Pituitary apoplexy – pathophysiology and clinical manifestations

Bari,
7-10 novembre 2013

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Focusing on…

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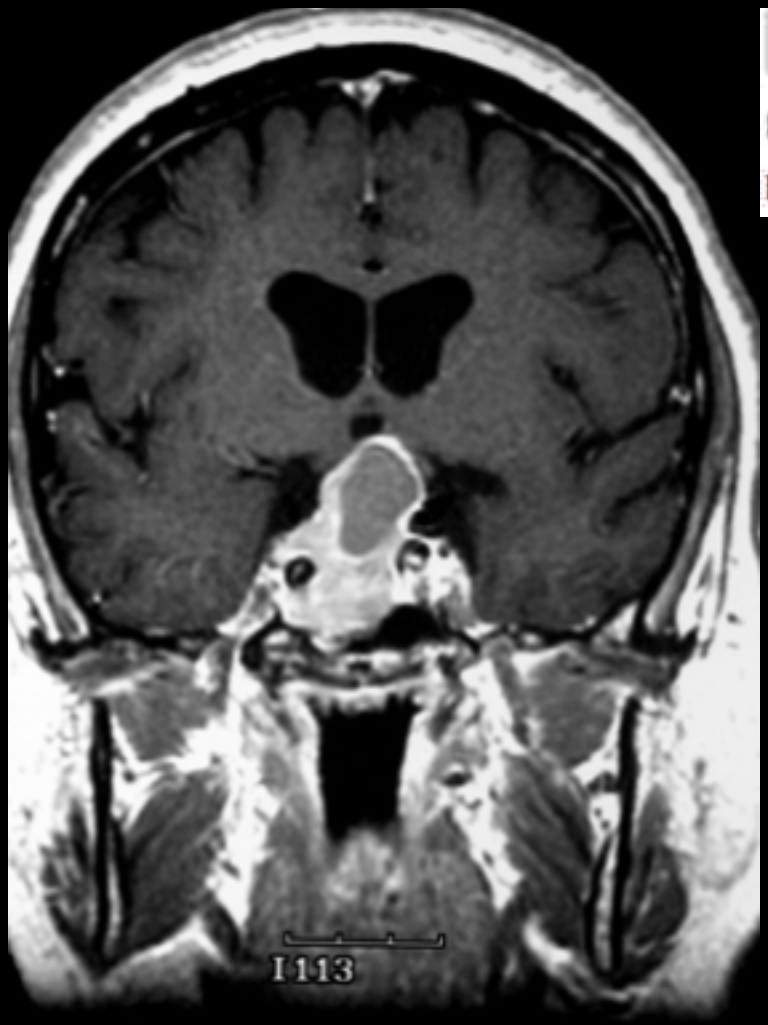
Pituitary apoplexy

New guidelines refine best practice, but some areas remain uncertain



BMJ | 26 MARCH 2011 | VOLUME 342

CLINICAL GUIDELINE

UK guidelines for the management of pituitary apoplexy

Pituitary Apoplexy Guidelines Development Group: May 2010

Clin Endocrinol 2011; 74: 9-20

Bellaria Hospital –
Centre of Surgery for Pituitary Tumours
(1998-2012):

- 1506 surgical procedures
- 76 pituitary apoplexy (5%)

Pituitary apoplexy – definition

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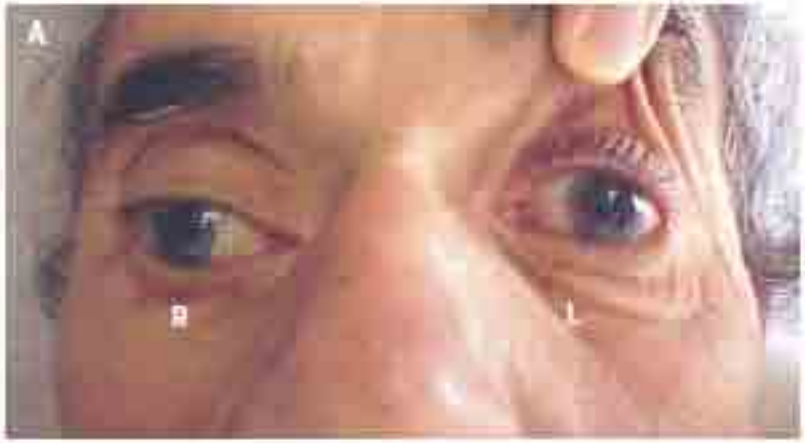
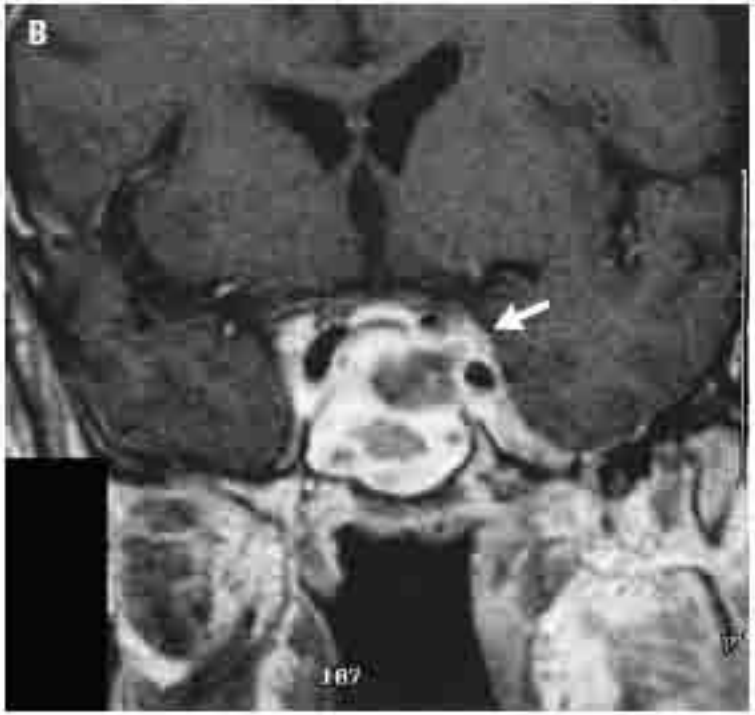
- Classical pituitary apoplexy is a *medical emergency* and rapid replacement with hydrocortisone maybe life saving.
- It is a clinical syndrome characterized by the *sudden onset of headache, vomiting, visual impairment and decreased consciousness* caused by haemorrhage and/or infarction of the pituitary gland.
- It is associated with the sudden onset of headache *accompanied or not by neurological symptoms involving the second, third, fourth and sixth cranial nerves*.
- If diagnosed patients should be referred to a *multidisciplinary team* comprising, among others, a neurosurgeon and an endocrinologist.

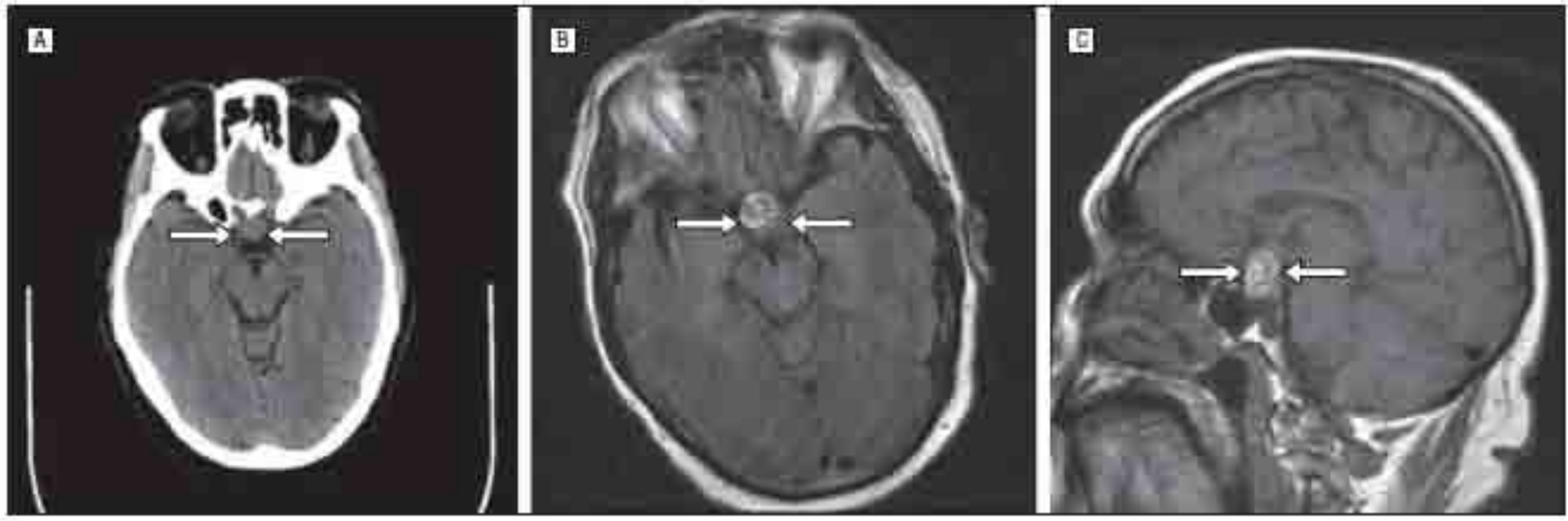
Clin Endocrinol 2011; 74: 9-20 [UK guidelines]

