Transsphenoidal surgery for a life-threatening prolactinoma apoplexy during pregnancy

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Abstract

Prolactinoma is the most common secreting pituitary adenoma. It is typically diagnosed in women of reproductive age and is common cause of infertility. Currently the treatment of choice is pharmacotherapy with dopamine agonists, whereas surgical treatment is reserved for a selected group of patients. Pituitary-tumor apoplexy is a rare, life-threatening condition associated with significant morbidity and mortality.

The authors present the case of a 25-year-old woman with prolactinoma treated with dopamine agonist. In course of such a treatment the patient became pregnant. The bromocriptine was gradually withdrawn. In the 14th week of pregnancy she was admitted for symptoms suggesting pituitary tumor apoplexy. The treatment with bromocriptine was reinitiated. In the 20th week of pregnancy further deterioration of the patient's neurological condition and visual-field abnormalities were observed. The patient was qualified for surgical treatment – selective transsphenoidal adenomectomy. The successful surgery led to improvement of neurological condition. The early postoperative PRL level decreased significantly and hormonal function of the pituitary was preserved. The pregnancy ended in 38th week with a caesarean section. Endocrinological evaluation conducted after the uneventful delivery confirmed normal function of the pituitary. Magnetic resonance imaging (MRI) did not reveal tumor re-growth. The patient is kept under constant medical care.

In this case study the authors discussed therapeutic management and reviewed literature regarding gestational pituitary-tumor apoplexy with particular emphasis on surgical treatment.

CASE REPORT

Abbreviations:

ACTH	- adrenocorticotrophic hormone
α-SU	- alpha subunit
b.i.d.	- bis in die (twice daily)
FSH	- follicle-stimulating hormone
GH	- growth hormone
LH	- luteinizing hormone
MRI	- magnetic resonance imaging
PRL	- prolactin
t.i.d.	- ter in die (three times daily)
TSH	- thyroid-stimulating hormone
TSS	- transsphenoidal surgery

INTRODUCTION

Prolactinoma is the most common type of secretory pituitary tumor. Tumor-induced hyperprolactinemia leads to oligo/amenorrhea, galactorrhea and infertility. In some cases expanding macroprolactinomas cause neurological symptoms resulting from "mass effect", such as headache, vomiting or visual disturbances. The treatment of choice for prolactinomas includes administration of dopamine agonists, such as bromocriptine or cabergoline. In 80–90% of cases pharmacological treatment normalizes serum prolactin levels, leading to restoration of regular menstrual cycles and fertility, and in case of pituitary macroadenomas dopamine agonists decrease tumor size and lead to regression of neurological symptoms and visual field abnormalities (Klibansky 2010; Melmed *et al.* 2011).

Indications for surgical treatment are limited and include: ineffectiveness of conservative treatment or inability to tolerate dopamine agonist therapy (Klibansky 2010; Melmed *et al.* 2011). Pituitary tumor apoplexy is a rare complication and one of few emergency states that is considered a life-threatening conditions. Particular risk is associated with hemorrhage into the pituitary tumor or its surrounding structures that occurs during pregnancy (Biousse *et al.* 2001; Ginath & Golan 2010; Rajasekaran *et al.* 2011). Due to advances in diagnostics and treatment of pituitary tumors, principles of monitoring pregnancy in women with pituitary adenomas, including complicated cases of prolactinoma with hemorrhagic tumor apoplexy, become more and more important issue

Pituitary apoplexy results from spontaneous bleeding within preexisting pituitary adenoma (hemorrhagic apoplexy) or from its ischemic necrosis. Most common symptoms of pituitary apoplexy include headache, nausea, vomiting, visual-field abnormalities, ophtalmoplegia and loss of consciousness, as well as symptoms resulting from acute pituitary insufficiency (Biousse *et al.* 2001; Ginath & Golan 2010; Rajasekaran *et al.* 2011).

