In the name of God

Case presentation

1402/5/09

Prepared by :Dr Nafise Hassanloo

A 33-year-old woman with persistent of Cushing’s syndrome

Patient ID:

- 33y/o woman
- Born in Shabestar, live in Pakdasht
- Two daughters (aged 7 and 12)
- Housewife
- Source of history: patient, reliable

Present Illness:

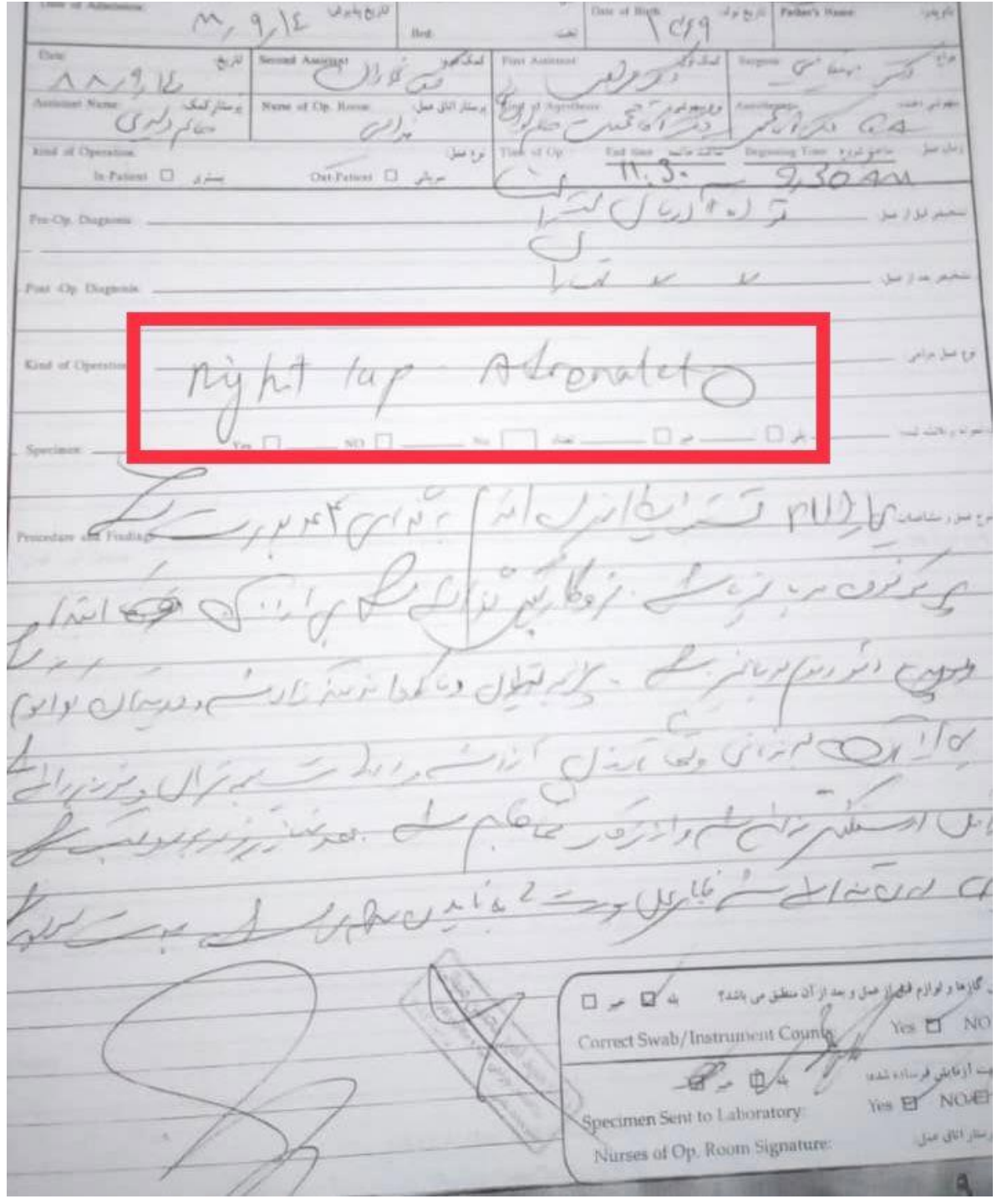
- A 33-year-old woman
- History of Cushing’s symptom (weight gain , purple stria, Moon face. Infertility)(1386-1388)
- Dx ACTH independent Cushing syndrome

Paraclinic evaluation:

1388	Result	Reference Range
24hr UFC	>1250 mcg/24 hr.	1.5 - 63
ACTH	2.4 pg/ ml	7.2 – 63.3

- **Abdominopelvic sonography:** A 20 *24 cm lesion, at the site of the right adrenal.
- **Abdominopelvic CT Scan:** A 25 *10 mm, partially enhanced, well defined lesion in favor of adrenal adenoma.
- **Pituitary MRI:** Nl

1388	Result	Reference Range
Urine Metanephrine	**148 µg/ 24hr.**	140- 785
Urine Normetanephrine	**136 µg/ 24hr.**	75- 375
Urine VMA	**5.4 µmol/24**	4- 35
DHEAS	**21 µg/dl**	65- 380


Night tap Atromalet
Correct Swab/Instrument Count:
Specimen Sent to Laboratory:
Nurses of Op. Room Signature:

آدرس دقیق:
تلفن :
بیمارستان:لباقی نژاد پزشک :دکتر سحاران تلفن:

Specimen :RIGHT ADRENAL .

Clin. data :ADRENAL MASS .

Macroscopic :Specimen received in formalin & consists of an irregular piece of fatty tissue with tumoral mass totally M: 6x3.5x3 cm & weighing 45 gr .The mass is well-defined & yellow M: 2.5 cm in diameter .On cutting,non homogenous ,yellow & hemorrhagic cut surface is seen .
R.S.S. IN 3 BLOCKS.

Microscopic :Sections show a adrenal neoplasm composed of cells with round to oval nuclei showing mild pleomorphicm & granular to homgenous pink cytoplasm .Tumor cells growing in trabecular solid pattern. Rare mitotic activity is present .No necrosis is identified.

iagnosis :RIGHT ADRENALECTOMY :
-ADRENOCORTICAL ADENOMA .

D-O :

patient's symptoms of Cushing's were controlled after adrenalectomy, and after a few months of pregnancy, she was fine until 1399, Again with the recurrence of symptoms such as

Weight gain, Headache, dizziness Striae, Round face, Dorsal fat pad

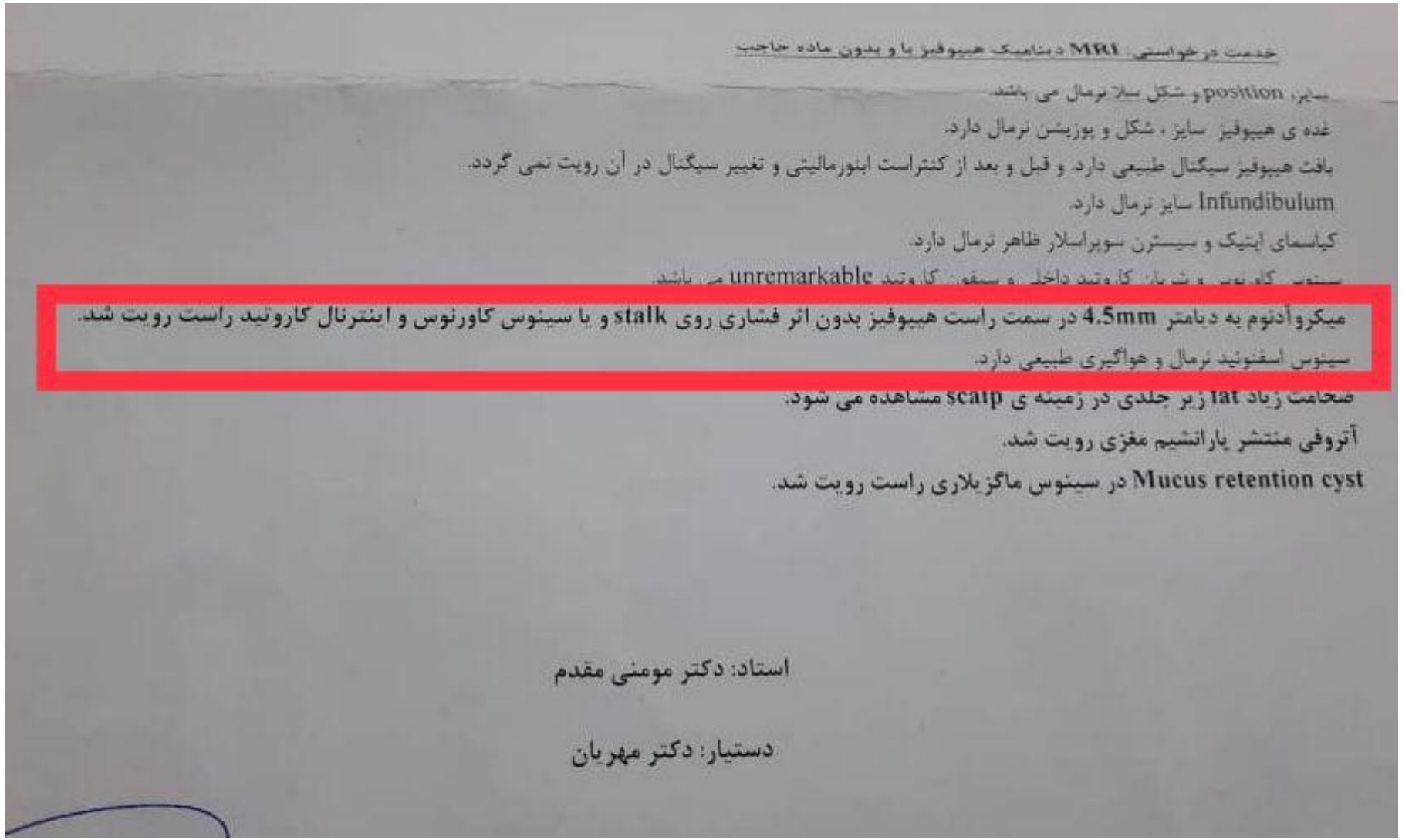
- Proximal muscle weakness
- Ecchymosis, easy bruising
- Hypertension (SBP: 190 mmHg),
- Dysglycemia
- Depression, mood change

which examined by an endocrinologist and with the

Laboratory tests: 1400.11.27

Date	Test	Result	Reference Range
1400.11.27	**24 hr. U. free cortisol**	**803 mcg/ 24 h**	1.5 - 63
1400.12.1	**24 hr. U. free cortisol**	**547 mcg/ 24 h**	1.5 - 63
1400.12.8	**ACTH**	**84.35 pg/ ml**	7.2 – 63.3
1400.12.14	**ACTH**	**101.1 pg/ ml**	7.2 – 63.3
1400.12.19	**Morning Cortisol**	**20.4 mcg/ dl**	3.7- 19.4
1400.12.21	**DST**	**9.3 mcg/ dl**	DST<5
1400.12.21	**24 hr. U. free cortisol (High Dexamethasone suppression Test)**	**6.4 mcg/ 24 h**	1.5 - 63

1400.12.21



خدمت درخواستی: MRI دینامیک هیپوفیز با و بدون ماده حاجب

سایز، position و شکل سلا نرمال می باشد.

غده ی هیپوفیز سایز ، شکل و پوزیشن نرمال دارد.

بافت هیپوفیز سیگنال طبیعی دارد و قبل و بعد از کنتراست اینورمالیتی و تغییر سیگنال در آن رویت نمی گردد.

Infundibulum سایز نرمال دارد.

کیاسمای اپتیک و سیسترن سوپراسلار ظاهر نرمال دارد.

سینوس کاورنوس و شریان کاروتید داخل و سیفون کاروتید unremarkable می باشد.

میکروآدنوم به دیامتر 4.5mm در سمت راست هیپوفیز بدون اثر فشاری روی stalk و با سینوس کاورنوس و اینترنال کاروتید راست روبت شد.

سینوس اسفنوئید نرمال و هواگیری طبیعی دارد.

ضخامت زیاد fat زیر جلدی در زمینه ی scalp مشاهده می شود.

آتروفی منتشر پارانشیم مغزی روبت شد.

Mucus retention cyst در سینوس ماگزیلاری راست روبت شد.

استاد: دکتر مومنی مقدم

دستیار: دکتر مهریان

Desmopressin stimulation test 1401.1.23

	Test : Cortisol		Test: ACTH	
	Result	Reference Range (6.2 – 20 mcg/ dl)	Result	Reference Range (7.2 – 64 pg/ ml)
-15 min	16 mcg/ dl		52 pg/ ml	
0 min	15 mcg/ dl		129 pg/ ml	
+15 min	18 mcg/ dl		98 pg/ ml	
+30 min	21 mcg/ dl		58 pg/ ml	
+ 45 min	23 mcg/ dl		99 pg/ ml	

- **serum cortisol:**
  using the criterion of a **greater than 20 percent** increase in serum cortisol, 80 to 85 percent of patients respond

- **plasma ACTH:**
  using criteria of a **30 or 50 percent** increase 95 and 81 percent of patients respond, respectively.

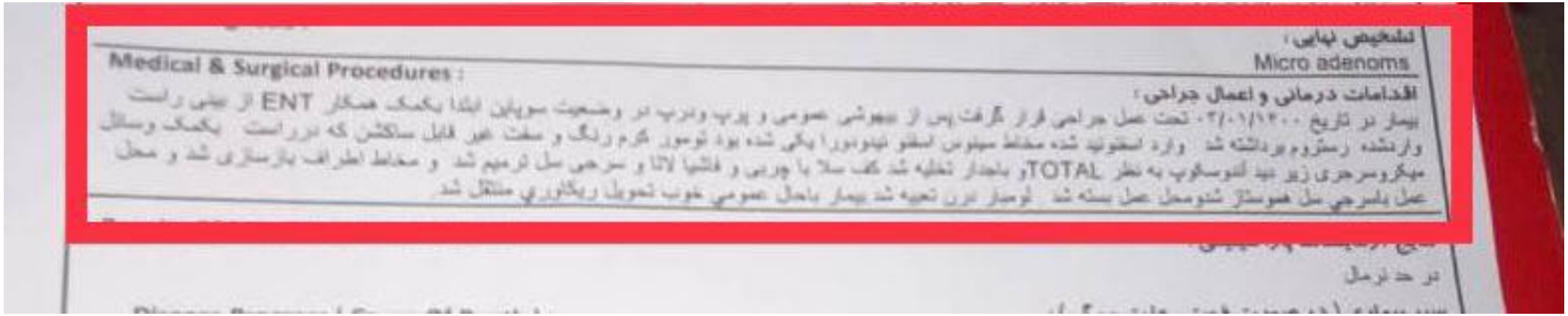
IPSS, 1401.1.27

ACTH			
	Right	Left	Peripheral
-5 min	143.1	54.91	56
0 min	169	41.2	49.54
+3 min	291.3	87.51	83.75
+5 min	265.3	128.4	135.6
+ 10 min	319.3	13.83	172.9

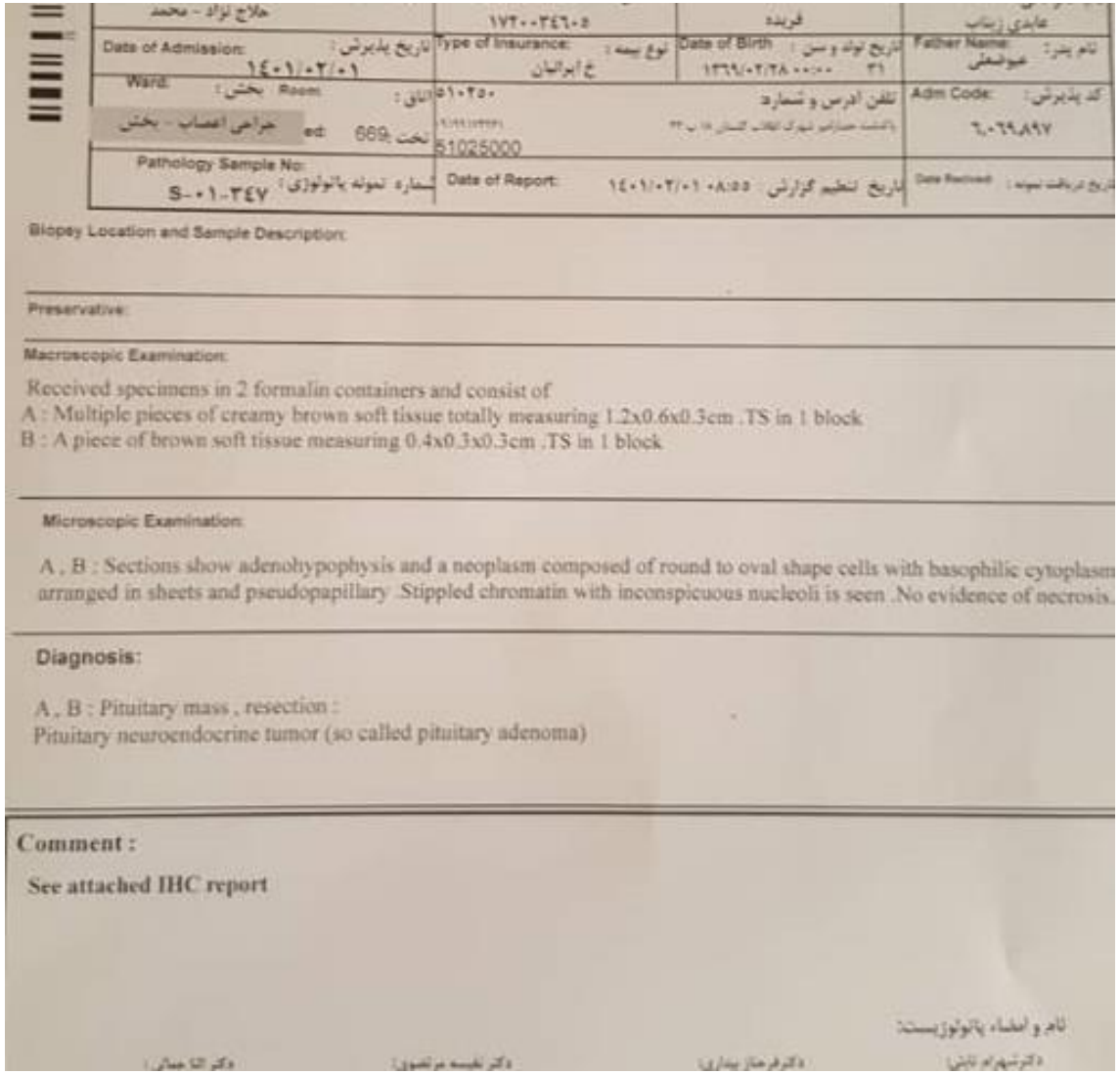
❖Prolactin 0 min :20ng/ml(2.8_26)

- **Pituitary source of ACTH**
- A central-to-peripheral plasma corticotropin **(ACTH) gradient** of:
  - **≥2 before CRH administration,**
  - **or ≥3 after CRH administration**

Pituitary mass resection,
TSS 1401.2.1



تومور کرم رنگ و سفت غیرقابل ساکشن در سمت راست به نظر توتال و با جدار تخلیه شد



Date of Admission: ۱۴۰۱/۰۲/۰۱ تاریخ پذیرش
Type of Insurance: ع ایرانیان نوع بیمه
Date of Birth: ۱۳۶۹/۰۲/۲۸ تاریخ تولد و سن ۳۱
Father Name: غیاثعلی نام پدر
Ward: Room: بخش: جراحی اعصاب - بخش ed: 669 تخت
Adm Code: ۶۰۰۶۹۸۹۷ کد پذیرش
Pathology Sample No: S-۰۱-۳۴۷ شماره نمونه پاتولوژی
Date of Report: ۱۴۰۱/۰۲/۰۱ ۰۸:۵۵ تاریخ تنظیم گزارش

Biopsy Location and Sample Description:

Preservative:

Macroscopic Examination:

Received specimens in 2 formalin containers and consist of
A : Multiple pieces of creamy brown soft tissue totally measuring 1.2x0.6x0.3cm .TS in 1 block
B : A piece of brown soft tissue measuring 0.4x0.3x0.3cm .TS in 1 block

Microscopic Examination:

A , B : Sections show adenohypophysis and a neoplasm composed of round to oval shape cells with basophilic cytoplasm arranged in sheets and pseudopapillary .Stippled chromatin with inconspicuous nucleoli is seen .No evidence of necrosis.