IMAGES IN CLINICAL MEDICINE

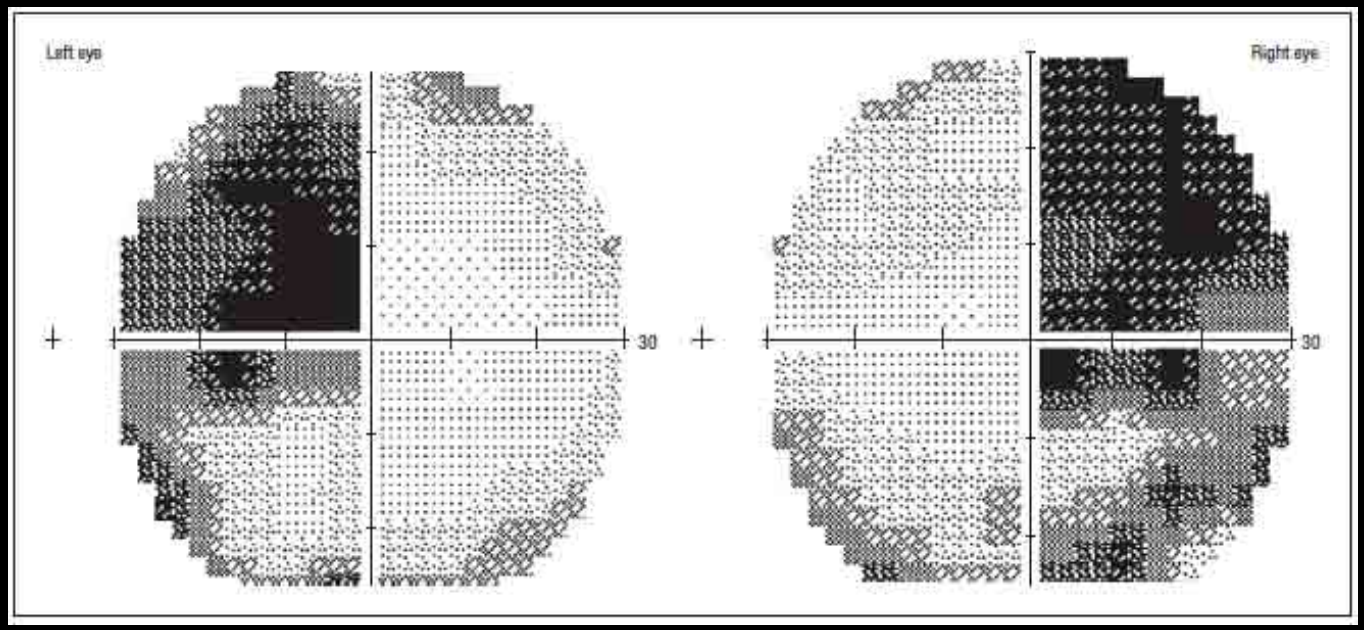
Pituitary Apoplexy



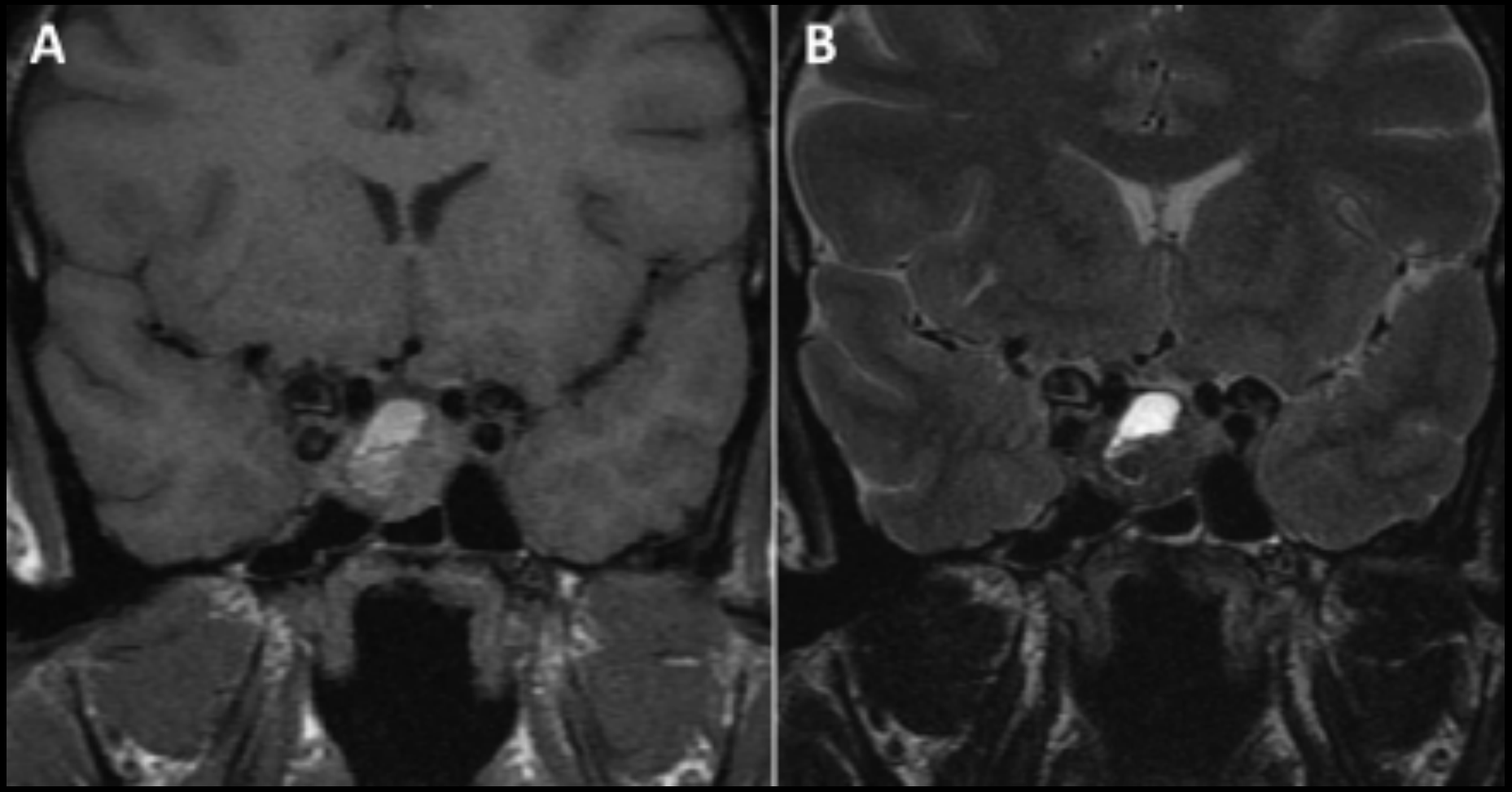




Classical features of pituitary apoplexy



Coronal T1-weighted (A) and T2-weighted (B) images



UK guidelines 2011

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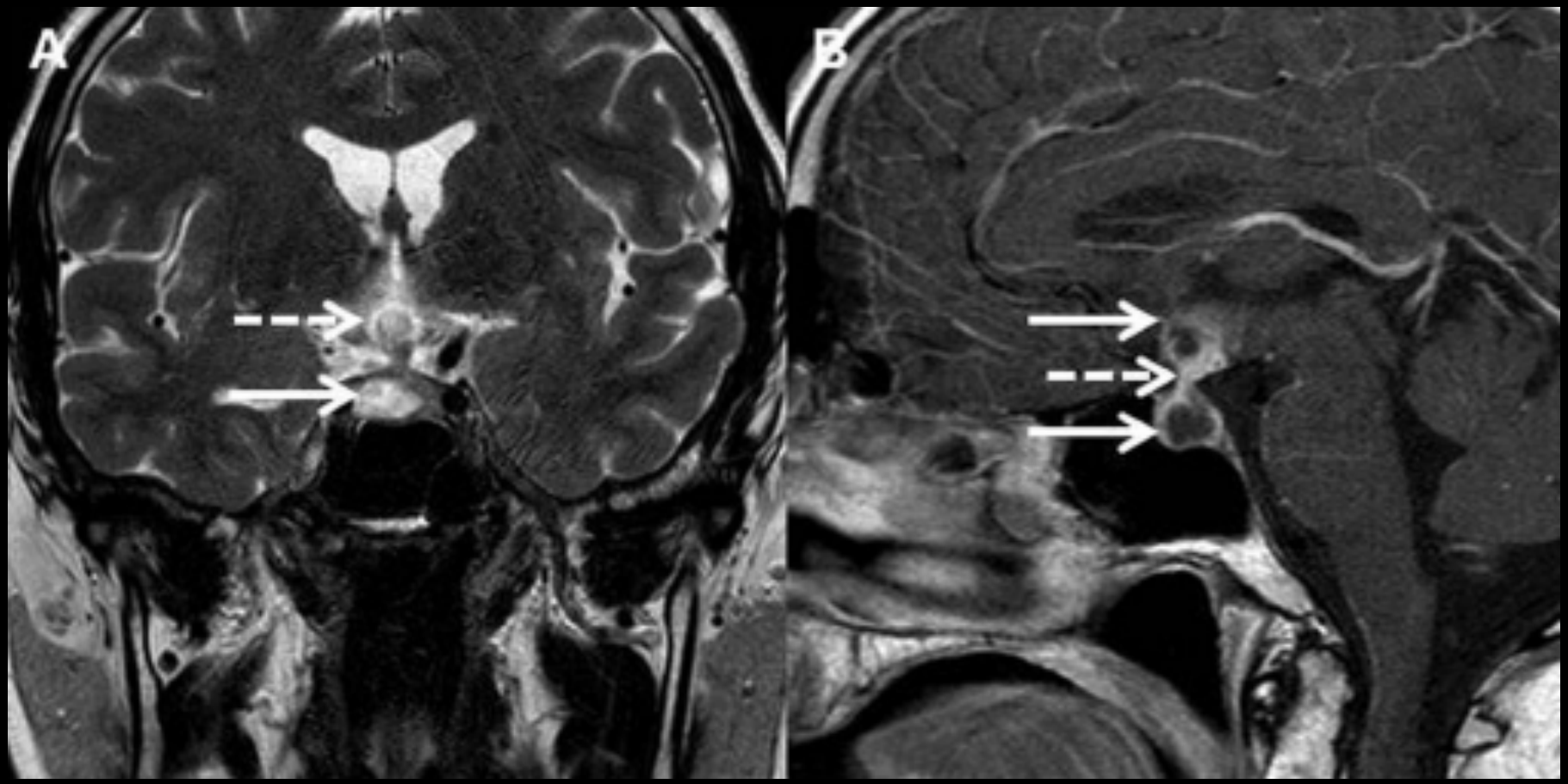
Definition of pituitary apoplexy

