Postoperative diabetes insipidus associated with pituitary apoplexy during pregnancy

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Abstract

BACKGROUND: Pituitary apoplexy during pregnancy is so rare that only 15 cases (12 pituitary adenomas, 2 lymphocytic neurohypophysitis, and 1 normal pituitary gland) have been published to date. Here, we report the case of a pregnant woman presenting with pituitary apoplexy from a nonfunctioning pituitary adenoma and provide a possible mechanism and management option for postoperative diabetes insipidus (DI).

CASE PRESENTATION: A 26-year-old woman presented with sudden onset of headache and bitemporal hemianopsia in the 26th week of her first pregnancy. Magnetic resonance imaging clearly revealed an 18 mm pituitary mass with a fluid–fluid level component displacing the optic chiasma upward. Endonasal endoscopic transsphenoidal surgery was successfully carried out 7 days after the onset of symptoms. DI became apparent immediately after the operation and was not controllable by arginine vasopressin (AVP) but by 1-desamino-8-D-arginine vasopressin (DDAVP) instead. This finding suggests an association between DI and vasopressinase secretion from the placenta, because vasopressinase can degrade AVP but not DDAVP. DI had diminished by the time the patient delivered a healthy girl at the 40th week of gestation.

CONCLUSION: Postoperative DI associated with pituitary apoplexy during pregnancy should be treated by DDAVP, which is not affected by placental vasopressinase secretion.

Abbreviations:

AVP	- arginine vasopressin
DDAVP	- 1-desamino-8-D-arginine vasopressin
DI	- diabetes insipidus
MRI	- magnetic resonance imaging
SIADH	- syndrome of inappropriate antidiuretic hormone secretion

CASE REPORT

INTRODUCTION

Pituitary apoplexy is a neurological and endocrinological emergency caused by hemorrhage and/or infarction in the pituitary gland. The incidence of pituitary apoplexy has been estimated at 0.5–17% in adenomas (Semple *et al.* 2005), but only 15 cases of pituitary apoplexy during pregnancy have been reported in the literature, which includes 2 cases of underlying lymphocytic neurohypophysitis and 1 with a normal pituitary gland (Table 1). Special care must be taken in controlling electrolytes, hormones, and water balance for such pregnant women. One of the symptoms of pituitary apoplexy is diabetes insipidus (DI) with resultant hyponatremia, the incidence of which is approximately 10% (Semple *et al.* 2005). To the best of our knowledge, no report has mentioned an association between pituitary apoplexy during pregnancy and DI. Here, we present the case of a pregnant woman who had developed pituitary apoplexy in a nonfunctioning pituitary adenoma and provide a possible mechanism and management option for postoperative DI.

CASE REPORT

A 26-year-old woman in the 26th week of her first pregnancy complained of sudden onset of headache and narrowing of the visual field. Her pregnancy course had been uneventful until then, and her past medical history was unremarkable, including an absence of irregular menstruation or galactorrhea. On physical examination, height was 158 cm and weight was 60 kg. Blood

Tab. 1. Summary of pituitary apoplexy during pregnancy confirmed by pathological or radiological study.

Case No.	Type of disease (Hormone)	Age	Gestation week	Symptoms	Treatment	Outcome	Delivery week	Prior treatment	Refs.
1	adenoma (PRL)	25	10	VFD	surgical decompression (TC)	panhypopituitarism	41	bromocriptine	[2]
2	adenoma (PRL)	26	23	H/A, DI	hormonal replacement	panhypopituitarism	38	none	[4]
3	adenoma (PRL)	29	34	H/A, VFD, III palsy	surgical decompression (TS)	good	39	bromocriptine	[8]
4	adenoma (PRL)	26	25	H/A, VFD, VAD	surgical decompression (TS)	good	39	HMG + HCG	[10]
5	adenoma (PRL)	33	30	H/A, VFD	surgical decompression (TC)	good	38	HMG	[13]
6	adenoma (PRL)	28	6	H/A, VFD	n.a.	good	32	bromocriptine	[14]
7	adenoma (PRL)	30	29	H/A, VI palsy	hormonal replacement	good	39	prior irradiation	[16]
8	adenoma (PRL)	34	29	VFD	surgical decompression (TC)	good	32	clomiphene	[21]
9	adenoma (PRL)	37	8	coma, III palsy	surgeical decompression (TC)	III palsy	n.a. (at term)	bromocriptine	[23]
10	adenoma (GH)	21	24	H/A, VFD, VAD	surgical decompression (TS)	good	n.a. (at term)	none	[19]
11	adenoma (GH)	29	24	H/A, VAD, VFD, DI	surgical decompression (TS)	good	40	clomiphene	[24]
12	adenoma (NF)	28	n.a.	H/A, VFD	surgical decompression (TS)	minimal diplopia	n.a.	none	[25]
13	lymphocytic neurohypophysitis	23	25	VFD	surgical decompression (TS)	good	n.a.	none	[7]
14	lymphocytic neurohypophysitis	26	24	H/A, VFD, VAD	surgical decompression (n.a.)	good	35	none	[17]
15	normal	28	7	coma, hyponatremia, DI	hormonal replacement	panhypopituitarism	spontaneous abortion	none	[15]
16	adenoma (NF)	26	26	H/A, VFD, VAD, DI	surgical decompression (TS)	good	40	none	Present case

