THE UNIVERSITY OF CHICAGO MEDICINE & BIOLOGICAL SCIENCES

75 y/o man with headache and double vision

Dr. Arosemena does not have any relevant financial relationships with any commercial interests.

75 y/o man with headache and double vision

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Endocrinology fellow
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Objectives

- Review the clinical presentation of pituitary apoplexy
- Evaluation and treatment of pituitary apoplexy
- Discuss conservative vs. surgical management in patients with pituitary necrosis

HPI

- 75 y/o M with PMH significant for cholangiocarcinoma on chemo (gemcitabine/cisplatin), metastatic prostate cancer s/p prostatectomy and HTN admitted on 11/12 after noticing a few days of dark stools. He also reported severe headache that lasted for 1 day associated with double and blurry vision.

- He described the headache as retroorbital, 6/10 in severity, he had associated diplopia but no nausea or vomiting.

- He called his PCP who recommended tylenol and ibuprofen PRN which relieved his headache. He reported diplopia was already improving when he presented to the ER.

- He had also noted some left eyelid dropping over last few days.

HPI

- During hospitalization he initially had a workup for suspected melena and underwent EGD which showed gastritis and esophageal erosions.

- Due to headache history primary team ordered a CT brain which showed: “ Mass-like enlargement of the pituitary gland with associated bony expansion of the sella, raising suspicion for underlying pituitary lesion”

MRI pituitary

What is the differential diagnosis?