Classical pituitary apoplexy refers to a clinical syndrome, characterized by sudden onset of headache, vomiting, visual impairment and decreased consciousness caused by haemorrhage and/or infarction of the pituitary gland. Pearce Bailey described the first case of pituitary tumour–associated haemorrhage in the year 1898.[10] The term pituitary apoplexy was first coined by Brougham *et al.*[11] in 1950, in a case series of five patients. Apoplexy usually occurs in patients with pre-existing pituitary adenomas and evolves within hours or days.[12]

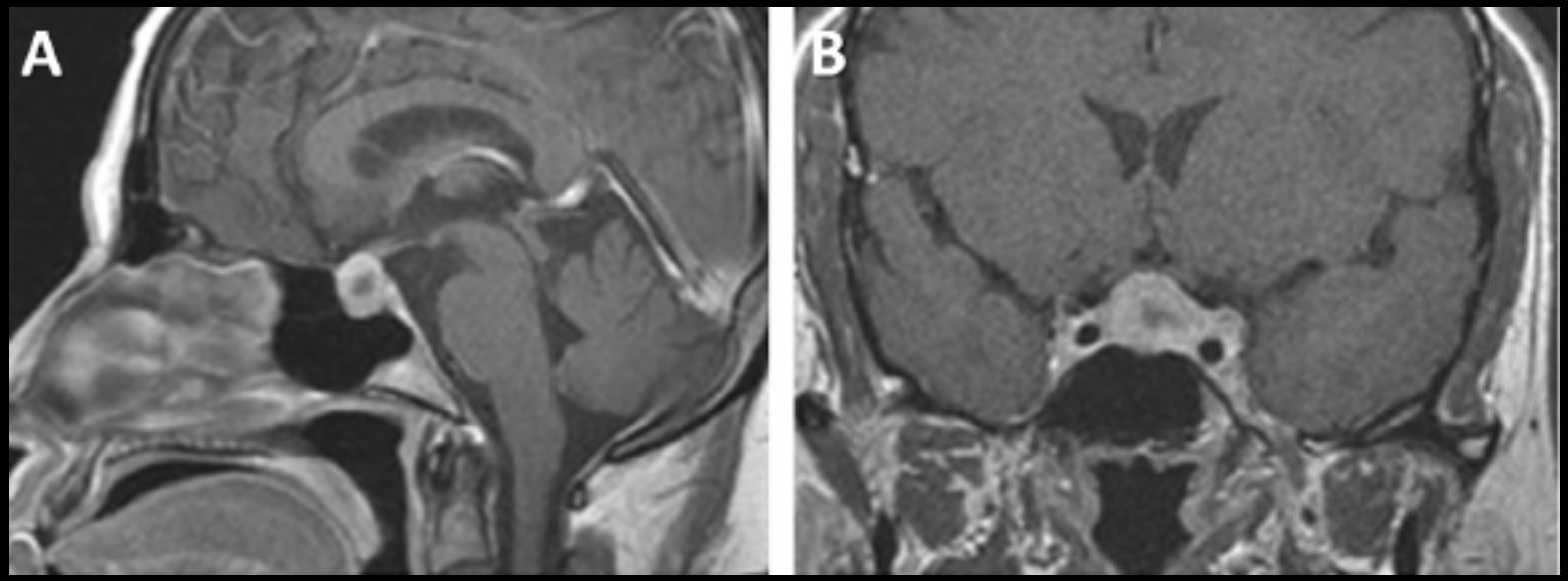
Asymptomatic pituitary haemorrhage and/or infarction ('subclinical pituitary apoplexy') may be detected on routine imaging or during histopathological examination. The frequency of subclinical haemorrhagic infarction is around 25%, but this does not constitute a diagnosis of pituitary apoplexy.[13,14]

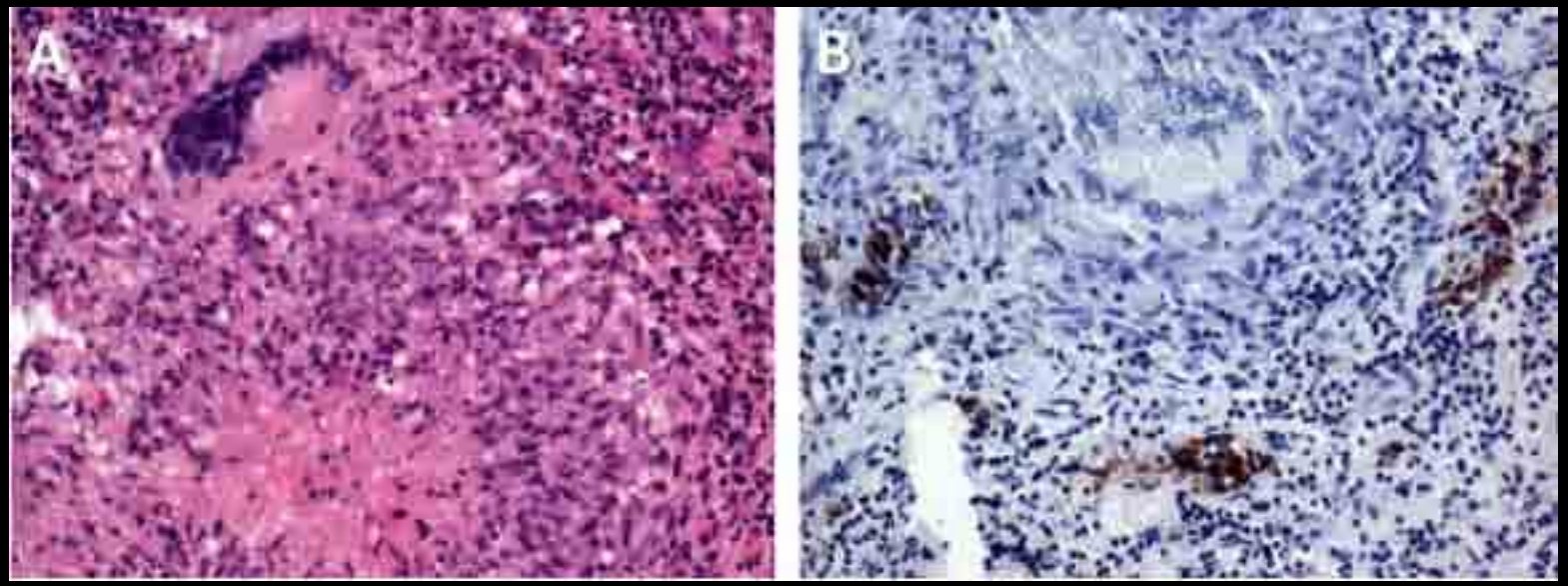
Chemical meningitis: A rare presentation of Rathke's cleft cyst



J Clin Neurosci 2013 (in press)

Idiopathic granulomatous hypophysitis





Pituitary Apoplexy Caused by Hemorrhage From Pituitary Metastatic Melanoma: Case Report

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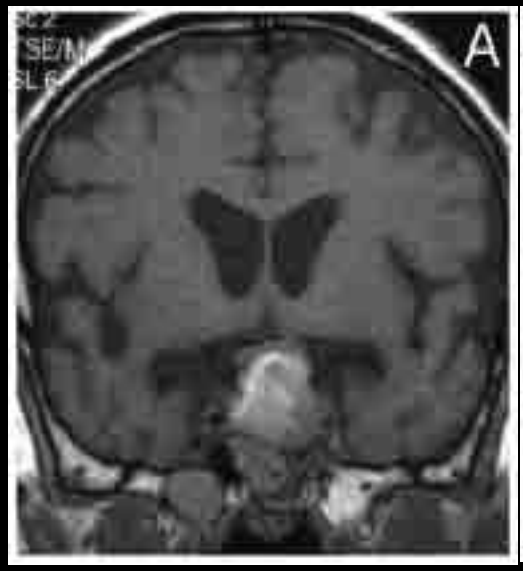