Diagnosis:

A , B : Pituitary mass , resection :
Pituitary neuroendocrine tumor (so called pituitary adenoma)

Comment :

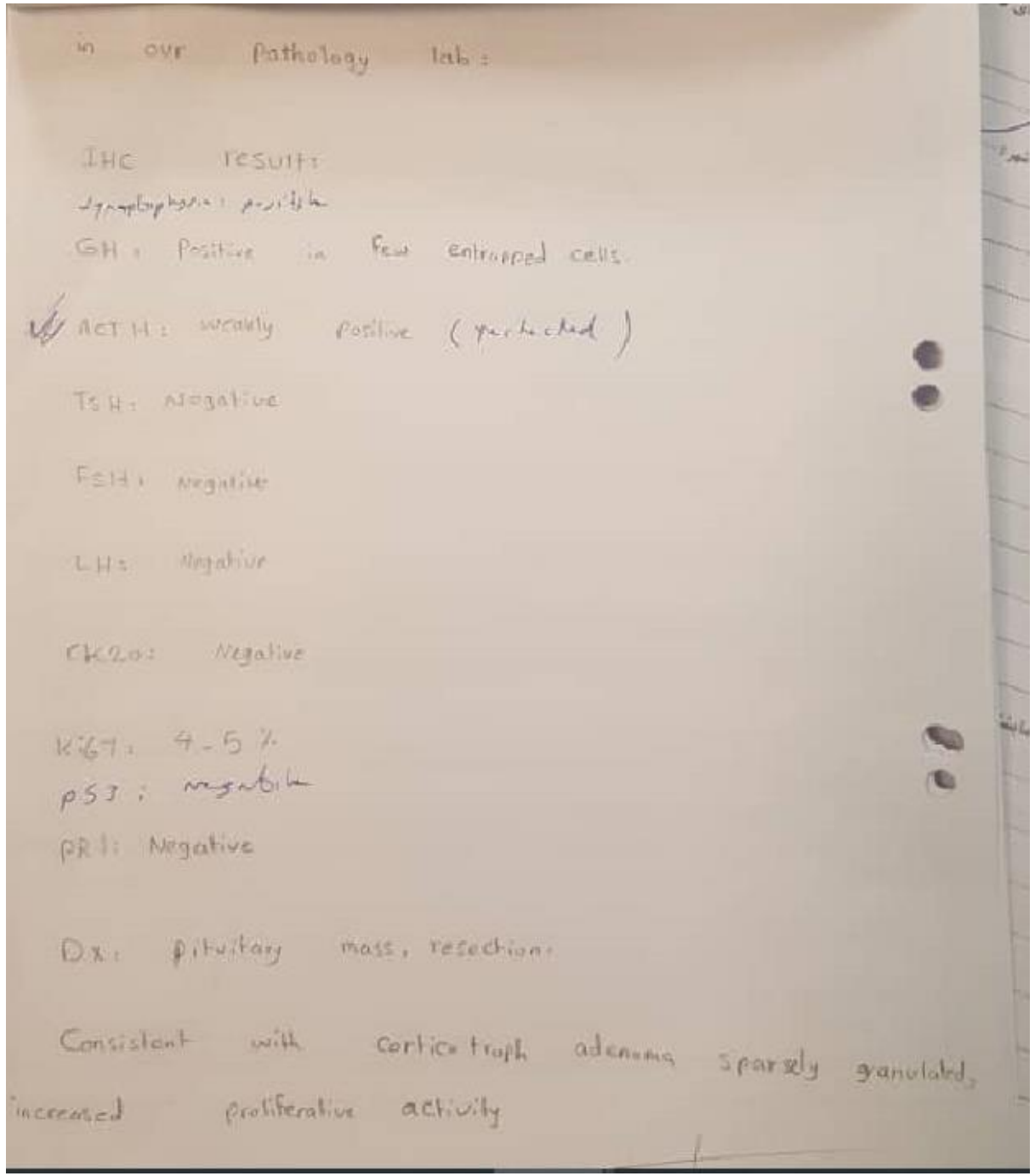
See attached IHC report

نام و امضاء پاتولوژیست:

Pituitary mass resection :1401.2.1

Pituitary neuroendocrine tumor(pituitary adenoma)

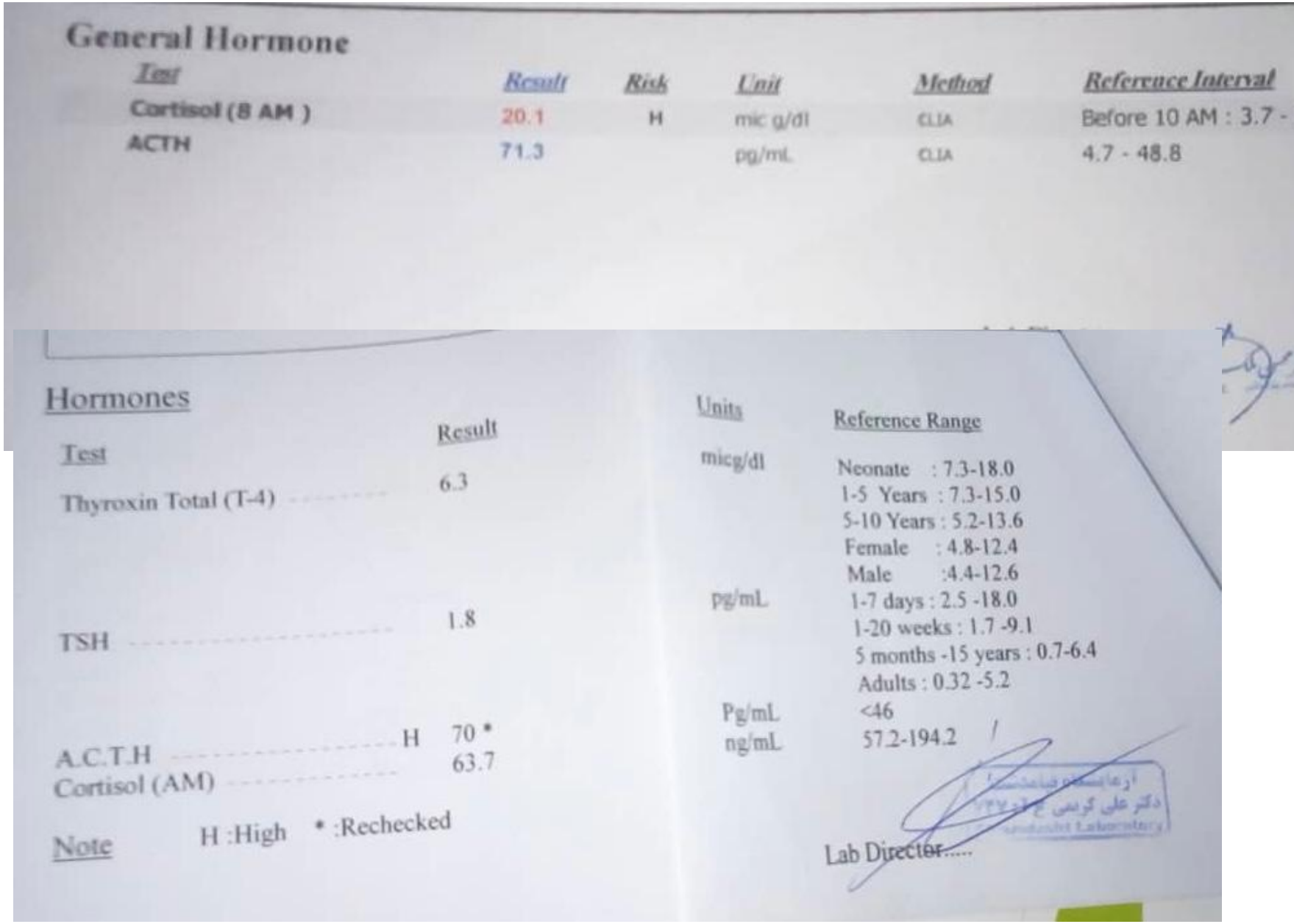
1.2*0.6*0.3cm



IHC : ACTH weakly positive

1401.2.4

1401.2.8
Cortisol:6.3µg/dl
(prednisolone)



General Hormone

Test	Result	Risk	Unit	Method	Reference Interval
Cortisol (8 AM)	20.1	H	mic g/dl	CLIA	Before 10 AM : 3.7 -
ACTH	71.3		pg/mL	CLIA	4.7 - 48.8

Hormones

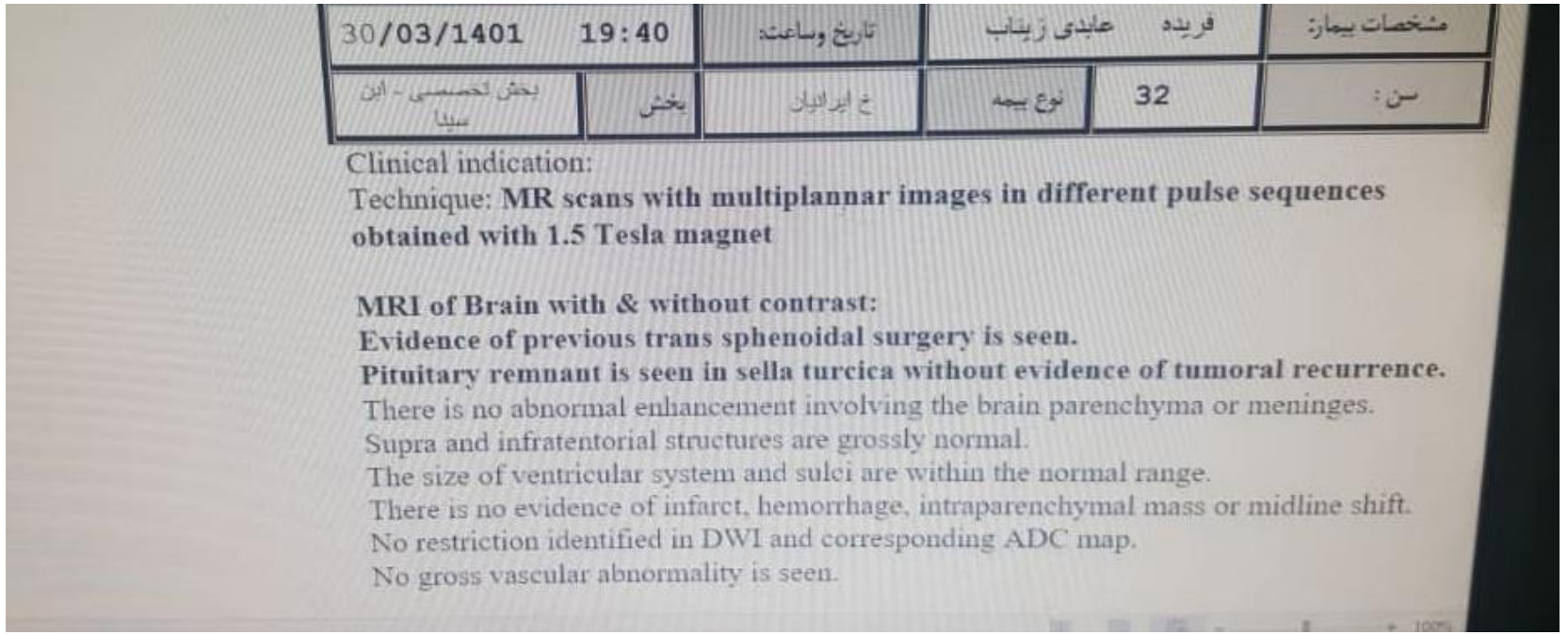
Test	Result		Units	Reference Range
Thyroxin Total (T-4)	6.3		micg/dl	Neonate : 7.3-18.0 1-5 Years : 7.3-15.0 5-10 Years : 5.2-13.6 Female : 4.8-12.4 Male :4.4-12.6
TSH	1.8		pg/mL	1-7 days : 2.5 -18.0 1-20 weeks : 1.7 -9.1 5 months -15 years : 0.7-6.4 Adults : 0.32 -5.2
A.C.T.H	70 *	H	Pg/mL	<46
Cortisol (AM)	63.7		ng/mL	57.2-194.2

Note H :High * :Rechecked

Lab Director.....

- **Brain MRI 1401.03.30**

Pituitary Remnant is seen
in Sella turcica w/o evidence
Of tumoral recurrence



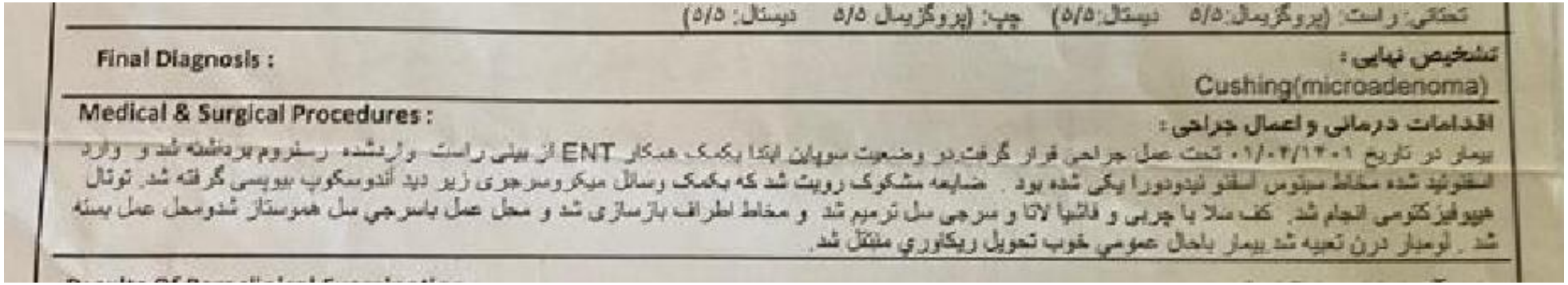
مشخصات بیمار:	فریده عابدی زیناب	تاریخ وساعت:	30/03/1401 19:40
سن: 32	نوع بیمه	خ ایرانیان	بخش تخصصی - این سینا بخش

Clinical indication:
Technique: **MR scans with multiplannar images in different pulse sequences obtained with 1.5 Tesla magnet**

MRI of Brain with & without contrast:
Evidence of previous trans sphenoidal surgery is seen.
Pituitary remnant is seen in sella turcica without evidence of tumoral recurrence.
There is no abnormal enhancement involving the brain parenchyma or meninges.
Supra and infratentorial structures are grossly normal.
The size of ventricular system and sulci are within the normal range.
There is no evidence of infarct, hemorrhage, intraparenchymal mass or midline shift.
No restriction identified in DWI and corresponding ADC map.
No gross vascular abnormality is seen.