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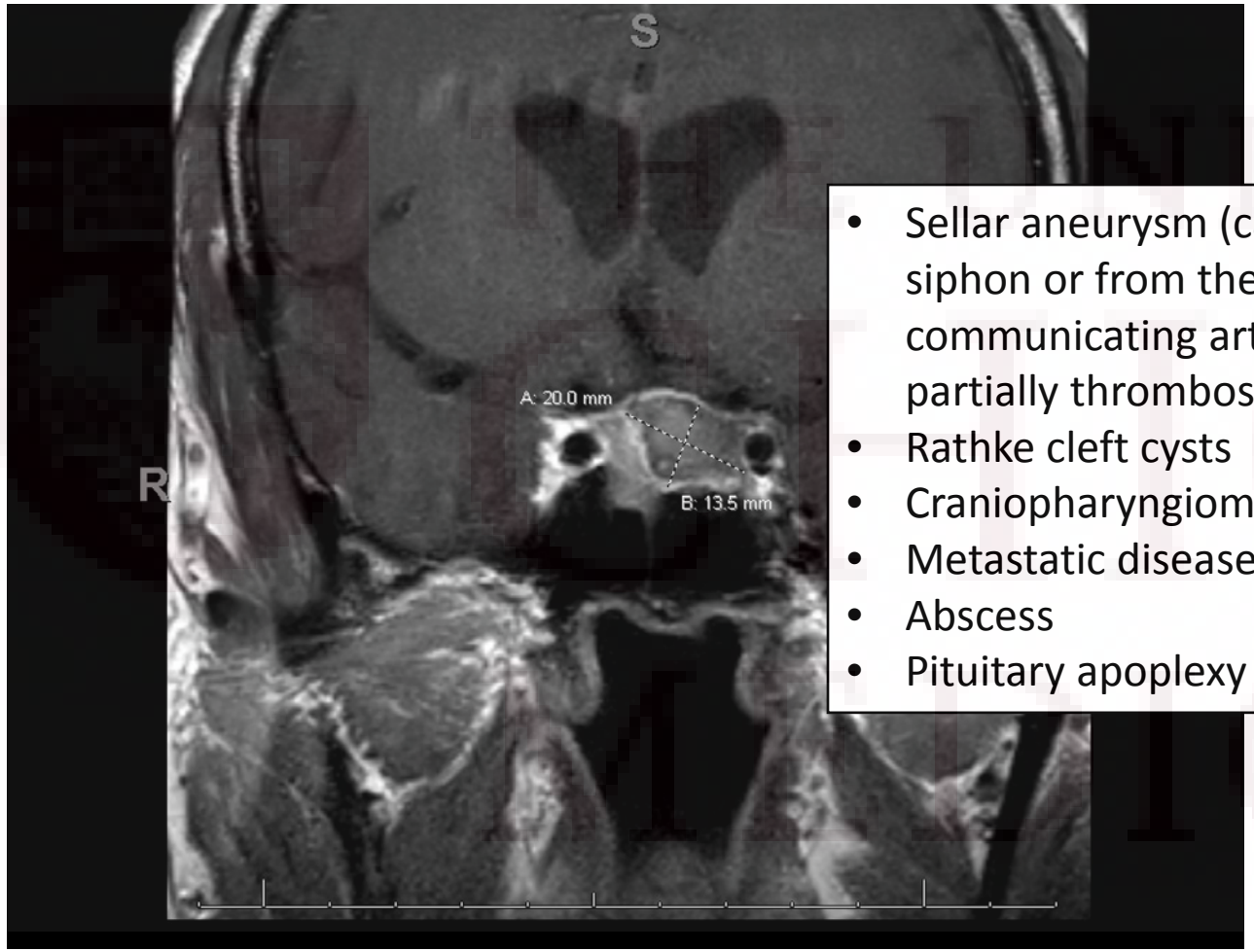
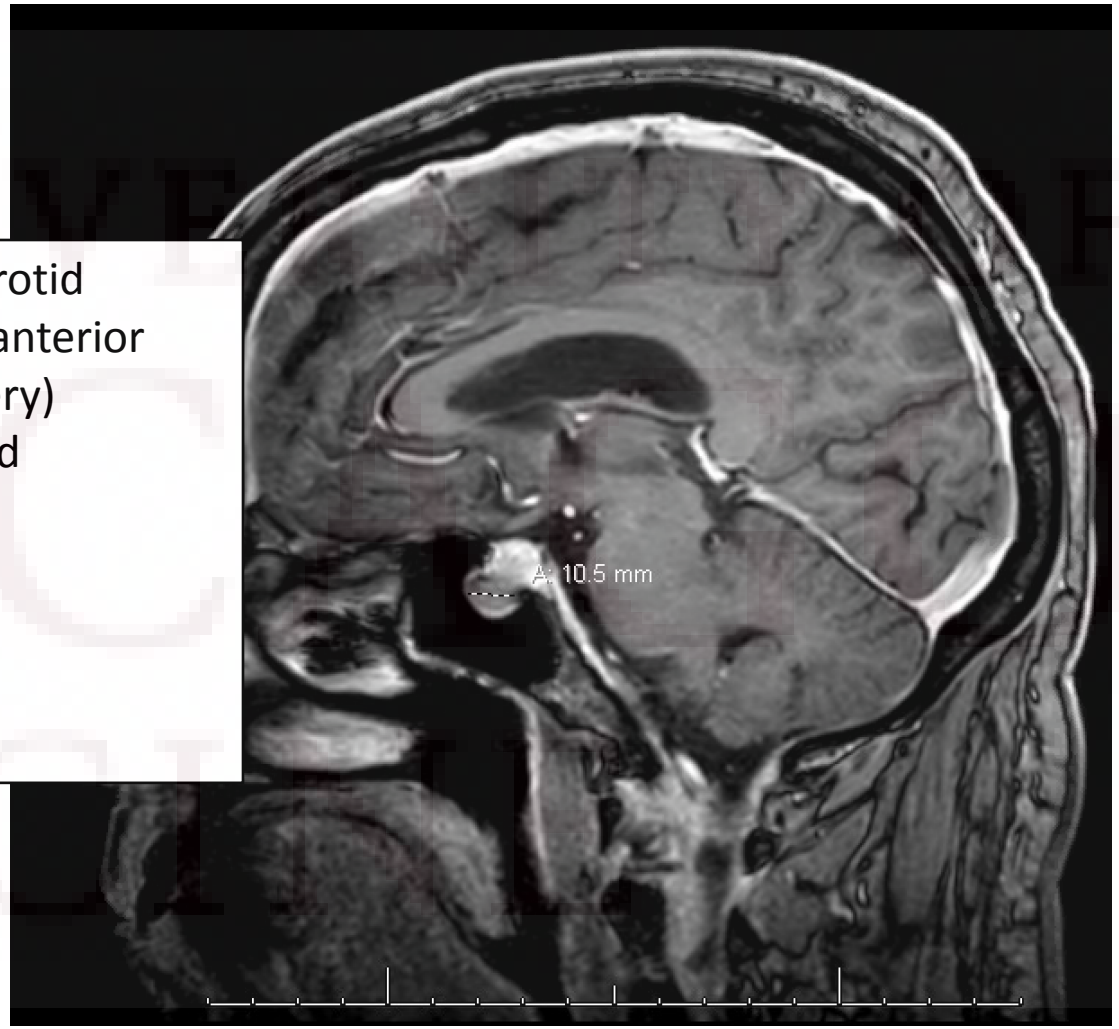


- Sellar aneurysm (carotid siphon or from the anterior communicating artery) partially thrombosed
- Rathke cleft cysts
- Craniopharyngioma
- Metastatic disease
- Abscess
- Pituitary apoplexy



Enhancing mass in the sella with mild extension into the sphenoid sinus and suprasellar cistern is favored to reflect a macroadenoma. Left aspect of the lesion demonstrates central T1 hyperintensivity suggestive of hemorrhage/apoplexy.

