Hypoprolactinemia is the most common disorder of the hypothalamo-pituitary axis, and prolactin (PRL) secreting tumors are the most common type of secreting pituitary tumors. The percentage of pituitary glands found to contain ranges from 1.7 to 27% in autopsy series. In women with prolactinomas, the stimulatory effect of the hormonal milieu that occurs during pregnancy may result in significant tumor enlargement during gestation.

Gestational gigantomastia is the massive over-development of the breasts occurring during the first or second trimester, typically returning to normal after delivery. Most cases of gestational gigantomastia respond well to bromocriptine therapy. High doses of this medication have often resulted in slowing or reversal of rapid breast growth during pregnancy. Bromocriptine is an ergot-derived compound that acts as a dopamine agonist in the hypothalamus, resulting in a significant decrease in the release of PRL from the anterior pituitary gland.

Non-puerperal mastitis is an inflammatory disease that resembles carcinoma; its course is insidious and it is frequently misdiagnosed. Circumscribed or diffuse non-puerperal mastitis is usually associated with local signs of inflammation. Mammography is an important diagnostic procedure for the demonstration of acute mastitis and its differentiation from an inflammatory carcinoma; it is also valuable in the control of treatment. PRL-lowering treatment alone seems reasonable in cases of abacterial mastitis or in combi-
nation with antibiotics in bacterial mastitis. Long-term lowering of the peripheral PRL level may prevent recurrences.

We present a case of non-puerperal mastitis in a young female with an incidentally detected pituitary microadenoma, which might also be the reason for habitual abortion in the patient.

Case Report
A 27 year-old female patient within the 19th week of her 4th gestation was admitted to our hospital with a 1-month history of progressive painful enlargement of both breasts. She had a history of antibiotic and anti-inflammatory drug therapy for the last 4 weeks that had been prescribed in another health center, with no response to treatment. There was no previous history of tuberculosis, sarcoidosis, and other infectious or granulomatous diseases. She had a history of three previous pregnancies, all of which resulted with spontaneous abortions. She had no family history of breast disease.

Physical examination revealed bilateral tenderness, hyperemia, engorgement of breasts, and marked peau d’orange covering the whole breasts raising the suspicion of inflammatory breast cancer (Figure 1 A-B). There was no nipple discharge, no palpable mass, or no enlarged axillary lymph node. She was severely limited by the pain in her breasts and their weight resulted in back pain. Mammography or magnetic resonance imaging (MRI) of the breasts could not be performed because of the intense pain and size of her breasts. Ultrasonography showed lymphatic dilatation, skin edema but no focal abnormality. The patient had a complete laboratory work-up, including a complete blood count, chemistry, liver function tests, coagulation screen and hormonal assay. Her hemoglobin was 11.1 mg/dL and the white blood cell count was 7,800/mm^3. All biochemical parameters and serum tumor markers were within normal limits. Serum PRL level was over 200 ng/mL (normal range; 1.2-30 ng/mL for females). MRI of the pituitary gland revealed a hypointense, well-circumscribed microadenoma with an 8 mm diameter, which was thought to be a prolactinoma. Ophthalmological examination revealed no visual field deficit. She was also consulted to obstetricians, hematologists, and endocrinologists in our hospital and serum cortisol, ACTH, follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone, and thrombophilia parameters screened for habitual abortion were normal. Ultrasound examination of the pelvis revealed a viable, progressing, normal fetus. Neurosurgeons thought that a prolactinoma of this size would not explain the pathology of the patient and they did not recommend surgical intervention. Bromocriptine 2.5 mg twice daily was initiated under the supervision of obstetricians. Unfortunately, 1 week after the initiation of treatment this gestation also resulted with abortion. At the same time, first signs of the resolution of the breast pathology appeared. She was discharged home 1 week later with antidopaminergic treatment (bromocriptine 2.5 mg bid). At the end of 1st month, she was seen in the outpatient clinic. Physical examination revealed that both breast pathologies had completely resolved (Figure 1 C-D). Serum PRL level had fallen within normal limits (28
ng/mL). Control MRI of the pituitary gland also revealed regression of previously detected adenoma and no mass was visible. The patient was reconsulted to obstetricians and endocrinologists, and she was advised to continue bromocriptine treatment for 1 year and to avoid pregnancy during this period. Reduction mammoplasty was planned for future treatment.

Discussion

In about one in every 100,000 pregnancies, the normal increase in size and weight of the breasts is exaggerated to enormous proportions. The resulting hypertrophy does not only deform the body appearance, but also may progress to skin ulceration or life threatening infections. The cause of gigantomastia remains a matter of speculation with the most common theories supporting hormonal imbalance or end organ hypersensitivity. There are some case reports with documented hyperprolactinemia.

