Case Report

Vanishing tumor in pregnancy

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ABSTRACT

A patient with microprolactinoma, who had two successful pregnancies, is described for management issues. First pregnancy was uneventful. During the second pregnancy, the tumor enlarged to macroprolactinoma with headache and blurring of vision which was managed successfully with bromocriptine. Post delivery, complete disappearance of the tumor was documented.

Key words: Bromocriptine, pregnancy, prolactinoma

Introduction

Hyperprolactinemia accounts for about one-third of all cases of female infertility. Prolactinoma accounts for the majority of cases of hyperprolactinemia. Dopamine agonists have become the primary mode of therapy of prolactinomas. In addition to bringing down the prolactin levels, they also reduce tumor size (50–75% by bromocriptine and 90% by cabergoline).[1] In women with prolactinomas, stimulatory effects of the hormonal milieu of pregnancy result in significant tumor enlargement during gestation.

Case Report

A 20-year-old housewife presented with secondary amenorrhea for 2 years in July 2001. She had a history of headache for 1.5 years. There was no history of galactorrhea. She consulted neurosurgery department in this hospital, where she was found to have prolactin level of 150 ng/ml (normal 5–25 ng/ml, CLIA). Her magnetic resonance imaging (MRI) brain showed a microadenoma of about 4 mm in the left half of the pituitary gland. She was started on bromocriptine 2.5 mg daily, which was stepped up to 7.5 mg subsequently. At 3 months of treatment, she had two menstrual cycles and her prolactin was 25 ng/ml. Then, she did not follow-up for 1 year, but she continued the drug. She followed up after 1 year, when she had missed a period. Her urine pregnancy test was positive and she was advised to stop bromocriptine. She was asymptomatic during her pregnancy. She delivered a full-term baby on 18/06/03. She followed up after 3 months of delivery. She was breastfeeding the baby and was asymptomatic.

Repeat MRI in April 2004 showed microadenoma of size 4 mm, which was the same as previous scan. In February 2004, after 2 months of stopping breastfeeding, her prolactin was >150 ng/ml. She was restarted on bromocriptine 7.5 mg daily in divided doses. After that, she had regular menstrual cycles for 2 years. MRI (11/08/05) showed a microadenoma of size 2 × 3 mm. She had spontaneous abortion in February 2006. After that, her menstrual cycles were normal for the next 4 months. She stopped bromocriptine on her own in June 2006 and presented in September with headache, blurring of vision and amenorrhea of 3 months duration. Urine pregnancy test was positive. MRI showed pituitary macroadenoma of 1.2 × 1.6 × 1.1 cm in the sellar region with suprasellar extension abutting of left side of optic chiasma [Figure 1]. The patient was admitted in the hospital where she was started on low dose of bromocriptine and the dose was slowly increased to 7.5 mg/day. She tolerated the drug well and her headache and visuals symptoms subsided. Her thyroid function tests and serum cortisol were normal. She was monitored with visual field charting

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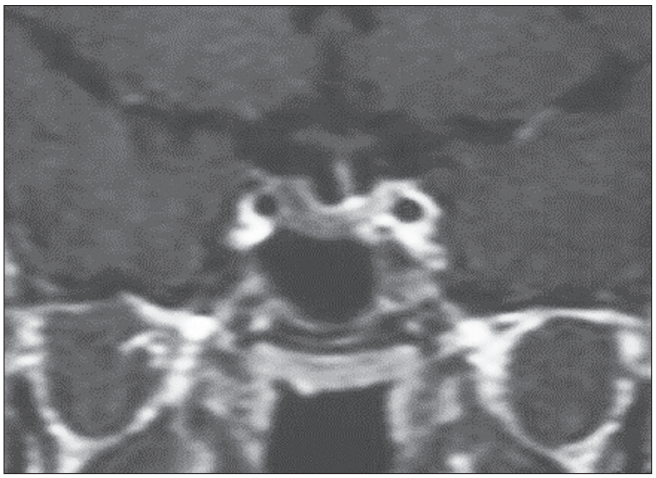

Figure 1: Magnetic resonance imaging at presentation showing a microadenoma of about 4 mm in the left half of the pituitary gland

