

# A rare case of pregnancy and delivery of a healthy neonate by a woman with microprolactinoma and review of the literature

**A. Kwaśniewska, M.D. Ph.D. Assoc. Prof.; M. Skoczyński, M.D. Ph.D.; M. Semczuk, Prof.**

*Department of Obstetrics and Gynecology, University of Medicine, Lublin (Poland)*

## Summary

A rare case of a term-pregnancy and delivery in a patient with microprolactinoma is presented. The patient had been treated with bromocriptine since she was 17 due to primary amenorrhea for 60 months with short intervals. Pharmacological tests with dopamine antagonists and X-ray diagnostics revealed the presence of microprolactinoma. The patient was constantly under specialist endocrinological care and the level of prolactin in her blood serum was continuously being monitored. After getting pregnant she was placed under strict gynecological scrutiny with special attention devoted to the developing fetus and possible congenital defects. The patient continued receiving bromocriptine therapy up to the 16th week of pregnancy. In the course of pregnancy in the 26<sup>th</sup> week, a circular suture was placed on the uterine cervix due to symptoms of isthmus-cervical insufficiency. In the 38<sup>th</sup> week of pregnancy a cesarean (C) section was performed and a healthy child in good general condition (Apgar score 10) was born. The child weighed 2,900 grams.

**Key words:** Microprolactinoma; Pregnancy; Hyperprolactinemia; Bromocriptine treatment.

## Introduction

Prolactin activity in the human body is multidirectional. Its influence on the female reproductive system mainly comprises affecting the mammary gland and hypothalamus-pituitary gland-ovary axis. Disturbances in proper hormonal functioning of the ovary may be caused by both excess and deficiency of prolactin. A normal level of prolactin in female blood serum is between 5-25 ng/ml. Hyperprolactinemia often disturbs ovary function, leading to infertility. Most frequently the symptoms which make patients with prolactin excess worried and force them to seek medical help are either amenorrhea or dysmenorrhea and galactorrhea. Keeping the level of prolactin as close to normal as possible and stable may be necessary to restore fertility in a woman. It seems that administration of dopamine antagonists may be indispensable even in the first weeks of pregnancy. Retrospective data presented in the available literature confirm the lack of harmful effects of these medicines on the development of the fetus [1-4].

## Case Report

The patient, B.G., aged 23, nullipara, went to see an endocrinologist for the first time when she was 17 due to amenorrhea. Sex hormone levels in blood sera were measured and it was found that the prolactin concentration was much higher than normal while the progesterone concentration was too low. The levels of other hormones were normal. Prolactin concentration was between 108 and 161 ng/ml. In December 1996 computed tomography (CT) examination was performed which showed

that the pituitary gland size was normal. The next stage in the diagnostic process involved a test with metoclopramide which revealed prolactin concentration levels corresponding to existence of microprolactinoma. Magnetic resonance imaging (MRI) of the pituitary gland was performed and a 4 x 6 mm hypointensive area was found on the right side of the gland. The image suggested existence of a microprolactinoma-type lesion. Since April 1997 bromocriptine had been administered to the patient at a dose of 5 mg a day. As a result of the therapy menorrhea occurred every 26-50 days lasting for five to seven days. Levels of prolactin concentrations during bromocriptine treatment were in the range of 5.42-42.2 ng/ml. Galactorrhea persisted. Control MRI of the pituitary gland was performed after two years in 1999 revealing existence of a focal lesion, 5 x 8 mm in size. The patient was treated with bromocriptine.

After confirming pregnancy bromocriptine treatment was continued for 16 weeks with a daily dose of 2.5 mg. Ultrasound examination results were satisfactory and the fetus did not reveal any features of intrauterine developmental arrest. In the 26<sup>th</sup> week of pregnancy due to isthmus-cervical insufficiency the patient had a circular suture placed on the cervix. The prolactin level at that time was 184.66 ng/ml. On February 9, 2003, at term, the patient was admitted to the hospital with initial labor pains. The suture was removed from the cervix and it was found that there was a 3-cm wide opening, retained amniotic sac and that the presenting part, the head, was slightly pushed into the inlet. Fetal heart rate was about 144 beats a minute. Due to the obstetric history and patient's request for a C-section it was decided that the pregnancy would be terminated surgically. A male was born in good general condition and weighing 2,900 grams. Rehabilitation after the C-section proceeded with no complications. The patient and the newborn were discharged without any complications on the fifth day after surgery. One month after delivery the prolactin level was 128 ng/ml. Within the third month after the delivery, control MRI was performed and the nodule was found to be a little smaller than before her pregnancy. The patient still remains under constant endocrinological care.