Your are paged about these findings… What is the next step?

Next step is:

- Perform Detailed Physical Exam Including Cranial Nerves and Visual Fields
- Evaluation of Endocrine Dysfunction/Empiric treatment
- Neurosurgery and Ophthalmology consult

What other information will you ask?

- He reported low libido for about 10 years.
- He did report fatigue and low energy since starting chemo
- Denied any galactorrhea or changes in the size of his hand, feet or hat size. He denied any history of headaches.
- Of note, his last chemo was 11/6 and he was prescribed PO dexamethasone to take 3 times a day for 2 weeks which he had been taking until day of admission.

PMH/PSH:

Cholangiocarcinoma

HTN

HLD

Kidney stones

OSA

OA

Osteopenia

Prostate cancer s/p prostatectomy

Prediabetes

Social history

Cigar smoker

No alcohol or drugs

Family history:

Cataract

Heart disease

Liver cancer

Medications:

Amlodipine

Atorvastatin

Vit D

Metformin

Compazine

Valsartan

Physical exam

- **Vitals:** BP: 163/77, HR: 60, RR: 20, SpO2: 95%, Height: 195.6 cm, Weight 117.2 kg, BMI: 30.63 kg/m^2

General: awake in NAD
Skin: no rashes or lesions
HEENT: EOM intact, anicteric, clear sclera. Left ptosis+
Neck: non tender, no lymphadenopathy appreciated.

Cardio: regular rate rhythm. S1, S2 no murmur/gallop/rub. No S3, S4.
Pulmonary: CTAB. No wheezes/rales/crackles.
Abdomen: soft, non-tender, non-distended.
Extremities: no cyanosis, clubbing or edema. No rash or lesions.
Neuro: Alert and oriented, no neurologic deficits except for left sided ptosis, visual fields intact

What is pituitary apoplexy?

- Pituitary apoplexy (PA) is a clinical syndrome due to abrupt hemorrhaging and/or infarction of the pituitary gland, generally within a pituitary adenoma.
- Clinical status may deteriorate dramatically (subarachnoid hemorrhage from the apoplectic adenoma, or cerebral ischemia secondary to cerebral vasospasm), or the patient may recover spontaneously.
- Universally considered a neurosurgical emergency in the past, but reports of spontaneous clinical recovery and/or tumor disappearance have led some specialists to adopt a conservative approach in selected cases.
- Most frequent in the fifth or sixth decade, with a male preponderance ranging from 1.1 to 2.3/1

Endocr Rev. 2015 Dec;36(6):622-45.

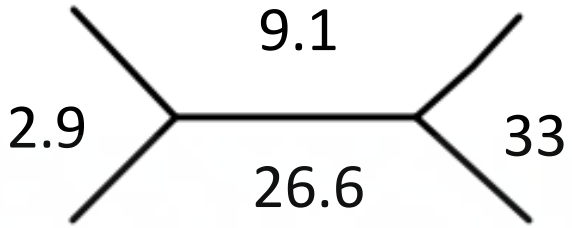
Clinical presentation

Table 2 Clinical manifestations of pituitary apoplexy.

Clinical manifestation	Frequency
Headache	Over 90%
Nausea and vomiting	43–80%
Visual impairment	85%
Rapid decrease in visual acuity (VA)	39–56%
Unilateral or bilateral blindness	Up to 30%
New visual fields (VF) defects	36–71%
Ocular paresis	40–78%
Diplopia	>50%
Possibly isolated acute cranial nerves (CN) palsies	Occasionaly reported
Third (more frequent)	
Fourth	
Fifth CN	
Altered mental state	13–42%
Coma	6.2%
Hypopituitarism	71–100%
Panhypopituitarism	70%
ACTH deficiency	70–76%
Gonadotrophin deficiency	76–79%
Central hypothyroidism	50–57%
Hydroelectrolytic disturbances	
Hyponatraemia	12–44%
Diabetes insipidus	0–8%
Other	
Meningeal irritation	Rare, secondary to the presence of blood in the suprasellar space
Unexplained hyperpyrexia	
Focal signs (cerebral infarction)	Exceptional (compression of the intracavernous carotid arteries)
Sudden death	Exceptional