The aim of this study is to report the case of a pregnant woman with macroprolactinoma diagnosed before pregnancy. The decision to remove pituitary tumor through transsphenoidal approach in 20th week of pregnancy was made due to occurrence of hemorrhagic pituitary-tumor apoplexy, resulting in neurological complications and possibility of life-threatening acute pituitary failure.

CASE REPORT

25-year-old woman was admitted to the Department of Endocrinology in October 2007. Earlier, since the beginning of 2005 she had symptoms of oligomenorrhea and finally amenorrhea. Due to weight gain, hirsutism and acne she had been diagnosed towards polycystic ovary syndrome. Despite negative result of progesterone test, the patient did not undergo any further hormonal assessment. In September 2007 the patient underwent outpatient prolactin measurement which revealed serum prolactin concentration as high as 270 μg/l (normal value: <25 μg/l).

Magnetic resonance imaging (MRI) revealed a sellar mass (16 mm × 12 mm × 14 mm) compressing and displacing optic chiasm, which was not enhanced after intravenous contrast agent, thus allowing identification of macroprolactinoma. Completion of diagnostic procedures and confirmation of normal thyreo- and corticotrophic pituitary function was followed by initiation of treatment with bromocriptine in the dose of 2.5 mg t.i.d. In Nov. 2007 (after 4 weeks of dopamine agonist treatment) the first menstruation re-occurred, followed by restoration of regular menses. MRI examination performed in Feb. 2008 revealed decrease in pituitary tumor size. Simultaneously, the resolution of hyperprolactinemia as well as correct thyreo- and corticotropic pituitary function was confirmed. Further assessment of the pituitary-gonadal axis demonstrated normal FSH/LH and estradiol levels and progesterone concentration typical for luteal phase which confirmed ovulation. Yet the expected menstrual cycle did not occur in Feb. 2008. Pregnancy test yielded positive result. The detailed clinical course, MRI results and results of hormonal assays are shown in Table 1.

After confirmation of pregnancy in ultrasonography examination, in accordance with the adopted agreements we began to gradually reduce bromocriptine dose until its complete discontinuation (Klibansky 2010; Melmed *et al.* 2011). The patient did not report any complaints and the course of early pregnancy was normal. Follow-up examinations revealed gradual increase in prolactin levels, but measurement results were within the limits typical for pregnancy.

In 14th week of pregnancy the patient reported worsening of her general condition, headaches, dizziness and visual abnormalities. MRI revealed features of tumor enlargement with optic chiasm displacement and focal hemorrhage within the tumor. Serum PRL concentration increased to the value of 263 μg/l. Due to the risk of acute pituitary failure as well as further tumor enlargement, the patient was administered hydrocortisone 200 mg i.v. and then orally in the dose of 40 mg/24h (20 mg-10 mg-10 mg). Bromocriptine

was reinitiated in the dose of 3.75 mg/24h resulting in rapid decrease of serum prolactin to upper limits of referral range (see Table 1). Consulting gynecologist recommended administration of tocolytic treatment, which included werapamil (40 mg b.i.d.) and fenoterol (5 mg b.i.d.).

Despite initiation of the above treatment the patient complained of persistent headaches and further visual impairment. Therefore in 19th week of pregnancy, she was consulted by neurosurgeon and referred to the Department of Neurosurgery. On admission the patient was conscious and well-oriented. The visual

Tab. 1. Clinical picture with detailed results of hormonal measurements.