Hypersensitivity of breast tissue to PRL appears to be a characteristic of pregnancy-induced gigantomastia because massive breast growth in such cases is usually slowed or reversed by PRL inhibition using bromocriptine.

The normal pituitary gland enlarges during pregnancy, predominantly because of estrogen-stimulated hyperplasia and hypertrophy of the PRL-producing lactotropes found in the anterior pituitary gland. PRL levels rise gradually throughout gestation. This stimulatory effect of pregnancy on the pituitary has important implications for the patient with a pre-existing prolactinoma who desires to become pregnant. Also in women with prolactinoma, the stimulatory effect of hormonal milieu that occurs during pregnancy may result in significant tumor enlargement during gestation.

PRL-secreting adenomas are the most common hormone-secreting (functional) pituitary tumors in both autopsy and surgical series. They are generally classified clinically by size: Microadenomas (<10 mm in diameter) and macroadenomas (>10 mm in diameter with or without extrasellar extension). Prolactinomas occur more frequently in women than in men and differ not only in size, but also in clinical presentation, invasive growth and secretory activity. The vast majority (95%) of prolactinomas in women are microadenomas, which present with the clinical manifestations of hyperprolactinaemia, and rarely lead to hypopituitarism or neurologic dysfunction. In contrast, men with prolactinomas often present with loss of libido or infertility, because of symptoms due to the size of the tumor rather than impotence.

There is a direct correlation between the degree of hyperprolactinemia and the likelihood of finding a PRL-secreting tumor. A serum PRL level greater than 200 ng per mL virtually assures the presence of prolactinoma. MRI of the pituitary fossa, preferably with gadolinium enhancement, should be considered if the serum PRL level is significantly elevated or if a pituitary tumor is suspected.

Tumors vary in how they affect pregnancy depending upon the hormone secreted. Some hormone oversecretion syndromes like Cushing’s disease and hyperthyroidism must be controlled to allow pregnancy to proceed without undue maternal and fetal morbidity, whereas treatment during pregnancy for other tumors is not necessary. The approach to the treatment of a patient with a prolactinoma depends on several factors including the severity of the patient’s symptoms, his or her desire for fertility, the likelihood of complications in relation to possible tumor expansion and the long-term consequences of untreated hyperprolactinaemia. Treatment goals include suppressing PRL secretion and its clinical and biochemical consequences, reducing the size of the prolactinoma, and preventing its progression or recurrence. Dopamine agonists are the preferred treatment for most patients with hyperprolactinemic disorders. Such agents are extremely effective in lowering serum PRL levels, restoring gonadal function, and decreasing tumor size. Bromocriptine and cabergoline are well-known dopamine agonists used in hyperprolactinemia. The number of studies investigating the safety of ca-
Bergolone during gestation is limited. The safety of fetal exposure to bromocriptine has been evaluated extensively, and this agent is not associated with increased rates of spontaneous abortion, fetal malformation, or adverse effects on postnatal development.\textsuperscript{13,14} Nevertheless, bromocriptine should be used cautiously during pregnancy.

Because of the inherent risks of surgery and the efficiency of dopamine agonists in treating patients with prolactinoma, surgical resection is rarely required.\textsuperscript{15} Surgery should be considered only in cases of resistance or intolerance to optimal medical therapy. Radiotherapy should be considered in patients with macroadenomas who are resistant to medical therapy or in whom surgery has failed.

To our knowledge, infection complicating the gigantomastia of pregnancy is very rare.\textsuperscript{6} Our case was interesting in that the patient had the signs of mastitis first and was put on antibiotic therapy. At the end of 4 weeks, she gave no response to this therapy and was referred to our department with the suspicion of inflammatory breast cancer. She had no signs of prolactinoma including galactorrhea (a major sign of prolactinoma in females). Further investigation revealed hyperprolactinemia and a pituitary microadenoma. The patient responded well to bromocriptine and serum PRL level returned to normal in a very short period. Unfortunately, the gestation terminated with spontaneous abortion 1 week after the initiation of bromocriptine, and we are not sure whether the reason of abortion is bromocriptine treatment or not. Another interesting finding was that the patient had experienced this disease only during her fourth gestation although the previous three gestations similarly ended with spontaneous abortions.

In conclusion, we think that the etiology of gestational gigantomastia and mastitis is a diagnostic dilemma and treatment of this condition is a matter of challenge.

\textbf{REFERENCES}