CASE REPORT

An unexpected headache: pituitary apoplexy in a pregnant woman on anticoagulation

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SUMMARY

Pituitary apoplexy is a rare event in which the pituitary gland undergoes infarction or haemorrhage, most commonly in the setting of an underlying tumour. We report on apoplexy of an undiagnosed pituitary adenoma precipitated both by physiological enlargement of the pituitary in pregnancy and prophylactic anticoagulation from a history of deep vein thrombosis. The haemorrhage was managed conservatively without significant complications.

BACKGROUND

This case highlights the theoretical increased risk of pituitary apoplexy during pregnancy due to physiological enlargement of the pituitary gland with increasing gestation. Further, anticoagulation in pregnancy is a common intervention and may contribute to precipitating pituitary apoplexy. As apoplexy is often the first presentation of an underlying pituitary adenoma, consideration of this as a differential diagnosis for headache and/or visual disturbance during pregnancy is important.

This case also contributes to the literature regarding conservative management of pituitary apoplexy, as pregnancy was a relative contraindication to surgical intervention. Controversy regarding management exists and some authors have advocated against the traditional surgical approach in circumstances of clinical stability and minimal neurology. However, in lieu of randomised control trials, the body of evidence currently is anecdotal and observational.

CASE PRESENTATION

A 30-year-old gravida 5 para 4 at 37 weeks 4 days gestation presented with the sudden onset of visual disturbance and severe occipital headache. She described having blurred vision for 3 h, with transient complete loss of vision for 45 min, and a background of intermittent visual disturbance for 4 weeks. Numbness and weakness of left upper and lower limbs, and transient left-sided facial numbness were reported. The patient was receiving prophylactic low-molecular-weight heparin throughout the pregnancy in the setting of recurrent provoked below-knee deep venous thrombosis and a strong family history of venous thromboembolism. She had a history of four previous caesarean sections.

On examination the patient was drowsy, but orientated with a stable blood pressure of 110/60 mm Hg and pulse rate of 80 bpm. Neurological examination revealed bilateral hemianopia, and

grossly normal visual acuity and extraocular movements. Loss of pain sensation in the left upper and lower limbs, and dysdiadochokinesis of the left upper limb were identified. Cardiotocography was reassuring for fetal well-being.

INVESTIGATIONS

Urgent MR angiography and venography (MRA/V) of the head and neck revealed enlargement of the pituitary gland to 12 mm diameter with evidence of a pre-existing underlying adenoma. Hypoechoic and hyperechoic areas were suggestive of both acute and subacute haemorrhage (figure 1). Unfortunately, targeted pituitary MRI was not performed in this emergency situation and in this case, the pituitary haemorrhage is better demonstrated on the axial than in the coronal images (figures 1 and 2). There was mild compression of the optic chiasm, but no expansion of the sella turcica. Early serological testing revealed adrenocorticotrophic hormone and cortisol deficiency, with other pituitary axes and biochemistry within normal limits (figure 3).

Figure 1 Axial view of MR angiography demonstrating enlargement of the pituitary gland with a fluid–fluid level and hypoechoic and hyperechoic areas consistent with acute and subacute haemorrhage.

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Figure 2 Coronal view of MR angiography in the venous phase also shows evidence of pituitary haemorrhage.

DIFFERENTIAL DIAGNOSIS

Pituitary apoplexy is an important potential pitfall in the diagnosis of headache in pregnancy that may be mistaken for pre-eclampsia, subarachnoid haemorrhage, meningitis, midbrain infarction or cavernous sinus thrombosis. More specifically, lymphocytic hypophysitis is an important differential consideration for headache with associated hypopituitarism. This condition most commonly occurs in pregnancy and the postpartum period, and is believed to have an autoimmune aetiology.^{1 2}

It may be differentiated from pituitary apoplexy by diffuse and homogenous contrast enhancement of the anterior pituitary on MRI.³

TREATMENT

The patient was transferred to a tertiary hospital for concurrent neurosurgical and obstetric care. The pituitary haemorrhage was managed conservatively with intravenous hydrocortisone 50 mg six-hourly and crystalloid fluid resuscitation. Delivery by caesarean section under spinal analgesia 2 days later was uncomplicated. Subcutaneous heparin 5000 IU twice daily was started postoperatively.

OUTCOME AND FOLLOW-UP

At discharge from hospital on day five, all neurological symptoms had resolved except for blurred vision. Visual acuity was 6/12 in the right eye and 6/6 in the left eye. Visual fields were assessed to be 86% intact in the right eye and 96% intact in the left eye, with bitemporal hemianopia. She was discharged on oral cortisone acetate for persistent hypocortisolism with no clinical or biochemical evidence of other pituitary dysfunction. Subcutaneous heparin 5000 IU twice daily was started postoperatively with the aim of restarting warfarin once a significant period had passed since the event of pituitary haemorrhage and neurological stability indicated it would be safe to do so.