Date	Results of hormonal measurements and MRI	Clinical course and treatment
01/2005-09/2007	Serum prolactin level (09.2007): 270 µg/l (normal value: <25 µg/l /ml).	Oligo/amenorrhea since 01/2005, hirsutism and acne since 11/2005. 10 kg weight gain; headaches since 2006. No visual disturbances. Height: 170cm; body weight: 65–75 kg; BMI: 22.5–26 kg/m^2
10/2007	TSH: 1.7 µIU /ml; fT4: 15.6 pmol/l; cortisol: 14.2 µg/dl; MRI showed pituitary macroadenoma (16x12x14 mm) compressing and displacing optic chiasm.	Initiation of bromocriptine treatment – (Bromergon) 2.5 mg t.i.d.; No necessity of hydrocortisone or L-thyroxin replacement.
11/2007	Serum PRL level (11.2007): 2.9 µg/l	Improved clinical condition. Decreased body weight. Regular menses re-occurred 4 weeks after treatment initiation. Weight: 72 kg
02/2008	PRL:1.94µg/l; FSH:1.17IU/l; LH:0.39IU/l; E_2:162 pg/ml; Progesteron: 17.7ng/ml; TSH: 0.82 µIU /ml; fT4: 13.9 pmol/l; cortisol: 9.6 µg/dl; S-DHEA: 2348 ng/ml (results typical for the luteal phase of the cycle). MRI revealed a heterogenous intrasellar mass (10x11x10 mm) without contrast media enhancement - shrinkage of the pituitary macroadenoma.	Further improvement of clinical condition. Subsidence of headaches. Bromocriptine 2.5 mg t.i.d. The expected menstruation did not occur in Feb. 2008. Positive result of pregnancy test.
03/2008	PRL: 41.7µg/l; TSH: 0.43 µIU /ml; fT4: 15.6 pmol/l;	Pregnancy confirmed in ultrasound examination. Gradual decrease of bromocriptine: the dose reduced to 1.25 and 0.625 mg/24 h. The medication was withdrawn in 03/2008.
04/2008	PRL: 141µg/l (02.04.2008) – 11th week of pregnancy. PRL: 263 µg/l (24.04.2008) – 14th week of pregnancy. MRI (without contrast media): enlargement of the pituitary adenoma (19×15×16 mm) - large hyperintensive intra- and suprasellar mass suggesting hemorrhage within a pituitary tumor with compressing the optic chiasm. PRL: 28.3 µg/l (30.04.2008) – 15th week of pregnancy (after bromocriptine); TSH: 0.297 µIU /ml; fT4: 16.4 pmol/l Cortisol: 17.3 µg/dl (on hydrocortisone treatment, 16 hours after the last dose);	In 11th week of pregnancy the patient reported no complaints. In 14/15th week of pregnancy: headaches and visual abnormalities. Following diagnosis of pituitary tumor apoplexy hydrocortisone 200 mg i.v. was administered followed by 40 mg/24h p.o. (20 mg-10 mg-10 mg). Bromocriptine was re-initiated in the dose of 3.75 mg/24h (1/2-0-1 tablet). Fenoterol 5 mg b.i.d. and verapamil 40 mg b.i.d. were introduced
05/2008	PRL: 111 µg/l	Persistent headaches, further visual field impairment. Bromocriptine dose was increased to 2.5 mg b.i.d. Oral hydrocortisone was maintained. Following the neurosurgical consultation the patient was referred to Dept. of Neurosurgery for surgical treatment.
06/2008	Preoperative tests: PRL: 98.7 µg/l; Preoperative MRI showed progression of the preexisting pituitary mass with optic chiasm compression; Postoperative tests: PRL (1st day after surgery) :1.4 µg/l; 7th day: PRL: 18.2 µg/l; TSH: 1.11 µIU /ml; fT4: 15.3 pmol/l; cortisol: 17.0 µg/dl; Early postoperative MRI revealed no residual pituitary adenoma.	Surgery without complications; Improvement in general and neurological condition. The patient was discharged on the 7th postoperative day.
09/2008	PRL: 31.0 µg/l; TSH: 0.54 µIU /ml; fT4: 13.0 pmol/l; cortisol: 29.2 µg/dl	Uneventful further course of pregnancy.
10/2008	PRL: 45.1 µg/l (1st day before delivery) PRL: 41.6 µg/l TSH: 1.68 µIU /ml; fT4: 11.0 pmol/l; cortisol: 30.8 µg/dl (1st day after delivery) MRI (1st day after delivery): no signs of residual pituitary adenoma.	Caesarean section performed at 38 weeks in the Department of Obstetrics and Gynecology. Delivery and puerperium without complications. Initiation of breast-feeding.
03/2010	PRL: 2.78 µg/l; TSH: 0.7 µIU /ml; fT4: 16.0 pmol/l; cortisol: 15.2 µg/dl; FSH: 4.85 IU/l; LH: 2.28 IU/l; E_2: 77.6 pg/ml; S-DHEA: 2450 ng/ml; progesterone: 12.1 ng/ml (II phase of the cycle) Follow-up MRI depicted secondary (postoperative) empty sella. Small pituitary gland (isointensive) is located on the right side of the enlarged sella. On the left side of the herniation of the suprasellar subarachnoid cistern through a widely opened diaphragm is visible. The pituitary infundibulum maintains a midline position. No tumor recurrence is noted.	After the restoration of regular menses and the end of lactation, normal thyreo-, cortico- and gonadotroph function of the pituitary was confirmed.

