل :

پس از بیهوشی عمومی

سپس بیمار پرپ درپ شد.

تزریق اپرون در دوسانتی متر بالای سوپرا استرنال ناچ تا پلن ساب پلاتیسمال زده شد و سپس فلپ سوپریور و اینفریور در بالا و پایین باز شد.در میدلاین عضلات استرپ در رافه میانب باز شد سپس تیروئید اکسپوز شد

در سمت چپ پل تحتانی تیروئید ادنوم بزرگ حدود یک تا دو سانتی متر ریت شد. عصب ریکارنت سمت چپ رویت و حفظ شد در سمت راست نیز ادنوم رزکت شد و عصب ریکارنت نیز حفظ شد

نمونه ها جهت پاتولوژی ارسال شد

درن همووواک هر دوسمت تعبیه شد

عضلات استرپ دوخته شد و سپس پوست در دولایه دوخته شد

پس از اطمینان از هموستاز بیمار تحویل همکاران محترم بیهوشی داده شد

ntinue:

Macroscopic :

Received specimen in fresh state for intraoperative consultation and consist of:

F1) A pink elastic irregular tissue measuring 2x0.7x0.6cm, W: 0.62gr. TS in 1 block.

F1SDX: Parathyroid tissue.

F2) A pink elastic irregular tissue measuring 1.8x1.1x0.5cm, W: 0.8gr. TS in 1 block.

F2SDX: Parathyroid tissue.

Microscopic :

Histologic findings, confirm the following diagnosis.

Diagnosis :

F1) Labeled as right parathyroid adenoma, resection (frozen and final diagnosis):

- Parathyroid tissue compatible with clinical diagnosis "parathyroid adenoma".

F2) Labeled as left parathyroid adenoma, resection(frozen and final diagnosis):

- Parathyroid tissue compatible with clinical diagnosis "parathyroid adenoma".

Pathologist: Dr. Parvizi MD/AP.CP Resident: Dr. Firouzi MD

1402.04.11

Calcium mg/dl	14.2	14.6 (1402.03.23)	13.8	12.3	11.6	10.1	9.5 4 TIR	7.8	8.5
Phosphorus mg/dl	2	2.2	1.8	1.5	1.3	1.2	1.2	1.4	1.3
Mg mg/dl	1.5						1.5		
ALB	3.8	3.9							
PTH Pg/dl		457							
25(OH) D3 ng/dl		19.4							

Present illness:

- She discharged;
  - Risperidone 2mg daily
  - Biperiden 2mg BD
  - Citalopram 20mg daily
  - Propranolol 20mg TDS
  - Clonazepam 1mg H.S
  - Depakine 500 daily
  - Quetiapine 25mg H.S
  - Calcium carbonate 500mg TDS
  - Rocaltrol 0.25mcg daily

	1402.05.18	1402.05.28
Calcium (mg/dl)	10.8	10
Phosphorus (mg/dl)	2.7	
ALB (g/dl)	4.4	
PTH (Pg/dl)	310	
25(OH)D3 (ng/dl)	36	

Present illness:

- (1402.06.10) hospitalized B1D +PF , DEMENTIA
- Persecutory delusion
- Control delusion
- Aggression
- Auditory hallucination
- Visual hallucination
- Talkative

خدمت درخواستی : MRI مغز بدون ماده حاجب

تکنیک تصویر برداری:ام ار ای مغز بدون کنتراست

یافته ها :

فضاهای اکسترا آگزیال :در سایز و شکل با توجه به سن بیمار نرمال هستند

خونریزی اکسترا آگزیال : ندارد

سیستم بطنی : در سایز و شکل با توجه به سن بیمار نرمال هستند

سیسترن های بازال : نرمال

شیفت میدلاین : ندارد

مخچه :نرمال

ساقه مغز : نرمال

کالواریوم : نرمال

سیستم عروقی :نرمال .

Signal void مناسب شریانی و سینوس های دورا رویت میشود.

بخش های قابل رویت سرویکال فوقانی :نرمال

Polyp/mucus retention cyst در سینوس ماگزیلاری چپ رویت شد.

ندول زیرجلدی به ابعاد 9×7mm در پریتال چپ به صورت Low T2/FLAIR و intermediate T1 رویت شد.

اربیت :در حد قابل رویت نرمال

ناحیه سلا و قاعده جمجمه نرمال

Brain Perfusion Scintigraphy

History:

The patient is a 53-year-old woman with history of psychosis, manic episode (B1D) and aggressive behavior who is referred for further evaluation.

