

Managing Prolactinoma during Pregnancy

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Received March 2010; Revised and accepted May 2010

Abstract

Objective: Prolactinomas are the most common pituitary tumors in pregnant women. We conducted this study on pregnant women with prolactinoma to determine their clinical symptoms and signs and eventual necessity to medical therapy.

Materials and methods: A descriptive study was performed on 85 pregnant women with prolactinoma. Patients were followed up by physical examination, imaging, and perimetry for diagnosis of visual field defect. If tumor was increased in size perimetry was performed in order to determine eventual visual field defect (VFD). Patients with progressive visual field defect had absolute indication for trans sphenoidal surgery (TSS). In other cases with progressive enlargement of adenoma size but without VFD bromocriptine was administered. Patients without increasing adenoma size were just followed up.

Results: In this study 72 patients (84%) had microadenomas, 7 patients (8%) had macroadenomas without previous medical or surgical therapy and 6 patients (7%) had macroadenomas with previous medical therapy with bromocriptine. Totally 20 patients (23 %) had tumor enlargement during pregnancy and was symptomatic in 7 patients (8.2%). There was significant difference between 3 groups according to incidence of symptomatic tumor enlargement ($p < 0.05$).

Conclusion: Macroprolactinomas are more likely to enlarge during pregnancy than microprolactinomas. In our study conservative management was successfully done in all patients without surgery or medical therapy.

Keywords: prolactinoma, pregnancy, transsphenoidal surgery, bromocriptine

Introduction

Prolactinomas are the most commonly encountered pituitary tumors in pregnant women (1, 2). These are classified according to size to microadenomas (size < 1 cm) and macroadenomas (size > 1 cm in diameter). More than 90% of prolactinomas are classified as microprolactinomas (3).

Women with prolactin-secreting tumors may experience further pituitary enlargement and must be closely monitored during pregnancy. Enlargement of pituitary gland during pregnancy depends on estrogen-stimu-

lated hyperplasia and hypertrophy of the prolactin-producing cells (4). Stimulatory effect of pregnancy on the pituitary has important effects in the patients with a pre-existing prolactinoma who want to become pregnant. In the other hand Hyper prolactinemia is responsible for about one third of female infertility (4,5).

Although the true prevalence of hyper prolactinemia is difficult to establish, it is estimated that among women presenting with reproductive disorders, approximately 15% with anovulation and 43% with anovulation and galactorrhea have hyper prolactinemia (6).

With appropriate management, most patients are expected to achieve successful pregnancies; however, managing prolactinomas during pregnancy remains a

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Table 1. Effect of pregnancy on prolactinomas

Tumor type	Prior therapy	Number of patients	Symptomatic tumor enlargement
Microadenomas	None	72	4
Macroadenomas	None	7	2
Macroadenomas	Yes	6	1

clinical challenge. For managing prolactinoma during pregnancy bromocriptine usually I successful in reducing the size of the tumor, but trans-sphenoidal surgery may be necessary (4,7).

We conducted this study to follow up pregnant women with Prolactinoma to determine their clinical symptoms, signs and eventual necessity to medical therapy.

Materials and Methods

A descriptive study, was performed on 85 pregnant women with prolactinoma in Rassolakram hospital, Tehran university of medical science, Iran from March 2007 to January 2011. Patients were included in this study with non-randomized method. Written informed consent was obtained from all patients, and the local institutional review board approved the study. We follow up all cases closely up to end up pregnancy.

Patients were classified according to adenoma diameter to microadenomas (size <1cm) and macroadenomas (size >1 cm).

We follow up patients with physical examination, imaging, and perimetry for diagnosis of visual field defect. If tumor was increased in diameter and size, we performed perimetry for determine eventual visual field defect (VFD). Patients with progressive visual field defect had absolute indication for trans sphenoidal surgery (TSS). In other cases with progressive enlargement of adenoma size but without VFD bromocriptine was administered (IRAN HORMONE CO, Iran, 2.5 mg tablet twice daily). Patients without increasing adenoma size were just followed.

Data were analyzed with SPSS software (version 13). P value <0.05 was considered statistically significant.

Results

Totally 85 pregnant women with prolactinoma were evaluated in this study. The mean age of patients was 29.3 ± 2.2 with the range of 21–36 years.

The mean period of follow up was 8.7 months and only one patient was visited before pregnancy.

Among the cases 65 women (76% patients) had successful previous pregnancy and 5 women (6% patients) had past medical history of infertility. Fifteen women (23% patients) were gravid one. All patients were referred from endocrine or obstetric clinics to neurosurgery unit.

In this study 72 patients (84%) had microadenomas, 7 patients (8%) had macroadenomas without previous medical or surgical therapy and 6 patients (7%) had macroadenomas with previous medical therapy with bromocriptine (Table 1). Twenty patients (23 %) had tumor enlargement during pregnancy that was symptomatic in 7 cases (8.2%) (Table 1).