prolactin (range: 1,9-25,0 µg/l); cortisol (range: 5-25 µg/dl) FSH: (range: follicular phase: 2.8-11.3 IU/l, luteal phase: 1.2-9 IU/l); LH: (range: follicular phase: 1.1-11.6 IU/l, luteal phase: 0-14.7 IU/l); estradiol: (range: follicular phase: 0-160pg/ml; luteal phase: 27-246 pg/ml); progesteron: (range: follicular phase: 0.3-2; luteal phase: 1.2-21ng/ml); TSH: (range: 0.4-4 µIU /ml; fT4: (range: 11.5-22.7pmol/l), in the presented case of female patient born in 1982, with pituitary apoplexy during pregnancy.
BP - blood pressure; MRI - magnetic resonance imaging; BMI - body mass index

acuity was decreased to 0.8 whereas visual field testing showed bilateral temporal field restriction. The optic discs were normal. Apart from the headaches and visual impairment, neurological examination did not reveal symptoms of increased intracranial pressure.

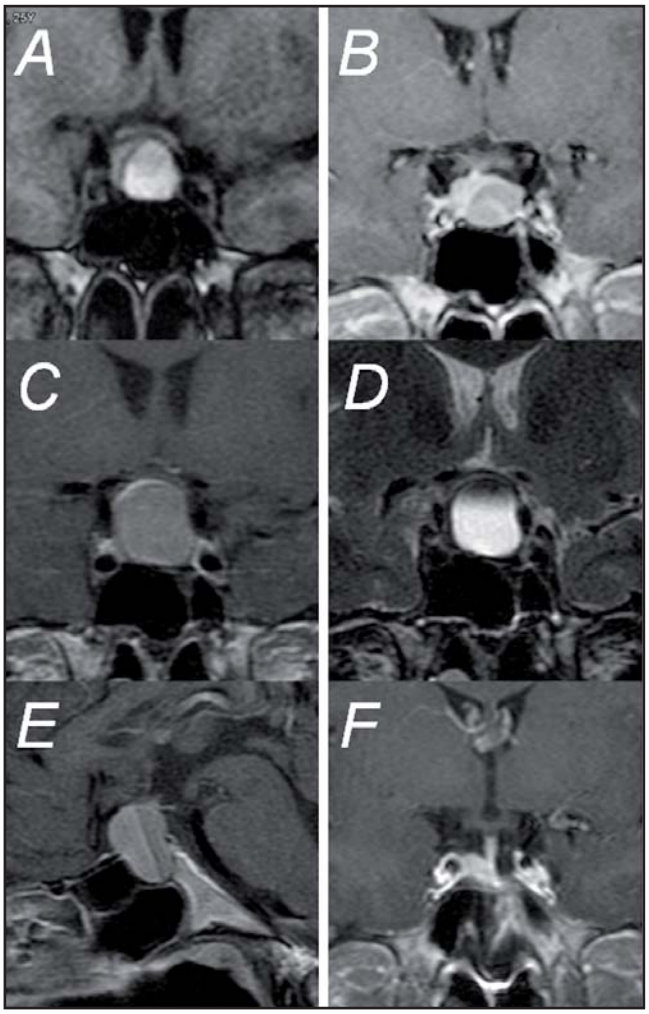


Fig. 1. MRI scans of the pituitary tumor in the presented patient (October 2007 – March 2010). **A** – initial MRI scans showing intra- and suprasellar pituitary adenoma (16x12x14 mm) compressing and displacing optic chiasm (coronal T1-weighted scans).
B – tumor shrinkage after treatment with bromocriptine shortly before pregnancy (coronal T1-weighted scans)
C,D,E – MRI images of pituitary-tumor apoplexy: Preoperative MRI (20th week of pregnancy) presenting enlargement of the preexisting pituitary mass (19×15×16 mm) - large hypointensive (Fig. 1C - coronal T1-weighted image) and hyperintensive (Fig 2D - coronal T2-weighted scan) intra- and suprasellar mass suggesting hemorrhage within a pituitary tumor, compressing the optic chiasm and displacing both cavernous carotid arteries. Note the hyperintensive area on Fig. 1E presenting subacute hemorrhage (sagittal T1-weighted MRI). **F** – Postoperative, follow-up MRI scan (2 years after surgery) depicted secondary (postoperative) empty sella. Small, isointensive pituitary gland is located on the right side of the enlarged sella. On the left side herniation of the suprasellar subarachnoid cistern through a widely opened diaphragm is visible. The pituitary infundibulum maintains a midline position. No tumor recurrence is noted (coronal T1-weighted scans).