Procedure:

The patient was placed in a quiet, dimly-lit room. Intravenous cannula was placed *10 to 15 min prior to* injection of 740 MBq 99mTc-ECD. The patient had their eyes open but was instructed not to speak, read or move for at least 5 minutes before to 5 minutes after the injection. SPECT was acquired *60 minutes* after injection with the patient lying in supine position.

Description:

The scan reveals mild to moderately decreased perfusion of bilateral anterior temporal lobes, more prominent on the right side. No significantly decreased or increased regional perfusion is evident in remainder of the brain hemispheres.

Impression:

- ***Mild to moderately decreased perfusion of bilateral anterior temporal lobes, more prominent on the right side.***

With respect to patient's history and complex neurologic medications she is receiving, the scan pattern is currently not specific. Initial stages of frontotemporal dementia may be DDx, in appropriate clinical setting.

Sincerely yours
G. Norouzi M.D.

Present illness:

Calcium	9.9	9.2	9.4	10.4	10.7
Mg	2.1				
Cr	0.74				
Tsh	2.17				
Alk P	220				
K	4.1				

Present illness:

- She discharged; (1402 MEHR)
  - psychotherapy
  - Valproate NA 200mg TDS
  - Biperiden 2mg BD
  - Haloperidol 5mg daily
  - Propranolol 20mg TDS
  - Memantine 10 BID
  - Donepezil 5mg H.S
  - Quetiapine 25mg H.S

Present illness:

	1402.07.10	1402.08.06
Calcium (mg/dl)	11	11.2
Phosphorus (mg/dl)		3.6
Mg (mg/dl)		2.4
ALB (g/dl)		3.7
PTH (Pg/dl)		284.4
25(OH)D3 (ng/dl)		25
K (mEq/l)	4.2	
TSH (µIU?/ml)	9.59	

	1402.10.17	1402.10.24
Calcium (mg/dl)	14.2 – 10.2	8.5
Phosphorus (mg/dl)		2.7
Mg (mg/dl)		1.6
ALB (g/dl)		3.7
PTH (Pg/dl)		550
25(OH)D3 (ng/dl)		35
K (mEq/l)	4	
TSH (µIU?/ml)	0.013	

- Hospitalized with weakness, fatigue, imbalance, drowsy since two weeks ago (1402.11.07)