DISCUSSION

Pituitary apoplexy is a rare cause for headache with potentially serious neurological and endocrine consequences. Precipitants for apoplexy include head trauma, hypotension, anticoagulants, surgery, pituitary dynamic testing, irradiation and hypertension.^{4 5} Pituitary apoplexy encompasses, but is not synonymous with, Sheehan's syndrome - a ischaemic infarction of the anterior pituitary gland resulting from postpartum haemorrhage.⁶ Profound postpartum hypotension is compounded by pituitary gland expansion of up to 136% by late pregnancy.⁷ Increase in size and associated changes in vascular supply and permeability may similarly precipitate haemorrhagic infarction during the antepartum period;^{5 8} however, these sequelae are rare and have only been documented in case reports.^{4 9}

Pituitary apoplexy occurs in patients previously asymptomatic of a pituitary tumour in 60–80% of cases.^{5 10} Headache occurs in 95% of cases and is sudden, severe and retro-orbital, bifrontal

	Value	Range		Value	Range
Haemoglobin	118g/L	115-160	Evening cortisol	96nmol/L	<330
WCC	14.6x10 ⁹ /L	4.0-11.0	Morning cortisol	80nmol/L	140-640
Platelets	274x10 ⁹ /L	140-400	ACTH	<10ng/L	10-50
Sodium	136mmol/L	135-145	FSH	<0.7U/L	1.0-8.0
Potassium	4.0mmol/L	3.5-5.1	LH	<0.2U/L	1.0-12
Creatinine	62µmol/L	32-73	Prolactin	1640mU/L	71-566
INR	0.9	0.9-1.2	IGF-1	62nmol/L	10.1-35.6
PTT	14s	12-15	Free T4	7.4pmol/L	7.0-17
APTT	27s	26-41	TSH	2.9mU/L	0.3-4.5
Fibrinogen	4.4g/L	2.0-4.5	Free T3	4.0pmol/L	3.5-6.0

WCC white cell count, INR international normalised ratio, PTT prothrombin time, APTT activated partial thromboplastin time, ACTH adrenocorticotrophic hormone, FSH follicle-stimulating hormone, LH luteinising hormone, IGF-1 insulin-like growth factor-1, T4 thyroxine, TSH thyroid-stimulating hormone, T3 triiodothyronine.

Figure 3 Serology values on presentation to hospital (morning cortisol 12 h post presentation).

or suboccipital.⁵ Other symptoms include diplopia (78%), vomiting (69%), visual field defects (64%), impaired visual acuity (52%) and altered level of consciousness.^{10 11} A rapid increase in pressure within the sella turcica causes superior compression of the optic tracts, chiasm or nerves and brain stem (causing altered levels of consciousness). Lateral compression of the oculomotor cranial nerves causes diplopia. Meningeal irritation and increased intracranial pressure lead to headache and vomiting. Leakage of blood or necrotic tissue into the subarachnoid space causes chemical meningitis and potential vasospasm of the intracranial arteries causing cerebral ischaemia (resulting in less specific symptoms). In this case, transient hemiplegia was observed, possibly secondary to vasospasm of the intracavernous carotid artery.^{5 10}

Hypopituitarism is an important complication of apoplexy and may be missed if not carefully investigated. In severe cases life-threatening hyponatraemia or hypotension may occur.¹² Biochemical evidence of hypopituitarism at presentation with apoplexy has been demonstrated with hypogonadotrophic hypogonadism in 79%, secondary hypothyroidism in 50%, secondary hypoadrenalism in 76%, hyperprolactinaemia in 6% and hyponatraemia in 44% of the patients.¹²

MRI/MRA is the modality of choice for diagnostic cranial imaging. In the first 24 h, hypointense changes are evident in T2-weighted images due to the presence of deoxyhaemoglobin. Subacute and chronic evidence of pituitary apoplexy includes focal hyperintensity on T1-weighted images and foci with both diminished and increased signal intensity on T2-weighted images.^{5 10} Within 2 weeks, a fluid level may be seen.