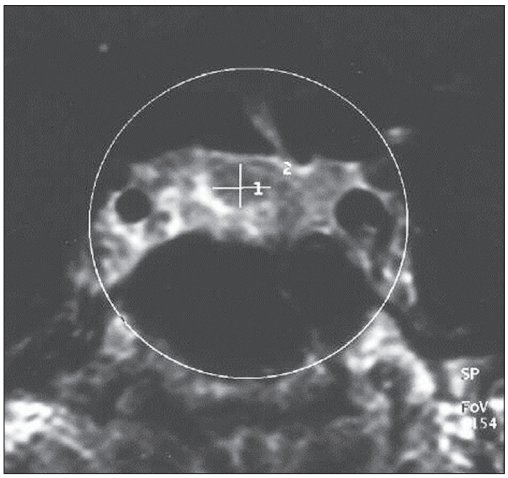

Figure 2: Magnetic resonance imaging after first delivery, showing a microadenoma of about 4 mm in the left half of the pituitary gland

two monthly, which were normal. Repeat MRI after 6 weeks showed tumor of same size. The patient delivered in March 2007 uneventfully. Baby was normal. Bromocriptine was stopped and she was advised to breastfeed the baby under close monitoring of visual field and symptoms. She was asymptomatic during this period. MRI was repeated after 3 months of delivery, which showed almost complete disappearance of the tumor [Figures 2-5].

Discussion

Pituitary gland enlarges during pregnancy, and by the end of pregnancy, it increases by 136%.[2] Mandel *et al*., summarizing 19 series, found that out of 376 cases of microprolactinoma, 6 (1.3%) had symptomatic tumor enlargement. Of 86 macroprolactinoma cases, 20 had tumor enlargement (23.2%).[3,4] Though dopamine agonists have been used during pregnancy to prevent tumor growth, it is prudent to reduce fetal exposure to drugs. In patients with microprolactinoma, they are advised to have menstrual periods occur naturally for a period of time (3–4 months) long enough to predict that a missed period may be due to pregnancy. Barrier contraception is advised during this period. Once pregnancy is confirmed, the drug is to be discontinued. In this way, these drugs will have been given only for 3–4 weeks of gestation. In 6239 pregnancies of patients managed in this manner, there was no increased incidence of abortions, prematurity, multiple births or fetal malformations above that expected in the control population.[5] There is no evidence that other dopamine agonists are less safe, but exposure to other agents during pregnancy is not well described. Such patients should be seen in each trimester and assessed for symptoms such as headache or visual problems.

Visual field testing needs to be done only if clinically indicated.[1] Treatment options for patients when the tumor is large or extends to the optic chiasma or cavernous sinus are 1) prepregnancy tumor debulking, 2) intensive monitoring without bromocriptine therapy and 3) continuous bromocriptine.[1] The safety of the last approach is not established, though it seems to be safe based on case reports. Mean offspring birth weight of the babies was normal in a series of 53 patients receiving bromocriptine. Long-term follow-up studies of 64 children of age between 6 months and 9 years whose mothers took bromocriptine have shown no ill effects.[6] Patients with macroadenomas should be seen monthly for clinical assessment and visual fields are to be tested during each trimester. Prolactin levels have little value in pregnancy.[1] When there is evidence of tumor enlargement during pregnancy, bromocriptine therapy is to be reinstituted immediately and the dosage increased as rapidly as possible. If there is no clinical response to bromocriptine on close monitoring, switching to cabergoline, transsphenoidal surgery or delivery (if the pregnancy is far enough advanced) should be considered.[4] The effects of transsphenoidal surgery during gestation are not known specifically, but would not be expected to be significantly different from the effects of other kinds of surgery.[7]

Cabergoline has been shown to cross the placenta in animal studies, but such data are lacking in humans. The data on safety of cabergoline during pregnancy and its effects on fetal development are scarce. The frequency of spontaneous abortions in pregnant women under cabergoline treatment in various series ranges from 7.2 to 10%.[8-15] In a series of 6329 patients treated with bromocriptine, Guillam *et al*. found the risk of spontaneous abortions to be 9.9%.[16] In the general population, Nybo

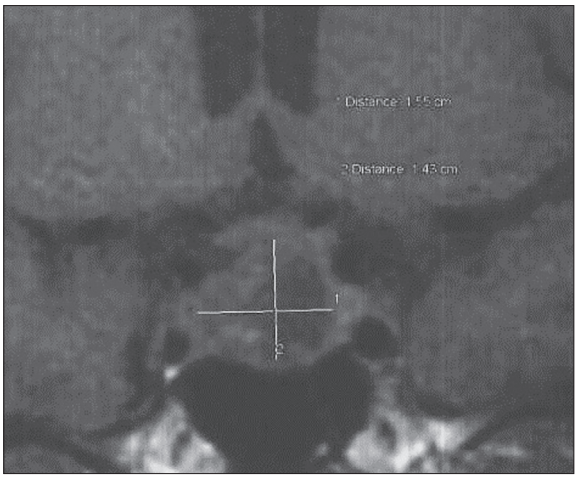

Figure 3: Magnetic resonance imaging showing a pituitary macroadenoma 1.2 × 1.6 × 1.1 cm in the sellar region with suprasellar extension abutting of left side of optic chiasma, after second pregnancy (spontaneous abortion), after stopping bromocriptine