- Due to the **lack of drop in cortisol and ACTH levels** and
- **lack of improvement in symptoms**,
- **Pituitary Remnant is seen**

➢**Total hypophysectomy on the date 1401/04/01**



تحتاني: راست: (پروگزيمال: ۵/۵ ديستال: ۵/۵) چپ: (پروگزيمال ۵/۵ ديستال: ۵/۵)

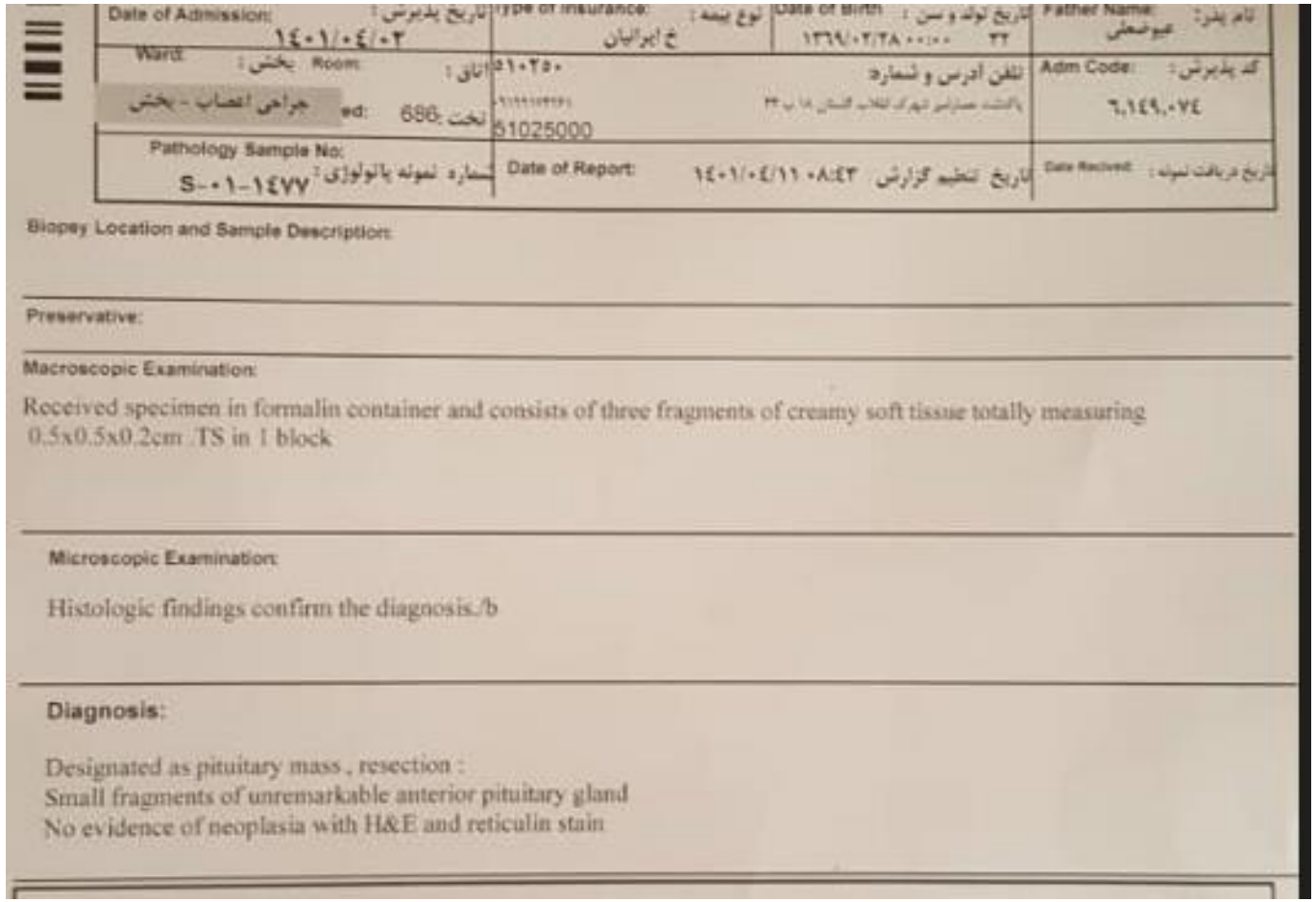
Final Diagnosis : **تشخیص نهایی :**

Cushing(microadenoma)

Medical & Surgical Procedures : **اقدامات درمانی و اعمال جراحی :**

بیمار در تاریخ ۰۱/۰۴/۱۴۰۱ تحت عمل جراحی قرار گرفت.در وضعیت سوپاین ابتدا بکمک همکار ENT از بینی راست وارد شده رسفروم برداشته شد و وارد اسفنوئید شده مخاط سپتوم اسفنو ئیدودورا یکی شده بود . ضایعه مشکوک رویت شد که بکمک وسایل میکروسرجری زیر دید آندوسکوپ بیوپسی گرفته شد. توتال هیپوفیزکتومی انجام شد. کف صلا با چربی و فاشیا لاتا و سرجی سل ترمیم شد و مخاط اطراف بازسازی شد و محل عمل باسرجي سل هموستاز شدومحل عمل بسته شد . بیمار درن تعبیه شد بیمار باحال عمومي خوب تحویل ریکاوري منتقل شد.

ضایع مشکوک رویت شد به کمک وسایل میکروسرجری بیوپسی گرفته شد.....
توتال هیپوفیزکتومی انجام شد



Date of Admission: ۱٤۰۱/۰٤/۰۳
Type of Insurance: خ ابرانیان
Date of Birth: ۱۳۶۹/۰۲/۲۸ ۰۰:۰۰ ۳۲
Father Name: عیوضعلی
Ward: جراحی اعصاب - بخش
Room: ۶۸۶ تخت
51025000
Adm Code: ٦,١٤٩,٠٧٤
Pathology Sample No: S-۰۱-۱٤۷۷
Date of Report: ۱٤۰۱/۰٤/۱۱ ۰۸:٤۳
Biopsy Location and Sample Description:
Preservative:
Macroscopic Examination:
Received specimen in formalin container and consists of three fragments of creamy soft tissue totally measuring 0.5x0.5x0.2cm .TS in 1 block
Microscopic Examination:
Histologic findings confirm the diagnosis./b
Diagnosis:
Designated as pituitary mass , resection :
Small fragments of unremarkable anterior pituitary gland
No evidence of neoplasia with H&E and reticulin stain

No evidence of neoplasia with H&E And reticulin stain

PARS Lab 1401.4.28

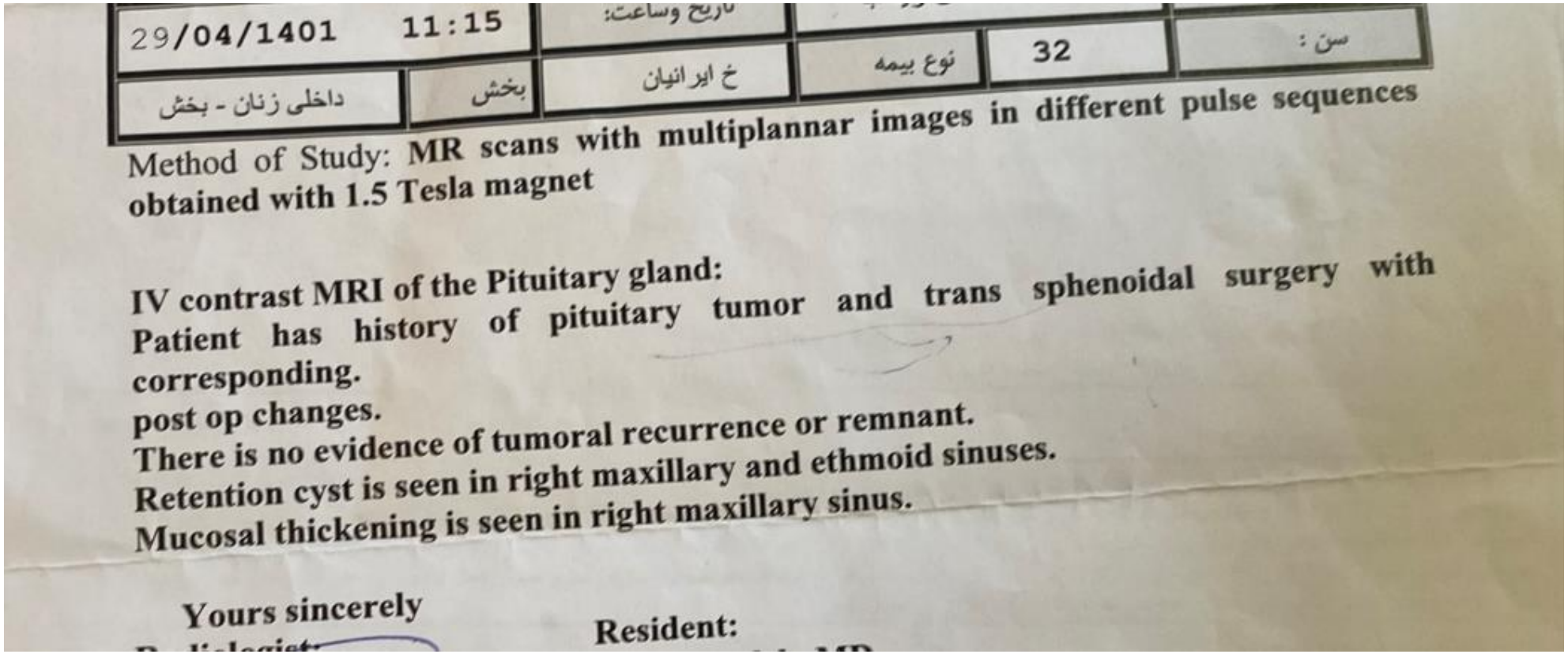
✓After second TSS

- **Cortisol**：**22 µg/dl**
- **ACTH** ： **82 pg/ml (7_64)**
- **UFC :** **219 µg/24h (36_137)**

Brain MRI 1402.4.29

There is NO evidence of pituitary tumoral recurrence or remnant

Retention cyst is seen



29/04/1401 11:15		تاریخ وساعت:			
داخلی زنان - بخش	بخش	خ ایرانیان	نوع بیمه	32	سن :

Method of Study: MR scans with multiplannar images in different pulse sequences obtained with 1.5 Tesla magnet

IV contrast MRI of the Pituitary gland:
Patient has history of pituitary tumor and trans sphenoidal surgery with corresponding.
post op changes.
There is no evidence of tumoral recurrence or remnant.
Retention cyst is seen in right maxillary and ethmoid sinuses.
Mucosal thickening is seen in right maxillary sinus.

Yours sincerely

Resident:

- **Ketoconazole Tablet 200mg BD started in 1401.4**

کدملی :	1720034605	تاریخ و ساعت گزارش:	1401/11/24 09:12
سن :	32 نوع بیمه	خ همگانی سلامت	بخش داخلی زنان - بخش

سی تی اسکن اسپیرال ریه و مدیاستن با تزریق:

مقاطع عرضی به ضخامت ۵ میلیمتر با تزریق انجام شد.

اینفیلتراسیون GG در ساب پلورال خلفی هر دو ریه رویت شد.

در اسکن انجام شده؛ در نواحی مدیاستن، تراشه و شاخه های برونش عارضه ای دیده نمیشود.

میدانهای ریوی طبیعی است و در نسج نرم و سیستم استخوانی توراکس عارضه ای دیده نمیشود.-0

سی تی اسکن اسپیرال شکم و لگن با تزریق:

تصویر یک round mass و اگزوفیتیک همراه با cresent sign 32*33mm در کولون نزولی که GIST در صدر تشخیص افتراقی قرار دارد.تصویر نواحی هایپودنس 35*30mm در سگمان II کبدی و 17mm در III و 11*7mm در سگمان V کبد و 10mm در سگمان II رویت گردید که تطابق با us و MRIدینامیک کبد جهت R/O متاستاز توصیه می شود. Mass هیپودنس آدرنال چپ رویت شد.سنگ 5mm در پل فوقانی کلیه چپ رویت شد.تصویر ناحیه هیپودنس با مرکز دانسیته چربی به دیامتر 9mm مطرح کننده لنف نود در RUQ رویت گردید.شواهد کوله سیستکتومی رویت نشد.

مجاری صفراوی، عروق پورت، پانکراس، نواحی پاراآئورت، طحال ابعاد طبیعی و دانسیته نرمال دارند.

دیامتر سیستم پیلوکالیسیل دو طرف طبیعی است.

در حد قابل بررسی در ناحیه معده، قوس های روده باریک، کولون و نواحی لگن عارضه ای دیده نمیشود./ب.

رادیولوژیست: دستیار رادیولوژی:

Exam Date: 04/30/2023(m/d/y)

تاریخ اسکن : ۱۴۰۲/۰۲/۱۰ ۱۳:۰۸
جناب دکتر : داودی - زهرا

PET/CT FROM VERTEX TO MID-THIGH
With Discovery 690 GE (General Electric), 64 Slice CT & Time-of-flight (ToF)

HISTORY: GIST
QUESTION: Metastatic Evaluation

TECHNIQUE:

Sixty minutes following administration of 513 MBq of FDG intravenously a partial body integrated PET-CT scan from vertex to proximal thighs was acquired. Sections were reconstructed in three standard orthogonal planes.
For anatomic referencing and for transmission correction purposes an unenhanced low dose CT was acquired and fused images were also generated.

BRAIN:

For evaluation of pituitary glands correlation with dynamic sellar MRI is recommended.
There is no midline shift or intracranial hemorrhage. The lateral ventricles are normal. The cerebellum and brainstem are intact. The basal cisterns are patent. The skull is intact.
Physiological FDG-uptake of the brain is seen.

NECK:

Increased metabolic activity in the anterior maxillary region and maxillary alveolar process region is seen (SUV max= 16.7). ENT and dental exam correlation is recommended.
Mucosal thickening in right ethmoid sinus and retention cyst in right maxillary sinus is seen.
The major salivary glands of the neck are normal. The epiglottis & aryepiglottic folds, true & false vocal cords, and supra & subglottic airways are intact. The thyroid lobes have normal size & texture. No cervical lymphadenopathy is detected.
Physiological FDG-uptake of the neck is seen.

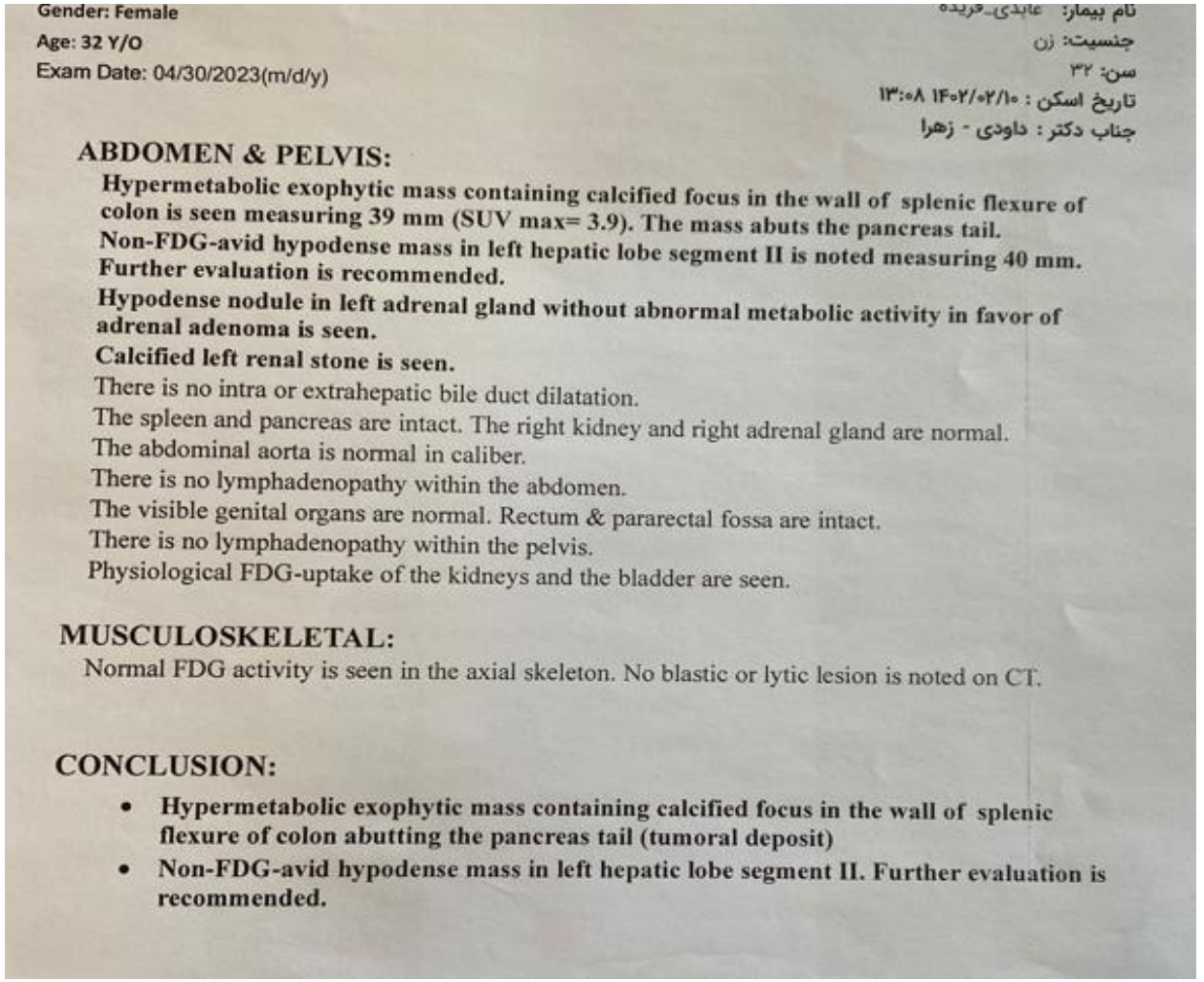
CHEST:

Band atelectasis in right middle lobe and left lower lobe are seen.
Otherwise lung fields are clear and no parenchymal infiltration is noted. No evidence of hilar or mediastinal adenopathy is seen. No mass lesion is detected. No evidence of pleural effusion is seen. Chest wall is unremarkable.
Heart size is normal. Physiological FDG-uptake of the heart is noted.