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## Discussion

A rare case of pregnancy and delivery of a healthy neonate by a patient with microprolactinoma has been presented. High levels of prolactin in female blood serum may lead to dysmenorrhea and be one of the reasons for infertility. In such case, getting pregnant is only possible after restoring prolactin levels back to normal [1-3]. Excess prolactin levels inhibit the pulsating secretion of GnRH, affects oocyte maturation, influences immunological mechanisms during pregnancy and may locally alter the function of the endometrium [1]. Increased prolactin levels are found in as much as about 30% of early miscarriage cases [1, 3]. However, it is still difficult to fully explain what role prolactin plays in reproductive processes [5]. Often, there are no clinical symptoms suggesting existence of hyperprolactinemia. One of the reasons to explain this is the existence of autoantibodies against one of the three prolactin isohormones with the largest molecule [1, 6].

For patients with increased prolactin levels, the choice of appropriate therapy may be crucial in pregnancy planning and carrying to term. Administering dopamine antagonists seems to be the treatment of choice [3]. In 80 to 90% of women such procedure restores ovulation and allows patients to get pregnant [3, 4, 7]. Administering bromocriptine to our patient at a dose of 5 mg a day in order to restore the appropriate prolactin level and, consequently evoke ovulation, allowed her to get pregnant without any other factors which might have contributed to infertility. During pregnancy, up to the 16<sup>th</sup> week, 2.5 mg of bromocriptine had been administered daily. This treatment method reflected a widely accepted medical procedure used in women with hyperprolactinemia, although the recommended period of administering dopamine antagonists is no longer than nine weeks of gestation [1, 2, 4]. Although administration of bromocriptine during pregnancy may be somewhat dubious due to the increased number of complications in the first weeks of pregnancy, the published data do not confirm these concerns [2-4, 8-10]. There are reports showing a significantly higher number of births healthy by women treated with bromocriptine compared to non treated women [1, 2, 11].

Despite this, our patient was under constant medical scrutiny directed towards possible congenital defects in the fetus because there is no way to disregard other endangering complications related to the existing microprolactinoma.

The most frequent complications in pregnant patients with hyperprolactinemia are miscarriage, tubal pregnancy, cystic mole and incomplete pregnancy [1, 2, 12]. Frequency of occurrence of tubal pregnancy (24%) was significantly higher in the group of women not treated with bromocriptine compared to the treated ones. The mechanism of occurrence of tubal pregnancy is most probably connected with the prolactin influence on estrogen functions and progesterone influence on uterine tube function [2].

Still opinions about the influence of pregnancy on pituitary tumors are divided [3, 13]. Badaway *et al.* found that in 45% of cases, pregnancy does not have any influ-

ence on the size of pituitary tumor, in 27% it can make the tumor smaller and also in 27% it can make the tumor larger but to a very limited extent. These results were confirmed by radiological examinations [14]. There is also a theory suggesting a beneficial influence of pregnancy on normalizing prolactin levels. What is more, there are examples of patients with hyperprolactinemia getting pregnant again without having been treated after a previous delivery [2, 8, 15, 16].

In our patient control X-rays performed two months after delivery revealed that the pituitary nodule was a bit smaller than before pregnancy. Also functional examinations using a dopamine antagonist, metoclopramide, showed that there was a prolactin profile similar to the one existing one year before the pregnancy.

We have presented a rare case of a patient with microprolactinoma. Medical procedures based on the knowledge of processes responsible for female fertility lead to achieving goals expected by the patient.

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Address reprint requests to:

A. KWAŚNIEWSKA, M.D.

Klinika Położnictwa ul. Staszica 16  
20-081 Lublin (Poland)