ORIGINAL ARTICLE

Isosexual Precocity in Girls

by

M. SUTAN ASSIN

(From the Clinic for Pediatric and Adolescent Endocrinology, Department of Child Health, Medical School, University of Indonesia, Jakarta).

Abstract

Puberty is considered precocious when the onset takes place prior to eight years of age. Isosexual precocious puberty indicates that sexual development has occurred appropriate to the individual's phenotype. This can be a) true sexual or b)pseudosexual. In true sexual precocity there is a premature activation of hypothalamic-pituitary axis, while pseudosexual precocity is due to disease of the gonads or adrenal glands or, rarely, other hormone producing tissues. Incomplete sexual development can be "premature thelarche" or "premature pubarche".

We have encountered 13 cases of precocious puberty in girls in 10 years time (1971 - 1980). Eight of them were idiopathic. Diagnostic procedures, medical treatment and psychosocial handling are discussed in this paper.

Presented at the first intensive Course in Obstetrics and Gynaecology, Asia and Oceania Federations of Obstetrics and Gynaecology, Bandung, June 12 - 14, 1982.

Introduction

Puberty is characterized by the development of secondary sex characteristics, adolescent growth spurt, changes in body composition, increased strength, change in behaviour, and finally the attainment of fertility (Kryston, 1981).

Puberty marks the end of the process which began in foetal life, the long period of development which prepares the individual for reproductive life. The time at which puberty is initiated varies with such factors as inheritance, nutrition and general health, geography, altitudes, chronic diseases and other environmental influences.

When the onset of puberty takes place prior to eight years of age in girls, then it is considered to be precocious.

Isosexual precocious puberty indicates that sexual development has occurred appropriate to the individual's phenotype. This can be True sexual or Pseudosexual (see Table 1).

In true sexual precocity there is a premature activation of the hypothalamic-pituitary axis leading to increased circulating levels of gonadotropins. The result will be a complete sexual development and eventually fertility. In pseudosexual precocity the sexual development is incomplete.

TABLE 1. *Causes of Isosexual Precocity in Girls.*

I. True Sexual Precocity	II. Pseudosexual Precocity
A. Idiopathic or Constitutional	
B. Intracranial processes	A. Ovarian tumors : granulosa cell tumors; thecal cell tumors; follicular cysts; teratomas etc.
1. post infectious : meningitis, encephalitis	B. Feminizing adrenal tumors.
2. trauma	C. Iatrogenic.
3. tumors	D. Estrogenic producing tumors
4. congenital anomalies	
5. diffuse cerebral atrophy	
6. primary hypothyroidism	
7. tuberous sclerosis	
8. various syndromes : McCune-Albright; Silver's; mongolism.	

True precocious puberty.

The majority of females with true precocious puberty has an idiopathic sexual precocity. The most striking clinical feature is the presence of secondary sex characteristics as a result of premature release of pituitary gonadotropins. The sequence of their appearance may not follow the normal pattern.

Premature puberty usually causes excessive linear growth and bone maturation and the patients are taller than their peers. However, liniar growth will terminate earlier due to epihyseal closure and their adult height is usually shorter then average. There is premature breast budding and growth of pubic hair and eventually axillary hair. Stimulation of the ovary by gonadotropins causes estrogen secretion, follicle maturation, ovulation and cyclic menstrual bleeding.

Plasma concentration of FSH and LH are usually elevated. Progesteron may be normal or elevated. Serum estrogen and urine 17-ketosteroid are also elevated. All laboratory values correlate better with the stage of sexual maturation and bone age than with the chronological age (Hung, 1978).

Sexual precocity secondary to cerebral organic cause is simulating the idiopathic type, with the difference that there is a lesion intracranially which causes the prematures onset of puberty. Tumors, encephalitis, meningitis, trauma, and other intracranial processes may cause true precocious puberty. Rare cases are McCune-Albright syndrome, mongolism, polydactylism and primary hypothyroidism.

Pseudosexual praecocity.