The patient was qualified for neurosurgical treatment. The surgery was performed in 20th week of pregnancy in the Department of Neurosurgery. She was operated on under general anesthesia with constant cardiotocography monitoring. The patient underwent a transseptal, transsphenoidal exploration of the pituitary region. Intrasellar and suprasellar hematoma was debulked and the mass of necrotic pituitary macroadenoma was totally excised. There were no intra-operative complications. Post-operative period was uneventful. Complete recovery of the visual acuity and visual field was observed. There were no signs of diabetes insipidus and fluid-electrolyte disturbances. Serum prolactin level on the 1st day after surgery was as low as 1.4 μg/l. The patient was discharged on 7th postoperative day on hydrocortisone replacement (in a dose of 30 mg/24h) until the further assessment of the pituitary-adrenal axis function. Treatment with bromocriptine was discontinued.

The next hormonal assessment of pituitary function after surgery was performed on the 8th postoperative day in the Department of Endocrinology. It confirmed normal thyreo- and gonadotroph function as well as normalization of serum PRL level. Histopathological, immunohistochemical and ultrastructural examination confirmed presence of sparsely granulated lactothroph pituitary adenoma (atypical subtype): GH(–), PRL(+), ACTH(–), TSH(–), FSH(–), LH(–), α-SU(–), MIB-1>3%; (Figures 2–4).

The further course of pregnancy was uneventful. The pregnancy ended in 38th week with a caesarean section. A healthy daughter was born (weight: 3310 g; height: 57 cm; with an Apgar score of 10). There were no complications in the puerperium period. The patient started nursing, which she carried on for a period of 18 months.

MRI of the pituitary performed shortly after delivery revealed no residual pituitary adenoma and the gland normally divided into anterior and posterior lobes. Hormonal measurements including serum cortisol level were within normal laboratory range (see Table 1), which allowed to withdraw hydrocortisone replacement.

MRI examination was repeated 6 and 18 months after the surgery, with no signs of tumor re-growth being observed. Since the delivery, pituitary function has been assessed every 6 months. Prolactin concentration remains within normal limits. The patient did not require neither hydrocortisone nor L-thyroxine replacement therapy.

