Clinics in Mother and Child Health
ISSN: 2090-7214

Jain D and Jain S, Clinics Mother Child Health
2015, 12:4
DOI: 10.4172/2090-7214.1000208

Case Report Open Access

Macroprolactinoma in Pregnancy-Successful Outcome and Follow Up

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Received date: July 23, 2015; **Accepted date:** November 6, 2015; **Published date:** November 14, 2015

Abstract

A 25 year old woman presenting with oligomenorrhoea was found to have a very high prolactin level. An MRI revealed a macroprolactinoma in the pitiutary gland. She was prescribed Cabergoline. However before the macroprolactinoma decreased in size she conceived. The patient was started with Cabergoline after the first trimester. She was observed with a careful history of headache, vomitings at each visit; periodic serum prolactin levels and visual field examinations. She had an uneventful course during pregnancy and delivered a healthy male baby. Cabergoline was stopped after delivery and she lactated the baby for six months. However she reported symptoms of head ache and an MRI diagnosed an expansion of the adenoma. Thereafter cabergoline was begun again and lactation was stopped in the interest of the mother. In this case cabergoline has been used to prevent tumour expansion in pregnancy and was found to be a safer, tolerable substitute to bromocryptine.

Keywords: Macroprolactinoma; Cabergoline; Magnetic resonance imaging (MRI); Thyroid stimulating hormone (TSH)

Introduction

With the advent of dopamine agonists for treatment of hyperprolactinemia, more number of women are presenting with macroprolactinoma in pregnancy. The tumour cells have estrogens receptors, and during pregnancy as the estrogens levels increase there occurs lactotroph cell hyperplasia resulting in increase in the tumour mass with grave consequences [1]. In case of macroprolactinoma, symptomatic tumour enlargement has been found to occur in 20-30% cases [2]. Bromocryptine has extensively been used in women with prolactinoma in pregnancy. In this case cabergoline was used to keep the tumour volume in check with a favourable maternal and fetal outcome.

Case Report

A 25 year old woman presented on Oct 13, 2012 with irregular cycles for last 2-3 years. Her menarche began at 13 years of age and now she was having periods every 2-3 months and the blood flow was scanty. On examination the girl was 5 feet 3 inches tall, she weighed 64 kg and her body mass index was 25. There was no acne or facial hair. There was no history of headache or giddyness. She was given medroxy progesterone acetate 10 mg once daily for five days and called on day 2 of the onset of menses. The girl reported on day 2 and a minimal investigative work up was done.

In view of the very high prolactin level of 476 .0 ng/ml, a magnetic resonance imaging was performed.

MRI revealed a well defined homogeneous lesion in sella on left side appearing hypo intense on TIW and mildly hyper intense on T2W images. The lesion measured 8 mm × 11 mm × 10 mm in size. No supra sellar extension of the lesion was seen. The pituitary stalk was deviated to the right (Figure 1).

Impression: MRI shows a homogenously homogenous lesion in sella likely to be a pituitary macro adenoma.

Diagnosis: A history of oligo menorrhoea with a very high prolactin level and a macro adenoma in the pituitary gland confirmed the diagnosis of a macroprolactinoma of the pituitary gland.

Name of test	Patient value	Normal range
Luteinising hormone	3.32 miu /ml	1.90-12.50 miu/ml
Follicle stimulating hormone	10.62 miu/ml	2.50-10.20 miu/ml
Thyroid stimulating hormone	1.91 miu/ml	0.35-5.50 miu/ml
Serum prolactin	476.0 ng/ml	2.80-29.20 ng/ml
Blood sugar fasting	80.25 mg/dl	Up to 110 mg/dl

Table 1: Patient report.

Treatment

The patient was started with cabergoline 0.5 mg twice a week along with a calcium and vitamin D supplement on Oct 27, 2012.

On Dec 8, 2012 , her serum prolactin level decreased to 55.74 ng/ml, and TSH was 2.26 miu/ml. An MRI done on February 2, 2013 showed no significant reduction in the size of the adenoma. She was continued on the same dose of Cabergoline and reported on March 3, 2013. She now had got married and was having regular menses with heavy blood flow and her serum prolactin level was 43.10 ng/ml. She was advised to avoid pregnancy till her prolactin become normal and an MRI showed reduction in size of the macro adenoma.