Pseudosexual praecocity is due to disease of the gonads or adrenal glands or, rarely, other hormone producing tissues. In these disorders there are no gonadotropins released by the pituitary so that in females no normal ovulation and cyclic menstrual bleeding will be established. FSH and LH levels in serum are not elevated. Serum estrogen is usually elevated, progesteron may be normal or increased. The bone age is accelerated. Vaginal smear mostly shows a significant estrogen effect.

Careful abdominal. pelvic and gynecologic examination should be done to detect an ovarian or adrenal tumor Pneumography, ultrasonography or laparoscopy may be necessary.

Premature Thelarche is precocious development of one or both breasts. The picture of sexual development is incomplete. No sexual hair is present, nor any other signs of puberty. The cause is likely a hypersensitivity of breast tissue to basal levels of estrogen. Iatrogenic premature thelarche is also possible.

Premature Pubarche is precocious development of sexual hair without other secondary sexual characteristics. Adrenal tumor or hyperplasia must be ruled out.

Incidence of all types of Isosexual Precocious Puberty in Girls.

Wilkina (1965) in a review from his own cases and three other investigators, Seckel (1965), Jolly (1955) and Thamdrup (1961) found that precocious puberty in girls was twice as common as in boys. Out of 601 girls with Precocities, 453 (75%) were of the idiopathic type, 31 (5 %) had proven or highly suspected intracranial lesions; 34 (6%) with Albright's syndrome; 81 (13%) had ovarian tumors; and only 2 (0,3 %) had adrenal lesions.

In our clinic for Pediatric Endocrinology in 10 years time (1971 - 1980) we had 13 cases of girls with precocious puberty (see table 2).

TABLE 2 :*Cases of Precocious Puberty in Girls (1971 - 1980).*

	age at onset (years)	number
Idiopathic	1 - 8	8
Post meningitis tbc	5	1
Albright syndrome	8	1
Ovarian cyst	8	1
Adrenal tumor	3	1
C.A.H.	5	1
		Total 13

Diagnostic procedures.

A detailed history concerning the onset of the breast enlargement, axillary and pubic hair growth as well as the vaginal bleeding should be taken. Intracranial lesions in the neonatal period or in childhood such as trauma, infections or other processes must be reviewed. Exposure to ingested or topical sex hormones during fetal life and childhood may also be a cause.

The following procedures should be done to reach the final diagnosis.

1. Accurate history and physical examination.
2. Evaluation of height and weight on the growth-chart.
3. X-ray examination :
   a. skull and sella tursica.
   b. bone age and epiphyseal discs
   c. prediction of adult height.
4. Laboratory :
   a. peripheral blood
   b. hormones in serum : FSH, LH, PRL, Estrogen, TSH, T4, T3 (when indicated)
   c. urine : 17-KS, 17-OHCS, Pregnandiol.
5. Vaginal cytology.
6. Gynecological examination.
7. Neurological examination.
8. When necesary ;
   a. CAT scan, pneumoencephalogram, arteriogram, EEG
   b. abdominal x-ray, IVP, USG
   c. adrenal arteriography
   d. laparoscopy
   c. exploration.

The finding of the cause of the precocious puberty is of utmost importance because the treatment depends upon the nature of the underlying disorder.

Mostly the Pediatric Endrocrinologist needs the assistance of an expert on Pediatric Gynecology for the diagnosis and the treatment as well.

Treatment and management of precocious puberty.

The principal objectives of treatment should be :

a. to postpone and control the progression of sexual development until the normal age for puberty;
b. prevention of premature epiphysial closure and short adult height;
c. removal of the underlying disorders: tumors, ingestion of sex hormones; infection, etc.
d. appropriate psychological and social handling.

Many attempts have been made to control the sexual and skeletal development by inhibiting the secretion of gonadotropins in true sexual precocity.

Moddock and associates (1956) used hog follicle stimulating hormone (FSH) to produce antihormones. These antihormones will cause the inhibition of ovarian function. This treatment, however, was not very effective.

In 1959 Glenn et al. (quoted by Hahn, 1964) introduced the oral preparatian of medroxyprogesterone (6 MAP), but other investigators found the result very disappointing.

