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Pituitary apoplexy complicated by a subarachnoid hemorrhage and ventricular extension: A rare case report and review of the literature

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Abstract

Background: Pituitary apoplexy is a rare endocrine emergency due to hemorrhage of the pituitary gland. Clinical presentation depends on the extent of bleeding and can deteriorate into a life-threatening condition if complicated by a subarachnoid hemorrhage.

Case report: A 60-year-old woman with a medical history of a macroprolactinoma treated with cabergoline and panhypopituitarism, presented with nausea, vomiting and an altered consciousness. CT scan of the brain revealed an extensive suprasellar hemorrhagic mass and a subarachnoid hemorrhage with ventricular extension. Angiography was negative for an arterial cerebral aneurysm. An external ventricular drain was placed urgently and one month after presentation a transsphenoidal resection of the hemorrhagic mass was performed. The patient had no neurological deficit. Visual field loss improved partially. Panhypopituitarism persisted. MRI pituitary three months postoperative showed resorption of the hemorrhagic mass with a residual collection.

Conclusion: To our knowledge, this is only the third case of pituitary apoplexy complicated by a subarachnoid hemorrhage in which an aneurysm was excluded. It is recommended to consider pituitary apoplexy in an angiographically negative subarachnoid hemorrhage. The clinical presentation, management and outcome of this and two previous case reports together with a review of the literature of pituitary apoplexy are discussed.

Keywords

Case report; Pituitary apoplexy; Subarachnoid hemorrhage; Prolactinoma.

Introduction

Pituitary apoplexy is an uncommon endocrine emergency due to abrupt hemorrhaging and/or infarction of the pituitary gland with a prevalence of 6.2 cases per 100,000 habitants [1]. In 75% of cases it concerns a patient with an unrecognised pituitary macroadenoma [1]. The clinical presentation depends on the extent of hemorrhage and can deteriorate into a life-threatening condition if pituitary apoplexy is complicated by a subarachnoid hemorrhage, as previously described in only two cases [2,3]. In patients known with a pituitary adenoma, an aneurysmal subarachnoid hemorrhage should still be excluded. We present a woman with pituitary apoplexy of a macroprolactinoma complicated by a subarachnoid bleeding and ventricular extension followed by a description of the clinical presentation, management and outcome of two previous cases.

Case Presentation

A 60-year-old woman presented herself at the emergency department because of confusion for several hours. She complained of nausea, vomiting and a mild headache since one day. Clinical examination revealed anisocoria with mydriasis of the right pupil in an agitated woman able to move her four limbs but unable to execute commands. The patient had a high-normal blood pressure (158/76 mmHg) and was subfebrile (38.2°C). Blood results showed a leucocytosis with a neutrophil left shift, normal kidney function and normal electrolytes. CT scan of the brain without contrast was urgently performed and revealed an extensive suprasellar hemorrhagic mass, a subarachnoidal bleeding around both anterior horns and extension to the lateral, third and fourth ventricles, the foramen of Monro and basal cisterns (Figure 1). There was no midline shift or hydrocephalus.

Seven months earlier, a macroprolactinoma was diagnosed as an incidental finding on a CT scan of the brain. Work-up with pituitary MRI revealed an adenoma with a craniocaudal diameter of 28 mm and compression of the optic chiasma (Figure 2). Hormonal work-up showed an elevated level of prolactin (147 µg/L, reference range 3-18.6 µg/L), central hypothyroidism, hypogonadal hypogonadism and cortisol and growth hormone deficiency confirmed by an insulin tolerance test (ITT) (Table 1). She was started on L-thyroxine 50 µg a day and Hydrocortisone 10 mg in the morning and 5 mg at noon and in the evening. Visual field examination was, unexpected, normal as examined by Humphrey Field Analyzer. Cabergoline 0.5 mg twice a week was started, resulting in a suppressed prolactin level one month later (Table 1). However, pituitary MRI five months after commencing cabergoline revealed unchanged dimensions of the adenoma and persistent compression of the optic chiasma. Further medical history consisted of arterial hypertension for which Belsar 20 mg/day was taken, hypercholesterolemia treated by Atorvastatin 20 mg/day, glaucoma and a hysterectomy.