DI, diabetes insipidus; GH, growth hormone; H/A, headache; HCG, human chorionic gonadotropin; HMG, human menopausal gonadotropin; n.a., not available; NF, nonfunctioning; PRL, prolactin; TC, transcranial decompressive surgery; TS, transsphenoidal decompressive surgery; VAD, visual acuity deficiency; VFD, visual field defect.

pressure was 128/72 mmHg. Her neurological manifestations were bitemporal hemianopsia and decreased visual acuity without any other cranial nerve dysfunction. She did not develop polyuria and polyposia.

Hematological data and electrolytes were normal for a pregnant woman in the end of the second trimester (WBC, 10,200/mm^3; RBC, 3.54×10^6/mm^3; hemoglobin, 10.4 mg/dL; platelets, 146×10^3 /mm^3; Na, 140 mmol/L; K, 3.6 mmol/L; Cl, 108 mmol/L). Hormonal data revealed a slight increase in cortisol and a decrease in free thyroid hormones. The former was considered a normal pregnancy event, but the latter was the result of hypothyroidism caused by the pituitary apoplexy (cortisol, 20.2 μg/mL [6.2–19.7]; ACTH, 27.9 pg/mL [<46]; PRL, 224.0 ng/mL [100–300 during pregnancy]; GH, 0.17 ng/mL [<2.1]; TSH, 1.11 μIU/mL [0.27–4.65]; FT3, 1.86 pg/mL [2.20–4.30]; FT4, 0.62 ng/dL [0.80–1.80]; LH, <0.5 mIU/mL [<0.5]; FSH, <0.5 mIU/mL [<0.5]). Magnetic resonance imaging (MRI) revealed an 18 mm pituitary mass with a clear fluid–fluid level component displacing the optic chiasma upward, consistent with intratumoral hemorrhage (Figure 1A and B).

The patient was referred to our hospital 6 days after the onset of symptoms and underwent an endonasal endoscopic transsphenoidal surgery on the following day to relieve the visual disturbance. Pathological examination revealed a nonfunctioning pituitary adenoma with hemorrhagic infarction (Figure 2A–C). Her visual symptoms immediately improved after the operation, though she developed polyuria (>8 L/day). This was considered to be masked diabetes insipidus (DI), which manifested following hydrocortisone administration (Figure 3). Arginine vasopressin (AVP) was first applied subcutaneously and then intravenously, both of which were ineffective. On postoperative day (POD) 6, hyponatremia became apparent (126 mmol/L), which required administration of sodium following water deprivation (<1 L/day) along with ceasing of AVP administration because syndrome of inappropriate antidiuretic hormone secretion (SIADH) was suspected. Instead of AVP, nasal administration of 1-desamino-8-D-arginine vasopressin (DDAVP) beginning POD 9 was found to be effective for DI and sodium loss.

Hormonal data on POD 10 were as follows: ACTH 32.8 pg/mL, cortisol 24.4 μg/mL, PRL 105.9 ng/mL, TSH 1.36 μIU/mL, FT3 1.27 pg/mL, and FT4 0.68 ng/dL. The patient began levothyroxine intake for hypothyroidism as well as DDAVP administration. She was released from DDAVP treatment by an uneventful vaginal delivery at the 40th week of pregnancy. MRI obtained 6 months after the surgery showed successful decompression of the chiasma and resumed hyperintensity at both the pituitary stalk and posterior lobe of the pituitary gland on a T1-weighted image, suggesting full recovery of the transient DI (Figure 1C and D).