The long-acting intramuscular medroxyprogesterone acetate (depo-MPA) first used by Kupperman and Epstein (1962) in children with constitutional precocious puberty gave better results. This was confirmed by Hahn et al. in 1964, but they found that although menses and breast development could be controlled effectively by MPA, the skeletal maturation and linear growth were not slowed down.

In our clinic we are still treating 4 girls (3 with idiopathic and 1 with post tbc. -meningitis precocity) with long-acting MPA (Depo Provera). The dosage we use is 150 mg. every 2 to 4 weeks. The results so far are quite satisfactory.

The introduction of a new drug, cyproterone acetate, by Neumann and Hamada in 1964 offers new possibilities in the treatment of precocious puberty.

Cyproterone acetate possesses antiadrogenic and antigonadotropic properties. The efficacy of the drug is much greater when it is given by mouth than by depot injections (Kauli et al., 1976). The recommended dosage is 70-150 mg/m^2 per day.

Its effect on slowing down growth and bone maturation is still debatable (Job, 1981).

The psychological and social handling of the patient is even of greater importance than the medical treatment. The child must be guided through the "dangerous" years and should be protected against sexual abuse by adults.

The best way to achieve this is a close cooperation between the patient her parents, her teachers, the psychologist and a team of clinician with enough experience in dealing with the problems of precocious girls.

REFERENCES

1. GLENN et al. quoted by HAHN, H.B.; HAYLES, A.B.;ALBERT, A.: In Medroxyprogesteron and Constitutional Precocious Puberty, Mayo Clin. Proc. 39:182-190 (1964).
2. HAHN, H.B.; HAYLES, A.B.; ALBERT, A.: Medroxyprogesteron and Constitutional Precocious Puberty, Mayo Clin. Proc. 39 : 182 - 190 (1964).
3. HUBBLE, D.: Paediatric Endocrinology (Blackwell Scient. Publ., Oxford and Edinburgh 1969).
4. HUNG, W., AUGUST, G.P., GLASGOW, A.M.; Pediatric Endocrinology. (Topan, Singapore (1978).
5. JOB, J.L.; PIERSON, M.: Pediatric Endocrinology, (John Wiley & Sons, New York 1981).
6. JOLLY H.; Sexual Precocity. Springfield, Thomas, 1955; quoted by Wilkins, L., in The Diagnosis and Treatment of Endocrine Disorders and Adolescence. (Charles C. Thomas Publ., Springfield III. 1965).
7. KAULI, R.; PERTZELAN, A.; PRAGER-LEWIN, R.; GRUNEBAUM, M.; LARON, Z.: Cyproterone acetate in treatment of precocious Puberty, Archs. Dis. Childh. 51 : 202 (1976).
8. KRYSTON, L.J.: Endocrine Disorders (Med. Exam Publ., New Work (1981).
9. KUPPERMAN, H.S., EPSTEIN, J.A.: Medroxyprogesterone acetate in the treatment of constitutional sexual precocity. J. Clin. Endocr. 22 : 456, 1962.
10. MADDOCK, W.D.; LEACH, R.B.; TOKUYAMA,I.; PAULSEN, A.; ROY, W.R.: Effects of hog Pituitary follicle-stimulating hormone in women : antihormone formation and inhibition of ovarian function. J. Clin. Endocr., 16 : 433, 1956.
11. NEUMANN, F.; HAMADA, H. (1965) quoted by KAULI, R. et al.: Cyproterone acetate in treatment of precocious puberty, Archs. Dis. Childh. 51 : 202 (1978).
12. SECKEL, H.P.G.; Med. Clin. N. Amer., p. 183,1946; quoted by WILKINS, L., in The Diagnosis and Treatment of Endocrine Disorders and Adolescence. (Charles C. Thomas Publi., Springfield, III. 1965).
13. THAMDRUP, E.; Precocious Sexual Development, Springfield, Thomas, 1961; quoted by Wilkins, L., in The Diagnosis an Treatment of Endocrine Disorders and Adolescence (Charles C. Thomas Publ., Springfield, III. 1965).
14. WILKINS, L.: The Diagnosis and Treatment of Endocrine Disorders of Child hood and Adolescence (Charles C. Thomas Publ., Springfield, III. 1965).