Four patients experienced headache, 2 patients experienced nausea and 1 patient had visual field defect. There was significant difference between two groups of patients according to incidence of symptomatic tumor enlargement and Patients with macroadenomas had more symptomatic tumor enlargement during pregnancy ($p < 0.05$).

Symptomatic patients were followed closely with MRI and perimetry every 3 weeks. Only 1 patient had stable visual field defect that was not worsened during pregnancy. Conservative management was done in all patients and no surgery or medical therapy was required.

Discussion

A woman with a prolactinoma should discuss her plans to conceive with her physician so that she can be carefully evaluated prior to becoming pregnant. This evaluation will likely include a magnetic resonance imaging (MRI) scan to assess the size of the tumor and an eye examination with a test of the visual fields.

The main investigations in the diagnosis of a prolactin-secreting adenoma are hormonal and radiological (8). As prolactin is a pulsatile hormone, it is a general rule to obtain several blood samples by taking a single sample on 3 separate days or 3 sequential samples (every 30 minutes) in restful conditions. Prolactin levels of 100 to 200 micrograms/L are commonly considered diagnostic for the presence of a prolactinoma; however, prolactinoma cannot be excluded in the

presence of lower levels, and prolactin levels >100 micrograms/L are present in some patients with idiopathic hyper prolactinaemia. Several dynamic function tests have been proposed to differentiate idiopathic from tumorous hyper prolactinaemia. To differentiate between a prolactinoma and a pseudo prolactinoma, thyrotrophin response to a dopamine receptor antagonist may be used, as only prolactinomas may have an increased response. A short course of dopaminergic drugs may also be of some help, as in macro prolactinomas only shrinkage may be observed. After hyper prolactinaemia is confirmed, imaging with magnetic resonance imaging (MRI) is necessary to define the presence of a lesion compatible with a pituitary tumor (8). There is now a general agreement that medical therapy is of first choice in patients with prolactinomas. Bromocriptine, the most common drug used in this condition inhibits prolactin synthesis and secretion (8).

In women with prolactinoma, the stimulatory effect of the hormonal change that occurs during pregnancy may result in significant tumor enlargement during gestation (9).

Micro prolactinomas (tumors <10 mm in diameter) tend to follow a benign course in non pregnant patients. A 5-year follow-up study¹⁵ of 30 women with untreated hyper prolactinemia associated with microadenomas showed that up to 35% of women resumed menses or had resolution of galactorrhea and none developed visual loss or pituitary insufficiency (10).

Surveys of women with micro prolactinomas during pregnancy have indicated that the risk of new neurologic sequel (optic nerve compression, headaches or stalk compression) ranges from 1.6% to 5.5% (11,12).

A recent study followed 80 pregnancies in 56 women with micro prolactinomas. During the 71 full-term pregnancies in this group, only 1 patient developed headaches (the headaches disappeared when bromocriptine was restarted), and 5 showed mild tumor growth on postpartum imaging (13).

No clinical trials have compared the outcomes of women with micro prolactinomas treated pharmacologically with those not treated during pregnancy. This has led to variability in management practices. Most specialists discontinue dopamine agonist treatment upon confirmation of pregnancy; some prefer to continue dopamine agonist treatment during pregnancy. The dopamine agonist most widely used during pregnancy is bromocriptine, which is a semi synthetic ergot alkaloid. Bromocriptine treatment leads to tumor shrinkage in approximately 90% of nonpregnant patients (14).

A survey of more than 1400 pregnant women who took bromocriptine primarily during the first few weeks of pregnancy found no evidence of increased rates of abortion or congenital malformations (4,15).

Experience with cabergoline during pregnancy is absolutely limited. For patients with micro adenomas or intra sellar macroadenomas, bromocriptine therapy is generally preferred to surgery because it is safe for the fetus when discontinued early in gestation and poses only a small risk of tumor enlargement for the mother. Such patients should be seen each trimester and assessed for symptoms such as headaches or visual problems. Visual field testing need only be done when clinically indicated (4,7).

Our practice with pregnant patients was to stop dopamine agonist therapy once pregnancy is confirmed. We informed patients about the small risk of tumor enlargement and ask them to contact us if any unusual symptoms such as headaches or visual problems occur. We followed up patients with physical examination, imaging, and perimetry for diagnosis of visual field defect. In our study patients with macro adenomas had more symptomatic tumor enlargement during pregnancy. Macroprolactinomas are more likely to enlarge during pregnancy than micro prolactinomas (16).

No randomized trial has compared various management strategies to reduce risk and improve outcomes for patients with macro prolactinomas during pregnancy. Management in these cases must be individualized and patients should be closely monitored by their family physicians along with a team of endocrinologists and neurosurgeons (16).

The risks of surgery versus medical therapy for prolactinoma should be explained in detail to each patient. More randomized clinical trials are recommended for reaching reliable guidelines for clinical practice.

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