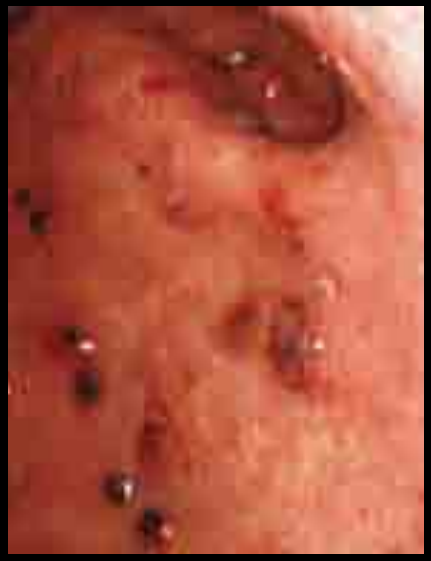

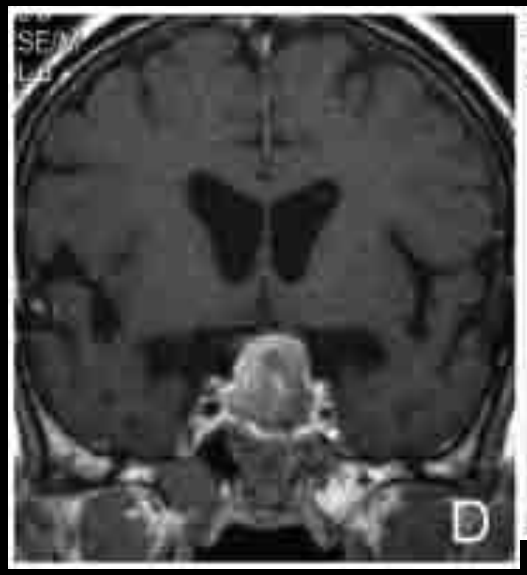

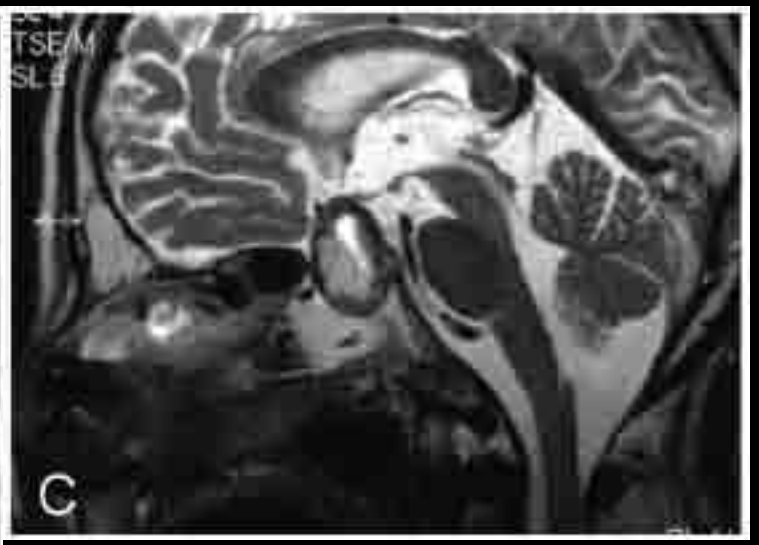

Neurol Med Chir 2013 (in press)

UK guidelines, 2011

Table 1. Precipitating factors in pituitary apoplexy

Systemic hypertension (26%)
Major surgery, in particular coronary artery bypass surgery
Dynamic pituitary function tests with GnRH, TRH and CRH
Anticoagulation therapy
Coagulopathies
Oestrogen therapy
Initiation or withdrawal of dopamine receptor agonist
Radiation therapy
Pregnancy
Head trauma

Pituitary apoplexy – pathophysiology (1)

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- …An epithelial tumor, probably a pituitary adenoma, gradually enlarges, expanding the pituitary fossa and compressing the remnants of functioning contiguous pituitary tissue. *As the tumor continues to enlarge*, it gains additional room for expansion by stretching the diaphragma sella. *Further expansion superiorly* may be accomplished if the attenuated diaphragm splits or if the diaphragmatic notch itself is usually voluminous. Otherwise the neoplasm must squeeze itself through a narrow channel between the firm fibrous peripheral limbs of the diaphragma sella and the hypophysial stalk centrally. *It is precisely at this juncture* where we believe the chain of events leading to pituitary apoplexy occurs…

Rovit anf Fein, *J Neurosurg* 1972; 37. 280

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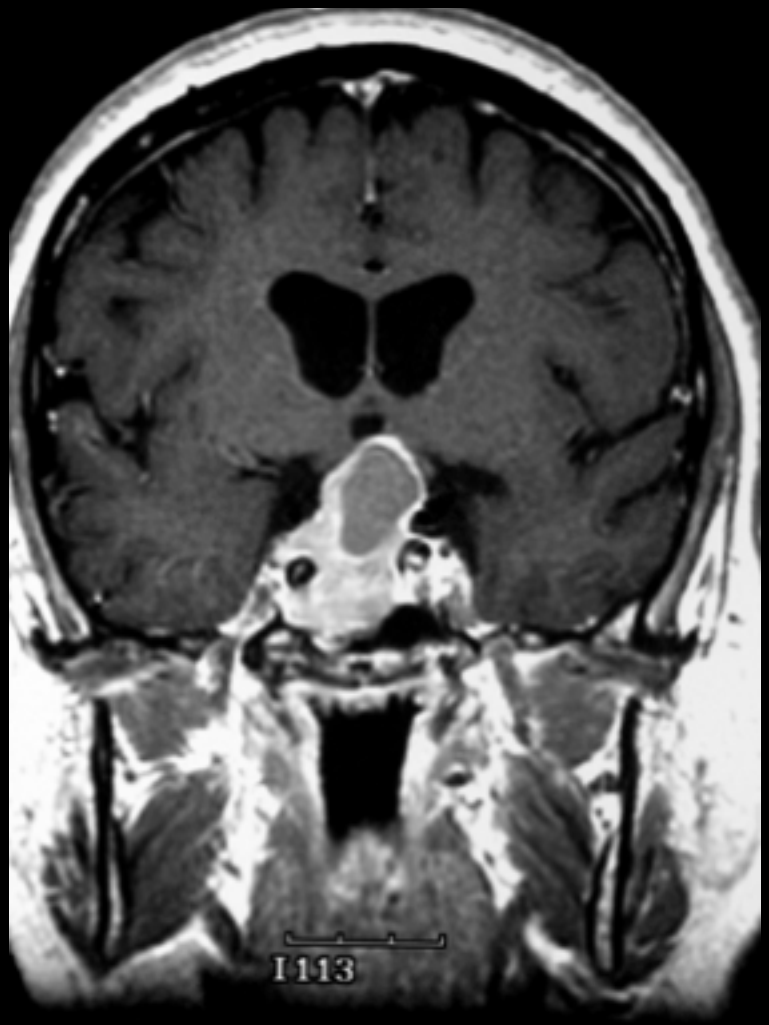

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Pituitary apoplexy – pathophysiology (3)

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- …The cavernous sinuses are acutely stretched, thus leading to *compression of the oculomotor nerves* and attenuation of the intracavernous internal carotid and inferior hypophysial arteries…
- …The hypophysial infarction may be so extensive as to disrupt the capsule of the tumor, allowing *escape of necrotic tissue and red cells into the chiasmatic cisterns* and thence into the general subarachnoid fluid circulation.

Rovit L & Fein JM, *J Neurosurg* 1972; 37. 280
Martin JB & Reichlin S. *Clinical Neuroendocrinology*, ed.2, 1987

Clinical presentation: how frequent are the various symptoms and signs?

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- Sudden, severe headache (up to 100%) often accompanied by nausea and vomiting (70%)
- Ocular palsies (nearly 70%)
  - Third cranial (oculomotor) nerve (nearly 50%)
- Decreased visual acuity and visual field defects (nearly 75%)
- Meningism (fever, photophobia, and altered consciousness level)
- Cerebral ischaemia (rarely), due to either mechanical compression of the carotid artery against the anterior clinoid or vasospasm secondary to subarachnoid haemorrhage.

UK guidelines, 2011

Clinical presentation: how frequent are the various symptoms and signs?

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Table 1 Presenting symptoms and signs ($n=35$)

Symptoms and signs	%	Relative involvement (%)
Nausea	80	–
Reduction of visual field	71	–
Ocular paresis	69	–
III rd Nerve palsy	–	67
IV th Nerve palsy	–	4
VI th Nerve palsy	–	29
Reduction of visual acuity	66	–
Vomiting	57	–
Photophobia	49	–
Pyrexia	20	–
Decreased level of consciousness	11	–

 Clinical Endocrinology, **51**, 181–188

What further investigations should be performed?

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A full anterior pituitary hormone profile, with an emphasis on identifying adrenocorticotrophin deficiency; repeated measurement of serum electrolytes, serum, and urine osmolalities; and strict monitoring of fluid balance.