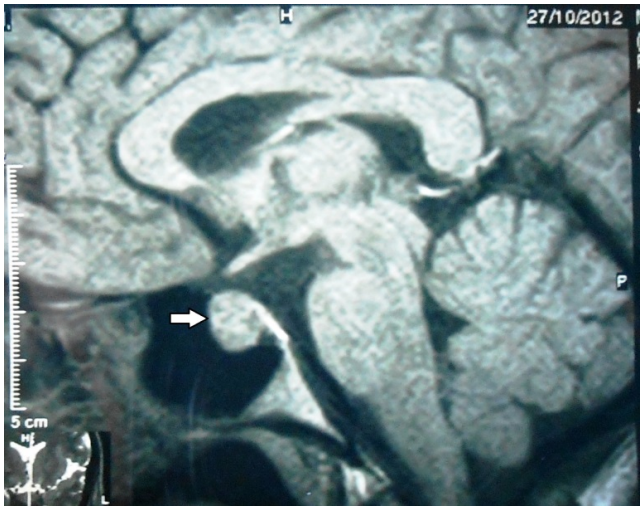

Figure 1: T1W sagittal image showing bulky pituitary gland with bulging superior border.

However she came on April 8, 2013 with 5 weeks amenorrhoea and a positive pregnancy test. The patient was counselled regarding the grave risk of expansion of prolactinoma in pregnancy; however she wished to continue the pregnancy. An MRI review of the earlier images showed that the prolactinoma was intrasellar and away from the optic chiasma and hence cabergoline was stopped . Investigations done revealed a TSH value 1.88 miu/ml, serum prolactin level 41.64 ng/ml and blood sugar by O, Sullivan glucose challenge test was 137 mg%. She was normotensive. A visual field examination was done which was normal and was repeated every month. The patient was asked to report in case of severe headache or vomiting.

Cabergoline was restarted at 14 weeks in a dose of 0.25 mg per week.An anomaly scan at 14 weeks and 19 weeks revealed no anomaly. She remained normotensive, normoglycemic throughout pregnancy. Her thyroid stimulating hormone remained below 5 miu/ml on repeat testing. Periodically performed visual field testing revealed no field defects. The serum prolactin level increased as the pregnancy advanced and the dose of cabergoline was enhanced gradually at each visit trying to keep serum prolactin level just above 100 ng/ml.

Date	Patient value	Weeks of pregnancy	Dose of cabergoline
April 10, 2013	41.60 ng/ml	5 + weeks	none
June 14 , 2013		14 weeks	Started 0.25 weekly
July 31, 2013	135.50 ng/ml	21 weeks	On cabergoline 0.25 weekly
Sept 7, 2013	168.0 ng/ml	26 weeks	cabergoline increased to 0.25 mg twice a week
Oct 26, 2013	212 ng/ml	32 weeks	cabergoline dose enhanced to 0.5 mg twice a week
Nov 11, 2013	102 ng/ml	37 weeks	Continued on cabergolin 0.5 twice weekly

Table 2: Serial serum prolactin values in pregnancy.

She went into spontaneous labour at 39 weeks. The woman delivered normally and a healthy male baby weighing 3 kg was delivered with a good apgar score .The baby was examined and had no anomalies. An echocardiography was done on the baby which revealed a normal heart.

Follow up after Delivery

The woman was allowed to lactate and cabergoline was stopped. After about 6 months she reported severe headache and serum prolactin level was 256 ng/ml. An MRI revealed a macroprolactinoma of size 12 × 14 mm, larger than the size prior to pregnancy (Figure 2). Lactation was stopped abruptly and dopamine agonist started. The patient improved rapidly and is on follow up. In the next visit we plan to shift the patient from cabergoline to bromocryptine because of the risk of cardiac valvulopathy with long term use of cabergoline.

