Bromocriptine or cabergoline induced pituitary apoplexy: Rare but life-threatening catastrophe

Sir,

Prolactin secreting pituitary tumor is one of the common causes of infertility in males and females. [1] Prolactin level is also high in non-prolactin secreting pituitary adenoma (e.g., growth hormone secreting) due to stalk effect. [2] Most of the prolactinomas can be managed medically with bromocriptine or cabergoline which are largely used as primary treatment for prolactinomas, as they help to normalize serum prolactin levels and induce reduction in the tumor size, promoting restoration of gonadal function, cessation of galactorrhea and improvement in visual defects in the majority of patients. [1,2]

Bromocriptine or cabergoline induced pituitary apoplexy is a life-threatening complication which is rare but well known. [2-5] This condition is characterized by sudden onset of headache, visual loss or deterioration, meningismus, altered mental status, and rarely, even death. [1,2] This pathology is caused by hemorrhagic necrosis of tumor or pituitary gland infarction, in which pituitary function is compromised, necessitating rapid administration of corticosteroids and endocrine evaluation. [1]

Rapid surgical decompression is required if there is sudden constriction of visual fields, and/or rapid deterioration of acuity, or neurological deterioration due to hydrocephalus. [1,2] These reports point toward the possibility of bromocriptine or cabergoline induced pituitary apoplexy, which should be kept in mind when a patient is neurologically deteriorating after starting these drugs. Careful follow-up is required when treatment with bromocriptine or cabergoline is attempted for prolactinoma in reproductive medicine clinic for infertility management in male and female patients.

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Thyroid and its indispensability in fertility

Sir,

Thyroid hormones are instrumental in reproductive physiology. In hypothyroidism, there is decreased synthesis of factors VII, VIII, IX, and XI [1] and estrogen break through bleeding secondary to anovulation, which may explain the frequent, prolonged, and heavy menstruation. Hyperthyroidism may be characterized by infrequent scanty menstruation or amenorrhea. Thyrotoxicosis (usually from Graves’ disease/gestational transient thyrotoxicosis) increases the risk of spontaneous abortions and especially if on methimazole, there is an amplified risk of congenital anomalies and aplasia cutis.

In males, thyrotoxicosis causes abnormal sperm motility, while hypothyroidism may result in abnormal sperm morphology and both may cause erectile abnormalities.

Ovarian surface epithelium and oocytes of primordial, primary, and secondary follicles, endometrial stromal and Ishikawa cells feature strong immunostaining of thyroid-stimulating hormone (TSH)-Receptor, thyroid hormone receptor TRα1 and TRβ1. TSH stimulated granulosa cells show a significant increase in cAMP concentrations via
activation through TSH-receptor.[2] Thyroid dysfunction may cause short luteal phase, failure to sustain a fertilized egg, and loss of early pregnancy. More than half of hypothyroid patients have menstrual irregularities and one third of subfertile patients have thyroid disease. Pituitary hormones such as TSH, prolactin, or growth hormone act synergistically with follicle-stimulating hormone (FSH) and luteinizing hormone (LH) to usher the follicles into the growth phase. About 46.1% of infertile patients with hypothyroidism exhibit hyperprolactinemia.[3] Hyperprolactinemia from longstanding primary hypothyroidism impairs pulsatile secretion of gonadotrophin-releasing hormone (GnRH) and causes ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea and polycystic ovaries when levels are high. Thyroid supplementation restores prolactin levels and normalizes ovulatory function. Thyroid hormones are vital for the production of both estradiol and progesterone lack of which may cause infertility independent of hyperprolactinemia.

Maternal thyroid dysfunction marrs fetal neuropsychological development and increases risk of preterm delivery, small for date offspring, fetal distress in labor, and probably gestation-induced hypertension and placental abruption. The recommended dose for iodine intake during pregnancy is increased from 200 to 250 µg/day.

A study showed that women who never achieved basal TSH <2.5 mIU/l or Thyrotropin releasing hormone-stimulated TSH <20 mIU/l had lower conception rates.[4] Women with TSH ≥2.5 mIU/l have significantly higher BMI, fasting insulin concentrations, total testosterone and free androgen indices and decreased sex hormone-binding globulin concentrations.

During super-ovulation for in vitro fertilization high estradiol enhances Thyroid Binding Globulin-TBG binding of thyroxine and may have effects on ovum quality, fertilization, conception, or ongoing pregnancy. Pregnancy rate and delivery rate are significantly higher in those treated with levothyroxine than placebo (35% and 10% vs 26% and 3%, respectively) and miscarriage rate is considerably lower (9% vs 13%).[5] Anti-thyroid peroxidase-TPO levels (>121 IU/mL) significantly correlate with early miscarriage (may affect post-implantation embryo development). In threatened abortions lower HCG, free T3 and free T4, but higher TSH4 serum concentrations are observed. In infertile women suffering from PCOS, clomiphene-resistant patients tend to have significantly more anti-TPO values compared to clomiphene and metformin responders.

Thyroid function is of paramount importance in fertility and adequate screening and treatment accordingly can improve conception and delivery rates apart from overall health.

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