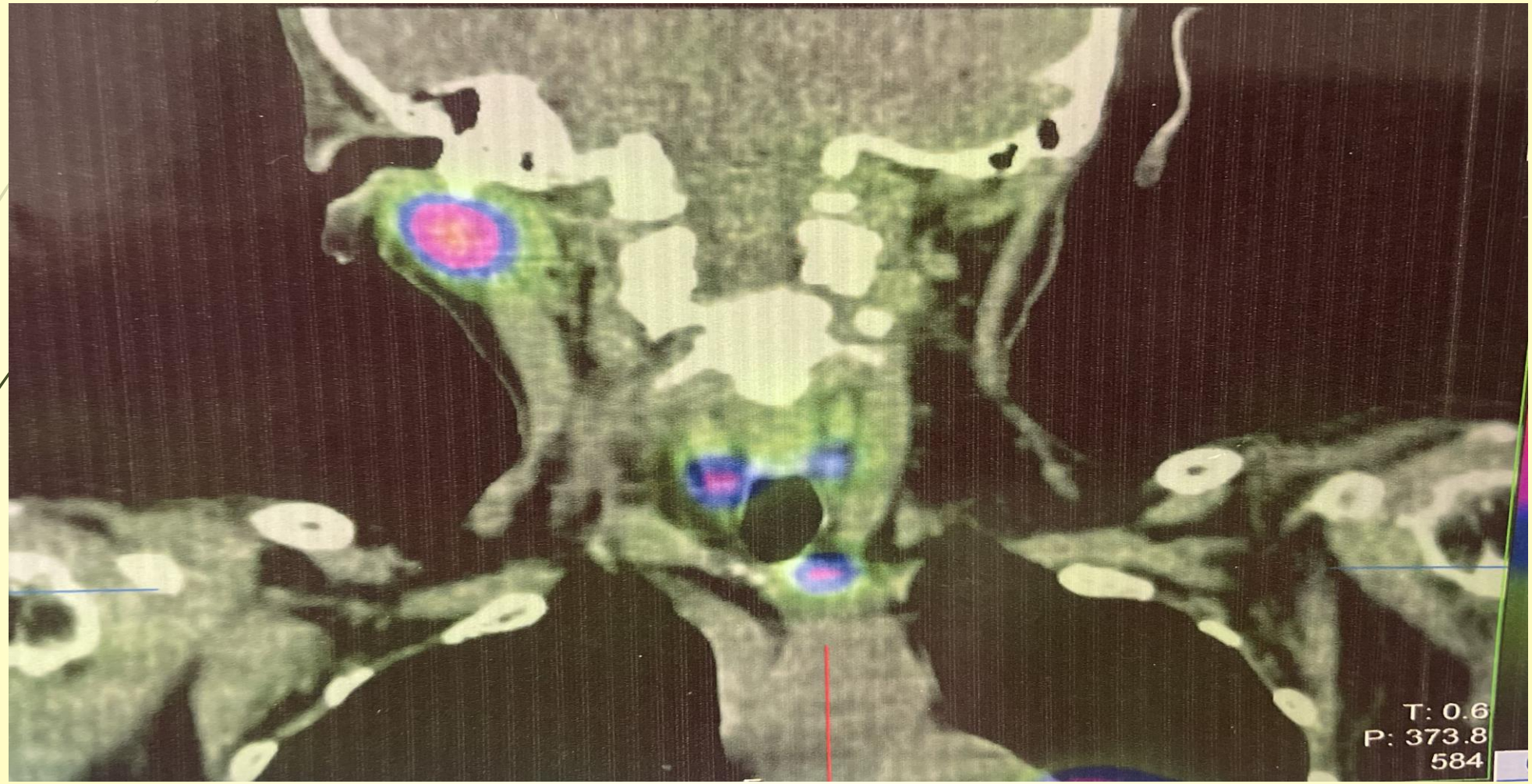
	7.11					9.11		11.11		12.11	
Calcium mg/dl	19.1	16.9	15.3	13.5	11.9	12.6	12	7.9	7.1	8.9	9.1
Phosphorus mg/dl	2.7			1.3	1.2	2.9	1	1.4	1.2	1.6	3
Mg mg/dl	1.4					1.2	1.5	1.9	1.3	1	1.2
ALB g/dl	3.4										
PTH Pg/dl	1099					204				114	
25(OH)D3 ng/dl	31.1										
K mEq/l	2.3	2.5	4.3	3	5.2	4.8		4.5			4.2

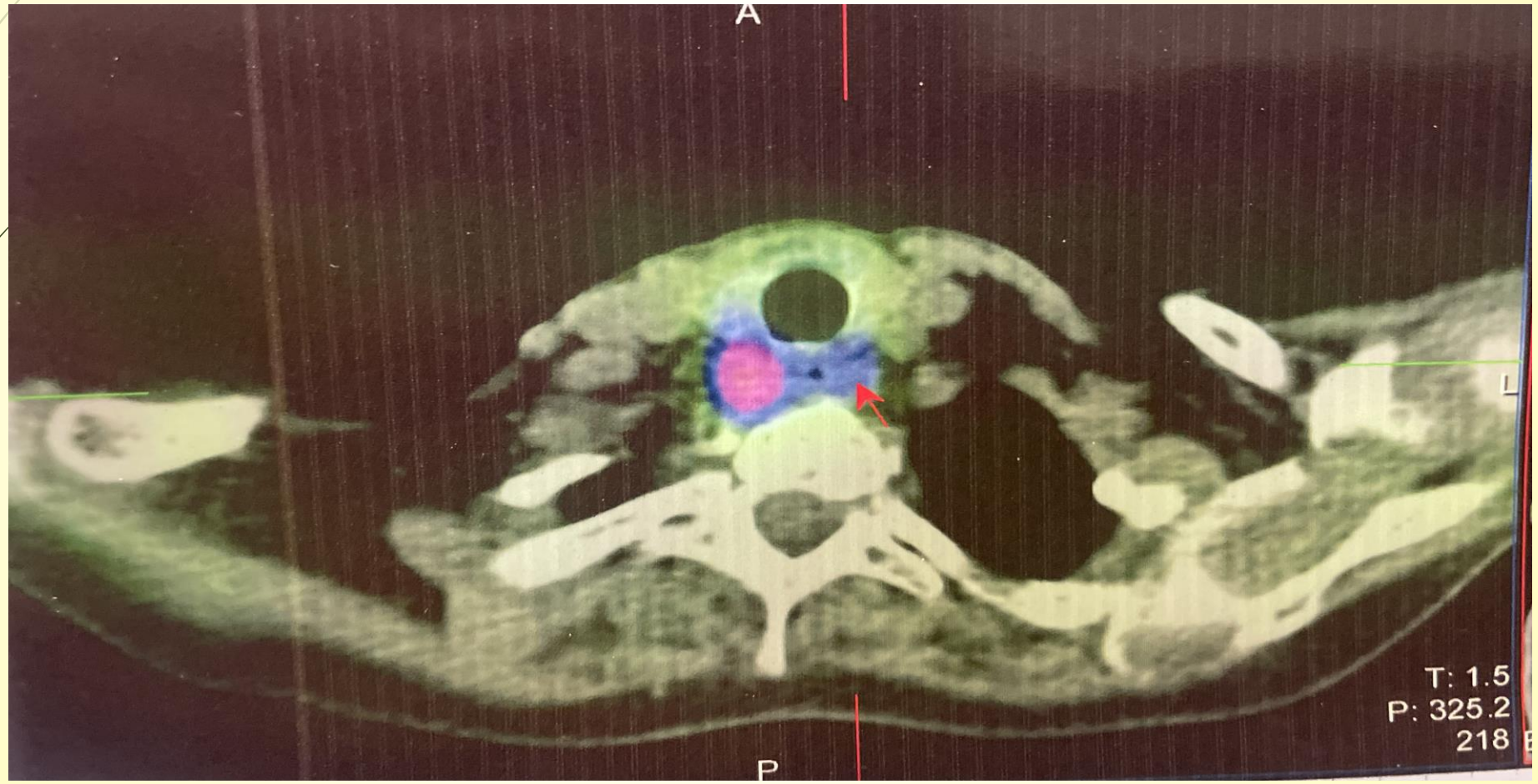
- Hydration (serum N/S 200 cc/h)
- Vial KCL 15% 20 cc/L
- Calcitonin 200 IU/ml s.c BID