FDG PET 1402.2.10
NECK: Increased metabolic in maxillary region
Chest: Atelectasis in right middle lobe

1. **Hyper metabolic mass focuses in the splenic Flexure of colon 39mm The mass abuts the pancreas tail**

2. **Non FDG avid hypodense mass in left hepatic lobe segment is noted measuring 40 mm.**



Gender: Female
Age: 32 Y/O
Exam Date: 04/30/2023(m/d/y)

نام بیمار: عابدی_فریده
جنسیت: زن
سن: ۳۲
تاریخ اسکن : ۱۴۰۲/۰۲/۱۰ ۱۳:۰۸
جناب دکتر : داودی - زهرا

ABDOMEN & PELVIS:

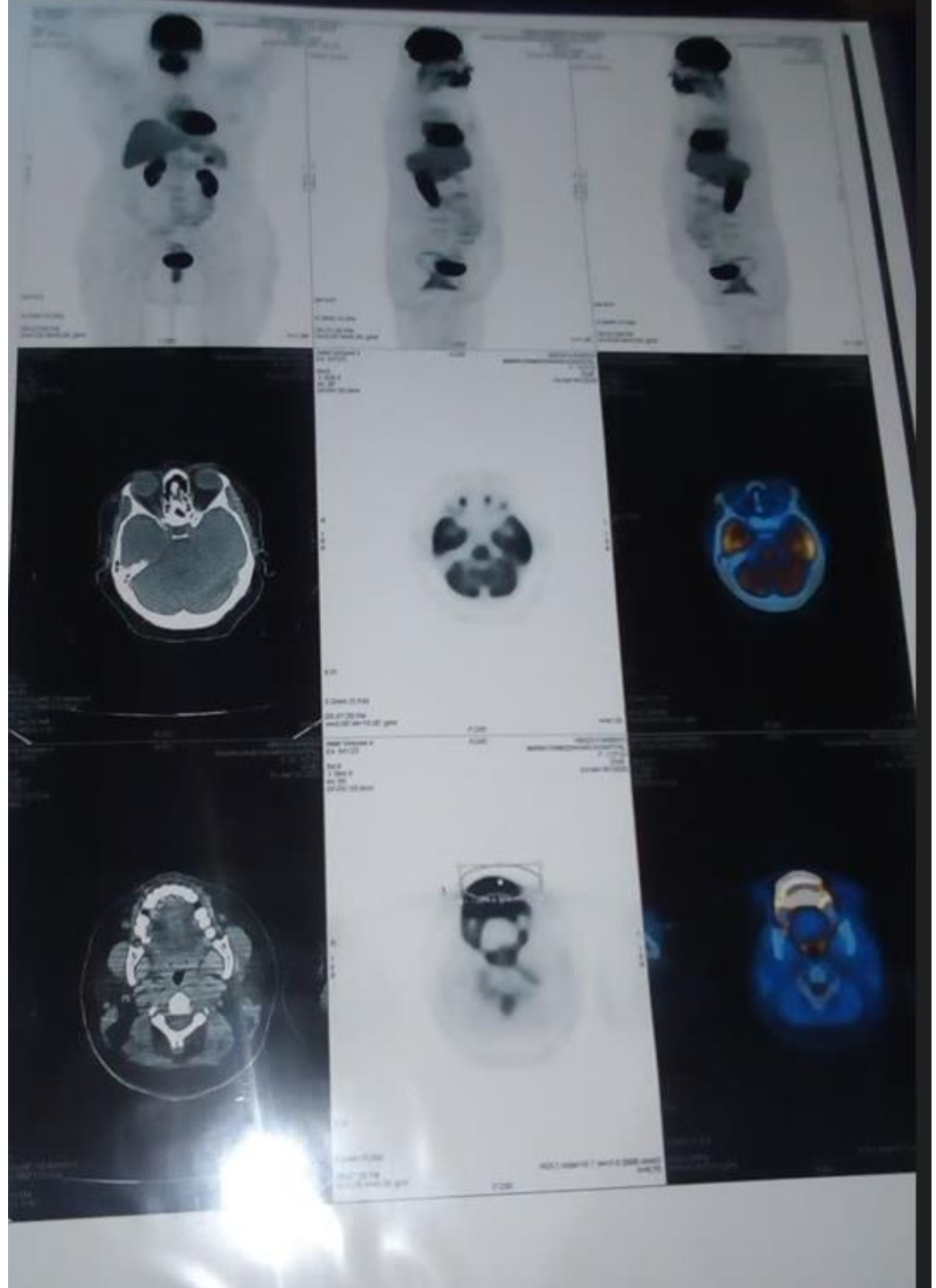
Hypermetabolic exophytic mass containing calcified focus in the wall of splenic flexure of colon is seen measuring 39 mm (SUV max= 3.9). The mass abuts the pancreas tail.
Non-FDG-avid hypodense mass in left hepatic lobe segment II is noted measuring 40 mm. Further evaluation is recommended.
Hypodense nodule in left adrenal gland without abnormal metabolic activity in favor of adrenal adenoma is seen.
Calcified left renal stone is seen.
There is no intra or extrahepatic bile duct dilatation.
The spleen and pancreas are intact. The right kidney and right adrenal gland are normal.
The abdominal aorta is normal in caliber.
There is no lymphadenopathy within the abdomen.
The visible genital organs are normal. Rectum & pararectal fossa are intact.
There is no lymphadenopathy within the pelvis.
Physiological FDG-uptake of the kidneys and the bladder are seen.

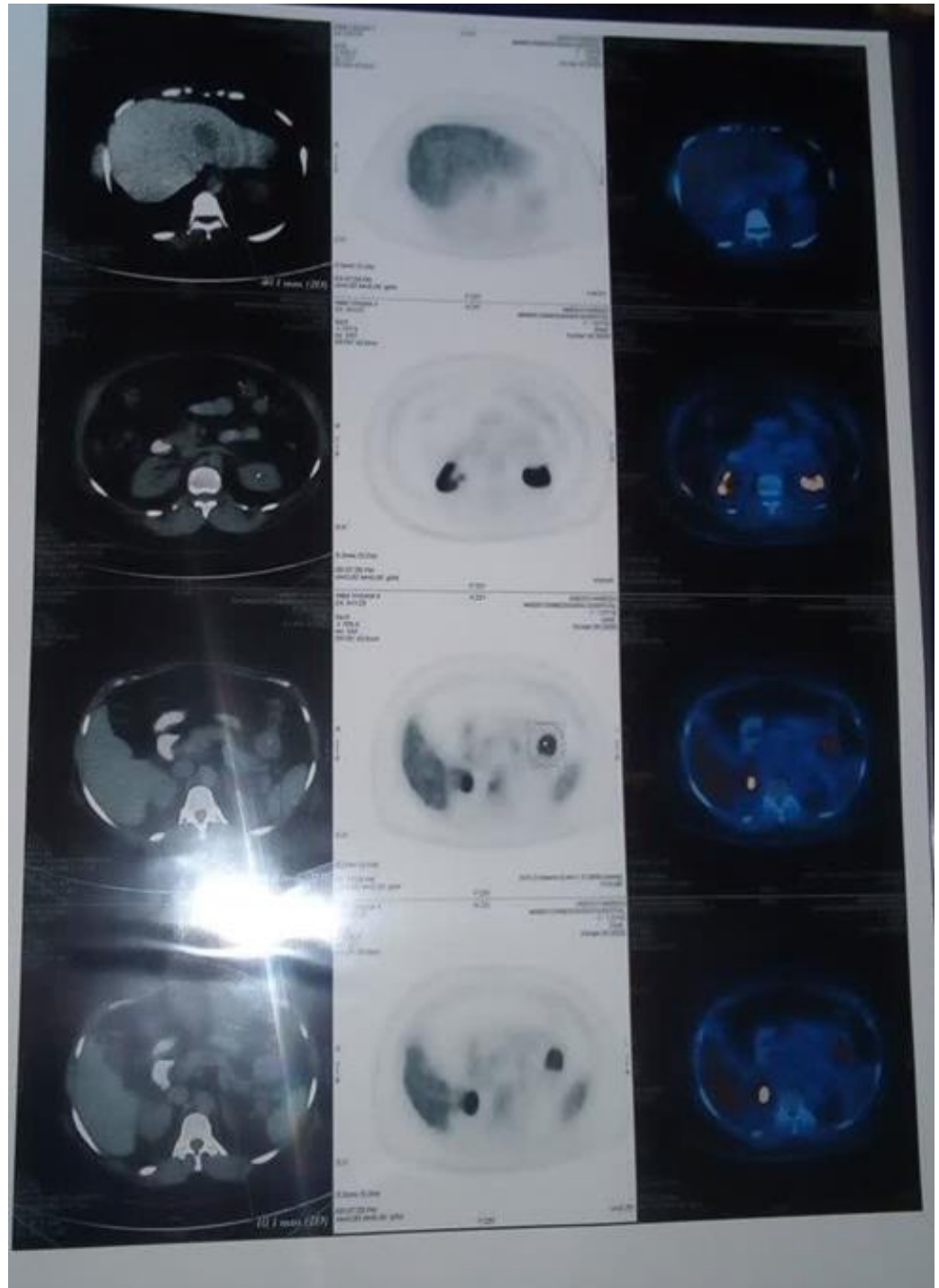
MUSCULOSKELETAL:

Normal FDG activity is seen in the axial skeleton. No blastic or lytic lesion is noted on CT.

CONCLUSION:

- **Hypermetabolic exophytic mass containing calcified focus in the wall of splenic flexure of colon abutting the pancreas tail (tumoral deposit)**
- **Non-FDG-avid hypodense mass in left hepatic lobe segment II. Further evaluation is recommended.**





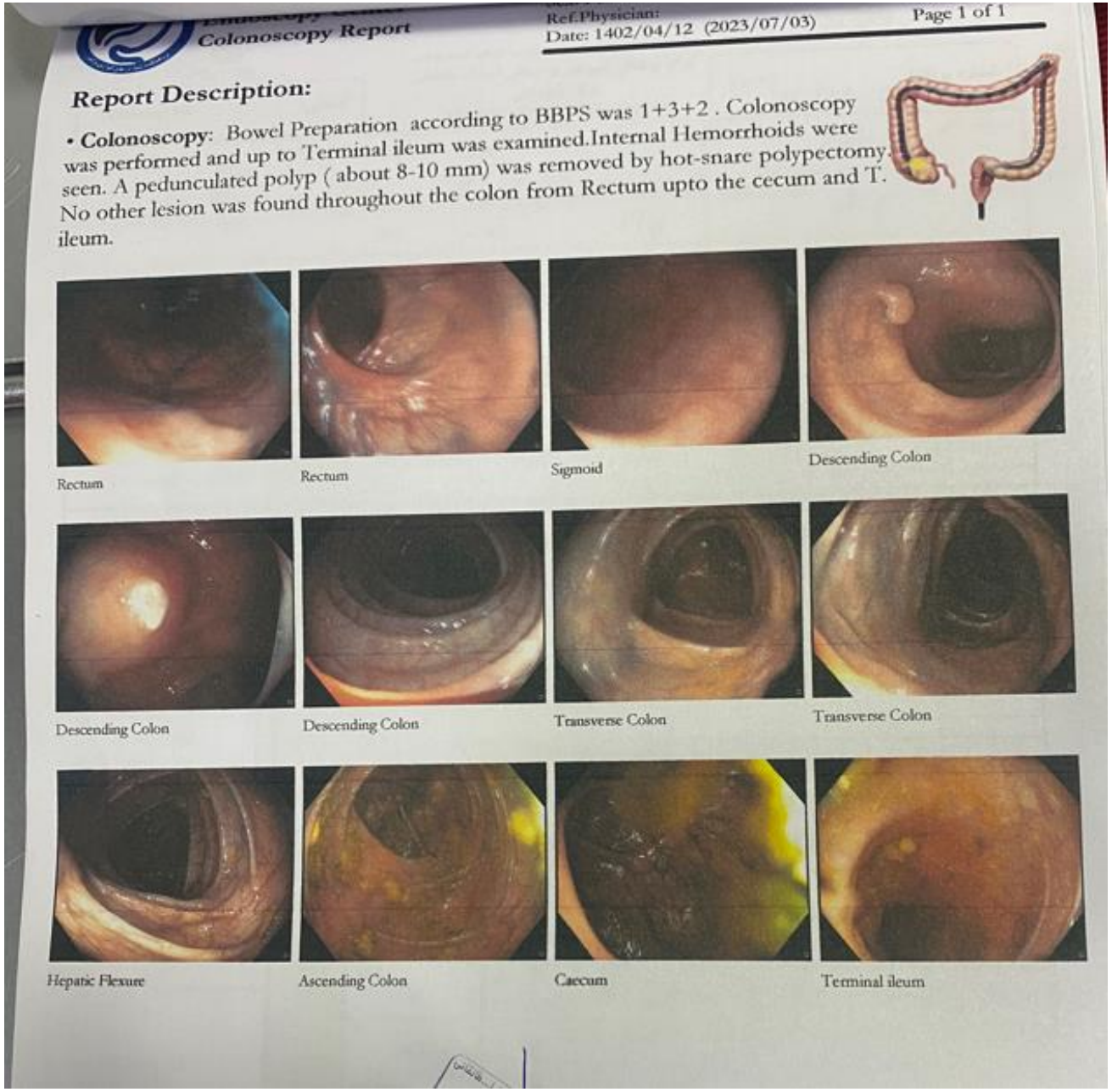
✓ **Ketoconazole200mg BD**

	1401.4 PARS lab	1401.7 PARS lab	1401.11 لقمان	1402.3 PARS lab
Cortisol	**22 µg/dl**	**15 µg/dl**	**27 µg/dl**	**19 µg/dl**
ACTH	**82 pg/ml (7_64)**	**67 pg/ml (7_64)**	**54 pg/ml**	**69 pg/ml (7_64)**
UFC	**219 µg/24h (36_137)**	**56 µg/24h (36_137)**	**340 µg/24h**	**385 µg/24h (36_137)**
HDDST UFC			<10	
TSH		**0.01**	0.1	
T4		**3.9 (5_14)**	4.2	
LH		**0.9 IU/L**		
FSH		**0.9 IU/L**		
Prolactin		**0.6 ng/ml**		
GH		**<0.05 ng/ml**		
IGF1		**108 ng/ml (109_300)**		

1402.3	PARS Lab
FBS	91
BUN	15
CR	0.8
AST	**18**
ALT	**40**
ALP	**326**

- The patient was admitted in Taleghani Hospital

In **1402/04/04**



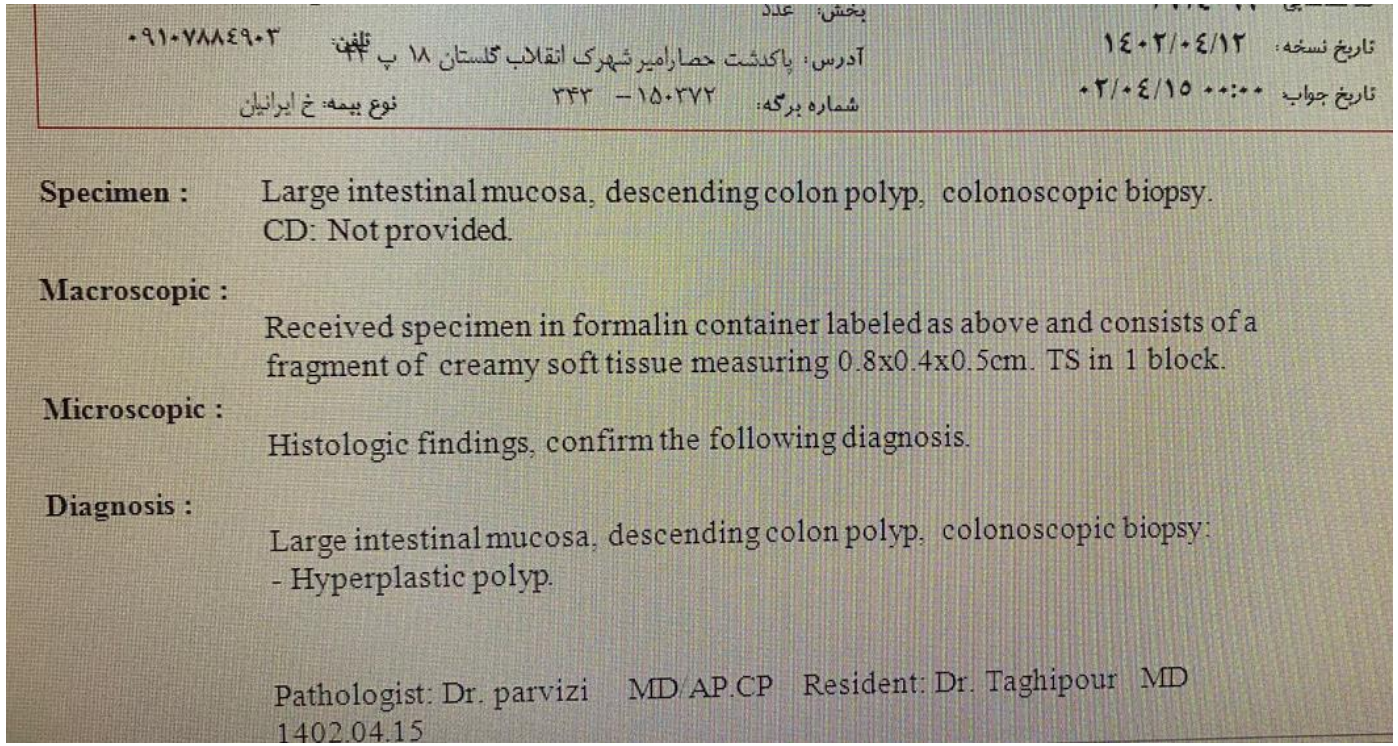
Colonoscopy Report

Ref.Physician:
Date: 1402/04/12 (2023/07/03)

Report Description:

• **Colonoscopy**: Bowel Preparation according to BBPS was 1+3+2 . Colonoscopy was performed and up to Terminal ileum was examined.Internal Hemorrhoids were seen. A pedunculated polyp (about 8-10 mm) was removed by hot-snare polypectomy. No other lesion was found throughout the colon from Rectum upto the cecum and T. ileum.

A pedunculated polyp (8_10mm)



بخش: عدد

آدرس: پاکدشت حصارامیر شهرک انقلاب گلستان ۱۸ پ تلفن: ۰۹۱۰۷۸۸۴۹۰۳

شماره برگه: ۱۵۰۳۷۲ – ۳۴۳ نوع بیمه: خ ایرانیان

تاریخ نسخه: ۱۴۰۲/۰۴/۱۲

تاریخ جواب: ۰۲/۰۴/۱۵ ۰۰:۰۰

Specimen : Large intestinal mucosa, descending colon polyp, colonoscopic biopsy.
CD: Not provided.

