A 4-Year-Old Girl with Precocious Puberty

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Abstract

Appearance of secondary sexual development before the age of nine in a male child and before the age of eight in a female child is called precocious puberty. Precocious puberty due to premature activation of the hypothalamic-pituitary axis is called central or complete precocious puberty. Incomplete precocious puberty is called if ectopic gonadotropin secretion occurs in boys or autonomous sex steroid secretion occurs in either sex. Here we report a case of a 4-year-old girl brought to a gynecologist by her parents because of breast development, pubic hair and periodic per vaginal bleeding. Her medical history was unremarkable. The parents were of average height, and the mother reported first menstruation when she was 11 years. On physical examination, the girl was 100 cm tall, weighed 17 kg, and had a body mass index 17. Her pubertal development is classified as Tanner stage 3 breast development and Tanner stage 2 pubic hair development.

Key words: Complete precocious puberty; Incomplete precocious puberty; Hypothalamic hamartoma

Introduction

Precocious puberty (PP) is reserved for girls who exhibit any secondary sex characteristics before the age of eight or menstruate before the age of ten.¹ This is due to excessive production of sex steroids which could be due to activation of hypothalamic-pituitary-gonadal axis [gonadotropin releasing hormone (GnRH) dependent PP], also known as central precocious puberty (CPP) or due to a non-hypothalamic mediated increase in sex steroid production (GnRH-independent PP). Out of these two types, GnRH dependent precocious puberty is more common and accounts for more than 90% of girls and about 50% of boys presenting with precocious puberty.²

The onset of puberty is marked by breast development and menstruation in girls. Tanner stage 3 breast development means appearance of the breast bud marking the onset of pubertal development.³ The most common mechanism of progressive precocious puberty is the early activation of pulsatile gonadotropin releasing hormone secretion which results in maturation of hypothalmo-pituitary ovarian axis which activates maturation of hormone responsive tissue such as breast, bones, pubic hair and endometrium. These girls have normal ovulation, menstruation and reproductive capacity.⁴ Isolated sexual precocity of unknown etiology carries no increased risk of mortality. However, distinguishing between children with idiopathic CPP and rare patient with a CNS, adrenal or ovarian tumor is important because the latter group may be at risk for tumor-related complication. Children with precocious puberty may be stressed because of physical and hormonal changes and they are too young to understand.⁵ Going through puberty early can also be difficult for a child emotionally and socially. For example, girls with precocious puberty may be confused or embarrassed about physical changes such as getting their periods or having enlarged breasts well before any of their peers.⁵ In case with progressive

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precocious puberty, they may present with adverse psychosocial outcomes, early menarche and short stature, because of early epiphyseal fusion.  

Here we present a case of a female child who was diagnosed as a case of precocious puberty.

Case report

A 4-year-old female child was brought by her parents to the Obstetrics & Gynecology outpatient department of Diabetic Association Medical College Hospital, Faridpur having bilateral enlargement of breasts, presence of pubic hair for one year and history of periodic bleeding per vagina for three months. According to the statement of patient her child was well one year back. Her milestones of development were normal. But she noticed gradual enlargement of her breasts and growth of pubic hair. Her mother also noticed that the girl was having per vaginal bleeding which evolved into monthly regular cycles of three to four days. She had no history of birth injury, head injury, encephalitis, headache or seizure.