- Surgery counsult

- O/P= 100 cc/h

Present illness:

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L
T: 1.5
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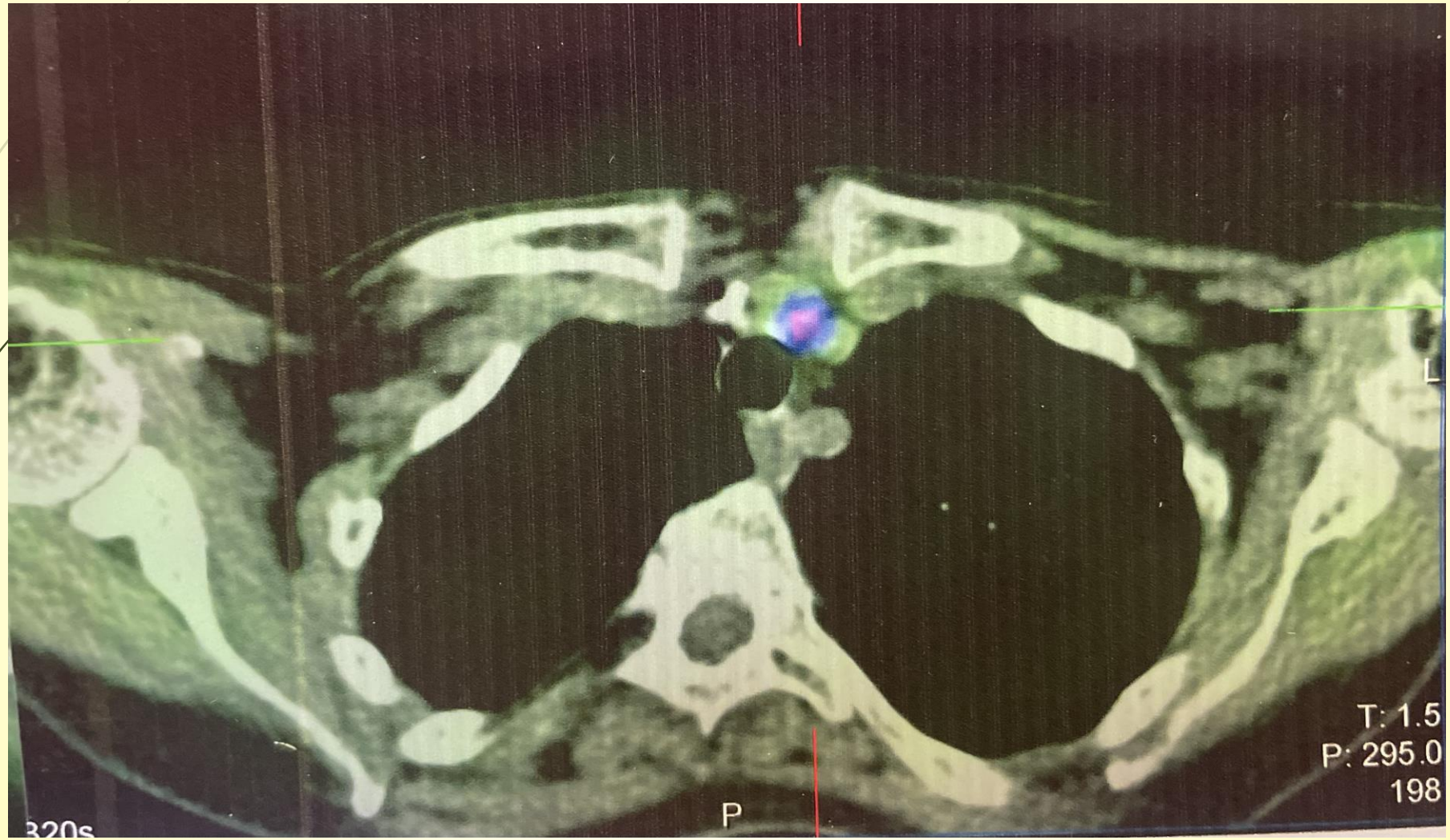
P