BMJ 2012;344:e2229 doi: 10.1136/bmj.e2229 (Published 4 April 2012)

Random cortisol
TSH, FT4
Serum sodium
Serum and urine osmolalities
Fluid balance

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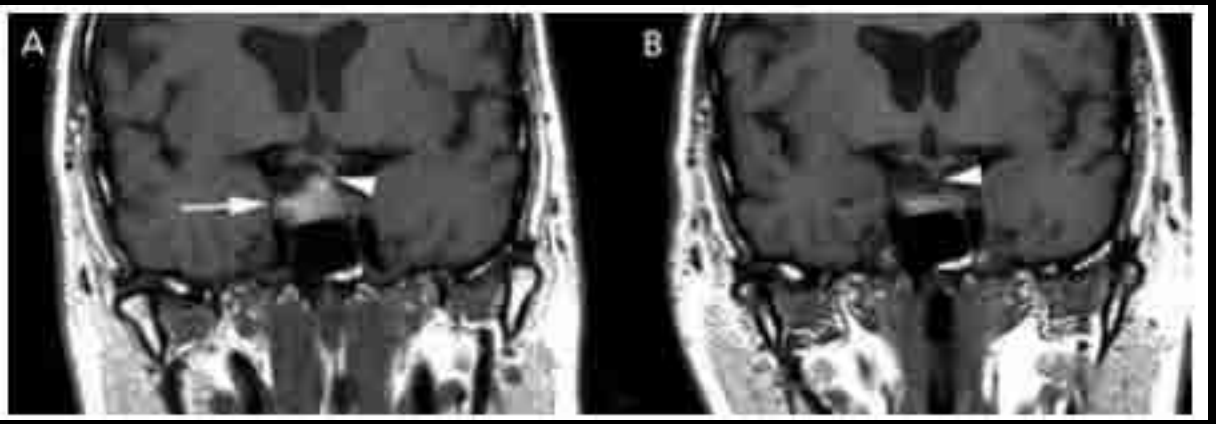
LESSON OF THE WEEK

Pituitary infarction: a potentially fatal cause of postoperative hyponatraemia and ocular palsy



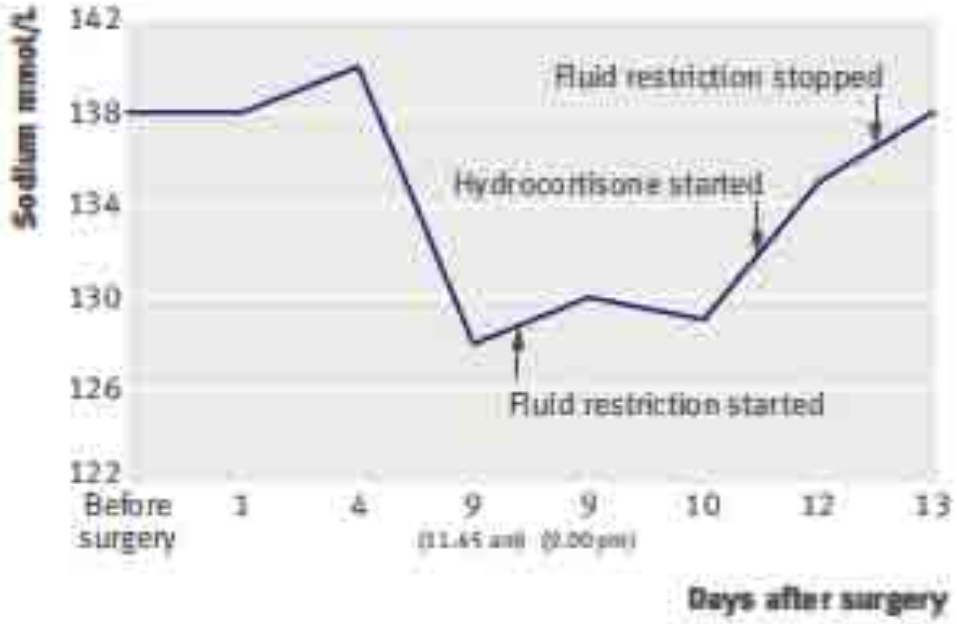


Fig 2 | Plasma sodium concentrations and response to interventions

Postsurgical hyponatraemia with ocular palsy suggests hypopituitarism from haemorrhagic infarction of an unsuspected pituitary adenoma

We describe a patient with haemorrhagic infarction of a pituitary adenoma and symptoms of blurred vision from oculoparesis who presented shortly after hip replacement, in whom hyponatraemia was caused by cortisol deficiency.

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Box 2: Common causes of sudden severe headache[1 14]

- Spontaneous (non-traumatic) subarachnoid haemorrhage
- Other secondary headache syndromes

  Vascular—intracranial venous thrombosis; intracerebral, intraventricular, extradural, or subdural haemorrhage; ischaemic stroke; arterial dissection; vasculitides

  Infection—for example, meningitis, encephalitis

  Acute hydrocephalus—for example, colloid cyst of the third ventricle)

  Intracranial tumour—including pituitary apoplexy

  Intracranial hypotension—spontaneous or after dural puncture

  Metabolic—for example, phaeochromocytoma, tyramine ingestion with monoamine oxidase inhibitors
- Primary headache syndromes[w2]

  Thunderclap headache

  Migraine

  Cluster headache

  Headache associated with sexual activity or exertion

Lumbar puncture

BMJ 2006; 333: 235

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Grading of recommendations (based on AHCPR, 1994)[1]

Grade	Evidence levels	Description
A	I a, I b	Requires at least one randomized controlled trial as part of the body of literature of over all good quality and consistency addressing the specific recommendation.
B	II a, II b, III	Requires availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation.
C	IV	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality
✔		Good practice point recommended by guideline development group

Appendix 1. Summary of recommendations

Clinical assessment

- *A diagnosis of pituitary apoplexy should be considered in all patients presenting with acute severe headache with or with out neuro-ophthalmic signs;* (✔)
- *Patients who have been diagnosed with pituitary tumour should be given clear information regarding the signs and symptoms of pituitary apoplexy and the precipitating factors;* (✔)
- *Patients known to have a pituitary tumour must be observed for signs and symptoms of pituitary apoplexy when performing pituitary stimulation tests, commencing anticoagulation therapy or undertaking coronary artery bypass or other major surgery;* (IV, C)

Clinical assessment

UK guidelines 2011

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- *Initial assessment of the patients presenting with symptoms consistent with pituitary apoplexy should include a detailed history focusing on symptoms of pituitary dysfunction e.g. symptoms of hypogonadism, followed by a thorough physical examination including cranial nerves and visual fields to confrontation;* (✔)
- *Formal visual fields assessment using Humphrey visual field analyzer or Goldmann perimeter must be undertaken when the patient is clinically stable, preferably within 24 h of suspected diagnosis;* (✔)
- *In haemodynamically unstable patients, in whom standard supportive measures are required to ensure haemodynamic stability, intravenous hydrocortisone should be administered after drawing blood samples for baseline endocrine function tests including random serum cortisol, FT4 and TSH.* (IV, C)

Endocrine assessment

- *All patients with suspected pituitary apoplexy should have urgent blood samples drawn to check electrolytes, renal function, liver function, clotting screen, full blood count, and random cortisol, PRL, FT4, TSH, IGF1, GH, LH, FSH and testosterone in men, oestradiol in women.* (**IV, C**)

Radiological assessment

- *Urgent MRI scan must be done in all patients with suspected pituitary apoplexy to confirm the diagnosis;* (**III, B**)
- *A dedicated pituitary CT scan is indicated if the MRI scan is either contraindicated or not possible;* (**IV,C**)
- *The results of the MRI or CT scan should be clearly explained to the patient as soon as possible after the investigation.* (✔)

Where should patients with pituitary apoplexy be managed?

- *Once the diagnosis has been confirmed, it is recommended that all patients be transferred once medically stabilized following liaison and advice from the specialist neurosurgical/endocrine team to the local neurosurgical/endocrine team as soon as possible. Neurosurgical HDU facilities must be available. This team must have access to specialist endocrine and ophthalmological expertise. (✔)*

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Suspected pituitary apoplexy

- Supportive measures to ensure haemodynamic stability
- Assessment and management of fluid/electrolyte balance
- Consider hydrocortisone replacement

- Urgent biochemical and endocrine assessment (FBC, U and E, LFT, clotting screen, IGF 1, GH, PRL, TSH, T4, LH, FSH, cortisol, testosterone or oestradiol)

- Urgent MRI to confirm diagnosis

or

- A dedicated pituitary CT scan if MRI is contraindicated

- Liase with regional endocrine and neurosurgical team immediately after the diagnosis confirmed

UK Guidelines, 2011

Areas for audit

UK guidelines 2011

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Table 3. Pituitary Apoplexy score

Variable	Points
Level of Consciousness	
Glasgow coma scale 15	0
Glasgow coma scale <8–14	2
Glasgow coma scale <8	4
Visual acuity	
Normal* 6/6	0
Reduced – unilateral	1
bilateral	2
Visual field defects	
Normal	0
Unilateral defect	1
Bilateral defect	2
Ocular paresis	
Absent	0
Present – Unilateral	1
Bilateral	2

A 44 year-old man presented to the Emergency Dept. with a 2-day history of acute, severe bitemporal headache coupled with vomiting and fever. He had received in vain NSAD.

Lumbar puncture was negative.

The day after, he complained of diplopia due to right VI c.n. palsy.

Brain CT scan showed a tumor in the sellar/ parasellar region.