Macroscopic :

Received specimen in formalin container labeled as above and consists of a fragment of creamy soft tissue measuring 0.8x0.4x0.5cm. TS in 1 block.

Microscopic :

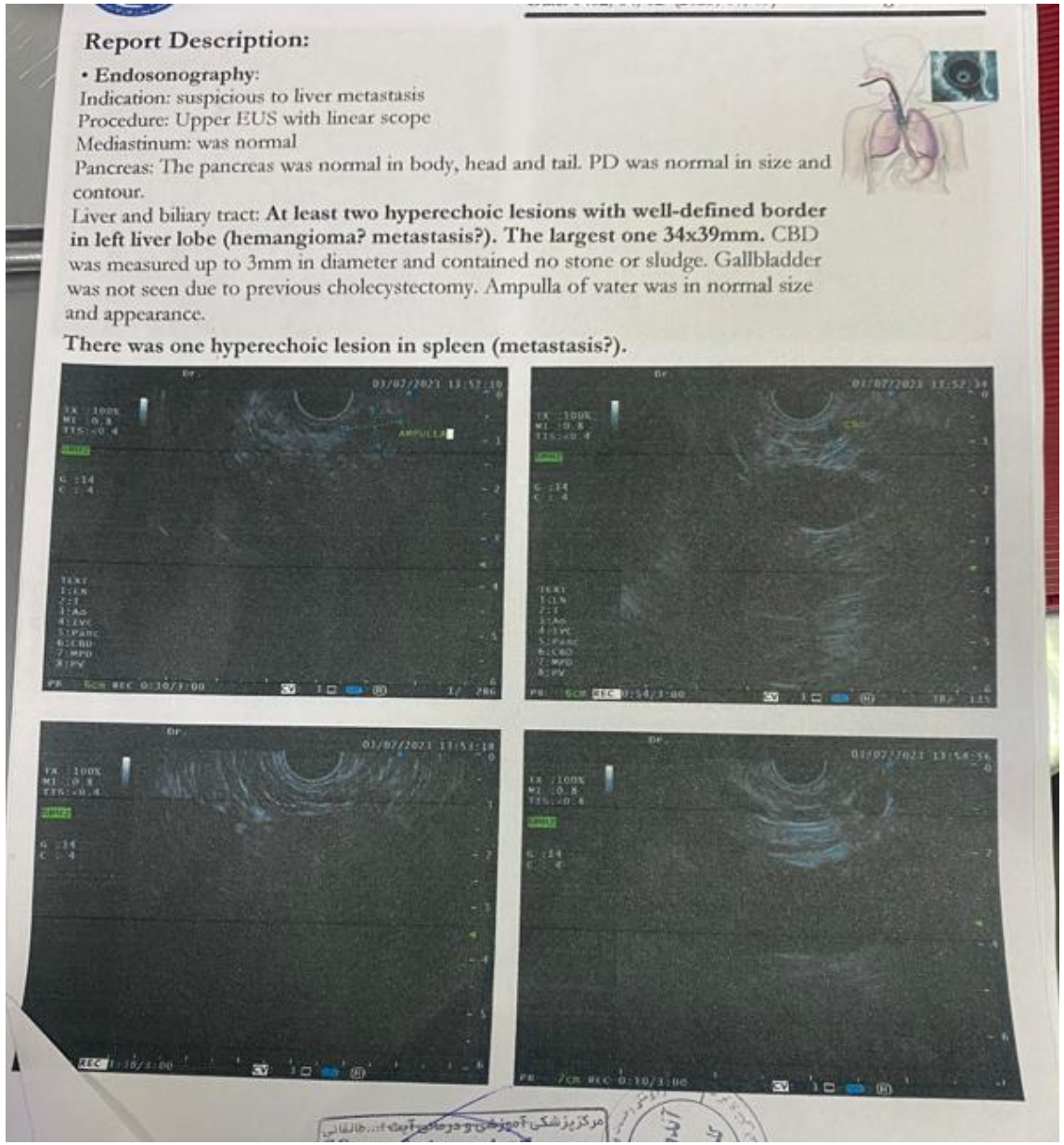
Histologic findings, confirm the following diagnosis.

Diagnosis :

Large intestinal mucosa, descending colon polyp, colonoscopic biopsy:
- Hyperplastic polyp.

Pathologist: Dr. parvizi MD/AP.CP Resident: Dr. Taghipour MD
1402.04.15

DX:
Hyperplastic polyp



Report Description:

• **Endosonography**:
Indication: suspicious to liver metastasis
Procedure: Upper EUS with linear scope
Mediastinum: was normal
Pancreas: The pancreas was normal in body, head and tail. PD was normal in size and contour.
Liver and biliary tract: **At least two hyperechoic lesions with well-defined border in left liver lobe (hemangioma? metastasis?). The largest one 34x39mm.** CBD was measured up to 3mm in diameter and contained no stone or sludge. Gallbladder was not seen due to previous cholecystectomy. Ampulla of vater was in normal size and appearance.

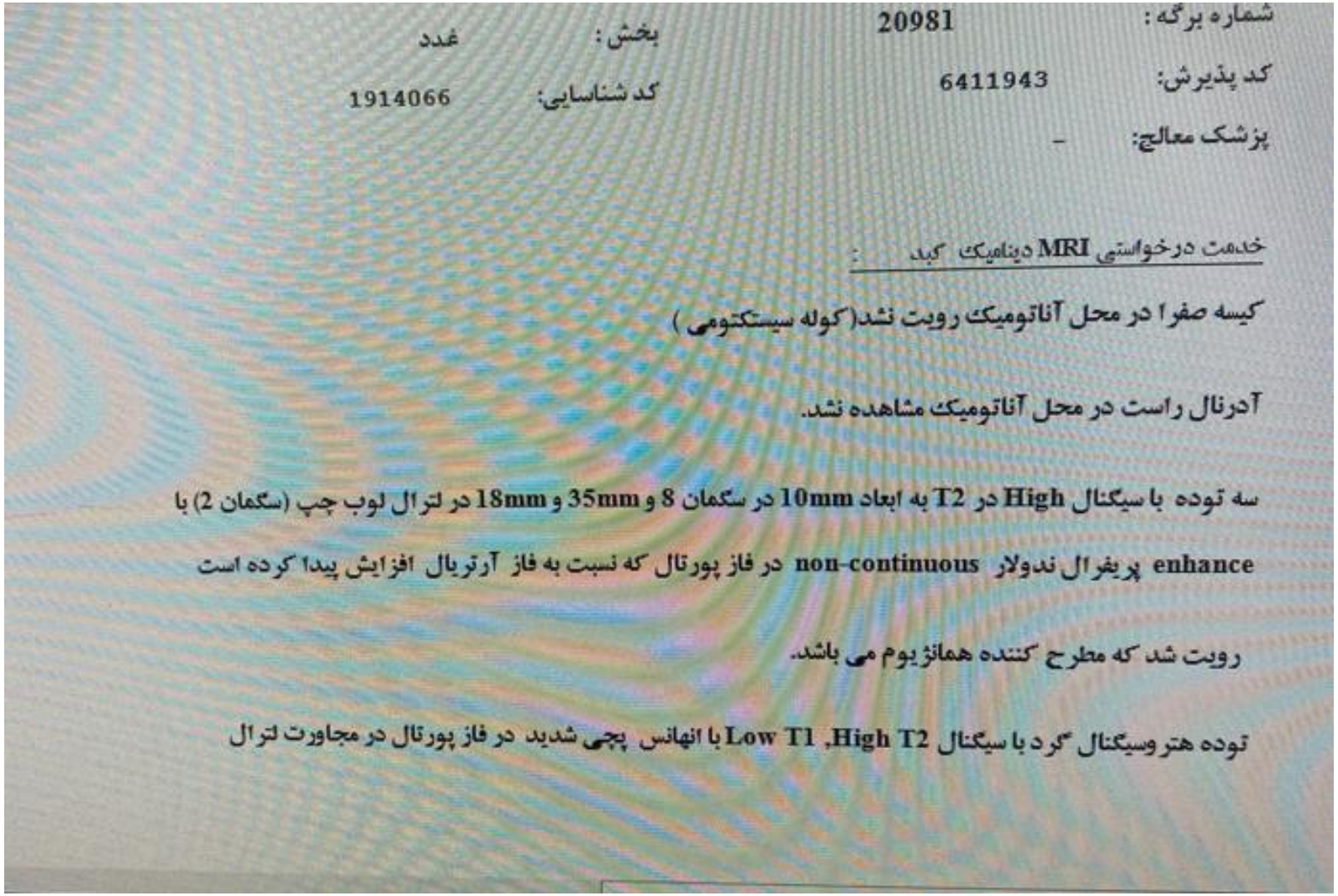
There was one hyperechoic lesion in spleen (metastasis?).

EUS 1402.4.10

2 Hyperechoic lesion in left liver lobe

Largest diameter 34 39 mm

Dynamic Liver MRI 1402.4.17
Hemangioma



شماره برگه : 20981 بخش : غدد

کد پذیرش: 6411943 کد شناسایی: 1914066

پزشک معالج: -

خدمت درخواستی MRI دینامیک کبد :

کیسه صفرا در محل آناتومیک رویت نشد(کوله سیستکتومی)

آدرنال راست در محل آناتومیک مشاهده نشد.

سه توده با سیگنال High در T2 به ابعاد 10mm در سگمان 8 و 35mm و 18mm در لترال لوب چپ (سگمان 2) با enhance پریفرال ندولار non-continuous در فاز پورتال که نسبت به فاز آرتریال افزایش پیدا کرده است رویت شد که مطرح کننده همانژیوم می باشد.

توده هتروسیگنال گرد با سیگنال High T2, Low T1 با انهانس پچی شدید در فاز پورتال در مجاورت لترال

کد پذیرش: ۶۴۱۱۹۴۳ کد شناسایی: ۱۹۱۴۰۶۶

پزشک معالج: -

خدمت درخواستی : MRI هیپوفیز و سلاتوریکا با و بدون ماده حاجب

سایز، position و شکل سلا نرمال می باشد.

غده ی هیپوفیز سایز ، شکل و پوزیشن نرمال دارد.

بافت هیپوفیز سیگنال طبیعی دارد. و قبل و بعد از کنتراست انورمالیتی و تغییر سیگنال در آن رویت نمی گردد.

Infundibulum سایز نرمال دارد.

سینوس کاورنوس و شریان کاروتید داخلی و سیفون کاروئید unremarkable می باشد.

سینوس اسفنوئید نرمال و هواگیری طبیعی دارد.

تغییرات post-op در ناحیه سلا تورسیکا و exsion هیپوفیز رویت شد.

تصویر ساختار تقریبا round به دیامتر ۱۲×۱۱۰۰ در مجاورت تحتانی سلا و در قدام clivus و با سیگنال بالا در T1 و signal drop در fat sat رویت شد که در درجه اول مطرح کننده fat در این ناحیه می باشد.

شواهد واضحی به نفع عود تومور سلاتورسیکا در حال حاضر رویت نشد بررسی آزمایشگاهی توصیه می شود.

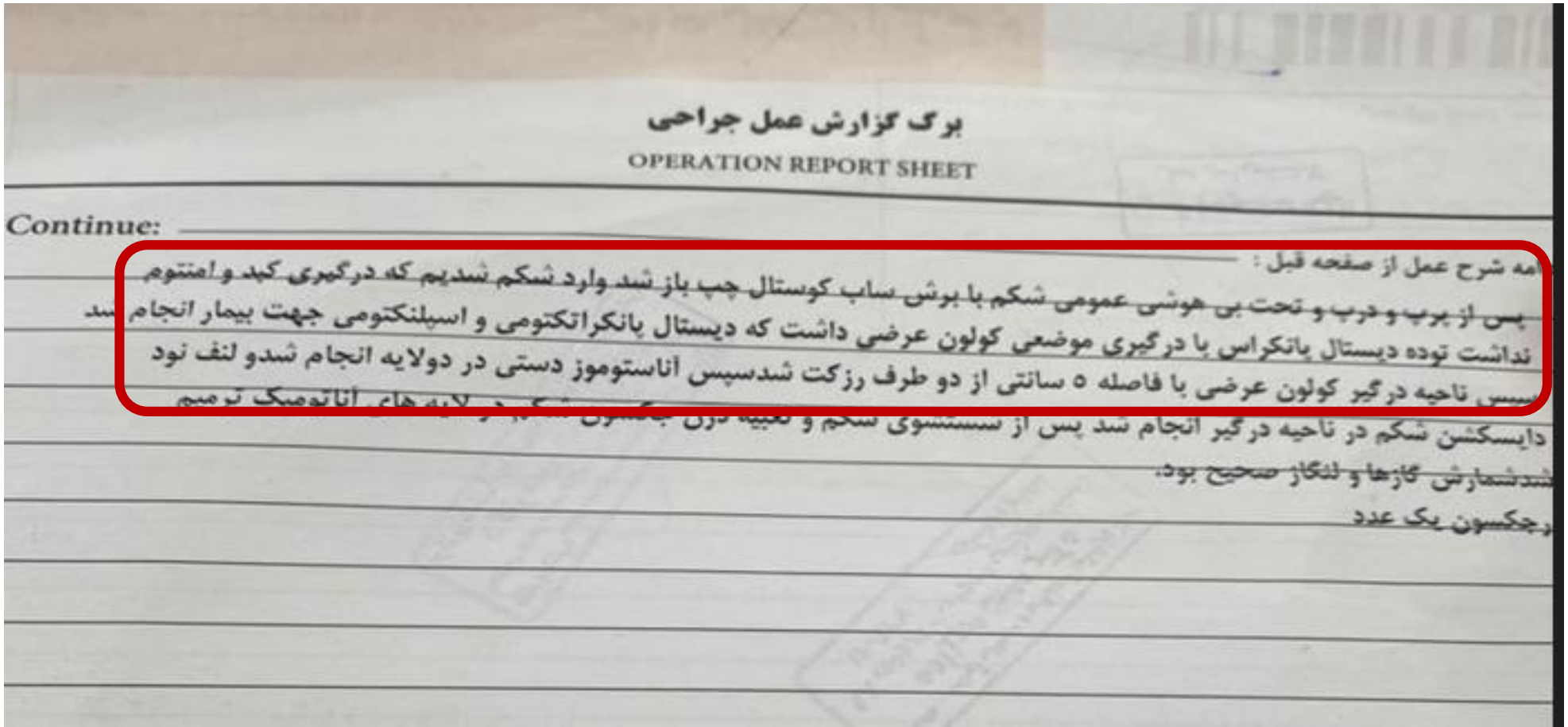
Polyp/retention cyst در ماگزیلاری راست و اسفنوئید راست رویت شد.

کدورت در سینوس اسفنوئید سمت راست رویت شد.

Pituitary MRI 1402.4

1402/04/20

Distal Pancreatectomy
+Splenectomy
+Partial colectomy



برگ گزارش عمل جراحی

OPERATION REPORT SHEET

Continue:

ادامه شرح عمل از صفحه قبل :

پس از پرپ و درپ و تحت بی هوشی عمومی شکم با بوش ساب کوستال چپ باز شد وارد شکم شدیم که درگیری کبد و امنتوم
ندانشت توده دیستال پانکراس با درگیری موضعی کولون عرضی داشت که دیستال پانکراتکتومی و اسپلنکتومی جهت بیمار انجام شد
سپس ناحیه درگیر کولون عرضی با فاصله ۵ سانتی از دو طرف رزکت شدسپس آناستوموز دستی در دولایه انجام شدو لنف نود
دایسکشن شکم در ناحیه درگیر انجام شد پس از ششستوی شکم و تخلیه درن
شدشمارش گازها و لنگار صحیح بود.
رجکسون یک عدد

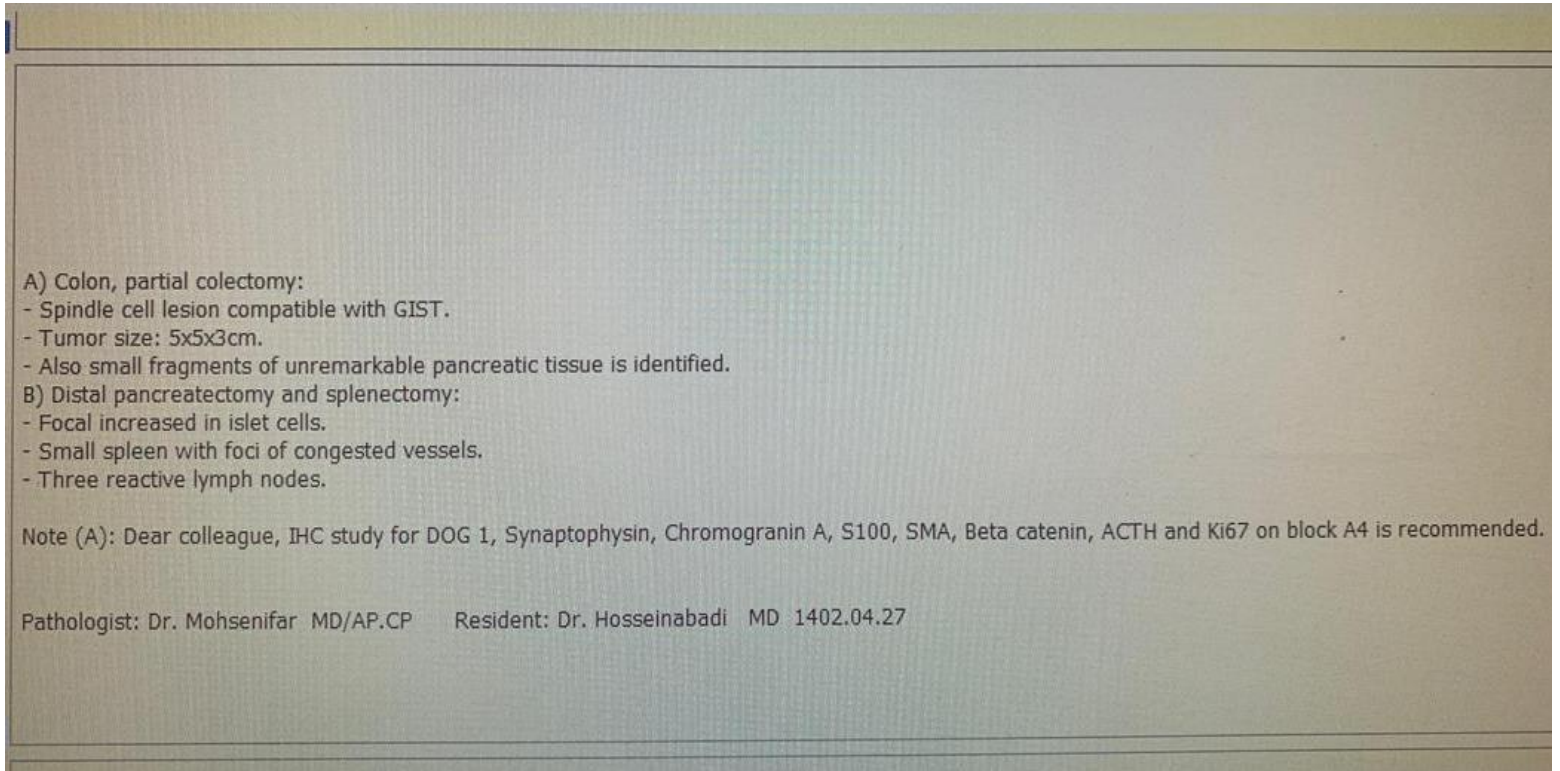
Pathology

Colectomy:

spindle cell compatible with GIST

Pancreatectomy and splenectomy:

Focal increase in islet cells Small spleen of congested vessels



A) Colon, partial colectomy:
- Spindle cell lesion compatible with GIST.
- Tumor size: 5x5x3cm.
- Also small fragments of unremarkable pancreatic tissue is identified.