Immediate management of pituitary apoplexy includes fluid and electrolyte replacement. Steroid supplementation may be indicated for both the replacement of cortisol and prevention of oedema of parasellar structures. A suggested regimen is hydrocortisone 50 mg intravenous six-hourly.^{5 10} Controversy exists regarding early transsphenoidal decompression of a pituitary

haemorrhage.¹² While advocated as first line by many authors,^{11–13} conservative management may be the preference in circumstances of minimal neurological disturbance and stable haemodynamic state.^{5 14–16}

The prognosis for resolution of visual symptoms is good; however, full recovery of pituitary function is less common. Improved visual acuity, visual fields and oculomotor function occurs in 86–100% of patients following both surgical^{11 12} and conservative management.⁵ Following surgical decompression, more than 50% of patients will have partial or complete recovery of pituitary function.¹⁰ Partial or pan-hypopituitarism is more common following non-operative management.⁵ Long-term hormone replacement is required in greater than 80% of patients (corticosteroids in 82%, thyroid hormone in 89%, testosterone (males only) in 64% and desmopressin in 11%).^{11 17 18}

Competing interests None declared.

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REFERENCES

- Thodou E, Asa SL, Kontogeorgos G, *et al.* Clinical case seminar: lymphocytic hypophysitis: clinicopathological findings. *J Clin Endocrinol Metab* 1995;80:2302–11.
- Tonda C, Rizvi AA. Headache, pituitary lesion and panhypopituitarism in a pregnant woman: tumor, apoplexy or hypophysitis? *Am J Med Sci* 2011;342:247–9.
- Powrie JK, Powell M, Ayers AB, *et al.* Lymphocytic adenohypophysitis: magnetic resonance imaging features of two new cases and a review of the literature. *Clin Endocrinol (Oxf)* 1995;42:315–22.
- Al-Sharafi BA, Nassar OH. Successful pregnancy in a female with a large prolactinoma after pituitary tumor apoplexy. *Case Rep Obstet Gynecol* 2013;2013:817603.
- Nawar RN, AbdelMannan D, Selman WR, *et al.* Pituitary tumor apoplexy: a review. *J Intensive Care Med* 2008;23:75–90.
- Matsuaki T, Khan KN, Inoue T, *et al.* Evaluation of obstetrical factors related to Sheehan syndrome. *J Obstet Gynaecol Res* 2014;40:46–52.
- Dinc H, Esen F, Demirci A, *et al.* Pituitary dimensions and volume measurements in pregnancy and post partum. MR assessment. *Acta Radiol* 1998;39:64–9.
- Onesti ST, Wisniewski T, Post KD. Clinical versus subclinical pituitary apoplexy: presentation, surgical management, and outcome in 21 patients. *Neurosurgery* 1990;26:980–6.
- Okafor UV, Onwuekwe IO, Ezegwui HU. Management of pituitary adenoma with mass effect in pregnancy: a case report. *Cases J* 2009;2:6350.
- Murad-Kejbou S, Eggenberger E. Pituitary apoplexy: evaluation, management, and prognosis. *Curr Opin Ophthalmol* 2009;20:456–61.
- Bills DC, Meyer FB, Laws ER Jr, *et al.* A retrospective analysis of pituitary apoplexy. *Neurosurgery* 1993;33:602–8; discussion 8–9.
- Randeva HS, Schoebel J, Byrne J, *et al.* Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinol (Oxf)* 1999;51:181–8.
- Epstein S, Pimstone BL, De Villiers JC, *et al.* Pituitary apoplexy in five patients with pituitary tumours. *Br Med J* 1971;2:267–70.
- Lloyd MH, Belchetz PE. The clinical features and management of pituitary apoplexy. *Postgrad Med J* 1977;53:82–5.
- McFadzean RM, Doyle D, Rampling R, *et al.* Pituitary apoplexy and its effect on vision. *Neurosurgery* 1991;29:669–75.
- Reid RL, Quigley ME, Yen SS. Pituitary apoplexy. A review. *Arch Neurol* 1985;42:712–19.
- Arafah BM, Harrington JF, Madhoun ZT, *et al.* Improvement of pituitary function after surgical decompression for pituitary tumor apoplexy. *J Clin Endocrinol Metab* 1990;71:323–8.
- Arafah BM, Kailani SH, Neel KE, *et al.* Immediate recovery of pituitary function after transsphenoidal resection of pituitary macroadenomas. *J Clin Endocrinol Metab* 1994;79:348–54.

Learning points

- ▶ Headache in pregnancy is a common clinical presentation with rare, serious pitfalls among the differential diagnoses.
- ▶ Physiological enlargement of the pituitary gland during pregnancy and anticoagulation use, common in this population, may precipitate haemorrhage.
- ▶ Pituitary apoplexy may be the first presentation of an underlying tumour and has a widely varied symptomatology—it should be considered as a differential diagnosis for headache, visual disturbance or symptoms of hypopituitarism in pregnancy.
- ▶ Conservative management of pituitary apoplexy is currently not common practice, but may be considered if neurological symptoms are minimal and the patient is clinically stable.
- ▶ Pregnancy is a relative contraindication to surgical decompression and urgent delivery by caesarean section might be indicated as a priority.

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