Eur J Endocrinol. 2015 May;172(5):R179-9

Laboratory assessment



Sodium	137
Potassium	3.8
Chloride	104
Gap	10
BUN	26
Creatinine	1.6
Calcium	8.8
Phosphorus	3.4

Cortisol	10.2
ACTH	17.1
Prolactin	30.10
FSH	10
LH	4
Total testosterone	117
IGF-1	77
TSH	0.10
fT4	1.47

What medications will you start?

- Recommended starting high dose steroids: Hydrocortisone 40 mg in the morning and 20 mg in the evening.
- Recommended starting Levothyroxine 75 mcg daily
- Recommended Neurosurgery and Ophthalmology consult

Pituitary apoplexy

- Acute secondary adrenal insufficiency is very frequent in patients with apoplexy, empiric parenteral corticosteroid supplementation (if possible preceded by blood drawing for subsequent serum cortisol determination) should be given to all patients with signs of PA

- Thus if the increase in cortisol levels is limited, adrenal failure should be suspected. A threshold of 15 g/dL (414 nmol/L) seems accurate for identifying patients with adrenal insufficiency in critical acute settings

Endocr Rev. 2015 Dec;36(6):622-4

What hormonal deficits are more common?

Pituitary Apoplexy

Claire Briet, Sylvie Salenave, Jean-François Bonneville, Edward R. Laws, and Philippe Chanson

Service d'Endocrinologie et des Maladies de la Reproduction and Centre de Référence des Maladies Endocriniennes Rares de la Croissance (C.B., S.S., P.C.), Hôpital de Bicêtre, Assistance Publique-Hôpitaux de Paris, Le Kremlin-Bicêtre F94275, France; Service d'Endocrinologie (C.B.), Centre Hospitalier Universitaire d'Angers, Angers 49000, France; Service d'Endocrinologie (J.-F.B.), Centre Hospitalier Universitaire de Liège, Liège B4000, Belgium; Unité Mixte de Recherche S1185 (P.C.), Université Paris-Saclay, Université Paris-Sud; and Institut National de la Santé et de la Recherche Médicale Unité 1185, Faculté de Médecine Paris-Sud, Le Kremlin-Bicêtre F94276, France; and Neurosurgery, Harvard Medical School, Brigham and Women's Hospital (E.R.L.), Boston, Massachusetts 02115

Corticotropic deficiency is the most common deficit observed in patients with PA, occurring in 50%– 80% of cases

Table 4. Percentages of Pituitary Deficiency at Time of PA Presentation in the Main Series Published Since 2000

First Author (Reference)	Year of Publication	Number of Patients	Any Pituitary Deficiency	Gonadotroph Deficiency	Thyrotroph Deficiency	Corticotroph Deficiency	Somatotroph Deficiency	Lactotroph Deficiency	Diabetes Insipidus
Sibal (13)	2004	45	76	76	57	60	NA	40	NA
Ayuk (12)	2004	33	72	72	37	50	NA	24	NA
Semple (27)	2005	62	73	40	55	61	6	2	8
Lubina (40)	2005	40	42	35	30	50	NA	NA	2
Dubuisson (29)	2007	24	71	67	67	62.5	58	58	0
Zhang (49)	2009	185	54		25	30	NA	NA	NA
Shou (45)	2009	44	NA	39	77	73	NA	NA	NA
Möller-Goede (31)	2011	42	45	43	14	7	NA	NA	2
Leyer (15)	2011	44	89	NA	NA	70	NA	NA	NA
Sarwar (42)	2013	25	13	1	9	13	NA	NA	NA
Kinoshita (38)	2014	58	NA	21	13	17	40	6	NA
Vargas (46)	2014	47	85	49	53	53	35	35	NA

NA, not available.

Back to our patient… Consultant response

- Ophthalmology: “No evidence of optic pathway involvement: vision stable, color vision full, PERRL with no RAPD, EOMs full, and no confrontational field defects at bedside.”