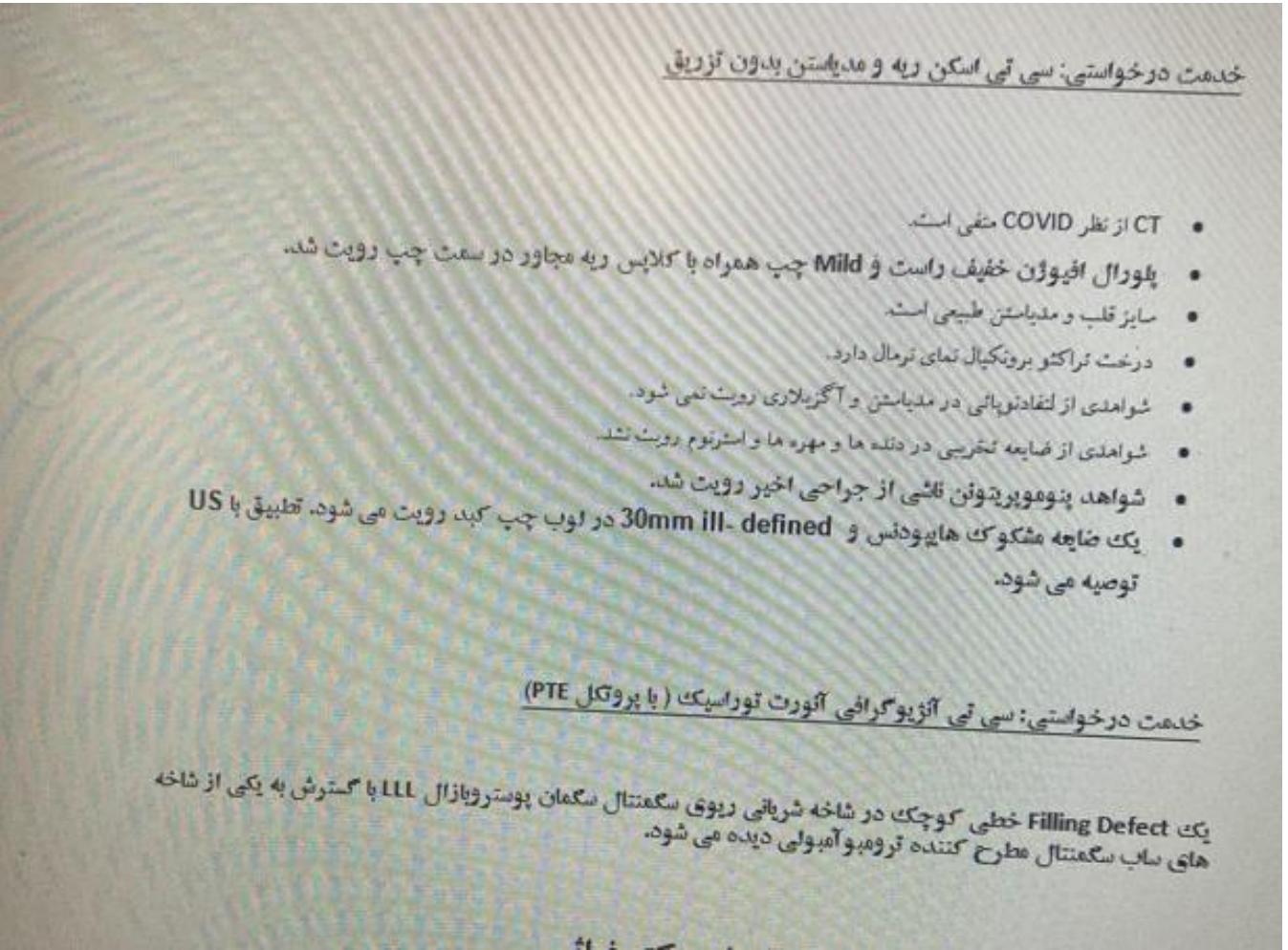
B) Distal pancreatectomy and splenectomy:
- Focal increased in islet cells.
- Small spleen with foci of congested vessels.
- Three reactive lymph nodes.

Note (A): Dear colleague, IHC study for DOG 1, Synaptophysin, Chromogranin A, S100, SMA, Beta catenin, ACTH and Ki67 on block A4 is recommended.

Pathologist: Dr. Mohsenifar MD/AP.CP Resident: Dr. Hosseinabadi MD 1402.04.27

Post Operative cortisol level

Date	cortisol	ACTH
1402/04/22	**37 µg/dl**	
1402/04/26	**46 µg/dl**	
1402/05/01	**34 µg/dl**	**32pg/ml (7_63)**



خدمت درخواستی: سی تی اسکن ریه و مدیاستن بدون تزریق

- CT از نظر COVID منفی است.
- پلورال افیوژن خفیف راست و Mild چپ همراه با کلاپس ریه مجاور در سمت چپ رویت شد.
- سایز قلب و مدیاستن طبیعی است.
- درخت تراکئو برونکیال تمای نرمال دارد.
- شواهدی از لنفادنوپاتی در مدیاستن و آگزیلاری رویت نمی شود.
- شواهدی از ضایعه تخریبی در دنده ها و مهره ها و استرنوم رویت نشد.
- شواهد پنوموپریتونئن ناشی از جراحی اخیر رویت شد.
- یک ضایعه مشکوک هایپودنس و 30mm ill- defined در لوب چپ کبد رویت می شود. تطبیق با US توصیه می شود.

خدمت درخواستی: سی تی آنژیوگرافی آئورت توراسیک (با پروتکل PTE)

یک Filling Defect خطی کوچک در شاخه شریانی ریوی سگمنتال سگمان پوستروبازال LLL با گسترش به یکی از شاخه های ساب سگمنتال مطرح کننده ترومبوآمبولی دیده می شود.

CT Angiography PTE:

Filling defect

Mild **pleural effusion** in left and right

Right **lung collapse**

1402.5.6	
WBC	14500
HB	7.7
PLT	**1035000**
BUN	15
Cr	1
PH **PCO2** **HCO3**	**7.47** **39** **28**
Na	143
k	3.6
AST	12
ALT	11
ALP	338
ESR	**79**
CRP	**57**

Drug History:

- Tab valsartan 80mg Daily
- Spray DDAVP 1puff Daily
- Levothyroxine 200µg/D
- Ketoconazole 200mg BD
- Rivaroxaban 15mg BD
- Amp Tavanex 750 mg /D
- Amp ampisulbactam 3gr/D
- Amp Vancomycin 1gr/BD

Review of Systems:

- Constitutional symptoms: weight gain (+)
- Head and neck: Round face (+)
- Cardiovascular: Hypertension (+)
- Respiratory: Nl
- Gastrointestinal: Constipation (+)
- Genitourinary: Menstrual changes (+)
- Musculoskeletal: Fracture (-)
- Skin: plethora (+), Ecchymosis (+), Easy bruising (+), Purplish stretch marks on the abdomen (+), Swelling (+),
- Neurological: proximal weakness(+), Headache (+), dizziness (+)
- Psychiatric: depression(+), anxiety(-), irritability (+)

Physical Examination:

- **GENERAL APPEARANCE:**
  - 33y/o women, awake and alert
- **Vital Sing:**
  - **BP: 130/75 mmHg, PR: 92/min, RR:22/min, OT: 36.8, SO_2: 82%**
- **BMI:**
  - **Weight: 97 Kg Height: 165cm BMI: 35.6**
  - Waist Circumference: 99 cm

Physical Examination:

- Round face, Facial plethora,
- normal thyroid size
- Dorsal fat pad
- Supraclavicular fullness
- Striae (red purple, >1cm wide),
- Lower : Force of muscles : 5/5

- **Past Medical History**

  - **ACTH independent Cushing** (Adrenalectomy 1388)
  - **ACTH Dependent Cushing (CD)** and TSS(1401/02/01) and (1402/04/1)
  - **HTN**
  - **Dysglycemia**

PROBLEM LIST

- A 33-year-old woman
- **Persistent Cushing symptoms**
- **High level cortisol post surgery**
- **PTE/ Pneumonia / Pleural effusion**
- **Spindle cell benign tumor**

- **Persistent Cushing syndrome**

AGENDA

- ✓Remission and recurrence rate after first and second TSS
- ✓Review of Nuclear medicine imaging in ectopic Cushing syndrome
- ✓Case Repot Diagnosis in occult ectopic Cushing syndrome in long follow-up
- ✓Pharmacologic Treatment in Persistent Cushing syndrome
- ✓Pitfalls in Performing IPSS
- ✓Treatment Plan

Long-term remission and recurrence rates after first and second transsphenoidal surgery for Cushing's disease: care reality in the Munich Metropolitan Region

C Dimopoulou[1,2], J Schopohl[2], W Rachinger[3], M Buchfelder[4], J Honegger[5], M Reincke[2,*] and G K Stalla[1,*]

[1]Department of Endocrinology, Max Planck Institute of Psychiatry, Kraepelinstrasse 2-10, 80804 Munich, Germany, [2]Medizinische Klinik und Poliklinik IV, Ludwig-Maximilians-University, Munich, Germany, [3]Department of Neurosurgery, Klinikum Grosshadern, University of Munich, Munich, Germany, [4]Department of Neurosurgery, University of Erlangen-Nürnberg, Erlangen, Germany and [5]Department of Neurosurgery, University of Tuebingen, Tuebingen, Germany
*(M Reincke and G K Stalla contributed equally to this work)

Correspondence should be addressed to C Dimopoulou
Email
dimopoulou@mpipsykl.mpg.de

To investigate the outcomes of patients with CD who underwent a second TSS.

- Highlight the time frame of the study**: 1990 to 2012.**

- Results:
  - Present the outcomes after the first TSS:
    - Remission: 71% (85/120)
    - Persistent disease: 29% (35/120)
    - Disease recurrence: 34% (29/85)
    - Mean time to recurrence: 54 months

  - Discuss the outcomes after the second TSS:
    - Remission: 42% (15/36)
    - Persistent disease: 58% (21/36)
    - Disease recurrence: 40% (6/15)
    - Mean time to recurrence: 42 months

- Conclusion:

- **Higher recurrence rates after the first TSS than** previously reported.

- **Second TSS** resulted in an additional **8% of patients achieving long-term remission.**

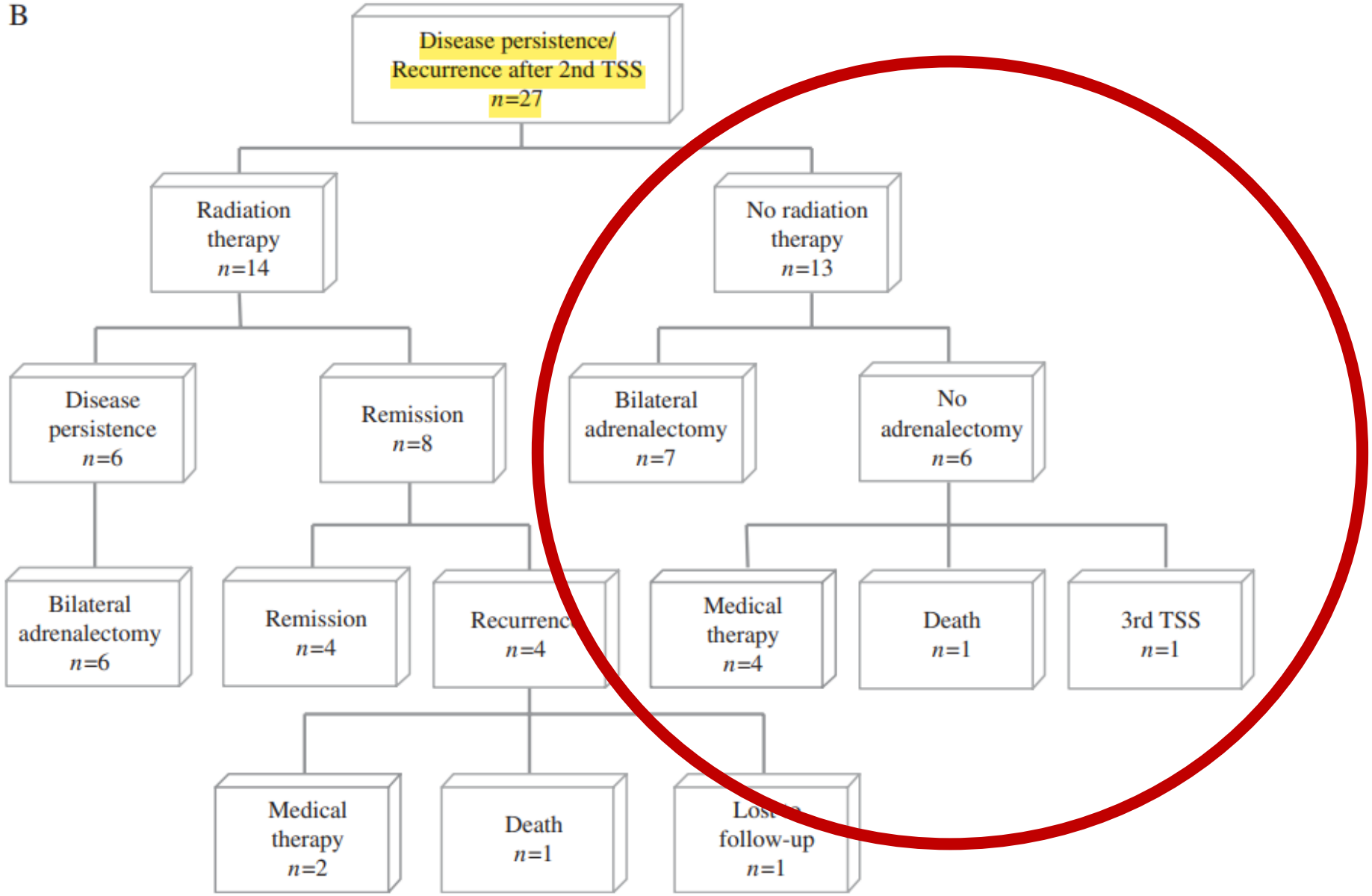
- After the second TSS, patients with **no visible tumor** on preoperative MRI showed a paradoxically **high remission rate of 75%.**

- **Postoperative hypocortisolism after the first TSS was associated with a lower risk of disease recurrence.**

Table 4 Remission rates, disease persistence, recurrence rates, and mean time to recurrence after first and second TSS and at final follow-up according to preoperative MRI. Comparisons between groups were calculated using χ^2 analysis.

	All patients	Macroadenoma	Microadenoma	No visible adenoma	*P* value
First TSS	*n*=120	*n*=32	*n*=58	*n*=30	
Remission	85 (71%)	22 (69%)	46 (79%)	17 (57%)	0.035
Disease persistence	35 (29%)	10 (31%)	12 (21%)	13 (43%)	0.082
Recurrence	29/85 (34%)	13/22 (59%)	10/46 (22%)	6/17 (35%)	0.007
Mean time to recurrence ±S.D. (months)	54±54	41±35	44±30	102±96	0.075
Second TSS	*n*=36	*n*=14	*n*=14	*n*=8	
Remission	15 (42%)	4 (29%)	5 (36%)	6 (75%)	0.124
Disease persistence	21 (58%)	10 (71%)	9 (64%)	2 (25%)	0.065
Recurrence	6/15 (40%)	3/4 (75%)	2/5 (40%)	1/6 (17%)	0.611
Mean time to recurrence ±S.D. (months)	27±29	35±36	15±16	120±0	0.522
Final follow-up	*n*=120	*n*=32	*n*=58	*n*=30	
Remission	110 (92%)	24 (75%)	56 (97%)	30 (100%)	0.000
Disease persistence	10 (8%)	8 (25%)	2 (3%)	0 (0%)	0.000

B


Disease persistence/ Recurrence after 2nd TSS n=27
Radiation therapy n=14
No radiation therapy n=13
Disease persistence n=6
Remission n=8
Bilateral adrenalectomy n=7
No adrenalectomy n=6
Bilateral adrenalectomy n=6
Remission n=4
Recurrenc n=4
Medical therapy n=4
Death n=1
3rd TSS n=1
Medical therapy n=2
Death n=1
follow-up n=1

Volume 100, Issue 9
1 September 2015

Conventional and Nuclear Medicine Imaging in Ectopic Cushing's Syndrome: A Systematic Review

FREE

Andrea M. Isidori, Emilia Sbardella, Maria Chiara Zatelli, Mara Boschetti, Giovanni Vitale, Annamaria Colao, Rosario Pivonello ✉, on behalf of the ABC Study Group

The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 9, 1 September 2015, Pages 3231–3244, https://doi.org/10.1210/JC.2015-1589

Published: 01 September 2015 **Article history** ▾

Systematic review of medical literature for ECS case series

- The analysis included 231 patients, with females accounting for 50.2% of the cases. The average age of the patients was 42.6 years.