L
T: 1.5
P: 295.0
198
P

سونوگرافی شکم و لگن:

در بررسی اولتراسونیک کبد دارای سایز و اکوی طبیعی است. حدود کبد منظم است.

قطر مجاری صفراوی داخل و خارج کبدی ،ورید پورت و ورید های هپاتیک طبیعی می باشند. (CBD = NL PVD = NL)

کیسه صفرا فاقد سنگ بوده ، و شکل و ضخامت جداری طبیعی دارد .

طحال (spleen span = NL) با سایز و اکوی طبیعی مشاهده می شوند.

در حد قابل بررسی پانکراس با سایز و اکوی طبیعی مشاهده می شود

ضایعه فضاگیر در احشای شکمی فوق مشاهده نگردید.

در بررسی اولتراسونیک کلیه راست با طول تقریبی NL و کلیه چپ با طول تقریبیNL در موقعیت طبیعی دیده می شود.

ضخامت و اکوی کورتکس در هر دو کلیه طبیعی است.اکوی مدولا و سینوس کلیه ها طبیعی می باشد.

علائمی به نفع وجود سنگ ادراری ، هیدرونفروز و ضایعه فضاگیر و کیستیک در کلیه ها مشاهده نمی گردد.

مثانه نیمه پر و در حد قابل بررسی حاوی ادرار و فاقد ضایعه جداری و اینترالومینال رویت شد.

مایع آزاد در فضای شکم و لگن رویت نشد .

ادامه شرح عمل از صفحه قبل :

ntinue :

پس از بروب و درپ و تخت جنرال آنستزی و در وضعیت سوپاین آنسزیون کولار در ناحیه قدام گردن داده شد و پوست ، زیر جلد و پلاتیسما باز شد. فلپ فوقانی و تحتانی بلند شد. عضلات استرپ توسط یک برش میدلاین از ناچ تیروئید تا استرنال ناچ باز شد. تیروئید اکسپوز شد و آزاد شد ولوب های تیروئید آزاد و دلیور گردید . غدد پارا تیروئید بزرگ شده در قسمت خلفی تیروئید داشت که به اندازه ۲ سانتی متر بود و رزکت شد و از بافت اطراف با حفظ عصب ریکارنت لارنژیال دایسکت شد و پدیکل عروقی آن دابل لیگاتور شد و جهت بررسی پاتولوژی فروزن شکسته ارسال شد و مقدار کمی از بافت پاراتیروئید سمت راست در عضله بایسپس سمت راست کاشته شد. طبق تماس با دکتر صیاد رزیدنت پاتولوژی نمونه frozen فقط بافت تیروئید داشت. پس از هموستاز و تعبیه هموک عضلات استرپ ترمیم شد . همچنین پوست و زیرجلد ترمیم شد و بیمار با حال عمومی خوب تحویل ریکاوری شد.

هم چنین CV لاین ساب کلاوین سمت راست برای بیمار تعبیه شد که پس از چک خونگیری و خون دهی از هر ۲ لومن فیکس و پانسمان شد.

Macroscopic :

Specimens received in two containers two in fresh state for intraoperative consultation (F1, F2) labeled as above and consist of:

F1) A fragment of creamy soft tissue measuring 3x1.5x0.8cm, weighing 0.99g. RSS in 1 block and TS in 2 blocks after formalin fixation.