- Neurosurgery: “No acute neurosurgical intervention needed at this time. Frequent neuro/vitals check q4h while inpatient. Recommend Dexamethasone 4 TID. Recommend to transfuse platelet with platelet goal >75K”

Conservative vs. surgical management

Table 3. Pituitary Apoplexy Score (PAS)

Variable	Points
Level of consciousness	
Glasgow coma scale 15	0
Glasgow coma scale 8–14	2
Glasgow coma scale <8	4
Visual acuity	
Normal 10/10 (or no change from pre-PA visual acuity)	0
Reduced, unilateral	1
Reduced, bilateral	2
Visual field defects	
Normal	0
Unilateral defect	1
Bilateral defect	2
Ocular paresis	
Absent	0
Present unilateral	1
Present bilateral	2

[From S. Rajasekaran et al: UK guidelines for the management of pituitary apoplexy. *Clin Endocrinol (Oxf)*. 2011;74:9–20 (17), with permission. © Blackwell Publishing Ltd.]

The PA score ranges from 0 to 10, and surgery usually is indicated for scores≥4

Our patient score: 2

Pituitary. 2018 Apr;21(2):138-144

Pituitary Apoplexy: Results of Surgical and Conservative Management Clinical Series and Review of the Literature

Joao Paulo Almeida[1,4], Miguel Marigil Sanchez[1], Claire Karekezi[1], Nebras Warsi[1], Rodrigo Fernández-Gajardo[5], Jyoti Panwar[3], Alireza Mansouri[1], Suganth Suppiah[1], Farshad Nassiri[1], Romina Nejad[1], Walter Kucharczyk[3], Rowena Ridout[2], Andrei F. Joaquim[4], Fred Gentili[1], Gelareh Zadeh[1]

Table 1. Baseline Characteristics

Patients and Tumor Characteristics	Surgical Treatment	Conservative Treatment	*P*
Age (years)	58.8 (±14.9)	53.8 (±19.4)	0.27
Gender			0.25
Male	32 (65.3)	9 (50)	
Female	17 (34.7)	9 (50)	
Known pituitary adenoma	8 (16.3)	8 (44.4)	0.02*
Symptoms			
Headache	44 (89.8)	16 (88.9)	0.91
Hypopituitarism	31 (64.3)	9 (50)	0.40
Visual decline	37 (75.5)	7 (38.8)	0.008*
CN palsy	27 (55.1)	5 (27.7)	0.057
III CN	14 (28.6)	3 (16.7)	
VI CN	7 (14.3)	1 (5.6)	
Multiple CNs	6 (12.2)	1 (5.6)	
Altered level of consciousness	7 (14.3)	3 (16.7)	1.00
Tumor characteristics			
Size (cm)	2.79 (±0.6)	2.25 (±0.6)	0.04*
Volume (cm^3)	8.38 (±0.7)	4.41 (±0.3)	0.02*
Knosp classification			0.02
0	2 (4.1)	5 (27.8)	
I	17 (34.7)	3 (16.7)	
II	15 (30.6)	8 (44.4)	
III	11 (22.4)	1 (5.6)	
IV	4 (8.2)	1 (5.6)	
Cavernous sinus invasion	15 (30.6)	2 (11.1)	0.12
Optic chiasm compression	47 (95.9)	10 (55.6)	0.001*

Table 3. Clinical Outcomes

Patients and Tumor Characteristics	Surgery Group, n (%)	Conservative Group, n (%)	*P*
Visual status at diagnosis			0.008*
No visual deficit	12 (24.4)	11 (61.1)	
Visual deficit	37 (75.5)	7 (38.8)	
Early follow-up*			0.67
Partial visual field improvement	17 (35.4)	2 (11.7)	
Complete visual field recovery	19 (39.6)	4 (23.5)	
Stable normal visual field	12 (25)	11 (64.7)	
Last follow-up†			0.63
Worsening	1 (2.1)	0	
No further improvement	3 (6.3)	0	
Partial visual field improvement	11 (22.9)	1 (6.7)	
Complete visual field recovery	21 (43.8)	3 (20)	
Stable normal visual field	12 (25)	11 (73.3)	
Cranial nerve deficit at diagnosis	27 (55.1)	5 (27.7)	0.057
Hormonal status at diagnosis			
Hypothyroidism	1 (2.0)	0	
Hypocortisolism	12 (24.5)	0	
Panhypopituitarism	18 (36.7)	9 (50)	
Hormonal function at follow-up*			
Hypothyroidism	2 (4.1)	1 (5.8)	
Hypocortisolism	9 (18.7)	2 (11.7)	
Panhypopituitarism	18 (37.5)	5 (29.4)	
Diabetes insipidus	3 (6.25)	1 (5.8)	

