PITUITARY PROLACTINOMA PRESENTING RARELY AS PRIMARY AMENORRHEA

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ABSTRACT

It is known that hyperprolactinemia can cause menstrual irregularities in adult females, but in adolescence, it is a rare cause of delayed or arrested puberty and growth disturbance. We are reporting a case of a 20-year-old girl with hyperprolactinemia with primary amenorrhea who had a normal development of secondary sexual characters except menarche. Her serum prolactin level was extremely high, but the other hormones examined were almost within the normal range and imaging studies showed pituitary macroadenoma. Hyperprolactinemia induced functional hypogonadotrophic hypogonadism with poor estrogen secretion results in primary amenorrhea, but with normal breast development. Prolactinoma in adolescence may also be easily and effectively managed by medical therapy. All clinicians who see patients with arrested puberty and/or primary amenorrhea should therefore be aware of the possibility of this diagnosis.

Keywords: Hyperprolactinemia, Pituitary microadenoma, Amenorrhoea.

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INTRODUCTION

Adolescent menstrual disorders are among the common gynecological complaint requiring the physician's attention. Primary amenorrhea is the failure to menstruate by age of 16 in the presence of normal secondary sexual development. In order to evaluate such cases the first line test is a pregnancy test to rule out the commonest secondary cause of amenorrhoea, then a thorough history, a complete physical examination and measurement of follicle stimulating hormone, thyroid stimulating hormone and prolactin, help identify the other causes of amenorrhea in most cases. Pituitary tumors in the brain occur most commonly between the age of 20 and 50, but are rare under 20. Prolactin secreting pituitary adenomas in particular are rare in childhood. Although hyperprolactinemia in adolescence is known yet rarely is a cause of delayed or arrested puberty. Its clinical presentation and response to treatment in prepubertal or peripubertal patients have seldom been reported in detail. Here we report the case of a 20-year-old girl who had hyperprolactinemia and primary amenorrhea.

CASE HISTORY

A 20 yr old girl presented to us in Endocrine Out Patient Department with history of primary amenorrhea. No history of poor linear growth or poor weight gain was present. No history suggestive of hypothyroidism, repeated infections, raised intracranial pressure was there. No history suggestive of defective smell and vision, difficulty in walking, deformity of extremities and nothing contributory from developmental and birth history. No similar history in family was present. According to the patient sparse axillary and pubic hair are present.

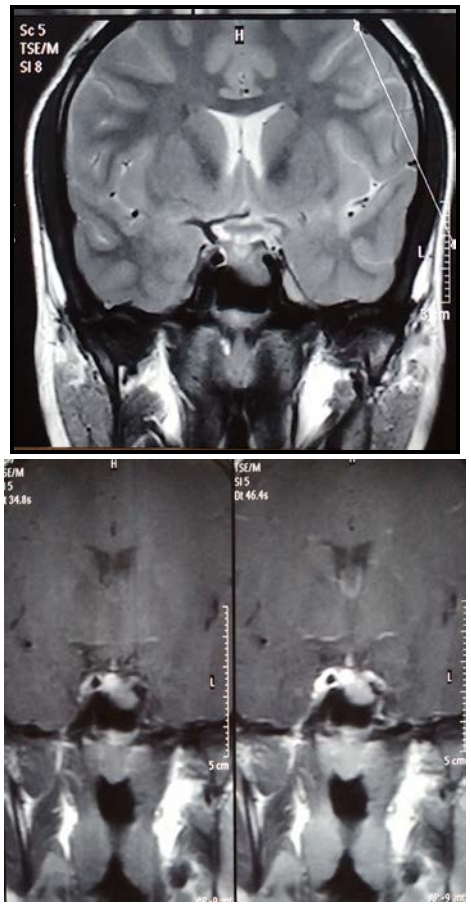
Physical examination revealed Height: 157 cms, MPH: 161cm, Weight: 45kg, BMI**:** 18.25 kg/m². Secondary sexual characteristic: Axillary hair A+, Pubic hair P2, Breast development B 3. No signs of hirsutism and no clitoromegaly was seen and vitals and other systemic examinations were normal. Urine pregnancy test was done and it was negative.