After presentation at the emergency department, the patient was sedated to enable placement of an external ventricular drain in the fourth ventricle and was admitted to intensive care. Solucortef 100 mg three times a day was administered. CT angiography excluded an arterial aneurysm. The day after admission the patient awakened and executed commands. Anisocoria disappeared. Two weeks later, the external ventricle drain was removed. The dose of corticosteroids was reduced to the dose of Hydrocortisone at admission. L-thyroxine 50 µg was continued and cabergoline was stopped at admission since high normal

tensions (systolic blood pressure 140-160 mmHg) were pursued as treatment of an intracerebral bleeding. Despite a diuresis up to 3.9 liters a day there were no arguments for diabetes insipidus since urine density remained normal. Visual field examination with automatic perimetry revealed bitemporal hemianopsia. MRI of the pituitary one month after admission showed a heterogenous suprasellar mass with following diameters: 28 mm craniocaudal, 19 mm laterolateral and 18 mm anteroposterior. Endoscopic transsphenoidal resection of the pituitary mass was performed and anatomopathological examination showed necrotic tissue. Unfortunately, immunohistological examination was not possible. Hormonal work-up five days postoperatively showed low levels of FT4 and FT3 and the dose of L-thyroxine was increased from 50 to 75 µg a day (Table 1). Hydrocortisone was continued at a dose of 20 mg a day. The postoperative level of prolactin was immeasurably low. Postoperative pituitary MRI showed a haemorrhagic suprasellar mass compatible with hemorrhagically residual adenoma but with a reduced mass effect on the optic chiasm (Figure 3). Because of this finding cabergoline was restarted at a dose of 0.5 mg twice a week. ITT six weeks postoperatively confirmed a persistent cortisol and growth hormone deficiency. Growth hormone was not substituted. Pituitary MRI three months postoperative revealed an important resorption of the hemorrhagic zone in the sellar and suprasellar region with a residual collection at the bottom of the sella turcica (Figure 4). Whether this collection is a residual hematoma or adenoma could not be differentiated. Visual field examination three months postoperatively showed improvement, but was not normal with a bitemporal quadrantanopia.

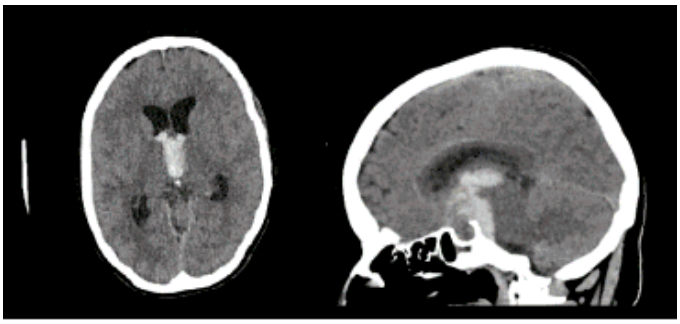

Figure 1: CT scan of the brain the day of admission showed an extensive suprasellar hemorrhagic mass and a subarachnoid bleeding around both anterior horns and extension to the lateral, third and fourth ventricles, the foramen of Monro and basal cisterns.

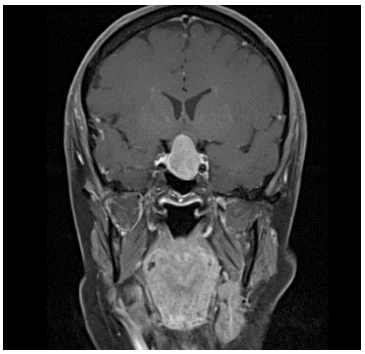

Figure 2: Pituitary MRI, seven months before presentation, showed a homogeneous adenoma with a craniocaudal diameter of 28 mm and compression of the optic chiasma.

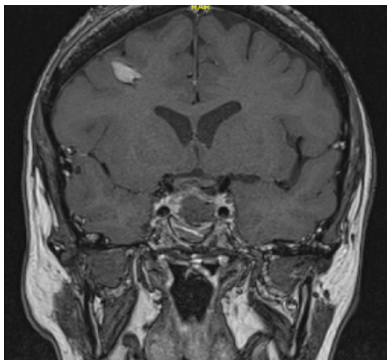

Figure 3: Pituitary MRI, six days postoperative, showing a haemorrhagic suprasellar mass compatible with a hemorrhagically residual adenoma but with a reduced mass effect on the optic chiasm.

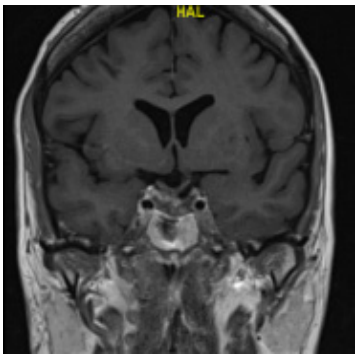

Figure 4: Pituitary MRI, three months postoperative, revealed an important resorption of the hemorrhagic zone in the sellar and suprasellar region with a residual collection at the at the bottom of the sella turcica.