A subsequent MR…

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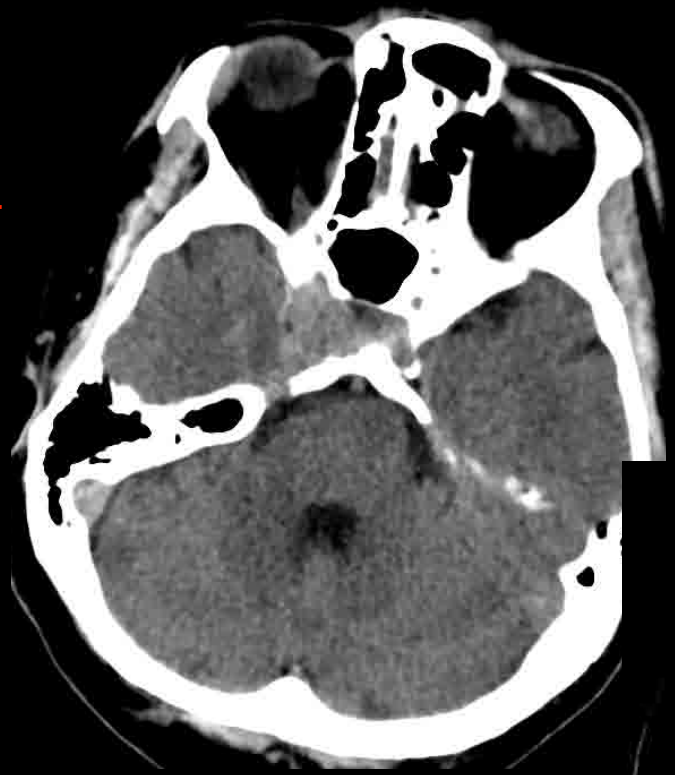
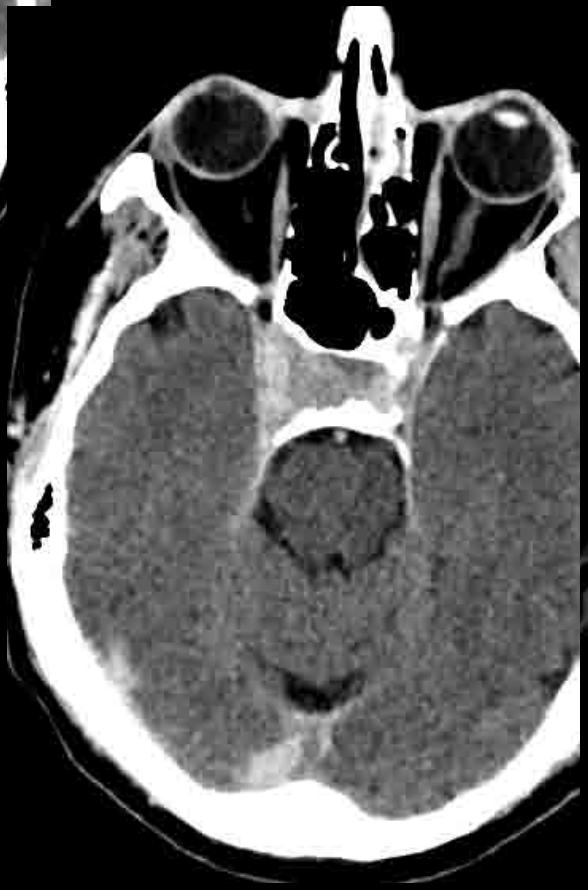
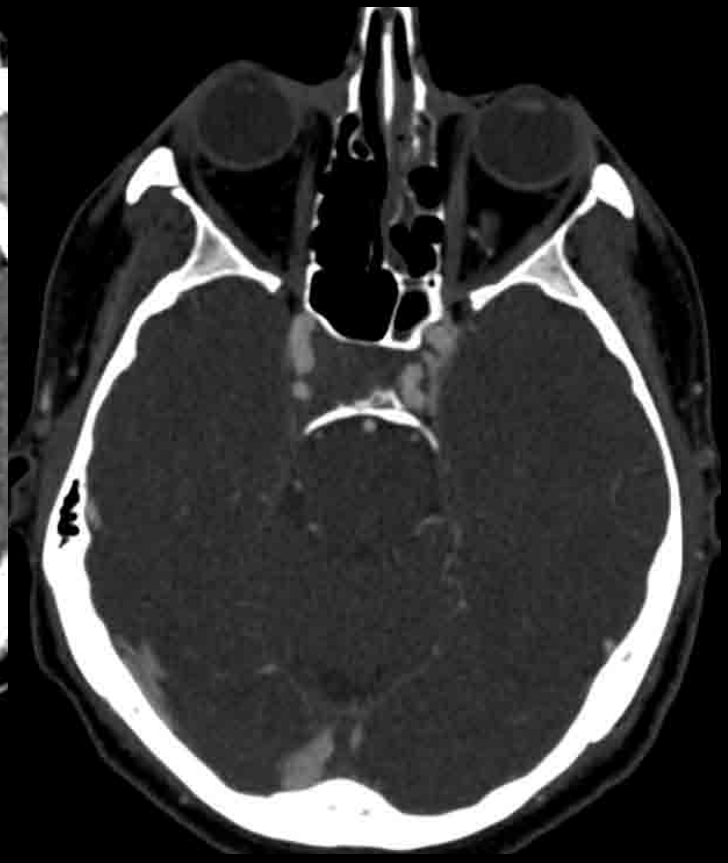
Pre-op CT scan