F1SDX: Parathyroid tissue.

F2) A fragment of creamy soft tissue measuring 4x1.5x1.2cm, weighing 1.2g. TS in 4 blocks.

F2SDX: Parathyroid tissue.

Microscopic :

Histologic findings, confirm the following diagnosis.

Diagnosis :

F1) Left parathyroid, resection (frozne and final diagnosis):

- Parathyroid hyperplasia.

F2) Right parathyroid, resection (frozne and final diagnosis):

- Parathyroid hyperplasia.

	7.11					9.11		11.11		12.11	
Calcium mg/dl	19.1	16.9	15.3	13.5	11.9	12.6	12	7.9	7.1	8.9	9.1
Phosphorus mg/dl	2.7			1.3	1.2	2.9	1	1.4	1.2	1.6	3
Mg mg/dl	1.4					1.2	1.5	1.9	1.3	1	1.2
ALB g/dl	3.4										
PTH Pg/dl	1099					204				114	
25(OH)D3 ng/dl	31.1										
K mEq/l	2.3	2.5	4.3	3	5.2	4.8		4.5			4.2

- Calcium carbonate 500 po TDS
- Rocaltrol 0.5 BID

- Calcium gluconate IV inf (24 h)

Drug history:

- Valproate NA 200mg TDS
- Biperiden 2mg BD
- Haloperidol 5mg daily
- Propranolol 20mg TDS
- Memantine 10 BID
- Donepezil 5mg H.S
- Quetiapine 25mg H.S

- PMH:
  - Renal stone (5 years ago)
  - B1D with psychotic feature
  - Parathyroidectomy
- PSH:
  - Parathyroidectomy
- FH:
  - Mother and Brother = HLP
  - Father : HTN, GOUT, IHD

REVIEW OF SYSTEM:

- Headache (-) Nausea & vomiting (-) Visual problems(-)
- Weight changes (+) appetite changes (-) sexual problems (-)
- Skin: pigmentation (-) diaphoresis (-) Dry & fragile hair (-)
- Ear , nose, mouth: NL
- Cardiovascular: NL palpitation (-)
- Respiratory: NL
- Gastrointestinal: NL
- Musculoskeletal: NL
- Neurological: AbNL
- Psychiatric: AbNL

PHYSICAL EXAMINATION:

- General appearance:
- A 53-year-old woman, disorient

- Vital sign:
  - BP:125/70 mmhg
  - HR=78
  - RR= 18
  - BMI= 18.51 kg/m2
  - W= 40 Kg
  - H=1.48 Cm

PHYSICAL EXAMINATION:

- Neck: Previose surgical scar
- Thorax: NL
- Lung: clear
- Heart: NL
- Abdomen: NL
- Extremities: NL

Problem list:

- A 53-year-old woman with the history Renal stone & parathyroid adenoma (2 adenoma) & Psychiatric disorders
- hyper calcemia (ca=19.1) & high PTH (1100)
- Osteoporosis
- Two parathyroidectomy (hyperplasia)
- Low ca, p, mg, k after parathyroidectomy

AGENDA:

- What are the causes of hypocalcemia in this patient ?
- Does this patient need a genetic test ?
- What is the course of lab data changes & treatment & expectations after treatment in this patent?

What are the causes of hypocalcemia in this patient ?

- **Hypoparathyroidism**
  - PTH ↓ (<15)
  - Ca ↓
  - P ↑
- **Hungry bone syndrome**
  - PTH (NL - ↑)
  - Ca ↓
  - P ↓
  - Mg ↓

Forestalling hungry bone syndrome after parathyroidectomy in patient with primary & renal hyperparathyroidism (2023 jun)

- **risk factors for HBS:**
- younger age at PTx,
- pre-operatory elevated bone alkaline phosphatase, and PTH, serum calcium.
- longer pre-surgery dialysis duration
- obesity
- an elevated pre-operatory calcitonin
- prior use of cinalcet
- the co-presence of brown tumors, and osteitis fibrosa cystica

- 15–25% to 92% of patients diagnosed with renal hyperparathyroidism (RHPT),
- up to 15–20% of individuals with PHPT

- Hypocalcemia (usually below the value of 8.2–8.4 mg/Dl
- post-operatory day to 3-day up to 30 days, requiring intravenous calcium replacement.
- hypophosphatemia, hypomagnesiemia, and, hyperkaliemia
- Early after PT surgery, normal or high (but lower than pre-operatory level) parathyroid hormone (PTH) is essential for establishing HBS diagnostic since non-low PTH is the clue to differentiate the condition from post-surgery hypoparathyroidism (low PTH)