Conservative and surgical treatments had similar visual and cranial nerve improvement rates (75% vs. 58.3%, P= 0.63 and 75% vs. 69.2%, P=1.0)

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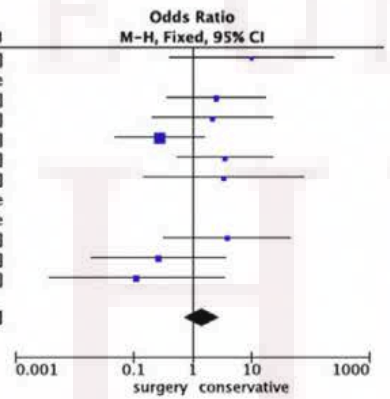
- Visual field recovery - OR: 1.45 (0.72-2.92)
- Cranial nerve recovery - OR: 2.30 (0.930-5.65)
- Hypopituitarism - OR 1.05 (0.64-1.74)
- Tumor recurrence - OR 0.68 (0.20-2.34)

A

Study or Subgroup	conservative Events	Total	surgery Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ayuk et al	6	6	4	7	2.2%	10.11 [0.41–247.48]
Bonick et al	0	0	0	0		Not estimable
Bujawansa	8	10	8	13	10.3%	2.50 [0.37–16.89]
Current study	3	4	21	36	7.7%	2.14 [0.20–22.65]
Giritharam et al	5	11	9	12	34.6%	0.28 [0.05–1.62]
Gruber et al	8	16	2	9	9.4%	3.50 [0.55–22.30]
Leyer et al	5	5	11	14	4.0%	3.35 [0.15–76.77]
Lubina et al	2	3	0	0		Not estimable
Maccagnam et al	0	0	0	0		Not estimable
Sibal et al	3	4	7	16	5.2%	3.86 [0.33–45.57]
Singh et al	2	3	31	35	12.0%	0.26 [0.02–3.53]
Teixeira et al	0	1	10	13	14.5%	0.11 [0.00–3.40]
Total (95% CI)		**60**		**155**	**100.0%**	**1.45 [0.72–2.92]**
Total events	40		103			

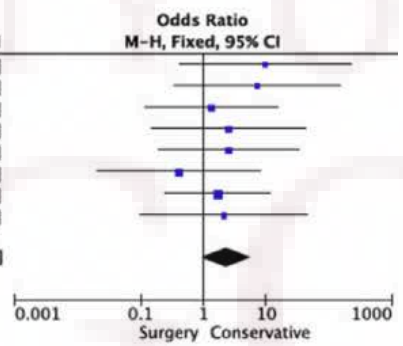
Heterogeneity: $\chi^2 = 10.79$, df = 8 ($P = 0.21$); $I^2 = 26\%$
Test for overall effect: $Z = 1.05$ ($P = 0.29$)



B

Study or Subgroup	conservative Events	Total	surgery Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ayuk et al	7	7	5	8	4.7%	9.55 [0.40–225.19]
Bujawansa	15	15	15	18	6.5%	7.00 [0.33–147.17]
Current study	3	4	18	26	17.5%	1.33 [0.12–14.87]
Gruber et al	10	12	2	3	7.8%	2.50 [0.15–42.80]
Leyer et al	10	11	8	10	11.1%	2.50 [0.19–32.80]
Lubina et al	1	2	10	14	18.3%	0.40 [0.02–8.07]
Sibal et al	6	8	9	14	23.9%	1.67 [0.24–11.58]
Singh et al	4	4	23	28	10.1%	2.11 [0.10–45.18]
Total (95% CI)		**63**		**121**	**100.0%**	**2.30 [0.93–5.65]**
Total events	56		90			

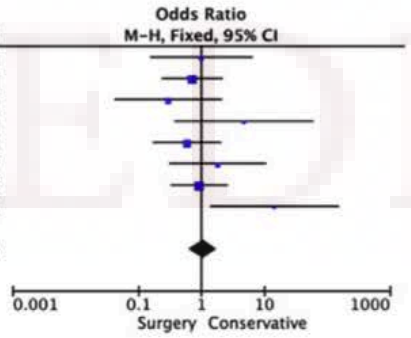
Heterogeneity: $\chi^2 = 2.91$, df = 7 ($P = 0.89$); $I^2 = 0\%$
Test for overall effect: $Z = 1.81$ ($P = 0.07$)