DISCUSSION

The presented case is an example of a rare and at the same time very difficult clinical situation. Whereas advances in diagnostics and treatment of prolactin-secreting pituitary tumors facilitate more frequent induction of pregnancy in patients with prolactinoma,

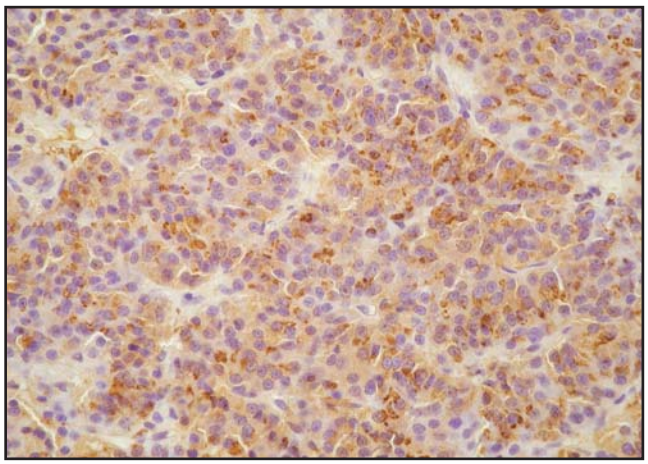
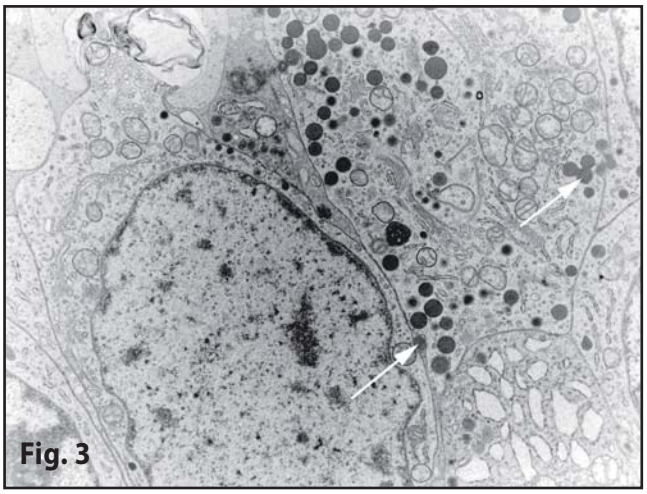
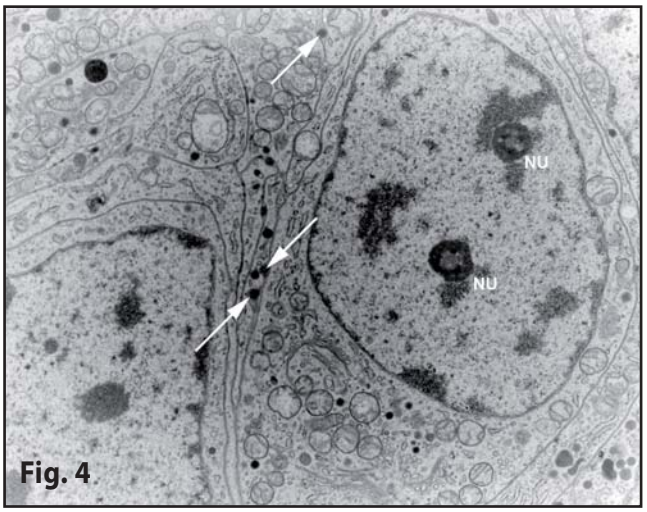


Fig. 2. Immunohistochemical localization of prolactin in sparsely-granulated lactothroph adenoma. Original magnification 400×.





Figs. 3 and 4. Ultrastructure of sparsely granulated lactothroph adenoma. Misplaced exocytosis of PRL-secretory granules (arrows); large nuclei with prominent nucleoli (NU). Original magnification 4800×.

gestational pituitary-tumor apoplexy is considered a very rare complication (Ginath & Golan 2010; de Heide *et al.* 2004; Okafor *et al.* 2009; Rajasekaran *et al.* 2011). Clinical practice and available recommendations issued by scientific societies suggest that patients with prolactinoma who have become pregnant should discontinue dopamine agonists (Klibansky 2010; Melmed *et al.* 2011). The risk of clinically significant enlargement of microprolactinoma in pregnancy is rather low. Therefore there is no need to perform neither routine MRI nor serum prolactin measurements. One should remember that PRL level during normal pregnancy may increase as many as 10 times and may reach concentration of even more than 300 μg/l (Klibansky 2010; Melmed *et al.* 2011).