- The pre-operatory use of anti-resorptives such as bisphosphonates (for example, pamidronate or zoledronic acid) in PHPT is controversial to associate benefits for HBS, but some authors reported it
- a 55-year-old female with a giant PT adenoma (of 5 cm, and a weight of 16 g) who was post-operatory re-admitted for HBS (the symptoms started 72 h after surgery and the patient remained hospitalized for one month

- **Hungry bone syndrome: still a challenge in the post-operative management of primary hyperparathyroidism: a systematic review of the literature 2013**

- Various risk factors of HBS
  - older age
  - weight/volume of the resected parathyroid glands
  - radiological evidence of bone disease
  - vitamin D deficiency.
- The syndrome is reported in 25-90% of patients with radiological evidence of hyperparathyroid bone disease vs only 0-6% of patients without skeletal involvement

[The hungry bone syndrome--an update]
2007

- Risk factors for the development of HBS
- Large parathyroid adenomas
- age > 60 years
- high preoperative levels of serum PTH, calcium and alkaline phosphatase

Does this patient need a genetic test ?

- Age <30-40
- Carcinoma
- Multiglands
- MEN syndrome
- First degree relatives >2 PHPT

Overview of the 2022 WHO Classification of Parathyroid Tumors

- Terms such as multi-glandular parathyroid disease and multiple multiglandular parathyroid adenomas have now replaced the historical term “parathyroid hyperplasia”.

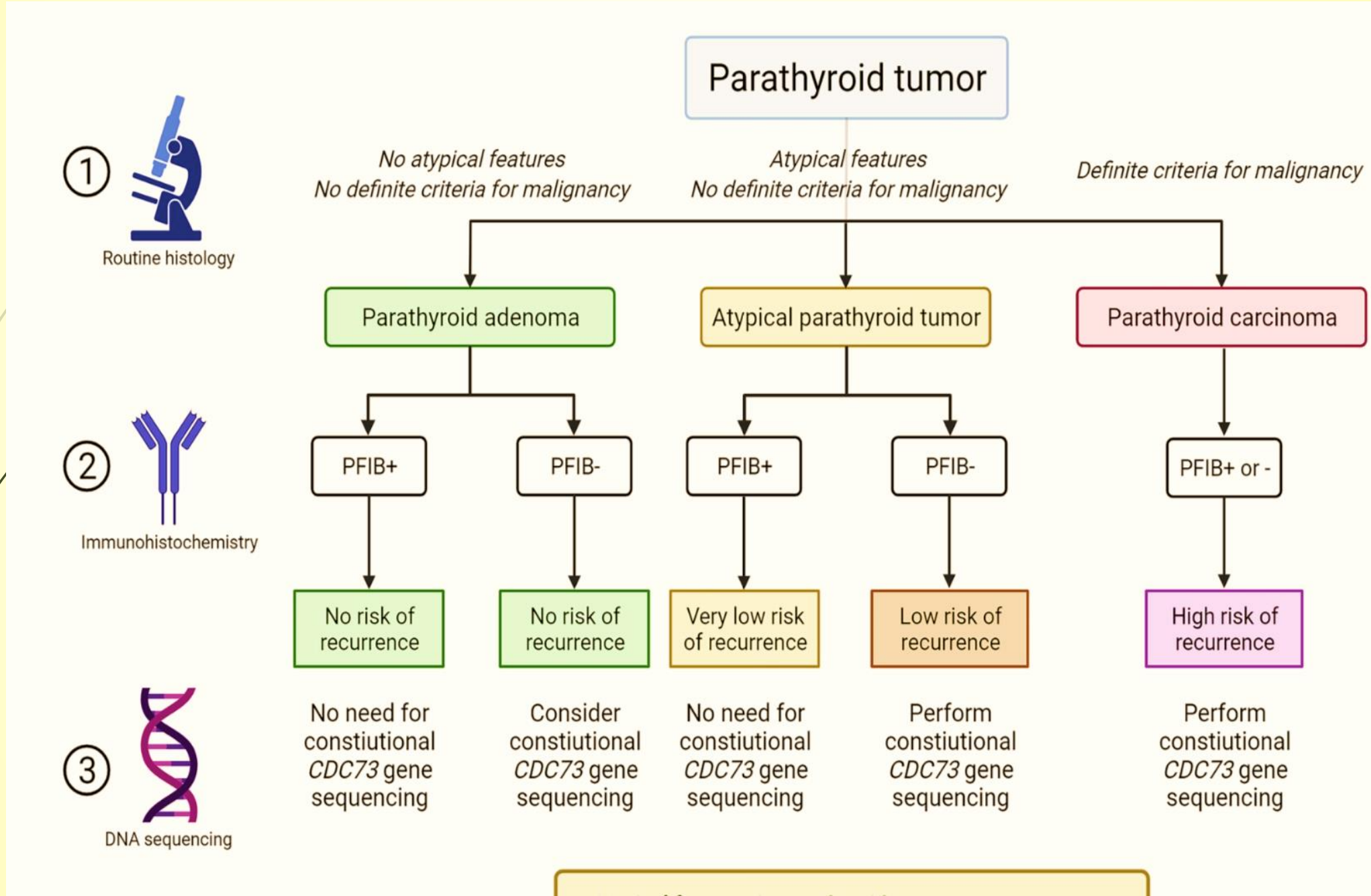
- the term “parathyroid hyperplasia” is now used primarily in the setting of secondary hyperplasia which is most often caused by chronic renal failure.