C

Study or Subgroup	conservative Events	Total	surgery Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bujawansa	20	22	30	33	7.3%	1.00 [0.15–6.53]
Current study	9	17	30	49	24.4%	0.71 [0.23–2.17]
Giritharam et al	8	11	18	20	11.7%	0.30 [0.04–2.13]
Gruber et al	19	20	8	10	1.8%	4.75 [0.38–60.14]
Leyer et al	14	25	13	19	21.8%	0.59 [0.17–2.05]
Sibal et al	16	18	22	27	6.6%	1.82 [0.31–10.59]
Singh et al	9	18	36	69	25.0%	0.92 [0.32–2.59]
Teixeira et al	8	9	5	14	1.5%	14.40 [1.37–150.81]
Total (95% CI)		**140**		**241**	**100.0%**	**1.05 [0.64–1.74]**
Total events	103		162			

Heterogeneity: $\chi^2 = 9.46$, df = 7 ($P = 0.22$); $I^2 = 26\%$
Test for overall effect: $Z = 0.20$ ($P = 0.84$)



D

Study or Subgroup	conservative Events	Total	surgery Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Ayuk et al	1	18	1	15	11.0%	0.82 [0.05–14.39]
Bujawansa	0	0	0	0		Not estimable
Current study	1	17	4	48	14.1%	0.69 [0.07–6.62]
Giritharam et al	0	11	4	20	10.3%	0.16 [0.01–3.26]
Gruber et al	0	20	6	10	10.2%	0.02 [0.00–0.36]
Leyer et al	4	24	0	19	10.4%	8.56 [0.43–169.70]
Lubina et al	0	0	0	0		Not estimable
Maccagnam et al	1	7	1	5	10.2%	0.67 [0.03–14.03]
Sibal et al	4	18	1	27	14.0%	7.43 [0.76–73.03]
Singh et al	0	18	4	69	10.5%	0.39 [0.02–7.64]
Teixeira et al	0	9	1	14	9.2%	0.47 [0.02–12.93]
Total (95% CI)		**142**		**227**	**100.0%**	**0.68 [0.20–2.34]**
Total events	11		22			

Heterogeneity: $\tau^2 = 1.46$; $\chi^2 = 13.68$, df = 8 ($P = 0.09$); $I^2 = 42\%$
Test for overall effect: $Z = 0.61$ ($P = 0.54$)

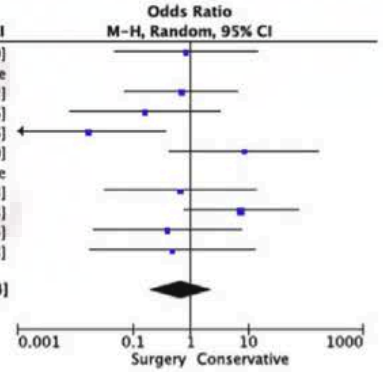


Figure 2. Surgery and conservative treatment results. Pooled analysis. (**A**) Visual field complete recovery, (**B**) cranial nerve complete recovery, (**C**) hypopituitarism, and (**D**) tumor recurrence rate. CI, confidence interval; df, degree of freedom; M-H, Mantel-Haenszel.

Most common pituitary adenomas…

- Non functioning pituitary adenomas (45–82%)
- Prolactinomas (5.5–31%)
- Growth hormone (7.2–25%)

- Rarely can happen in sellar tuberculoma, pituitary metastasis, abscess, lymphocytic hypophysitis, craniopharyngioma, sellar hemangioblastoma and Rathke's cleft cyst.

Eur J Endocrinol. 2015 May;172(5):R179-9

What precipitated the apoplexy?

- Angiography
- Orthopedic surgery
- Cardiac surgery
- Dynamic tests
- GnRH agonists ?
- Anticoagulants/Coagulation disorders ?
- DAs
- Head trauma

He was on Lupron several years ago.