In case of prolactin-secreting pituitary macroadenomas the situation is more complex. It is recommended to appropriately prepare a given female patient for pregnancy in order to achieve the greatest possible shrinkage of tumor volume. Estradiol levels which tend to increase during pregnancy are associated with the risk of further enlargement of initially large prolactin-secreting tumors. If conservative treatment with dopamine agonist (either bromocriptine or cabergoline) does not lead to distinct reduction of tumor size it is recommended to perform pre-pregnancy debulking surgery. However, if a patient becomes pregnant despite presence of a large pituitary tumor, then it is recommended to perform a visual field test once every trimester. In case of deterioration or occurrence of neurological symptoms, it is necessary to perform an MRI visualization of pituitary and – if necessary – to re-introduce treatment with a dopamine agonist (Klibansky 2010; Melmed *et al.* 2011).

In the presented case, the patient became pregnant as early as 3 months after starting dopamine agonist treatment. It facilitated achievement of PRL level normalization and return of regular menses. The partial decrease in tumor size was also achieved. Based on available recommendations, bromocriptine treatment was gradually discontinued (Klibansky 2010; Melmed *et al.* 2011). The dopamine-agonist was re-introduced in 14th week of pregnancy due to neurological symptoms, particularly visual impairment. The single-phase MRI examination confirmed features of hemorrhagic apoplexy of the pituitary tumor. However, despite decrease in serum prolactin level and administration of glucocorticosteroids it was not possible to achieve neurological improvement which necessitated search for other therapeutic options.

As it was already mentioned, hemorrhagic apoplexy of the pituitary tumor is considered an endocrine emergency (Biousse *et al.* 2001; de Heide *et al.* 2004; Rajasekaran *et al.* 2011). However – according to literature data and our own experience – occurrence of the pituitary apoplexy cannot be predicted. The condition may occur in both sexes and at any age. According to Biousee *et al.* (2001) it cannot be ruled out that rare cases of apoplexy within pituitary tumors

(in particular prolactinoma) occurring in pregnancy are associated with stimulating effect of endogenous estrogens and – on the other hand – with discontinuation of dopamine agonist treatment which inhibits tumor enlargement. It is possible that simultaneous effect of a strong stimulating factor together with discontinuation of an effective drug are conducive of tumor apoplexy occurrence (Biousse *et al.* 2001). This was also the case in the presented patient.

Surgical treatment of pituitary tumors during pregnancy is difficult and associated with worse prognosis both for the mother and the child, particularly in case of emergency surgeries. Brodsky *et al.* (1980) observed a 1.5-fold increase in risk of miscarriage if the surgery is performed in the 1st trimester and even 5-fold increase if the surgery is performed in the 2nd trimester (Brodsky *et al.* 1980). Risk for the mother may be associated with possible occurrence of iatrogenic pituitary failure, including diabetes insipidus and irreversible vision loss. Belchetz *et al.* (1986) report their experience with sudden expansion and re-growth of prolactin-secreting tumor after performing debulking surgery for prolactinoma in a pregnant woman (Belchetz et al.1986).

Okafor *et al.* (2009) describe the case of a pregnant woman with macroprolactinoma in advanced pregnancy. Shortly after giving birth by caesarean section in 33rd week followed by initiation of conservative treatment with bromocriptine there occurred sudden deterioration of the patient's general condition, hypertensive crisis, cardiac arrest and death of the patient, most probably in the course of pituitary apoplexy (Okafor *et al.* 2009).