Results of Hormonal testing were as below

TSH: 8.08 μIU/ml	Cortisol : 24.13
Free T_4: 0.00 ng/dl,	Estradiol (E_2): 24.95 pg/ml
Free T_3: 4.01 pg/ml	Prolactin: >200 ng/ml
FSH: 21.7 mIU/ml	testosterone : 29.20 ng/dl
LH: 0.17mIU/ml	

IMAGING STUDIES

Ultrasonography of pelvis showed small Uterus 46x28x18mm, ovaries NDF b/l &endometrial thickness 4 mm and MRI sella with Gadolinium Enhanced Dynamic Scan showed pituitary macro adenoma of size 14 x 14 x 10 mm hypointense on T1 WI. It is extending into the left cavernous sinus with partial encasement of the left internal carotid artery.



MRI sella coronal cuts showing pituitary macro-adenoma

DISCUSSION

In the present case the girl presented to us with history of primary amenorrhea and appearance of thelarche (breast) at the age of 14 years. She also developed axillary and pubic hair, which she had noticed

since 2 years with normal external and internal genitalia. Hyperproactinemia with pituitary adenoma was documented on further evaluation, but there was absence of galctorrhea, visual difficulties and raised intracranial pressure symptoms which was atypical of prolactinoma tumor. The patient was started on tablet Cabergoline 0.5mg twice weekly with small dose of Thyroxine in view biochemical evidence of hyperprolactinemia and central hypothyroidism. Hyperprolactinemia due to a prolactin secreting pituitary adenoma is now a well recognized cause of secondary amenorrhea in women.[1] Such patients often respond well to orally active dopamine agonists, which usually lead to normal serum prolactin levels and normal gonadal function. In the majority of cases, shrinkage of the adenoma occurs, even in the presence of a large extrasellar extension.[2] On review of literature, we found few case reports of hyperprolactinemia with primary amenorrhea. Howlett et al[2] reported 14 peripubertal cases of prolactinoma, of which nine cases had macroadenomas demonstrated by CT scan and/or pneumo-encephalography and the other five had microadenomas. In the brain tumor registration in Japan between 1969 and 1981, 3,152 cases were registered under age 14 and only 36 (1.1%) of them had pituitary adenoma.[3] Among all the cases of prolactinoma only 0.47% of them were under the age of 20 years. Pre and peripubertal cases of prolactinoma are therefore rare and we should therefore observe such cases very carefully, as they may reveal certain clinical features which are specific to their age and are not fully understood.

In the present case also her puberty has started with breast development and reached nearly adulthood on appearance, but she had not had menarche. We guess that her hyperprolactinemia had already been present by that time. It appears that hyperprolactinemia can cause several different symptoms, according to the different timing of onset of hyperprolactinemia and they include delayed puberty, arrested puberty, primary amenorrhea and secondary amenorrhea. During normal physiological states associated with elevated prolactin (PRL), luteinizing hormone (LH) levels are lowered e.g., during pregnancy, pseudopregnancy, postpartum and lactation. Hyperprolactinemia inhibits the postcastrational rise in LH levels in a dose-dependent fashion in male rats.[4] One hypothesis to explain these findings is that elevated PRL levels act centrally to inhibit gonadotropin hormone releasing hormone (GnRH) release, which in turn results in lowered LH levels. There are animal studies by Koike et al,[5] Fox SR et al[6] and Park et al[7] that report documentation of reduced release of GnRH hormone from the pituitary gland by hyperprolactinemia explaining primary amenorrhea in our patient.

Breast development requires lower levels of estrogens, while uterus and endometrium require higher level of estrogens. The index patient with prolactinoma had normal breast development, but small uterus, which suggests that she has been exposed to estrogen, albeit at lower concentrations. The source of estrogen in this patient despite hyperprolactinemia includes increased prolactin-mediated adrenal androgen production, which provides a

substrate for the synthesis of weaker estrogens in adipose tissue[8] and partial suppression of hypothalamo–pituitary–ovarian axis, thereby allowing measurable levels of FSH, which is required for induction of aromatase activity.

CONCLUSION

Prolactinoma in adolescence is a rare cause of primary amenorrhea, delayed or arrested puberty. Furthermore, it may be effectively managed by medical therapy. All clinicians who come across the patients with these symptoms should therefore be aware of the possibility of this diagnosis.

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