CASE REPORT

Management of macroprolactinomas in Pregnancy- Report of two cases

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ABSTRACT

Management of a pregnant patient with prolactinoma is complex. The propensity for tumor growth under estrogenic stimulation of pregnancy and effects of therapy on fetal development are major concerns. Monitoring of these patients with regular prolactin assays is difficult due to elevations of prolactin seen during normal pregnancy and lactation. Many studies have reported a 20-30% risk of tumor progression during pregnancies in patients with macroprolactinoma. Based on these studies, regular field testing / imaging in these patients is advocated. Imaging studies are expensive and unpractical in Indian context. We report course of two successful pregnancies in patients with macroprolactinomas. Monitoring of these patients with prolactin levels and timely institution of bromocriptine therapy may be sufficient for managing pregnancy in these patients. Pituitary apoplexy could occur even when prolactin levels are maintained in the normal (for pregnancy) range with bromocriptine. [IJEM 2007;(3&4):35-37]

Key words- Macroprolactinoma, pregnancy, lactation, apoplexy, cabergolin, galactorrhea

INTRODUCTION

Management of a pregnant patient with prolactinoma is complex. The propensity for tumor growth under estrogenic stimulation of pregnancy and effects of therapy on fetal development are major concerns. Also, monitoring of these patients with regular prolactin assays is difficult due to elevations of prolactin seen during normal pregnancy and lactation. Many studies have reported a 20-30% risk of tumor progression during pregnancies in patients with macroprolactinoma(1,2,3,4,5). Based on these studies, regular field testing / imaging in these patients is advocated. Imaging studies are expensive and unpractical in Indian context. We report course of two successful pregnancies in patients with macroprolactinomas.

Case 1

This patient age 23 years, married for two years presented with complaints of galactorrhoea, irregular periods and infertility. Investigations revealed high prolactin levels(186.7ng/ml) and pituitary macroadenoma. Cabergoline initiation resulted in resumption of normal periods and a positive pregnancy test four months later. Therapy was stopped and patient was advised to follow up with monthly prolactin monitoring. Table 1 gives the prolactin levels throughout pregnancy and lactation. Bromocriptine was initiated only when prolactin levels rose to above 250ng/ml. Bromocriptine was stopped postdelivery, MRI done fourth month postpartum did not reveal any appreciable change in size of the pituitary tumor. She has been restarted on bromocriptine therapy.

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Table 1: Prolactin levels of patients 1 and 2 during pregnancy

PATIENT 1

Month of gestation	Prolactin levels (ng/ml)	Intervention
First	35.2	-
Second	81.3	-
Third	135.4	-
Fifth	302	Bromocriptine 2.5 mg
Sixth	208	-
Seventh	224	-
Eighth	307	-
Ninth	Delivered	-
First month lactation	145.6	-

PATIENT2

Month of gestation	Prolactin levels (ng/ml)	Intervention
Second	0.5	-
Fourth	23	-
Fifth	326	Bromocriptine 2.5
Sixth	160	-
Seventh	95	-
Ninth	124	-
First month lactation	252	-

Case 2

A 22 year old lady, married for two years presented with a history of secondary amenorrhoea and galactorrhoea for 10 months. Investigations revealed primary hypothyroidism and hyperprolactinemia (T4 - 0.54 (0.89-1.76 ng/dl), TSH - 42.7 mU/L (0.3 - 4 mU/L), serum prolactin - 472 ng/ml (6-29ng/ml). Hyperprolactinemia persisted even after attaining a euthyroid status. MRI sella revealed pituitary macroadenoma. The visual field charting was normal. A diagnosis of macroprolactinoma with primary hypo-thyroidism was made. She was prescribed Tab Cabgoline 0.5 mg twice a week and 50 micrograms of thyroxin daily. Contraception was advised. Patient had single menstrual period after one month of starting therapy followed by amenorrhoea next month. Preg colour test was found positive. Hormonal profile was (PRL < 0.5 ng/ml,T4= 8 (5.1 – 14 microg/dl) and TSH = 3.48 mU/L). Cabgoline was stopped and she was advised to continue on thyroxine 50 micrograms/day and she was advised to follow up with prolactin levels. 6 weeks later, she had severe headache from temples to occiput with altered consciousness. She was taken to a local hospital where she was given intravenous fluids. This headache subsided over two days. She was normotensive at this visit, prolactin levels were 23 ng/ml. Visual field charting was normal. Prolactin levels rose to 326 ng/ml next month when she was initiated on bromocriptine 2.5 mg/day. She was admitted to Gynecology in the second trimester (sixth month) with complaints of fever and headache. Prolactin levels were 160 ng/ml. MRI sella revealed intratumoral bleed. She was treated conservatively with intravenous fluids, head ache and fever improved. She delivered at 33 weeks, birth weight of the child was-2.28 kg. Normal lactation was established, post delivery MRI showed no change in the size of the tumor.