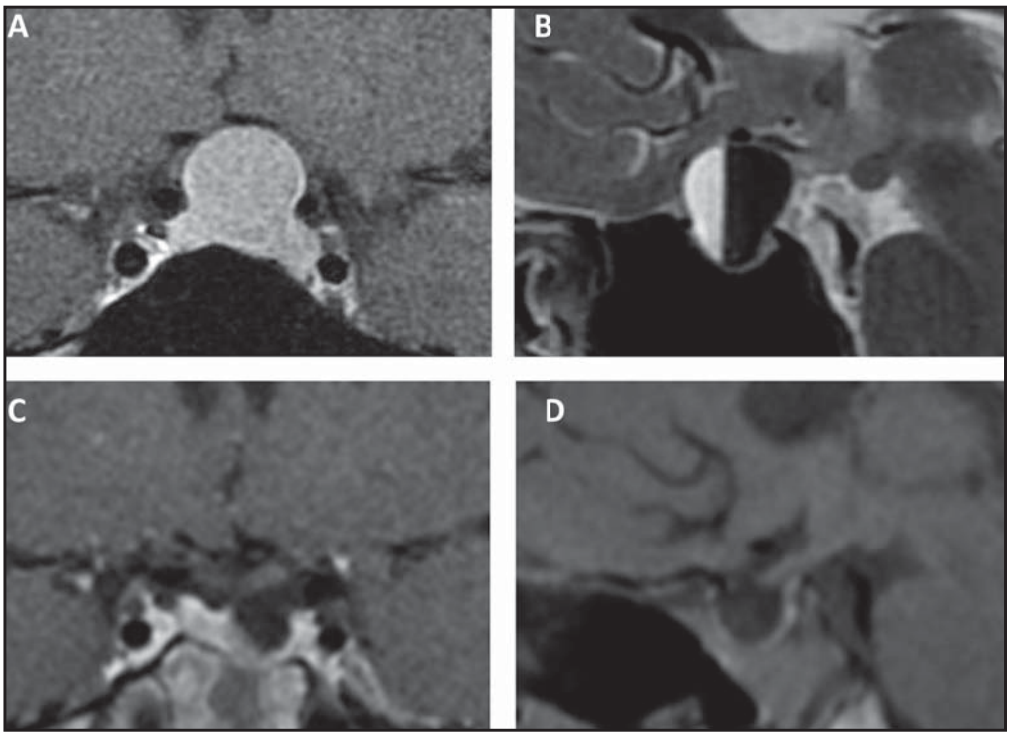

Fig. 1. Pre- and postoperative MR images. (A) Preoperative coronal section of Gd-enhanced T1-weighted image (WI) showing an intrasellar mass extending into the suprasellar region. (B) Preoperative T2WI showing a mass containing a clear fluid–fluid level, indicating intratumoral hemorrhage. (C) Postoperative coronal section of Gd-enhanced T1WI showing decompressed chiasma and pituitary gland. (D) Postoperative sagittal section of T1WI revealing a hyperintensity area from the pituitary stalk to the posterior part of the pituitary gland, indicating preservation of posterior pituitary function.