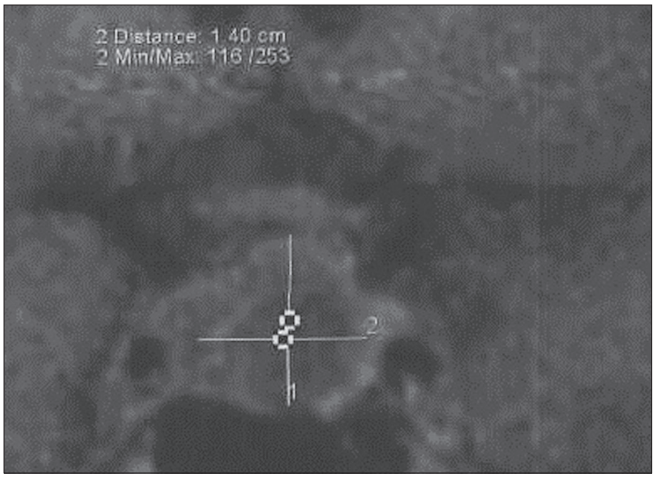

Figure 4: Magnetic resonance imaging in February 2007, during third pregnancy, after 6 weeks of bromocriptine

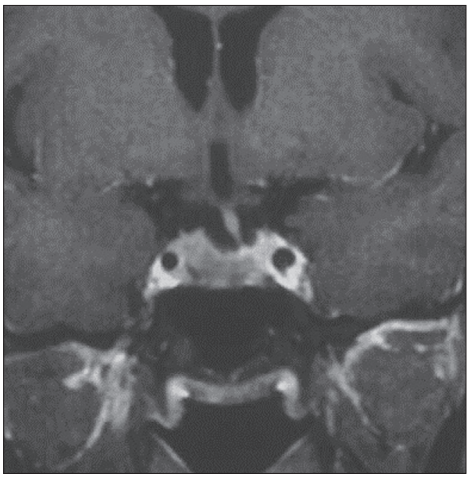

Figure 5: Magnetic resonance imaging 3 months after delivery, showing complete disappearance of tumor

Andersen *et al*. found a risk of spontaneous abortions of 10.9% in 1,221,546 pregnancies.[17] Also, the risk of embryo-fetal malformation does not look elevated based on the present data.[11,18-20] Though cabergoline database is small, for a woman who is intolerant to bromocriptine and doing well with cabergoline, continuing cabergoline may be reasonable. It has been shown that cabergoline treatment causes further shrinkage of tumor in patients previously treated with bromocriptine and those considered resistant to dopamine agonists.[21]

Cabergoline has a high affinity to 5HT2B receptors besides D2 receptors, and this forms the basis of action of cabergoline on cardiac valves. Valvular regurgitation and restrictive valvulopathy has been described in Parkinson's patients receiving high doses of cabergoline (nearly 20 times the typical doses used for prolactinoma).[22] Literature review shows that 11 studies have assessed the potential association between valve regurgitation and the use of cabergoline in patients treated for prolactinoma.[23] In total, 795 patients, treated with cabergoline at a median cumulative dose of 290 mg and a median duration of 59 months, and 1202 healthy control individuals were included in these studies. Five of these studies did not report any relevant cardiac findings, although increased prevalence of regurgitation in any valve was reported in five studies, and one study reported an increased tenting of the mitral valve. In light of these data, it is controversial whether prolactinoma patients receiving cabergoline for long term should be monitored with echocardiography or not.

The safety database of pergolide and quinagolide are very much limited. Although suckling stimulates prolactin secretion in normal women for the first few weeks to month postpartum, there are no data suggesting that breastfeeding can cause tumor growth. There seems to be no reason to discourage nursing in women with prolactinomas.[1] The possibility of the enlargement being entirely due to lymphocytic hypophysitis, which is known to present with mass lesion during pregnancy and spontaneously resolves postpartum, was considered in our patient. However, serum cortisol and thyroid functions which were normal are not in keeping with the diagnosis of lymphocytic hypophysitis This case report illustrates an unusual presentation of microprolactinoma which had symptomatic enlargement during pregnancy, which resolved completely in the postpartum period with medical line of therapy.

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