09.10.13

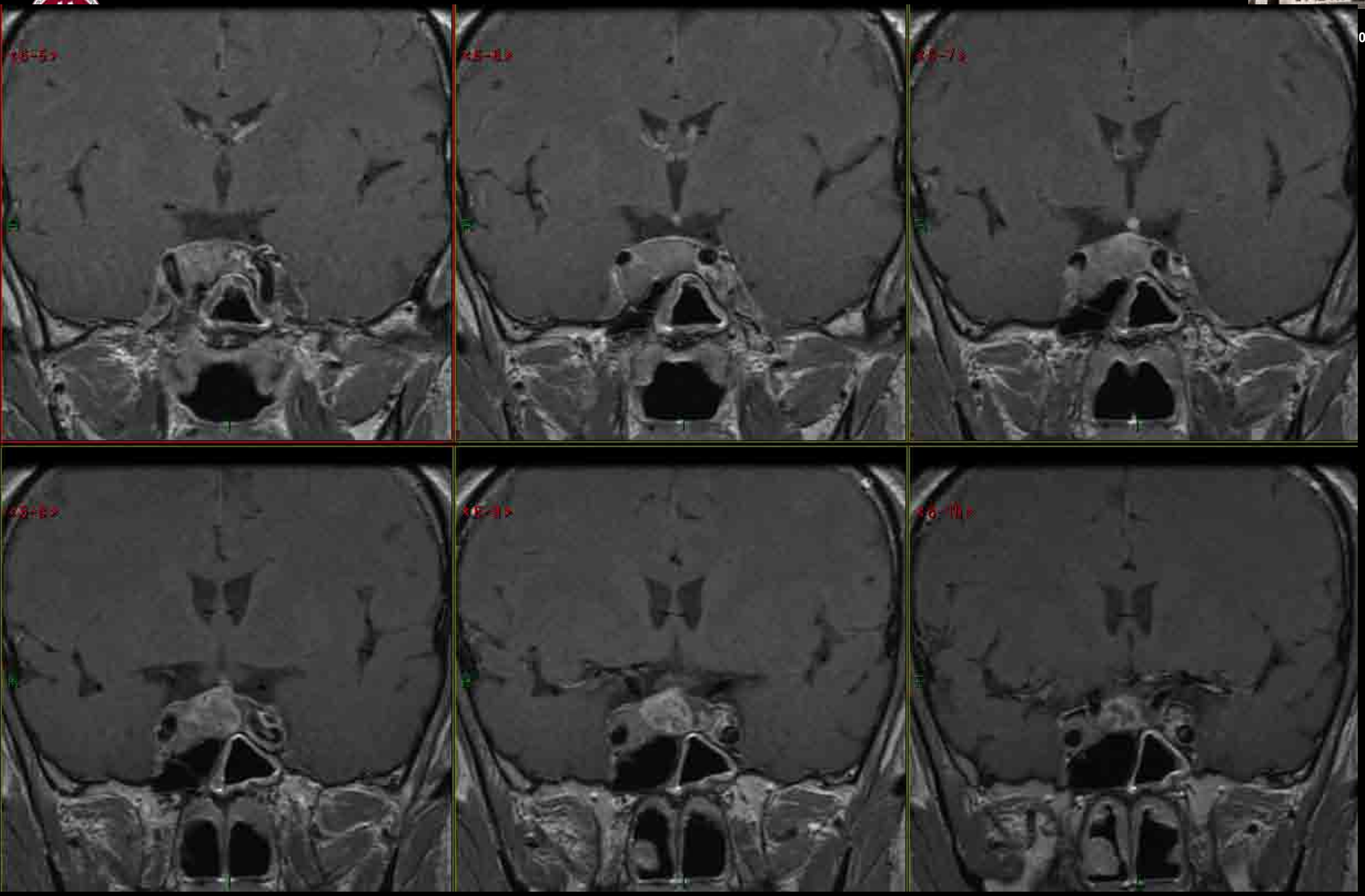


Pre-op Angio-CT scan
10.10.13





Pre-op MRI 10.10.13



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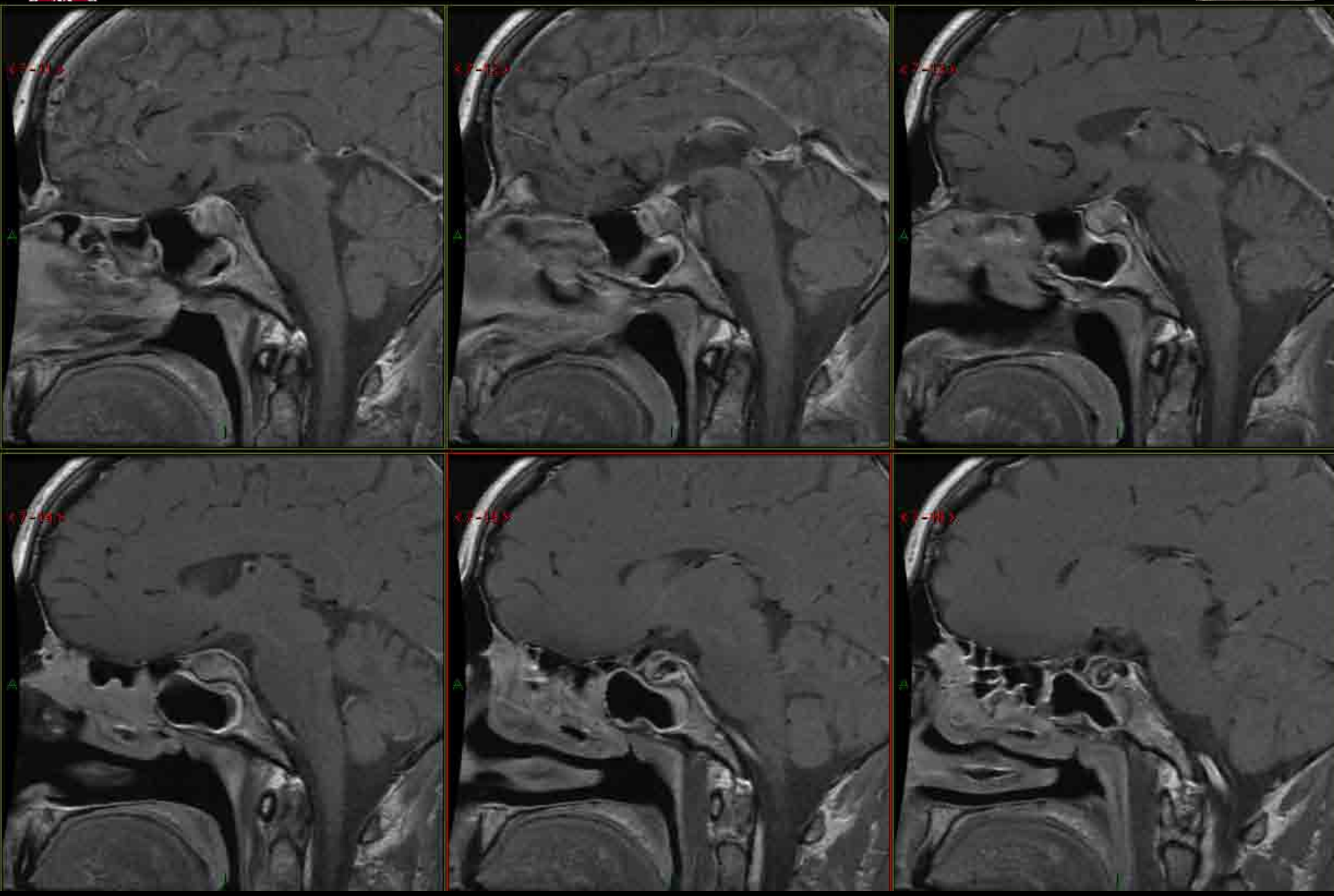
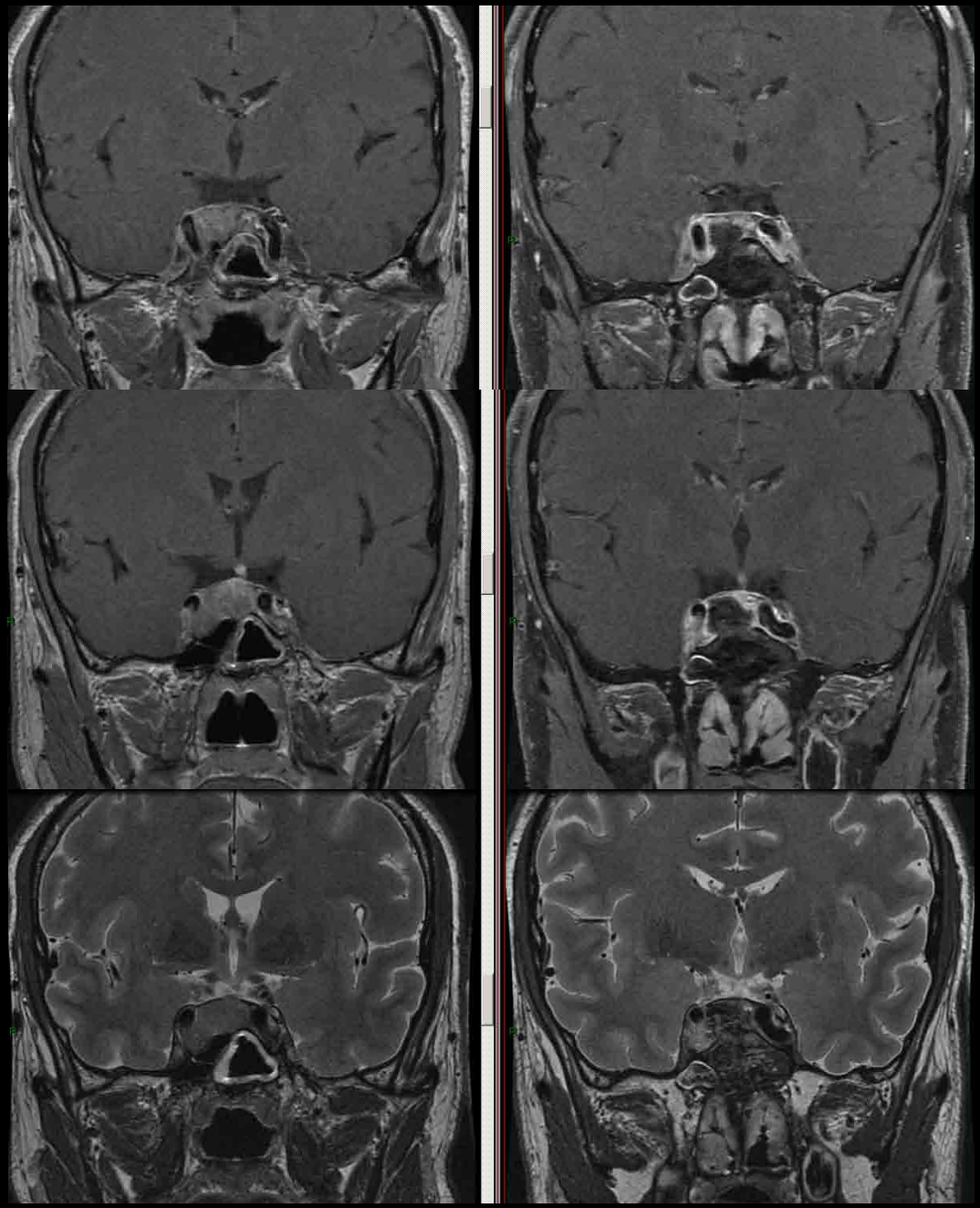
Pre-op MRI 10.10.13



Pre-op Post-op



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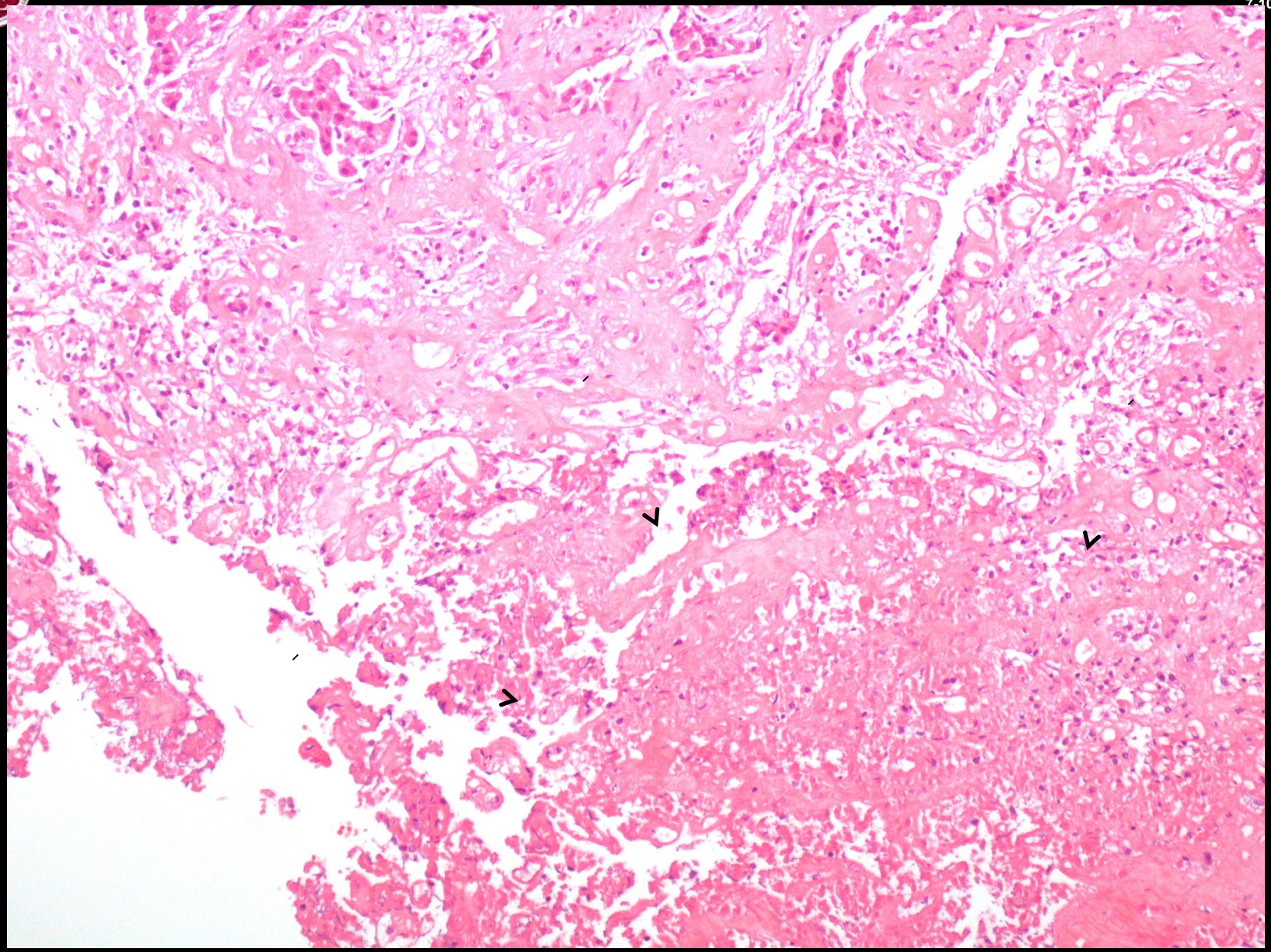
Ischemic necrosis in a pituitary tumour