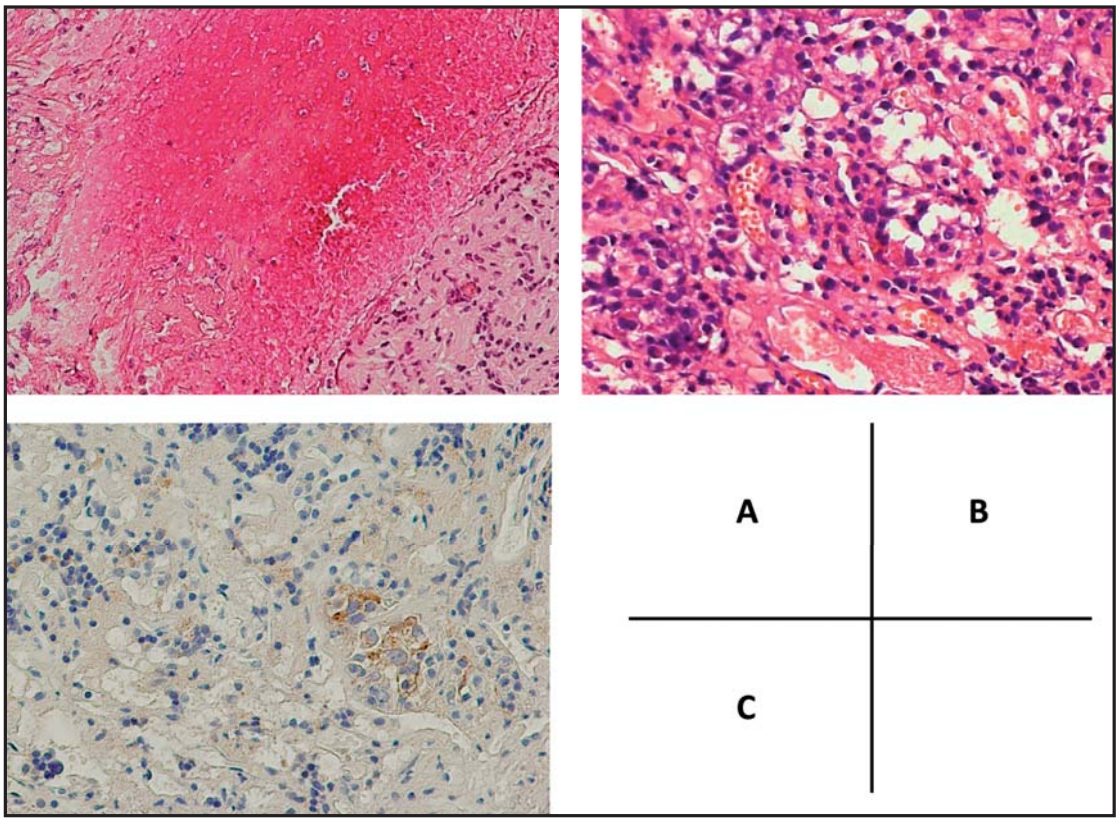

Fig. 2. Pathological study of the surgical sample. (A) HE staining of the surgical specimen revealing intratumoral hemorrhagic necrosis, suggesting hemorrhagic infarction. (B) Pituitary adenoma with rich vascularity is shown. (C) Anti-PRL staining showing faint positive cells in the adenoma, consistent with a nonfunctioning adenoma in pregnancy.

DISCUSSION

Peri- and postpartum cases of pituitary apoplexy contribute to hypovolemic shock and are widely recognized as Sheehan syndrome, but only 16 cases, including our case, have been reported and confirmed by radiological and/or pathological exploration (Table 1) during pregnancy. In these gestational pituitary apoplexy cases, 13 were caused by pituitary adenomas (Burry *et al.* 1978; de Heide *et al.* 2004; Gondim *et al.* 2003; Hervet *et al.* 1975; Kajtar & Tomkin 1971; Kannuki *et al.* 1993; Lamberts *et al.* 1979; Lunardi *et al.* 1991; Nagulesparan & Roper 1978; O'Donovan *et al.* 1986; Ohtsubo *et al.* 1991; Onesti *et al.* 1990), 2 by lymphocytic neurohypophysitis (Fujimaki *et al.* 2005; Lee & Pless 2003), and 1 was a normal pituitary gland (Krull *et al.* 2010). Nine out of the 13 adenomas were prolactinomas with or without pretreatment for infertility. The rapid growth of pituitary adenomas with visual dysfunction during pregnancy has been reported in macroprolactinomas treated with dopamine agonists (Dommerholt *et al.* 1981). It is recognized that the normal pituitary gland is physiologically enlarged throughout pregnancy (up to 136% at the end of the pregnancy) as a result of hyperplasia of the lactotroph cells stimulated by placenta-produced estrogens (Elster *et al.* 1991; Scheithauer *et al.* 1990).

Although the etiology of pituitary apoplexy due to pituitary adenoma is not fully understood, various precipitating factors, such as an anticoagulated state, head trauma, dopamine agonist treatment, and endocrine stimulation tests, have been suggested (Semple *et al.* 2007). Our case was caused by hemorrhagic infarction derived from a pre-existing, nonfunctioning pituitary adenoma confirmed by pathological examination and consistent with no symptoms of amenorrhea or galactorrhea before pregnancy. It is likely that the increase in internal estrogen production and water volume during pregnancy led to hemorrhagic infarction or bleeding from fragile tumor vessels of the adenoma. The fact that only some macroprolactinomas show visual disturbance during pregnancy (Imran *et al.* 2007) suggests a much higher incidence of asymptomatic or subclinical pituitary apoplexy.