- The study found that 52.4% of the patients had "overt" ectopic Cushing syndrome (ECS), while 18.6% had "occult" ECS, and 29% had "covert" ECS.

- lung most common site (55.3% of cases).
- Mediastinum-thymus (7.9%),
- pancreas (8.5%),
- adrenal glands (6.4%),
- gastrointestinal tract (5.4%),
- thyroid (3.7%),
- other sites (12.8%).

- **Conventional imaging techniques**
- CT localized tumors in 66.2%,
- magnetic resonance imaging (MRI) in 51.5%,
- octreotide scan (OCT) in 48.9%.

- **Molecular imaging techniques**,
- FDG-PET (positron emission tomography), F-DOPA-PET
- 68Ga-SSTR-PET/CT (68Gallium-labeled somatostatin receptor PET/CT),

provided additional value in identifying tumors that were not detected by conventional radiology

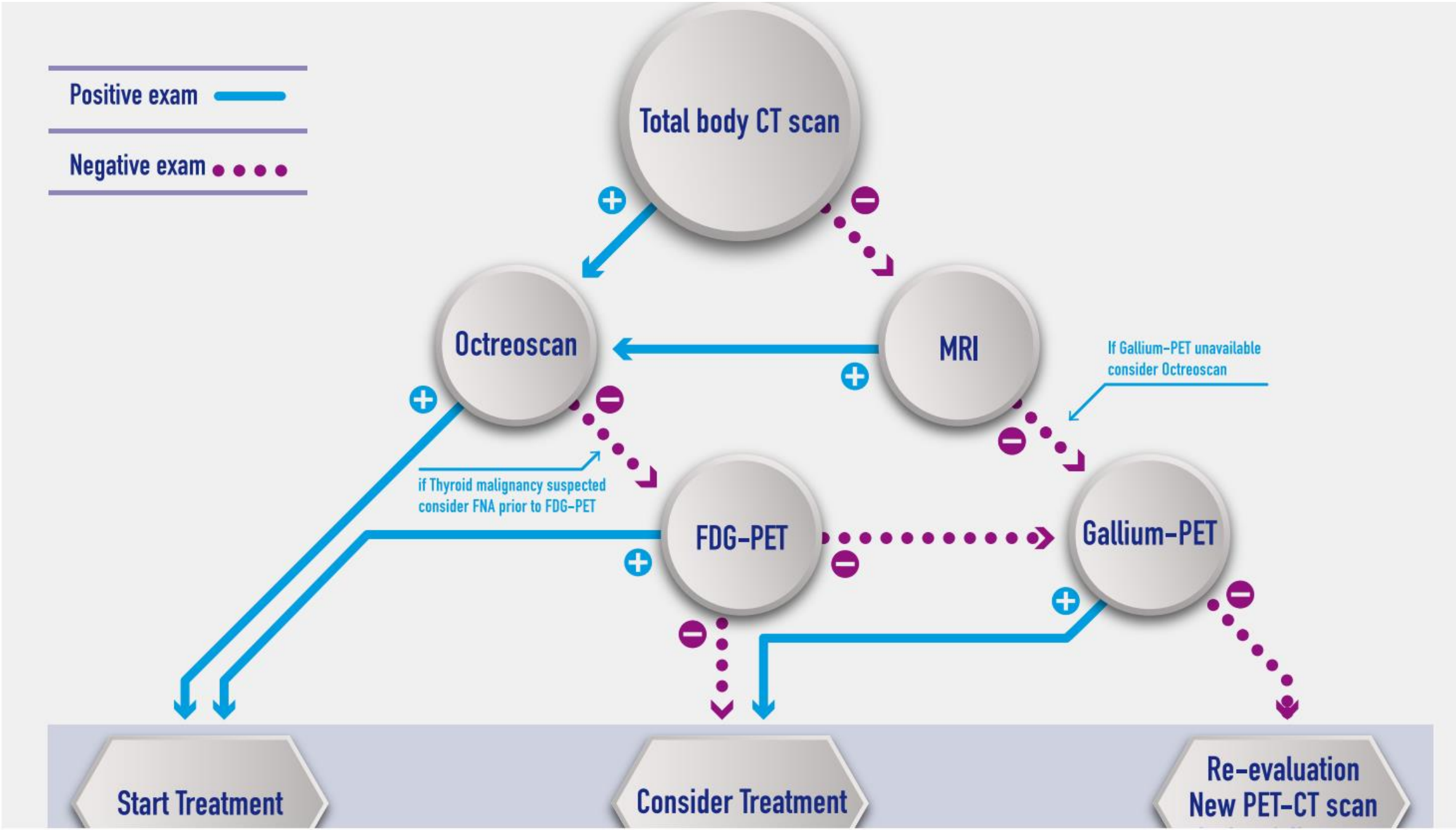
- Among the molecular imaging techniques,

OCT was the most commonly used and had a detection rate of 64%.

FDG-PET had a detection rate of 59.4%.

F-DOPA-PET showed a sensitivity of 85.7%

68Ga-SSTR-PET/CT demonstrated a sensitivity of 100% in covert cases, suggesting it to be the most sensitive imaging technique for ECS.


Positive exam
Negative exam
Total body CT scan
Octreoscan
MRI
If Gallium-PET unavailable
consider Octreoscan
if Thyroid malignancy suspected
consider FNA prior to FDG-PET
FDG-PET
Gallium-PET
Start Treatment
Consider Treatment
Re-evaluation
New PET-CT scan

- Despite intensive investigations, 18.6% of ACTH-secreting tumor sources remained occult.

- **68Gallium-SSTR-PET/CT shows potential superiority over other imaging techniques.**

- **It demonstrated the highest sensitivity in localizing covert ECS and consistently helped identify its source.**

- These findings suggest that OCT, FDG-PET, F-DOPA-PET, and 68Gallium-SSTR-PET/CT can be useful secondary and tertiary imaging modalities after a negative CT or MRI scan in identifying the tumor site associated with ACTH production

- Considering the potential for false-positive results, it is important to adopt a double-step approach with sequential use of detection and confirmatory exams.

This helps mitigate the risk of inaccuracies, especially when dealing with small lesions. Additionally, complications arise when multiple distinct neuroendocrine tumors (NETs) coexist

The degree of hypercortisolism can also influence the interpretation of 68Gallium-SSTR-PET/CT positivity.

	CT	MRI	OCT	FDG-PET	F-DOPA-PET	MIBG	^{68}Gallium-SSTR-PET/CT
All patients (n = 231)							
Sensitivity, % (95% CI)	66.2% (59.5–72.3)	51.5% (41.9–60.9)	48.9% (41.5–56.3)	51.7% (41.5–61.8)	57.1% (36.6–75.5)	30.8% (12.7–57.6)	81.8% (61.5–92.7
n	137/207	53/103	84/172	46/89	12/21	4/13	18/22
True positive	63.7%	50.5%	48.3%	51.1%	54.5%	26.7%	78.3%
n	137/215	53/105	84/174	46/90	12/22	4/15	18/23
False negative	33.6%	47.6%	50.6%	47.8%	40.9%	60%	17.4%
n	70/215	50/105	88/174	43/90	9/22	9/15	4/23
False positive	3.7%	1.9%	1.1%	1.1%	4.5%	13.3%	4.3%
n	8/215	2/105	2/174	1/90	1/22	2/15	1/23

	CT	MRI	OCT	FDG-PET	F-DOPA-PET	MIBG	^{68}Gallium-SSTR-PET/CT
Overt (n = 121)							
Sensitivity % (95% CI)	98.3% (93.9–99.5)	92.9% (81.0–97.5)	63.5% (52.9–72.9)	71.1% (55.2–83)	53.9% (29.1–76.8)	37.5% (13.7–69.4)	70% (39.7–89.2)
n	113/115	39/42	54/85	27/38	7/13	3/8	9/13
True positive	97.4%	92.9%	62.1%	71.1%	50,0%	30%	69.2%
n	113/116	39/42	54/87	27/38	7/14	3/10	9/13
False negative	1.7%	7.1%	35.6%	28.9%	42.9%	50%	30.8%
n	2/116	3/42	31/87	11/38	6/14	5/10	4/13
False positive	0.9%		2.3%		7.1%	20%	
n	1/116		2/87		1/14	2/10	
Covert (n = 67)							
Sensitivity, % (95% CI)	43.6% (31.4–56.7)	44.8% (28.4–62.4)	64.0% (50.1–75.9)	59.4% (42.3–74.5)	85.7% (48.7–97.4)	50% (9.5–90.6)	100% (61–100)
n	24/55	13/29	32/50	19 /32	6/7	1/2	9/9
True positive	39.3%	41.9%	64.0%	57.6%	85.7%	50%	90.0%
n	24/61	13/31	32/50	19/33	6/7	1/2	9/10
False negative	50.8%	51.6%	36.0%	39.4%	14.3	50%	
n	31/61	16/31	18/50	13/33	1/7	1/2	
False positive	9.8%	6.5%		3.0%			10.0%
n	6/61	2/31		1/33			1/10

Table 3. Sensitivity (95% CI) of Diagnostic Techniques in Primary Source Localization According to Tumor Site

Site (Positive Finding)	CT +	MRI +	OCT +	FDG-PET +	F-DOPA-PET +	MIBG +	^{68}Gallium-SSTR-PET/CT +
Lung	79.4% (70.3–86.2)	66.7% (48.8–80.8)	60.9% (50.2–70.8)	54.6% (38.0–70.2)	71.4% (45.4–88.3)	50% (9.5–90.6)	77.8% (45.3–93.7)
n	77/97	20/30	50/82	18/33	10/14	1/2	7/9
Thymus, mediastinum	85% (63.9–94.8)	62.5% (30.6–86.3)	85.7% (60.1–96.0)	62.5% (30.6–86.3)	33.3% (6.2–79.2)	nd	50% (15.0–85.0)
n	17/20	5/8	12/14	5/8	1/3		2/4
Pancreas	85.7% (60.1–96.0)	87.5% (52.9–97.8)	66.7% (35.4–88)	100% (61–100)	nd	Out of 1 case: 0 TP, 1 FN	100% (34.2–100)
n	12/14	7/8	6/9	6/6			2/2
Adrenal gland	100% (72–100)	100% (57–100)	60% (23.1–88.2)	100% (44–100)	100% (20.7–100)	50% (15–85)	nd
n	10/10	5/5	3/5	3/3	1/1	2/4	
Gastrointestinal tract	90% (59.6–98.2)	71.4% (35.9–91.8)	50% (21.5–78.5)	57.1% (25.1–84.2)	100% (20.7–100)	nd	100% (34.2–100)
n	9/10	5/7	4/8	4/7	1/1		2/2
Thyroid	80% (37.6–96.4)	100% (20.7–100)	66.7% (20.8–93.9)	100% (43.9–100)	nd	Out of 3 cases: 0 TP, 1 FP, 2 FN	100% (34.2–100)
n	4/5	1/1	2/3	3/3			2/2
Carotid glomus, atrium, para-aortic region	33.3% (6.2–79.2)	33.3% (6.2–79.2)	80% (37.6–96.4)	100% (34.2–100)	nd	nd	nd
n	1/3	1/3	4/5	2/2			
Head: ethmoidal-paranasal-sphenoid-sinus, olfactory bulb, skull base, etc	57.1% (25.1–84.2)	87.50% (52.9–97.8)	80% (37.6–96.4)	71.4% (35.9–91.8)	Out of 1 case: 0 TP, 1 FN	nd	100% (43.9–100)
n	4/7	7/8	4/5	5/7			3/3
Abdomen/other (abdominal paraganglioma, ovary)	60% (23.1–88.2)	66.7% (20.8–93.9)	20% (3.6–62.5)	100% (20.7–100)	nd	100% (34.2–100)	nd
n	3/5	2/3	1/5	1/1		2/2	

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Clinical Case Seminar

A2(1-8)

Non Obvious Diagnosis of an Occult ACTH Dependent Cushing Syndrome

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Abstract

- **A 54 years old man**
- Presenting Symptoms: Progressive **signs and symptoms of Cushing syndrome**

- Biochemical Diagnosis: Adrenocorticotropic Hormone **(ACTH)-dependent** hypercortisolism

- Diagnostic Tests:
  - High dose 8 mg overnight Dexamethasone Suppression Test (HDDST)
  - (DDAVP) stimulation test
  - Magnetic Resonance Imaging (MRI)
- Conflicting Results: **Led to the diagnosis of ectopic ACTH syndrome** following Bilateral Inferior Petrosal Sinus Sampling (BIPPS)

OctCT	2009	ACTH suppression after 4 h: 89.5% Cortisol suppression after 4 h: 63.4%	See table 3 for details
CgA	2008	46 ng/mL (RV <101.9)	
NSE	2009	21.6 µg/L (RV 0-12.5)	
Calcitonin	2009	2 pg/mL (RV 1-12)	
Imaging			
Total body CT	2008	Negative	
OCT	2009	Negative	
Total body CT	2010	Negative	
PET	2010	Small focus in the right lung	
			Computed tomographies performed between 2010-2014 are not currently available. They always showed a negative result
PET	2014	Small focus in the right lung	
Pituitary MRI	2014	Negative	
Total body CT	2015	Negative	
PET	2017	Moderate focus in the right lung	
Total body CT	2017	Focal lesion in the right lung	

- Localization Challenges:
  - Imaging Exams: Most imaging exams gave **negative results**
  - **Prolonged Follow-up**: Chest Computed Tomography (CT) scan provided morphological confirmation of a **small focus in the right lung**
  - Previous Detection: **68Gallium-DOTATOC-Positron Emission Tomography (PET) identified the lung focus**

- Treatment and Surgery:
  - Surgery: Right lower lobectomy of the lung performed
  - Pathology: ACTH-positive typical pulmonary carcinoid diagnosed

  - Pre-surgery Management: **Good management of hypercortisolism achieved with somatostatin analog lanreotide**

Table 6. Main therapeutic steps. 24hCLU before and after therapeutic modifications are reported.

Therapy	Posology	Year of prescription	24hCLU (µg/24h) RV 10-110		Notes
Ketoconazole	400 mg/die	November 2008	\		Discontinued 2 weeks before performing march 2009 hormonal evaluation
Lanreotide			Before	After	
	60 mg im/28 days	April 2009	\	\	
	90 mg im/28 days	September 2010	\	2013: 75 2013: 69 2014: 10 2014: 13	
	120 mg im/28 days	June 2015	379	2010: 76 2010: 72	
Pasireotide			Before	After	Discontinued in june 2017, before performing right lower lobectomy of the lung. The patient showed a poor biochemical control of hypercortisolism in the last month before discontinuation.
	0.6 mg sc twice/daily	January 2017	309 348	76 45.5	
Surgery		June 2017			Right lower lobectomy of the lung

- **68Gallium-SSTR (Somatostatin Receptor)-PET**

✓**greatest sensitivity** in localizing **covert cases**

✓**best follow-up imaging technique**

✓Has aspecificity ranging 88-95%

Medical therapy for Cushing's disease

1. **Control of hypercortisolism in preparation** ,medical therapy is often required when surgery is delayed
2. Management of hypercortisolism if surgery is contraindicated
3. Management of persistent or recurrent hypercortisolism after initial surgery
4. Patients who have undergone radiation therapy – Control of hypercortisolism while waiting for the effect of pituitary radiation
5. Patients with ectopic ACTH syndrome – Treatment of occult or metastatic ectopic ACTH syndrome

Diabetes-endocrinology October 2021
Consensus on diagnosis and management of Cushing's disease: a guideline update

Table 2. Summary of Medical Therapies for CD

Target	Drug	Commonly used doses	Efficacy	Adverse effects	Key considerations
Adrenal steroidogenesis	Ketoconazole	400–1200 mg/d PO, dosing BID	Retrospective studies: ~65% UFC normalization initially, but 15-25% escape	GI disturbances, ↑ liver enzymes, gynecomastia, skin rash, AI	• *EMA approved for treatment of endogenous CS, off-label use in US* • Increasing doses needed to counter escape • Needs gastric acid for absorption (avoid PPIs) • Decrease in testosterone would be preferred in women; men need follow-up for hypogonadism • Risk for serious hepatotoxicity; mostly transient but regular LFT monitoring required • Risk of QTc prolongation • Careful review of other medications for potential drug-drug interactions is essential
	Osilodrostat	2-7 mg/d BID PO as maintenance; 30 mg/d BID maximum	Phase 3 randomized withdrawal study: 86% UFC normalization	↑ Androgenic and mineralocorticoid precursors (hirsutism, hypertension, hypokalemia), GI disturbances, asthenia, AI	*FDA approved for patients with CD in whom pituitary surgery is not an option or has not been curative* • *EMA and Japan approved for treatment of endogenous CS* • Not yet widely available • Rapid decrease in UFCHas • Risk for hypocortisolism, hypokalemia, and QTc prolongation • Cross-reaction in routine assays with 11-deoxycortisol • Careful monitoring for hyperandrogenism in women
	Metyrapone	500 mg/d to 6 g/d; dosing q 6-8 h	UFC normalization Retrospective studies: ~70% Prospective study: 47% at week 12	↑ Androgenic and mineralocorticoid precursors (hirsutism, hypertension, hypokalemia), AI	• *EMA approved for treatment of endogenous CS, off-label use in US* • Rapid decrease in UFC, typically in first month • Possible cross reactivity with 11-deoxyxortisol in cortisol immunoassays • Hyperandrogenism needs to be monitored with long-term use in women
	Mitotane	250-500 mg/d PO up to 8 g/d	Retrospective studies: ~80% UFC normalization	GI disturbances, dizziness, cognitive alterations, AI ↑ Liver enzymes; treatment should be stopped if elevations are >5 × ULN	• *FDA and EMA approved for treatment of adrenal cancer with endogenous CS* • Slow onset of action, highly variable bioavailability • Narrow therapeutic window (dose titration based on mitotane plasma levels) • Neurological toxicity could be a limiting factor

Somatostatin receptor	Pasireotide	0.3-0.9 mg/mL BID SC	Phase 3 study: 15-26% UFC normalization	Hyperglycemia, T2DM, diarrhea, nausea, abdominal pain, cholelithiasis, fatigue	• *Widely approved for patients with CD in whom pituitary surgery is not an option or has not been curative* • Decreases tumor volume • High risk for hyperglycemia requires careful patient selection • Risk of QTc prolongation
	Pasireotide LAR	10-30 mg monthly IM	Phase 3 study: 40% UFC normalization Clinical signs and symptoms of hypercortisolism improved		
Dopamine receptor	Cabergoline	0.5-7 mg weekly PO	Retrospective studies: ~40% UFC normalization initially, but ~25-40% escape Clinical signs and symptoms of hypercortisolism improved	Headache, nasal congestion, hypotension, depression, dizziness	• *Off-label use only for CD* • Decreases tumor volume in up to 50% of the patients evaluated • Clinical signs and symptoms of hypercortisolism improved • Poor response may be due to under-titration • Risk for treatment-induced impulse-control disorder; unclear risk for cardiac valvulopathy
Glucocorticoid receptor	Mifepristone	300-1200 mg/d PO	Open-label phase 3 study: significant improvement in glycemia (~60%) and blood pressure Clinical signs and symptoms of	GI disturbances, headache, hypokalemia, arthralgia, peripheral edema, hypertension, vaginal bleeding, AI	• *FDA approved for hyperglycemia associated with CS* • No laboratory markers of efficacy • Challenging to use outside specialized clinical practice • Risk of hypokalemia and adrenal insufficiency; needs close monitoring • Careful review of other medications for potential drug-drug interactions is essential

JOURNAL ARTICLE

Cabergoline in severe ectopic or occult Cushing's syndrome

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Published: 01 July 2019 **Article history** ▾

Context

Cabergoline has been shown to have some effect in the treatment of moderate Cushing's disease, but its effectiveness in Cushing's syndrome of ectopic or occult origin remains to be investigated.