Table 1: Pituitary function.

	At diagnosis of macroprolactinoma (12 February 2021)	**One month after treatment with cabergoline** (02 April 2021)	**Six days postoperative** (05 October 2021)	**Six weeks postoperative** (9 November 2021)	*Reference level*
TSH (mU/L)	3.12	2.45	0.07	0.02	*0.55-4.78*
FT4 (pmol/L)	6.72	8.1	11.4	16.9	*11.5-22.7*
FT3 (pmol/L)			3.0	3.8	*3.5-6.5*
Prolactin (µg/L)	178	<1	0.4	0.4	*2.8-29.2*
FSH (E/L)	1.2		0.3	<0.3	
LH (E/L)	<0.1		<0.1	<0.1	
Oestradiol (ng/L)	19		<5	<5	
IGF-1 (ng/mL)	77	76	53	62	*55-204*
ACTH (pg/mL)	15	21.3	<2	<2	*7-63*
Cortisol (ng/mL)	51	88	4.9	1	*62.4-180*

Table 2: Summary of three cases of pituitary apoplexy complicated by a subarachnoid bleeding.

	Satyarthee et al. [2]	**Nakahara et al. [3]**	**Current report**
Date of publication	2005	2006	2022
Age (year)	13	46	60
Sex	Men	Female	Female
Symptoms at presentation	Headache	Headache, vomiting	Headache, vomiting, confusion
Visual field disturbances	Bitemporal hemianopsia	no	Bitemporal hemianopsia
Awareness	Normal	Normal	Reduced
Pituitary insufficiency	No	No	Panhypopituitarism
Known pituitary adenoma	No	No	Yes
Treatment	Transsphenoidal resection	Transsphenoidal resection	Transsphenoidal resection
Visual deficit recovery	yes	x	Partially
Pituitary function postoperative	Thyrotropic and corticotropic deficiency	Normal	Panhypopituitarism

Discussion

Pituitary apoplexy is a rare clinical syndrome which results from infarction or haemorrhage of the pituitary gland, generally within a pre-existing pituitary macroadenoma. Less often, intrasellar cysts rupture and cause apoplexy. With a prevalence in the general population of 6.2 cases per 100 000 habitants and between 2 and 12% in patients with a pituitary adenoma, pituitary apoplexy is very rare [1,4]. Pituitary apoplexy is the first manifestation of an underlying pituitary macroadenoma in 80% of patients and is most frequently seen in the fifth or sixth decade of life with a slight male preponderance of 1.1-2.3/ 1 [1,5]. Pituitary apoplexy complicated by a subarachnoid bleeding is very rare since this is only the third case described so far.

The pituitary is densely vascularised. The anterior lobe is provided with a capillary network supplied by the superior hypophyseal artery which is a branch of the internal carotid artery [6]. Pituitary adenomas are prone to bleed because of the rich and complex vascularisation, incomplete maturation of

the vessels and fragmented basal membranes [7]. Incomplete maturation of the vessels is more frequent in prolactinomas [8]. Bleeding from the pituitary tumor may extravasate from the sella turcica into the adjoining subarachnoid space and ventricles.

Many patients with pituitary apoplexy have precipitating factors including angiographic procedures, cardiac or orthopedic surgery, head trauma, anticoagulation therapy, bleeding disorders, thrombocytopenia, pregnancy, pituitary irradiation, treatment with gonadotropin releasing hormone for prostate cancer or endocrine stimulation tests with thyroid releasing hormone [1,5,9,10]. Pituitary apoplexy is typically associated with macroadenomas and is rarely seen in microadenomas. Regarding the type of pituitary macroadenoma associated with apoplexy, data is inconsistent because hypersecretion can be clinically or immunohistological determined. The review of Briet et al. revealed 48% of adenoma were non-functioning whereas secretion of prolactin, growth hormone and ACTH was seen in 40%, 7% and 5% respectively [1].

The most common clinical features of pituitary apoplexy are headache (80%), nausea and vomiting (40-80%), visual disturbances (40-90%) and oculomotor nerve palsy (50-80%). Less frequent symptoms include altered consciousness (5-40%), pyrexia (10-25%) and meningeal irritation (5-15%) [6]. The majority of patients will have an acute endocrine dysfunction at presentation; 50-80% corticotropic deficiency, 30-70% thyrotropic deficiency and 40-75% gonadotropic deficiency [1,6]. Diabetes insipidus is infrequent in pituitary apoplexy being reported in approximately 5% of cases [1]. Clinical status may deteriorate dramatically if pituitary apoplexy is complicated by a subarachnoid hemorrhage or cerebral ischemia secondary to cerebral vasospasm.