Thrombocytopenia (Platelets 33)

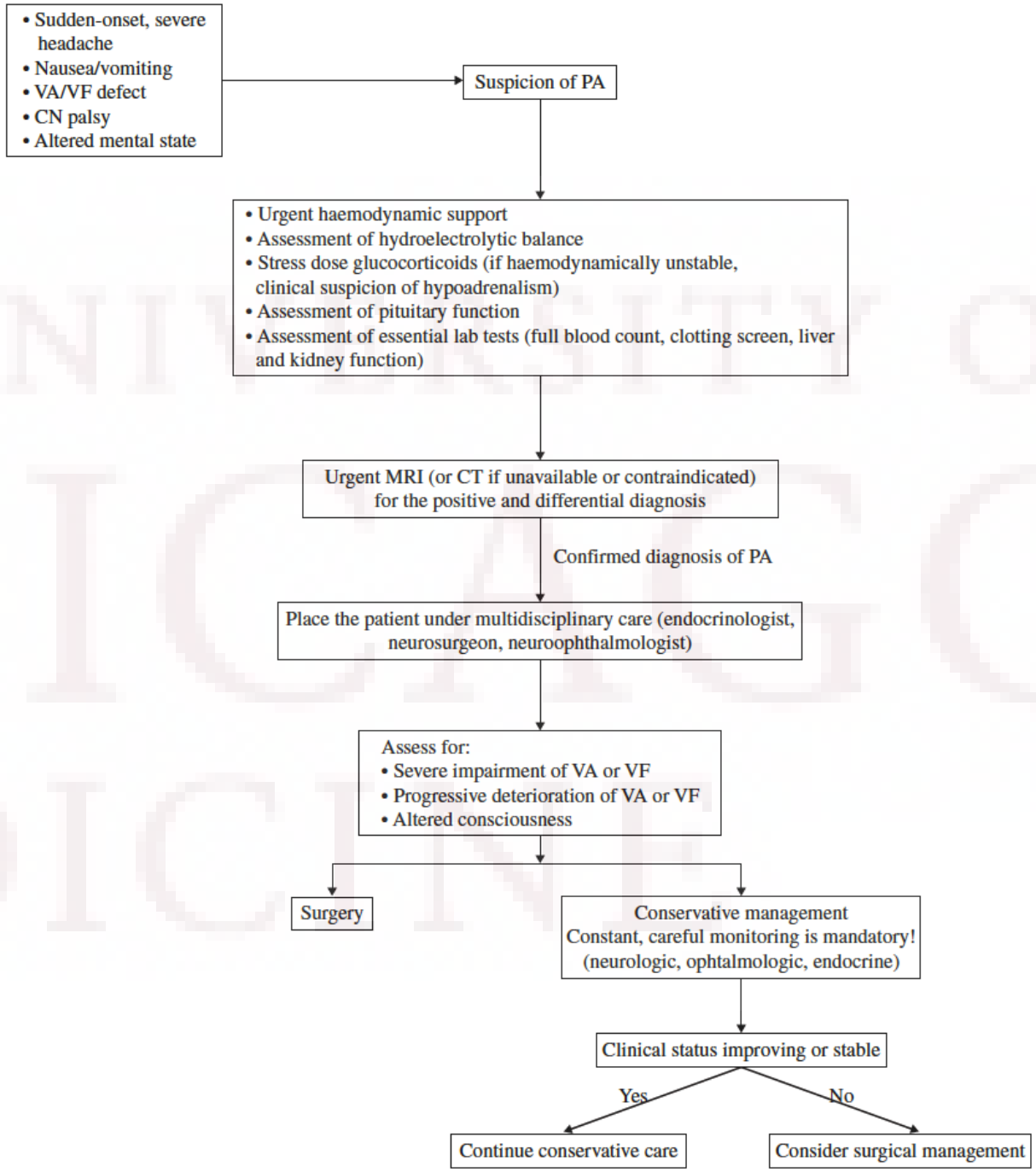
Endocr Rev. 2015 Dec;36(6):622-45.

Back to our patient…

- Discharged on hydrocortisone 20/10 and levothyroxine 75 mcg daily

- Seen in clinic 1 month after, visual symptoms and headache completely resolved.
- Continues on hydrocortisone 20/10
- Levothyroxine decreased to 50 mcg daily
- Receiving chemotherapy for his cholangiocarcinoma
- Started on insulin for steroid induced diabetes

Pituitary apoplexy emergency management summary



Eur J Endocrinol. 2015 May;172(5):R179-90

Take home points:

- Pituitary apoplexy is universally considered a neurosurgical emergency.
- Precipitating factors include: increase in intracranial pressure, arterial hypertension, major surgery, anticoagulant therapy or dynamic testing.
- Corticotropic deficiency with adrenal insufficiency may be life threatening if left untreated.
- Conservative management is increasingly used in selected patients (those without important visual acuity or field defects and with normal consciousness).