Treatment options for pituitary apoplexy consist of correction of the hormonal deficiency, close surveillance of the patient status, and transsphenoidal decompressive surgery. In general, conservative therapy for pituitary apoplexy can be acceptable only for selected patients whose symptoms are mild and can be controlled by hormonal and electrolytic correction (Maccagnan *et al.* 1995). Prolactin (PRL) stabilization by dopamine agonists for pregnant women with prolactinoma manifesting visual deficiency is preferred as

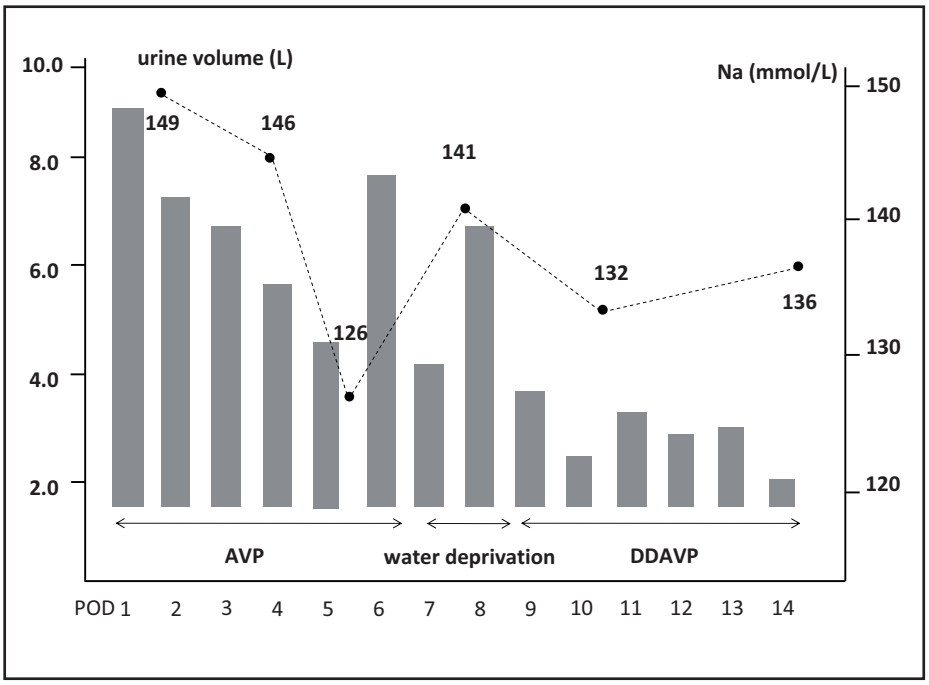

Fig. 3. Graph showing postoperative course of urine volume (columns) and serum sodium. Abbreviations: AVP, arginine vasopressin; DDAVP, 1-desamino-8-D-arginine vasopressin; POD, postoperative day.

long as the clinical symptoms and laboratory data are not severe. However, cases with sudden, remarkable clinical deterioration require emergent neurosurgical intervention (Imran *et al.* 2007). This is in agreement with previous studies that have established transsphenoidal decompressive surgery as the treatment of first choice for symptomatic pituitary apoplexy (Verrees *et al.* 2004). It is also reported that surgical intervention within the first 8 days after pituitary apoplexy improves clinical outcome regarding both visual impairment and pituitary dysfunction (Randeva *et al.* 1999). Moreover, transsphenoidal surgery under general anesthesia does not appear to present teratogenic risk to the fetus (Czeizel *et al.* 1998). According to the previous reports, 12 women who underwent decompressive pituitary surgery appeared to have good outcomes in terms of symptoms and deliveries (Table 1), suggesting that pituitary surgery for pregnant women with symptomatic pituitary apoplexy is a feasible option.

DI and electrolyte abnormalities are common complications of pituitary surgery (18–75%) (Nemergut *et al.* 2005). In addition to postoperative dysfunction of vasopressin secretion, the condition called gestational diabetes insipidus (GDI) has been reported as a rare complication (up to 1 in 30,000 pregnancies). It is associated with activated placental vasopressinase secretion that can degrade AVP and oxytocin but not DDAVP (Iwasaki *et al.* 1991; Ananthakrishnan 2009). The level of this enzyme increases 1,000-fold in the third trimester, although the plasma levels of AVP are similar to nonpregnant levels (Gordge *et al.* 1995; Lindheimer & Davison 1995). To date, only 3 cases out of 15 reported cases of pituitary apoplexy during pregnancy developed DI, all of which were controlled not by AVP but by DDAVP, although no explanation for this was offered (de Heide *et al.* 2004; Krull *et al.* 2010; Ohtsubo *et al.* 1991). Taking into consideration vasopressinase secretion during pregnancy, the use of DDAVP to treat pregnant women with postoperative DI seems a more reasonable strategy than treatment with AVP.

CONCLUSION

Here, we report the case of a pregnant woman with pituitary apoplexy caused by a pre-existing, nonfunctioning pituitary adenoma successfully treated by transsphenoidal decompression. Postoperative DI might be associated with vasopressinase secretion, which can be controlled by DDAVP.

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