Case series

In this case series, cabergoline was used in combination with steroidogenesis inhibitors in nine patients with severe Cushing's syndrome of ectopic or occult origin. Cabergoline's effectiveness enabled rapid withdrawal of the steroidogenesis inhibitors and long-term control of the hypercortisolism in three of the cases.

Review of the literature

In the literature, we found only 11 cases of ectopic or occult Cushing's syndrome treated with dopamine receptor agonists, alone or in combination. Yet of these 11 cases, 10 responded.

Conclusions

Although limited, the existing experience highlights the potential value of cabergoline in the treatment of ectopic or occult Cushing's syndrome.

Cabergoline plus Lanreotide for Ectopic Cushing’s Syndrome

- 35-year-old man with symptoms suggesting an ectopic corticotropin syndrome related to a carcinoid tumor.
- Tests confirmed the diagnosis, and imaging revealed a lung tumor.
- Surgery was performed to remove the tumor, but Cushing's syndrome persisted afterward.
- Since reoperation was not possible, the patient was started on lanreotide therapy, a somatostatin analogue. Initially, there was a decrease in corticotropin and cortisol secretion, **but over time**, the tumor became **resistant to the treatment**. After one year, lanreotide therapy was stopped the long-term effectiveness

- of combined treatment with a somatostatin analogue and a dopamine agonist in a patient who no longer had a response to either agent alone and supports the hypothesis that somatostatin and dopamine receptors interact and that somatostatin and agonists may potentiate actions.

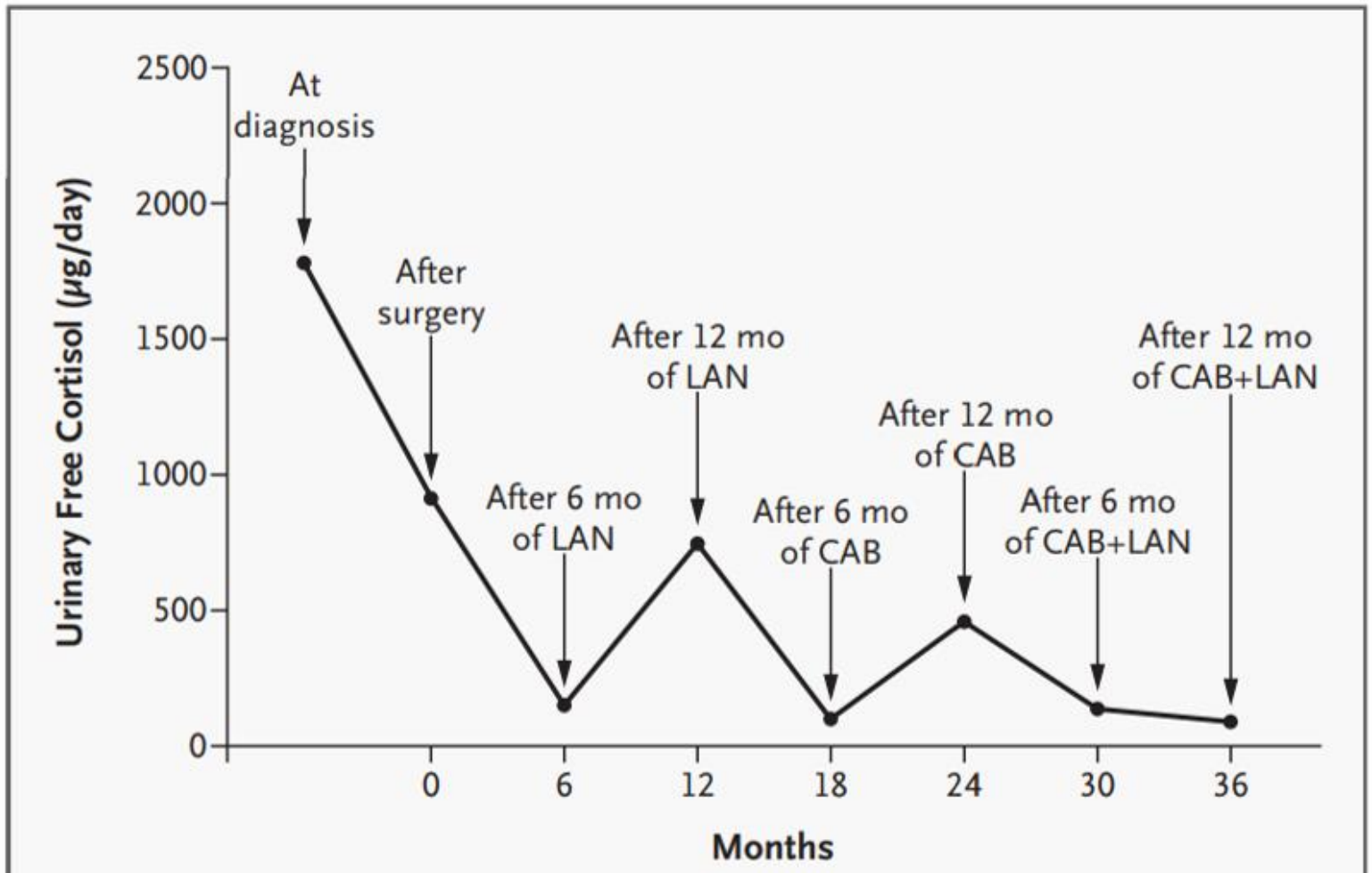


Figure 1. Urinary Cortisol Levels after Various Treatments in a Patient with the Ectopic Corticotropin Syndrome Associated with a Corticotropin-Secreting Lung Carcinoid.

LAN denotes lanreotide, and CAB cabergoline.

Pitfalls In Performing And Interpreting Inferior Petrosal Sinus Sampling: Personal Experience And Literature Review

Article *in* The Journal of Clinical Endocrinology and Metabolism · January 2021

DOI: 10.1210/clinem/dgab012

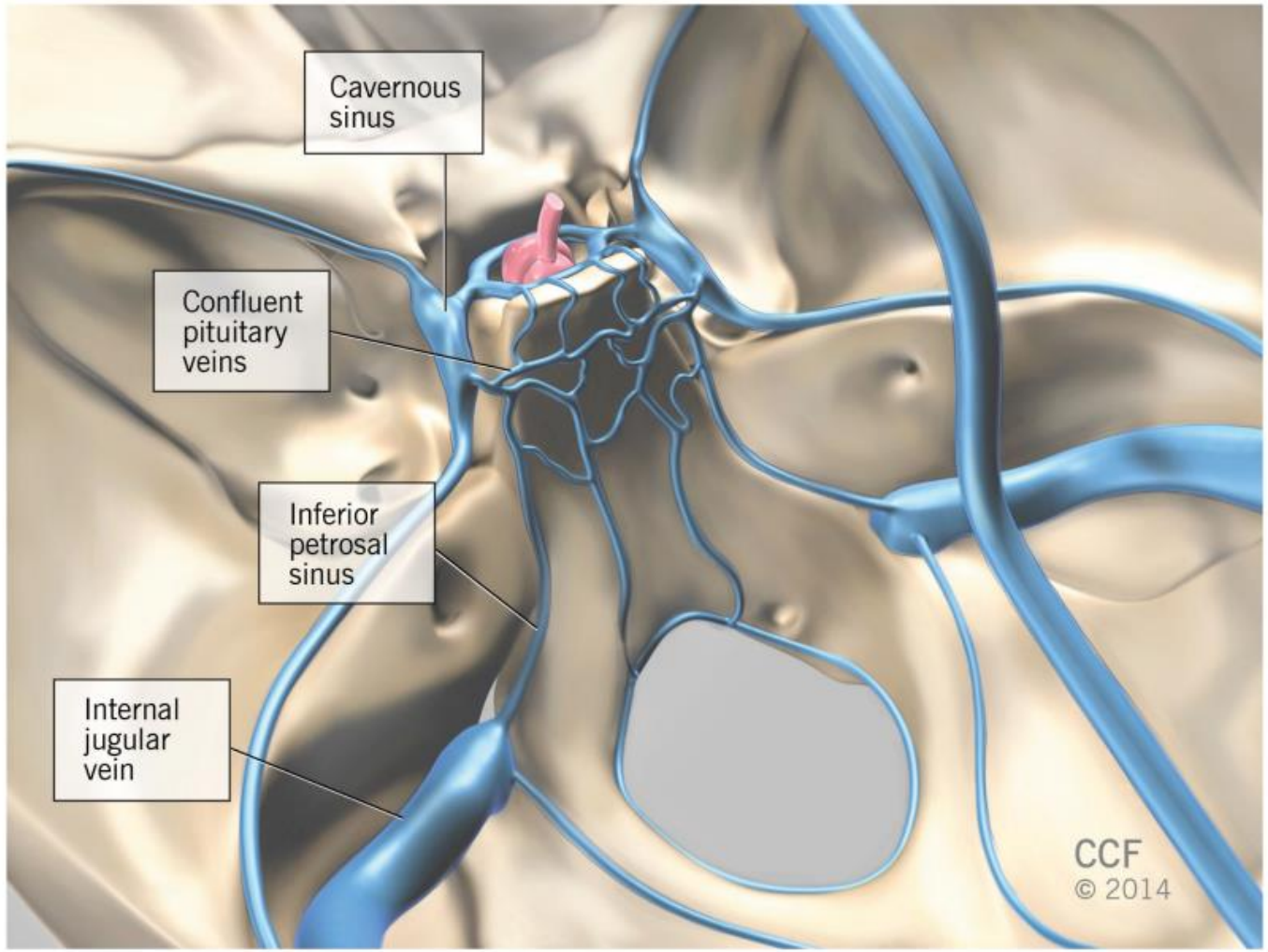


Figure 2. In this schematic, the infundibulum and pituitary gland are marked in red. The pituitary gland sits in the sella. The relevant venous structures are designated in blue.

Important steps in performing and interpreting IPSS results

- **IPSS** cannot be used to confirm the diagnosis of **ACTH-dependent Cushing syndrome (CS)** ,It is essential to establish ACTH-dependent hypercortisolism before the procedure.

- This study confirms that **IPSS should not** be used to distinguish pseudo-Cushing states from CD. Pseudo-Cushing states must be eliminated as potential causes of ACTH-dependent hypercortisolism before referring a patient for IPSS

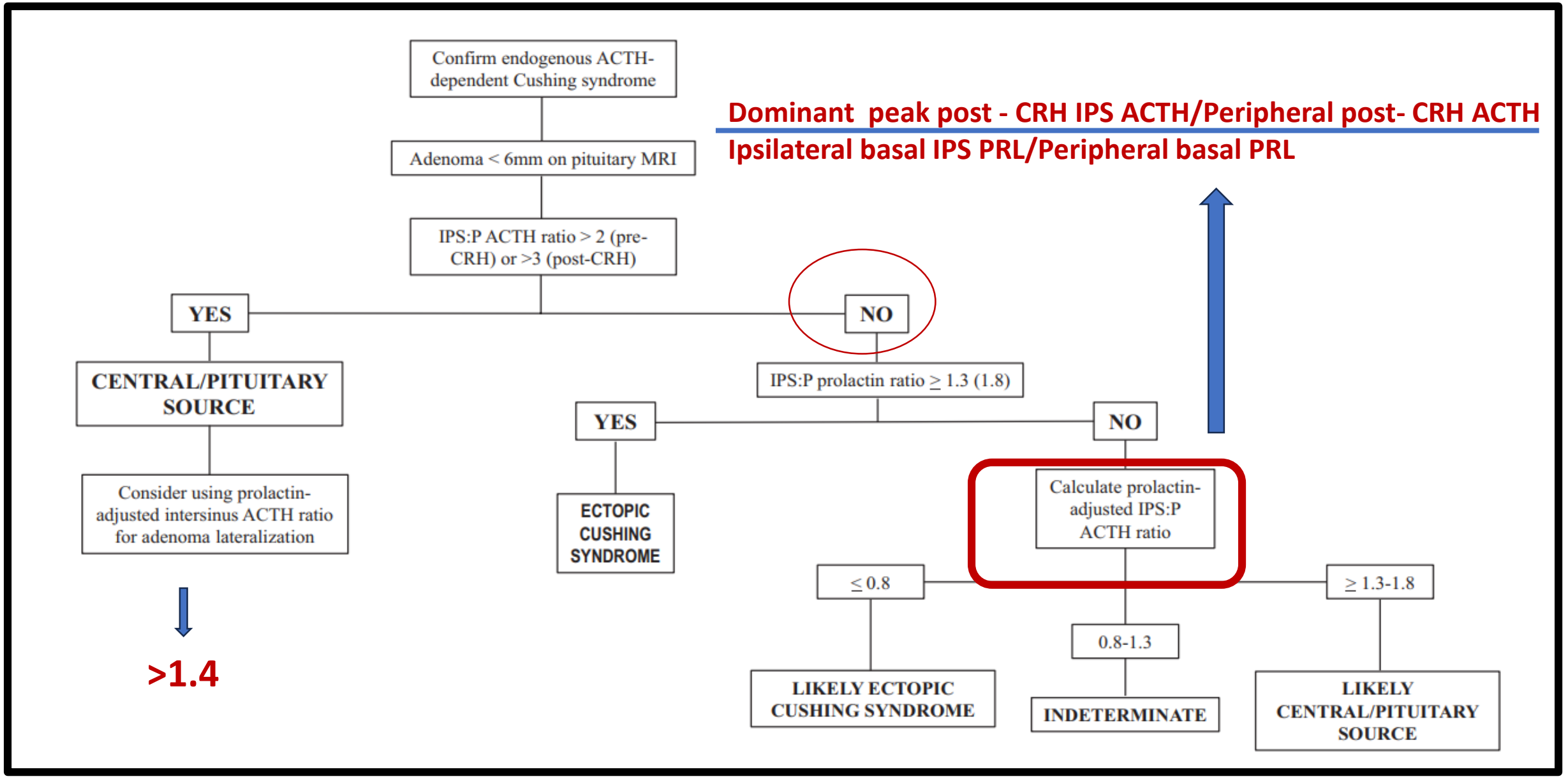
- The **absence of sustained hypercortisolism** can cause **misleading IPSS results** measure **serum cortisol** the morning of scheduled IPSS and proceed only if the value is **> 10 µg/dl**

- The prolactin-adjusted IPS:P ACTH ratio can improve differentiation between Cushing disease and ectopic ACTH syndrome when there is a lack of proper IPS venous efflux based on IPS:P prolactin ratio

- An absolute IPS ACTH level < 200 and < 400 pg/mL preand post-CRH stimulation and a < 35% increase in ACTHto-CRH in the periphery may suggest failed IPS cannulation

- A **lack of significant IPS:P ACTH gradient** in **unilateral successful IPS catheterization** does not rule out a corticotroph adenoma to the contralateral gland

- The **value of the intersinus ACTH gradient to predict tumor lateralization may be improved by using a prolactin-adjusted ACTH ratio >1.4**


Confirm endogenous ACTH-dependent Cushing syndrome
Adenoma < 6mm on pituitary MRI
IPS:P ACTH ratio > 2 (pre-CRH) or >3 (post-CRH)
YES
NO
CENTRAL/PITUITARY SOURCE
Consider using prolactin-adjusted intersinus ACTH ratio for adenoma lateralization
>1.4
IPS:P prolactin ratio ≥ 1.3 (1.8)
YES
NO
ECTOPIC CUSHING SYNDROME
Calculate prolactin-adjusted IPS:P ACTH ratio
≤ 0.8
0.8-1.3
≥ 1.3-1.8
LIKELY ECTOPIC CUSHING SYNDROME
INDETERMINATE
LIKELY CENTRAL/PITUITARY SOURCE
Dominant peak post - CRH IPS ACTH/Peripheral post- CRH ACTH
Ipsilateral basal IPS PRL/Peripheral basal PRL

Treatment Plan

- Increase dose of Ketoconazole 400mg BD
- Adrenalectomy candidate after the improvement of the patient's clinical condition