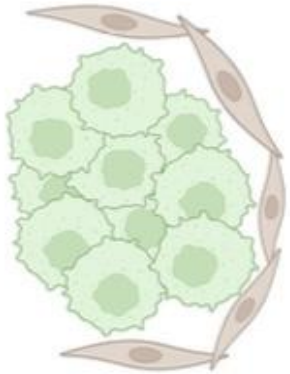
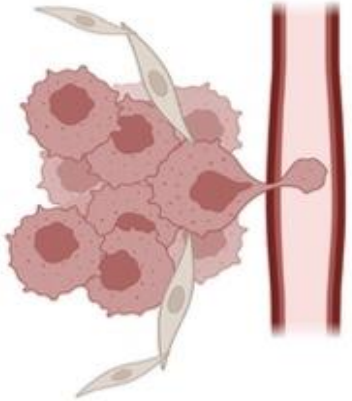
Overview of the 2022 WHO Classification of Parathyroid Tumors

- **Definite criteria of malignancy:**
  - Angioinvasion
  - Lymphatic invasion
  - Perineural invasion
  - Unequivocal invasion into adiacent structures
  - Histologically confirmed metastasis

Overview of the 2022 WHO Classification of Parathyroid Tumors

- **Atypical features in parathyroid tumors:**
  - Cellular nests in a thickened connective tissue
  - Tumour cells in capsule
  - Adherence to adiacent structures without frank invasion
  - Band-like fibrosis
  - Trabecular growth
  - Increased mitotic activity (>5 per 10 mm2)
  - Atypical mitotic figures
  - Coagulative necrosis
  - PFIB loss
  - Ki-67 labeling index >5%
  - Other immunohistochemical aberrancies


Parathyroid tumor
① Routine histology
No atypical features
No definite criteria for malignancy
Atypical features
No definite criteria for malignancy
Definite criteria for malignancy
Parathyroid adenoma
Atypical parathyroid tumor
Parathyroid carcinoma
② Immunohistochemistry
PFIB+
PFIB-
PFIB+
PFIB-
PFIB+ or -
No risk of recurrence
No risk of recurrence
Very low risk of recurrence
Low risk of recurrence
High risk of recurrence
③ DNA sequencing
No need for constiutional CDC73 gene sequencing
Consider constiutional CDC73 gene sequencing
No need for constiutional CDC73 gene sequencing
Perform constiutional CDC73 gene sequencing
Perform constiutional CDC73 gene sequencing

Parathyroid adenoma	Atypical parathyroid tumor	Parathyroid carcinoma
		
PFIB +	PFIB + or -	PFIB -
PGP9.5 -	PGP9.5 + or -	PGP9.5 +
APC +	APC + or -	APC -
GAL-3 -	GAL-3 + or -	GAL-3 +
Ki-67 ↓	Ki-67 ↓ ↑	Ki-67 ↑

Does this patient need a genetic test ?

- MEN 1 (menin)
- MEN 4
- CDC 73
- MEN 5 (MAX)
- FIHP (GCM2)

What is the course of lab data changes & treatment & expectations after treatment in this patent?

- Ca = 8.5 -9 mg/dl
- PTH < 2ALN

- IF NOT:
- Ca > 9.5 mg/dl
- PTH > 2 ALN
- Persistent disease should be evaluate again

THANKS FOR YOUR ATTENTION