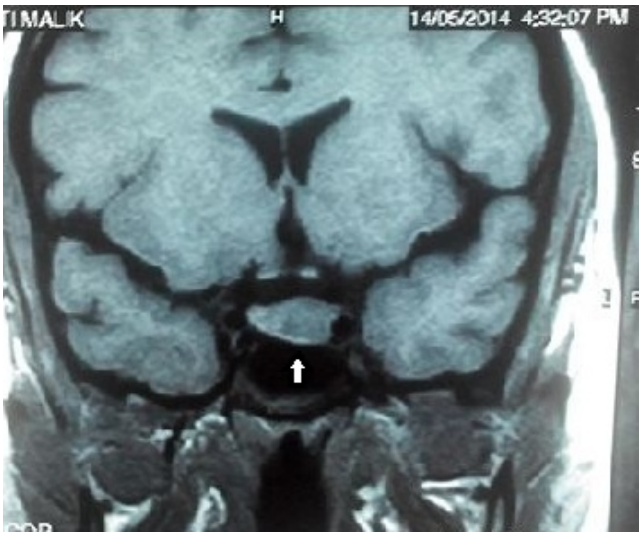

Figure 2: T1W coronal image of sella showing bulging left side of sella with a relatively hyperintense lesion in left side of sella – macroadenoma.

Discussion

The treatment of macroprolactinoma in pregnancy is very challenging because of the very high risk of tumour expansion and resulting visual loss and loss of pituitary function as well. Moreover at present there are no clear guidelines regarding management during pregnancy. Both bromocryptine and cabergoline have been used to restore fertility in prolactinoma. Some authors suggest stoppage of dopamine agonist with onset of pregnancy in case of intrasellar prolactinoma, followed by periodic visual field testing, careful history with recording of symptoms and MRI if headache or visual field disturbances occur. If MRI reveals increase in tumour volume then dopamine agonist should be urgently started [3]. In a report , a pregnant woman with a macroprolactinoma who was well controlled with bromocryptine, the drug was stopped as pregnancy was diagnosed on her. Around the twentieth week she presented with headache, visual loss and MRI showed pituitary apoplexy with compression of optic nerve and optic chiasma [4].

However in other studies dopamine agonist has been discontinued as pregnancy occurs and restarted after first trimester [12]. Bromocryptine is a time tested dopamine agonist used extensively in pregnancy. Among 6329 patients on bromocryptine the risk of spontaneous abortion was 9.9%, no greater than the general population [5]. In another study with women taking bromocryptine in early pregnancy the incidence of congenital malformations, abortions, ectopic pregnancy was not higher as compared with normal women [6].

However bromocryptine causes severe nausea and vomiting, which are common complaints in pregnancy and thus can cause aggravation of the same resulting in very poor tolerability. Bromocryptine has to be given two to three times daily. Cabergoline has a longer half life resulting in much less frequent dosing, just once or twice a week. The easy dosing schedule and fewer side effects of cabergoline as compared to bromocryptine was why cabergoline was used in this woman.

Here in this patient near normal prolactin levels were achieved with cabergoline when the patient conceived. Considering concerns regarding safety of cabergoline during first trimester , cabergoline was stopped as soon as her pregnancy test became positive. Moreover the stoppage of cabergoline was also considered because the macroadenoma was confined to the sella and well away from the optic chiasma. Cabergoline has a long half life and the beneficial effect lasts for about 3 months, during which time the organogenesis was completed. The drug was restarted at 14 weeks in a small dose. In one study where 350 pregnant women were given cabergoline during first trimester there was no significant difference in the incidence of neonatal malformations, spontaneous abortions or preterm delivery [7,8].

Till now there are a few published reports of serum prolactin levels in pregnancy for the dose titration of dopamine agonist when given in pregnancy [9]. This woman was given minimum possible dose of cabergoline to keep the serum prolactin level between 100 ng/ml-150 ng/ml .

Magnetic resonance imaging can be performed during pregnancy without gadolinium. However an MRI was not required in this woman as signs and symptoms of tumour enlargement were not evident at antenatal visits.

Two studies have demonstrated complete remission of hyperprolactinemia and macroprolactinoma following pregnancy in 64%-70% cases [10,11]. The mechanism behind this is not known but could be because of autoinfarction of the pituitary gland. Moreover there is no evidence to support enlargement of macroadenoma during breastfeeding owing to increased prolactin levels [11,12]. Contrary to this report , in our patient the prolactinoma expanded considerably during lactation, thus close supervision is absolutely necessary while the woman is breastfeeding.

Conclusion

When a woman with macroprolactinoma conceives, Cabergoline, a newer dopamine agonist can be given during pregnancy to maintain safe serum prolactin levels and may help in preventing expansion of the tumour, thus avoiding sudden catastrophe in terms of visual loss. Cabergoline was tolerated well, equally efficacious when compared to bromocryptine and had an excellent safety profile; as seen by the uneventful course during pregnancy and a favourable neonatal outcome.

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