Three Patients with Autism and Central Precocious Puberty

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Abstract. We have experienced three patients of autism combined with precocious puberty. Their age at diagnosis of precocious puberty ranged from 6 yr and 9 mo to 9 yr and 6 mo. All patients showed pubertal growth spurt and elevated levels of basal LH and FSH, and experienced menstruation. One patient was diagnosed as having central precocious puberty according to the diagnostic guidelines. The other two patients were on borderline sexual precocity. They have been treated with GnRH analog for the purpose of stopping menstruation, which was not tolerated for their mentality. Similar to known combination of CNS disorders and precocious puberty, patients with autism may be susceptible to the early onset of puberty.

Key words: central precocious puberty, autism, GnRH analog

Introduction

It is not well described so far that the combination of precocious puberty and autism frequently occur, although clinicians experience that patients with autism tend to have early sexual maturation. Patients diagnosed as having autism are increasing in recent years, because of widened awareness and the changes in the diagnostic criteria. We report three cases of autism combined with central precocious puberty.

Patient Report

Patient 1

Patient 1 was a 6 yr and 11 mo old female. She was born of a normal pregnancy and delivery at 41 wk of gestation. There was no family history of neurological and psychiatric disorders. From infancy she showed impaired language communication and diagnosed as autism at the age of 5 yr and 6 mo. Breast budding was noticed at 5 yr and 9 mo. At 6 yr and 9 mo old, her height was 119.3 cm (+0.41 SD), her weight was 21.64 kg (%overweight: –4.4%), and the height velocity was 9.3 cm/y (+5.0 SD) (Fig. 1). Pubertal stages were Tanner III for breast and Tanner I for pubic hair. Her bone age was 10 yr and 9 mo according to the TW-2 (J-RUS) methods. Her ovaries, uterus and adrenal glands were normal in size for her age. LH showed response from 4.18 to 40 mIU/ml, FSH from 4.2 to 17.4 mIU/ml after GnRH loading, which was pubertal levels. Diurnal variations of LH and FSH were determined by every twenty-minute blood sampling for three hours during day and night. Nocturnal secretion (3 h during sleep) showed mean LH of 7.26 mIU/ml, FSH of 6.55 mIU/ml. Daytime secretion (3 h) showed mean LH of 0.30 mIU/ml, FSH of 2.83 mIU/ml. Serum E2
was 61.9 pg/ml, IGF-1 was 210 ng/ml and DHEA-S was 115 ng/ml. Serum HCG and AFP were within normal range. A cystic lesion on pituitary was observed in MRI, which was suspected to be pituitary microadenoma or a cyst.

### Patient 2
Patient 2 was a 10 yr and 1 mo old female. She was delivered by cesarean section at 41 wk of gestation. Her family history was unremarkable. The diagnosis of autism was made during infancy according to her behavior. At the age of 8 yr and 9 mo, breast budding was noticed by the family. At 9 yr and 4 mo, she had menarche. At the age of 9 yr and 6 mo, she was referred to our hospital for the assessment of puberty. Her height was 140.7 cm (+1.16 SD), her weight was 33.16 kg (% overwt 4.6%), her height velocity was 9.0 cm/yr (+4.25 SD) in this year and 7.0 cm/yr (+2.13 SD) in the last year (Fig. 2). Her pubertal stages were Tanner III to IV for breast and Tanner III for pubic hair. Basal LH was 1.69 mIU/ml, FSH was 9.44 mIU/ml, E2 was 27.1 pg/ml, IGF-1 was 600 ng/ml. Brain MRI showed no abnormality.

### Patient 3
Patient 3 was a 10 yr and 11 mo old female. She was born by vaginal delivery at 42 wk of gestation without complications. Her father has dyschromatopsia. She was diagnosed as Gianotti syndrome at 2 yr old and as having atypical autism. At the age of 8 yr and 3 mo, she showed breast budding and at the age of 9 yr and 4 mo, she had menarche and showed development of pubic hair. At 9 yr and 6 mo old, her height was 136.8 cm (+0.44 SD), her weight was 31.75 kg (% overweight 1.2%), the height velocity in this year was 10 cm/yr (+5.5 SD) and in last year was 8.4 cm (+3.88 SD) (Fig. 3). Pubertal stages were Tanner III for breast and pubic hair. Her bone age was 11 yr and 7 mo by the TW-2
Autism and Precocious Puberty

(J-RUS) method. LH and FSH responses to GnRH loading test were from 8.36 to 93.6 mIU/ml, and from 5.82 to 18.5 mIU/ml, respectively. Serum E2 was 30.0 pg/ml, IGF-1 310 ng/ml and DHEA-S 175 ng/ml. Brain MRI showed normal pituitary, cavum vergae and cyst at septum pellucidum.

These three patients have been treated with GnRH analog for the purpose of stopping menstruation. Patient 1 started GnRH analog at 6 yr and 10 mo, Case 2 started at 9 yr and 6 mo, case 3 started at 9 yr and 8 mo.

Discussion

Autism is a disease of wide spectrum with developmental disorders characterized by impairments of social interaction, language communication, imaginative play, range of interests and activities. Patients with autism are increasing in recent years, due to heightened awareness and the changes of diagnostic criteria.

Clinically, it is observed that patients with autism tend to have early sexual maturation (1, 2). However, the frequency of precocious puberty in autism has not been clearly documented. Mouridsen SE et al. (2) reported a case of pervasive development disorders and idiopathic precocious puberty (2). Their case showed Tanner stage II for breast development and Tanner I for pubic hair at the age of 5 yr and 10 mo. Her bone age was 8–10 yr, and the brain MRI was normal.

Here we report three patients of autism combined with sexual precocity. Patient 1 met the diagnostic guidelines of central precocious puberty (2001 edition by the Study group of precocious puberty in Ministry of Health, Labor, and Welfare). On the other hand, patients 2 and 3 were suspicious of central precocious puberty. Two of three patients showed abnormal/subnormal findings in brain MRI; microadenoma or cyst in pituitary was suspected in patient 1 and cavum vergae, cyst of septum pellucidum was found in patient 3. It is not clear that these brain abnormalities can be an etiology for early pubertal maturation. Mouridsen et al. (2) reported that there was no lesion in the brain and the endocrine glands.

All three patients have been treated with GnRH analog. The purpose of the treatment is mainly to stop the regular menstruation, which is hard for them to manage.

In conclusion, patients with autism are relatively susceptible to the early onset of puberty. Treatment for sexual precocity should be considered upon not only bone age maturation and growth but also their mental maturation.

References