General physical examination of the patient was within normal. Her height was 100 cm, weight 17 kg and there was no skin pigmentation. Examination of breasts revealed that her both breasts were enlarged and firm in consistency. Nipple and areola were found developed. There was no discharge. Axillary and pubic hair was long, curved and dark. On per abdominal examination, there was no palpable lump. She had normal hematological and biochemical profiles. Hormonal analysis revealed pubertal response of gonadotropins with luteinizing hormone (LH) of 2.30 mIU/mL (N <0.6 mIU/mL), follicle-stimulating hormone (FSH) of 4.98 mIU/mL (N <0.6 mIU/mL), and estradiol (E2) of 9.6 pg/mL (N <5 pg/mL), with normal thyroid functions. Radiography of the left wrist revealed bone age greater than chronological age. Ultrasonography of abdomen showed prominent ovaries (right ovary 2.8 x 1.0 cm and left ovary 1.9 x 1.0 cm) and follicles were present in each ovarian parenchyma, uterus was measuring about 4.7 x 1.3 cm (L x AP). Tumor markers such as carcinoembryonic antigen (CEA), CA 125, alpha fetoprotein and human chorionic gonadotropin (HCG) were negative. MRI of brain showed hypothalamic hamartoma (Fig 1). Finally the girl was diagnosed as a case of central precocious puberty due to hypothalamic hamartoma. After counseling patient’s guardian, treatment was started. GnRH agonist, Inj. Decapeptyl 3.75 mg every 4 weeks was prescribed (the drug should be continued up to 11 years of age). One month after treatment she still had menstruation and there was increased pubic and axillary hair. But after two years of follow-up, there was subsidence in size of the hypothalamic hamartoma, reversal of secondary sexual characters and regression of monthly menstrual cycles.

Fig 1. Midsagittal and coronal MRI of brain showing hypothalamic hamartoma

Discussion

Precocious puberty is an unusually early onset of puberty, statistically defined as -2.5 to 3.0 SD below the average age of onset of puberty in healthy children. It is a rare condition. The gonadotropin-dependent type (GDPP), also known as central precocious puberty, is the most common subtype and is characterized by an early maturation of the hypothalamic-pituitary-gonadal axis. This is much more common in girls than in boys. Here the pattern and timing of pubertal events progress in the normal sequence. Eighty to ninety percent of GDPP will have no identifiable cause (idiopathic GDPP) and this condition will have a striking female predominance. The other important causes include CNS tumors, trauma, infections, primary hypothyroidism, hydrocephalus, cysts etc.

Hypothalamic hamartoma is a relatively rare congenital malformation usually associated with central precocious puberty and gelastic seizures. This tumor is composed of redundant brain tissue with a haphazard assembly of neurons, nerve fibers and neuroglial cells in inappropriate distributions and proportions. The association of hypothalamic hamartoma with precocious puberty has long been recognized. In fact, hypothalamic hamartoma is one of the most common cerebral lesions associated with precocious puberty.

Children with precocious puberty due to hypothalamic hamartomas usually present before four years of age. Although the mechanism for precocious puberty is not
known, the prevailing view is that hypothalamic hamartomas contain ectopic luteinizing hormone releasing hormone (LHRH) neurosecretory neurons which are unrestrained by the normal negative feedback mechanisms and produce secretory bursts of LHRH.¹¹

This patient had a normal pattern of pubertal growth, a quicker skeletal maturity and an elevated level of luteinizing hormone (LH). All these findings are characteristic of GDPP or central precocious puberty.¹² MRI is the primary imaging modality for detection of hypothalamic hamartomas, allowing better tissue characterization and greater anatomic details.¹² The imaging features most commonly consist of a hypothalamic mass isointense to grey matter on T1W sequence, and increased signal intensity on T2W and FLAIR (fluid attenuated inversion recovery) sequence.⁸ The MRI of this patient revealed all these features.

Medical treatment with long-acting GnRH agonists is the first choice of treatment in patients with CPP due to hypothalamic hamartoma.¹³ In particular, depot preparations ensure an adult height within the genetic height potential with normal body proportions, bone density and reproductive function.¹⁴ Surgical resection of the hypothalamic hamartoma is indicated only in cases of progressive neurological deficit, hydrocephalus, and progressive enlargement of the mass and intractable seizures.¹⁵

Conclusion

Thorough history taking and careful examination are required to determine the possible causes of precocious puberty. Additional evaluation should include hormonal assays and bone age assessment (E2, LH and TSH). If a randomly measured level of LH is in the pubertal range, an MRI brain should be obtained. A pelvic ultrasound scan is required to rule out an ovarian tumor or cyst, mainly if the E2 level is elevated. A GnRH or GnRH-agonist stimulation test is the gold standard for diagnosing CPP, and is recommended to assess the activation of the gonadotrophic axis, for predicting the progression of puberty. In case of progressive CPP, treatment with a depot GnRH agonist is suggested and is generally continued for 11 years, even though the best duration of therapy is undecided.

References