Gondim *et al.* (2003) achieved complete recovery of a pregnant patient with microprolactinoma complicated with hemorrhage into the tumor during the third trimester of pregnancy following a transsphenoidal removal of hematoma in the sellar region. In 39th week of gestation the patient spontaneously delivered a healthy newborn (Gondim *et al.* 2003).

Also in the presented case we managed to achieve complete success of the transsphenoidal procedure. The decision to perform surgery was made only after conservative treatment with dopamine agonist proved ineffective and after careful preparation of the patient. This included initiation of tocolytic treatment, antithrombotic prophylaxis and administration of glucocorticosteroids, displaying anti-edematous action and protecting against possible acute pituitary insufficiency. Permanent endocrinological care and periodic assessment of cortico- and thyreotropic pituitary function provided safe pregnancy course and fortunate delivery. Thus, the described case was managed in accordance with later recommendations included in *Pituitary Apoplexy Guidelines Development Group* (2010), which emphasize the fact, that the surgery should be performed in maximally stable state and in a center with substantial experience in performing surgical procedures of pituitary tumors (Rajasekaran *et al.* 2011).

However one should remember, that due to substantial risk of recurrence of PRL-secreting pituitary tumors even many years after the surgery, the patient will require prolonged endocrinological follow-up, including hormonal assessments and MRI of the pituitary (Klibansky 2010; Melmed *et al.* 2011).

We are convinced that transsphenoidal removal of macroprolactinoma complicated with hemorrhagic apoplexy performed in the described case was a life-saving procedure both for the mother and the child. Excellent collaboration between endocrinological and neurosurgical teams further contributed to the final success achieved in the treatment of this rare and dramatic complication of pregnancy, i.e. hemorrhagic apoplexy of pituitary tumor.

SUMMARY

The presented case demonstrates that transsphenoidal selective adenomectomy performed after appropriate preparation and stabilization of patient's condition may be regarded as a safe and valuable treatment method of hemorrhagic apoplexy of pituitary tumor occurring during pregnancy.

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Written consent of the patient for presentation and publication of her clinical case was obtained.

REFERENCES

1 Belchetz PE, Carty A, Clearkin LG, Davis JC, Jeffreys RV, Rae PG (1986). Failure of prophylactic surgery to avert massive pituitary expansion in pregnancy. Clin Endocrinol **25**: 325–30.
2 Biousse V, Newman NJ, Oyesiku NM (2001). Precipitating factors in pituitary apoplexy. J Neurol Neurosurg Psychiatry. **71**: 542–545.
3 Brodsky JB, Cohen EN, Brown BW Jr, Wu ML, Whitcher C (1980) Surgery during pregnancy and fetal outcome. Am J Obstet Gynecol **138**: 1165–7.
4 Ginath S, Golan A (2010) Gestational pituitary – tumor apoplexy. N Engl J Med. **363**(7): e10.
5 Gondim J, Ramos F Jr, Pinheiro I, Schops M, Tella OL Jr (2003). Minimal invasive pituitary surgery in a hemorrhagic necrosis of an adenomaduring pregnancy. Minim Invasive Neurosurg. **46**(3): 173–6.
6 de Heide LJ, van Tol KM, Doorenbos B (2004). Pituitary apoplexy presenting during pregnancy. Neth J Med. **62**(10): 393–396.
7 Klibansky A (2010). Prolactinomas. N Engl J Med. **362**(13): 1219–1226.
8 Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA, Wass JAH (2011). Diagnosis and treatment of hyperprolactinemia: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. **96**(2): 273–288.
9 Okafor UV, Onwuekwe IO, Ezegwui HU (2009) Management of pituitary adenoma with mass effect in pregnancy: a case report. Cases J. **2**: 9117.
10 Rajasekaran S, Vanderpump M, Baldeweg S, Drake W, Reddy N, Lanyon M, *et al.* (2011). UK guidelines for the management of pituitary apoplexy. Pituitary Apoplexy Guidelines Development Group: May 2010. Clin Endocrinol. **74**: 9–20.