Atypical pituitary adenoma

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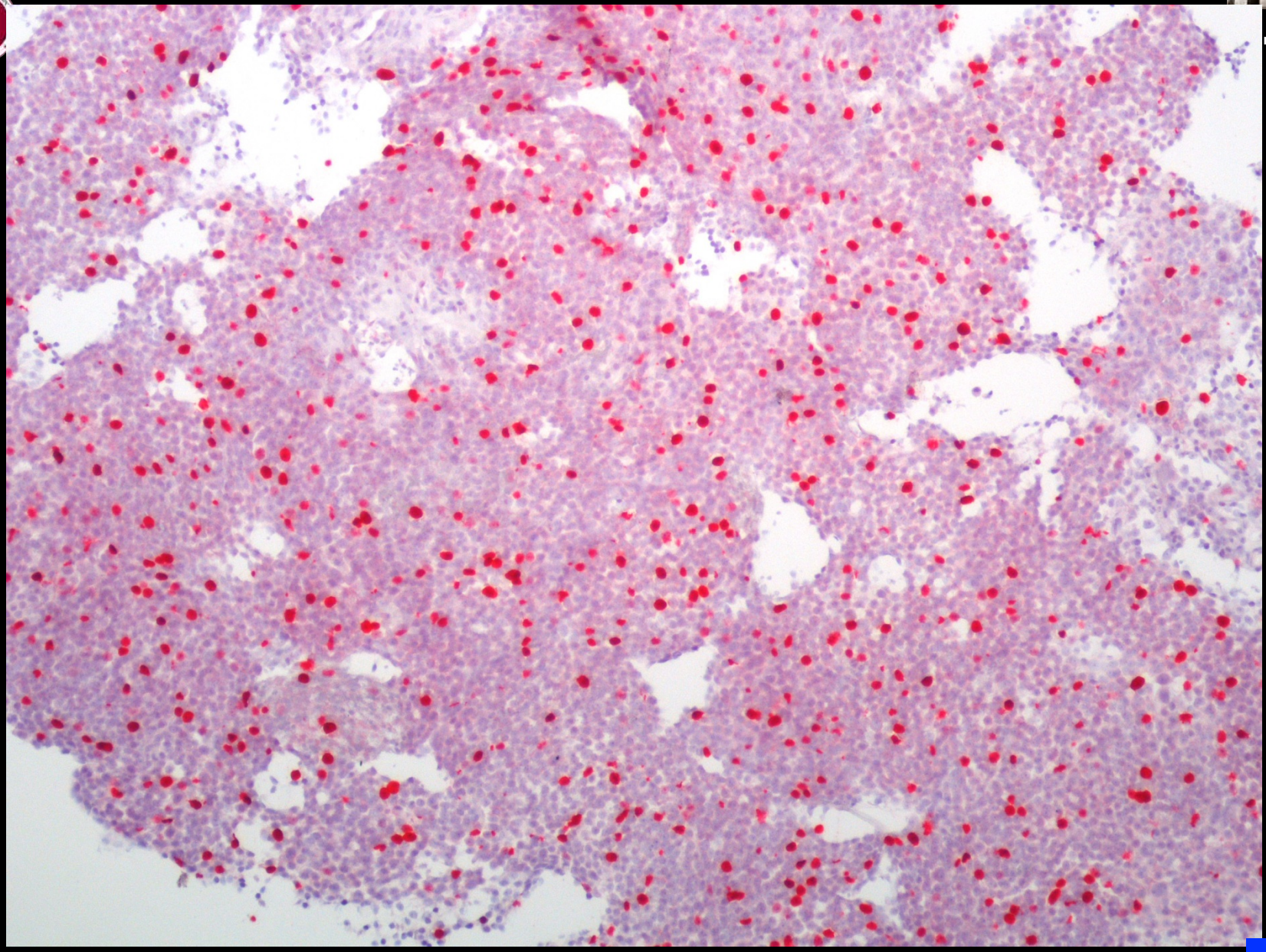
novembre 2013



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Atypical pituitary adenoma

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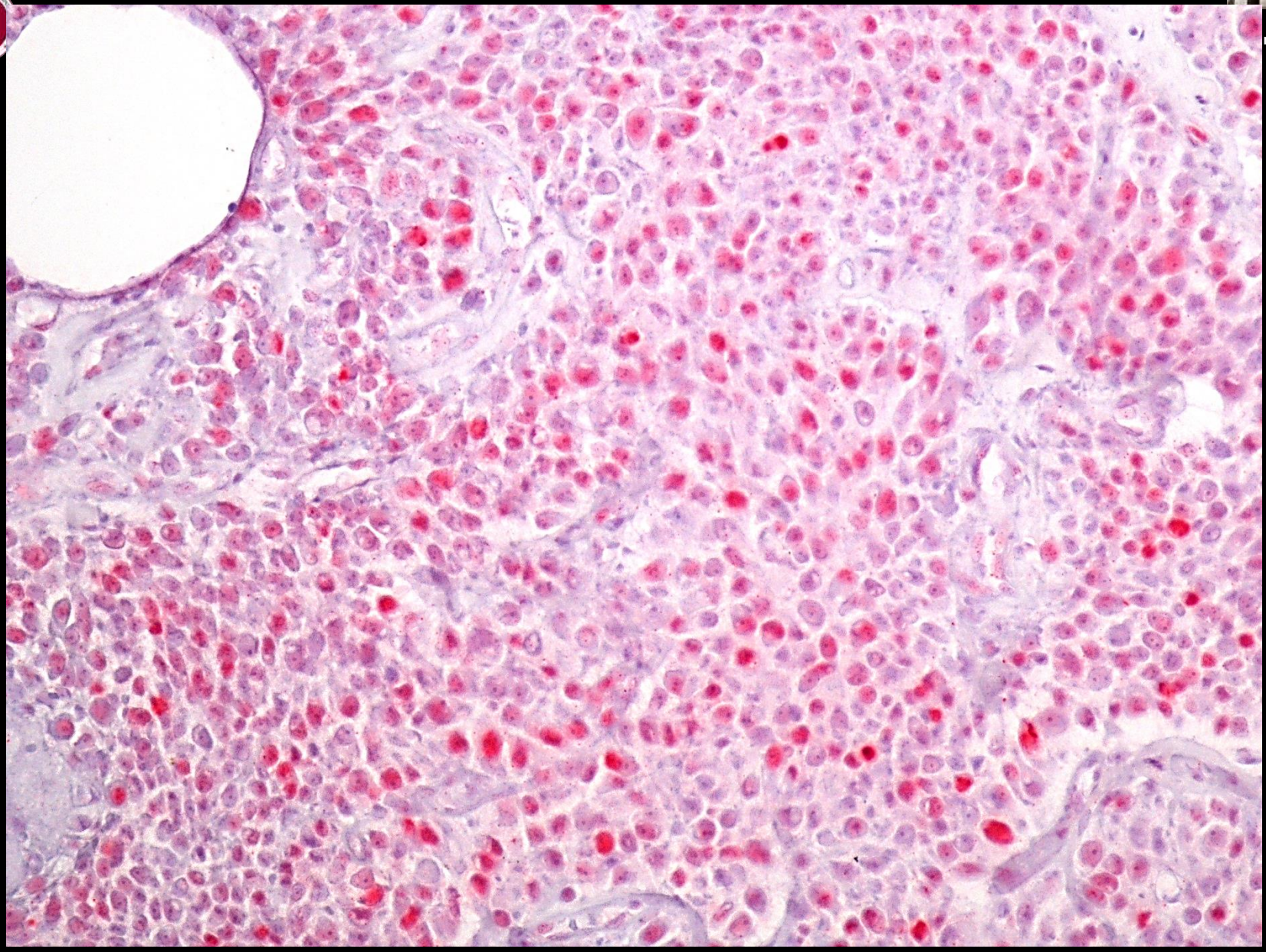

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Focusing on…

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The Bellaria Hospital's jazz band

Giorgio Frank (trumpet and conductor)

Diego Mazzatenta

Matteo Zoli

Ernesto Pasquini

Vittorio Sciarretta

Marco Faustini Fustini

Antonella Bacci