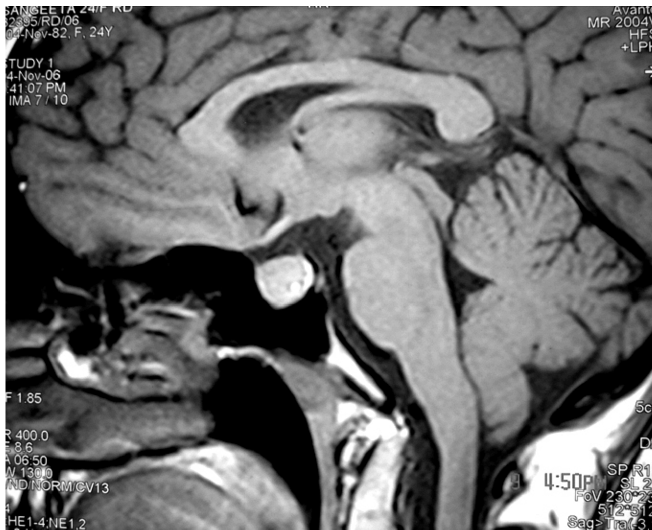

Figure 1: MRI of patient 2 showing intratumoral bleed

DISCUSSION

Prolactinomas are common pituitary tumors usually presenting as infertility in women. The impaired reproductive endocrine axis in these patients is mostly reversible with therapy. However, enlargement of tumor due to stimulatory effect of estrogens on lactotrophs is a major concern. A recent meta analysis has reported a 2.6% risk of symptomatic increase in size in microprolactinomas during pregnancy(6). In comparison, the risk of tumor progression during pregnancies for patients with macroprolactinoma is much higher, around 31%(1,2,3,4). Therefore, we advise contraception during treatment in patients with macroprolactinoma. Some patients, however, do not follow this advice and present with conception a few months after initiation of therapy.

Prolactin rises linearly throughout normal pregnancy reaching concentrations of 150 –200 ng/ml at term(7). Levels of prolactin reach as high as 60-70ng/ml during the first trimester, increasing to 100 ng/ml during the second trimester and peaking to 140-180 ng/ml during the third trimester(7,8,9). Prolactin levels remain high till upto six months postpartum with levels as high as 150 ng/ml in the first month of lactation. Based on the natural progression history of macroprolactinomas, it is generally agreed that routine visual field testing/imaging be undertaken in a patient with macroprolactinoma. In the Indian context however, routine repeated imaging is unpractical.

Given the tranplacental transfer of all the dopaminergic agents, stopping of medical therapy is recommended during pregnancy in patients with prolactinoma. In case of symptomatic enlargement, however, use of bromocriptine therapy is advocated with a greater experience and least incidence of side effects compared to other formulations. Cabergoline has also been found to be safe, but due to its use in a limited number of patients, its use is restricted to patients intolerant to bromocriptine. Data in about 350 cases of use of cabergoline during pregnancy has shown no increased risk of adverse effects on fetus such as spontaneous abortions, congenital malformations, multiple pregnancies or prematurity(10,11,12).

Our first patient was managed conservatively with monitoring of monthly prolactin levels. Bromocriptine was instituted only when serum prolactin levels rose to more than

250 ng/ml, levels more than in a normal pregnancy. MRI done postpregnancy did not reveal any appreciable change. In comparison, the second patient had a more dramatic course with pituitary apoplexy necessitating hospital admission. Pituitary apoplexy is a known complication related to the hypervascularity of pituitary gland during pregnancy. Lactation was successfully established in both patients.

In conclusion, it is possible to maintain prolactin in the normal range (for pregnancy) with bromocriptine therapy. Monitoring of these patients with prolactin levels and timely institution of bromocriptine therapy may be sufficient for managing pregnancy in these patients. Pituitary apoplexy could occur even when prolactin levels are maintained in the normal (for pregnancy) range with bromocriptine.

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