Since in many patients pituitary adenoma is unrecognised prior to pituitary apoplexy, diagnosis can be missed. It is recommended to consider pituitary apoplexy in an angiographically negative subarachnoid hemorrhage and in 80% of cases pituitary tumor can already be visualised on the urgent CT scan of the brain [1]. However, even in patients with a medical history of a pituitary adenoma, a cerebral aneurysm still needs to be excluded since it is much more frequent and since a pituitary adenoma has been reported to coexist with arterial aneurysms in 8.3% as compared in 2.4% of the general population [11].

The management of pituitary apoplexy is a matter of debate as some advocate early surgical decompression in all patients whereas others adopt a conservative approach for patients without visual field defects and with normal consciousness. All patients should receive corticosteroids even if they do not present symptoms of an adrenal crisis [5]. Tumor shrinkage is common after apoplexy but long-term follow-up studies have shown recurrence of these adenoma in 11.1% [12]. Several studies comparing surgical and conservative approaches have shown comparable outcomes in terms of pituitary function and visual deficit recovery [13]. No literature was found about the treatment of adenomas with residual tumor after resection of the hemorrhagic mass. Despite the choice of therapeutical approach, endocrine prognosis is poor in patients with pituitary apoplexy because of frequently irreversible pituitary damage [1].

So far, to the best of our knowledge, only two cases of pituitary apoplexy complicated by a subarachnoid bleeding have been previously described. The main characteristics of these two and the current case are summarized in Table 2 [2,3]. The first case reported by Satyarthee et al. in 2005 was

about a 13-year-old boy who went to the emergency room with a sudden headache and a bitemporal field defect since some weeks prior to presentation [2]. He had signs of meningeal irritability. CT scan showed a massive subarachnoid hemorrhage with extension into the third ventricle. Pituitary MRI demonstrated a large suprasellar, heterogeneous mass, suggestive of pituitary apoplexy. He had no medical history and hormonal work-up was normal. A cerebral aneurysm was excluded. Transsphenoidal decompression of the pituitary adenoma was performed and histopathology revealed a pituitary adenoma with extensive necrosis. Immunohistological staining was negative. Postoperatively, his visual field defect almost completely recovered but he developed a corticotropic and thyrotropic deficiency. The second case described by Nakahara et al. in 2006 was a 46-year-old woman presenting with a sudden headache, nausea and vomiting [3]. She had no visual field disturbances and neurological investigation was normal. CT scan of the brain showed a diffuse subarachnoidal bleeding with extension into the fourth ventricle and basal cisterns and a hyperdense suprasellar mass. Cerebral angiography was negative for an aneurysm. MRI showed a pituitary mass with intratumoral hemorrhage. Hormone status was normal. The patient underwent transsphenoidal resection of the pituitary adenoma and immunohistological staining was negative. Pituitary function remained normal. Four other case reports have been published between 1948 and 1981 but a cerebral aneurysm was not excluded by angiography [14-17].

Our case report described a patient with a pre-existing macroprolactinoma and a severe and life-threatening presentation of pituitary apoplexy with reduced consciousness. Prolactinomas are more prone to bleed, certainly if larger than 10 mm. In the past, dopamine agonists were seen as a predisposing factor to pituitary apoplexy but the review of Carija et al. has shown that the incidence of apoplexy in prolactinoma with or without treatment with dopamine agonists was equal [18]. In contrast to previous studies, the study of Möller-Goede et al suggested that arterial hypertension does not predispose patients to pituitary apoplexy [19]. Therefore, besides having a macroprolactinoma, this patient had no predisposing factors for apoplexy.

Conclusion

Pituitary apoplexy is a rare endocrine emergency due to hemorrhage of the pituitary gland. Clinical status may dramatically deteriorate if pituitary apoplexy is complicated by a subarachnoid bleeding. Since pituitary adenoma and cerebral aneurysm can coexist, a cerebral angiography is necessary to exclude an aneurysmal bleeding. The endocrine prognosis is poor because of frequently irreversible pituitary damage. This is the third case of a pituitary apoplexy complicated by a subarachnoid hemorrhage and ventricular extension without an arterial aneurysm.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: An informed consent for publication of this case report was obtained in Dutch (patient's native language) and can be requested if necessary.

Availability of data and materials: Data sharing is not applicable to this article as no datasets were

generated or analysed during the current study.

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