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Typology and Etiology of Precocious Puberty in Sub-Saharan Africa: Report of 8 Cases in Abidjan, Ivory Coast

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Abstract

Introduction: Early puberty is defined by development of secondary sexual characteristics before the age of 8 years in girls and 9 years in boys. In the West, one in five children out of 100,000 is concerned. Little information on sub-Saharan African patients exists concerning this pathology. **Objective:** To determine the etiology and clinical characteristics of early puberty in a cohort of Ivorian children. **Methods:** We conducted a cross-sectional study between 2015 and 2017 in children admitted to early puberty in the unique Endocrinology Service of the country. The epidemiology and clinical characteristics were assessed. **Results:** The eight patients involved were all females. Their mean age at diagnosis was 7 years and 3 months and the mean age of first symptoms begun at 5 years and 6 months. Seven patients had a central precocious puberty (CPP) including five cases of idiopathic CPP (ICPP) treated by (GnRH agonist) and two cases with secondary precocious puberty (SPP). One of them has a hypothalamic hamartoma and the other a sequelae of encephalopathy. The last case had a peripheral precocious puberty (PPP) causes by ovarian dystrophy. **Conclusion:** Our results confirm the predominance of idiopathic central precocious puberty particularly in girls.

Keywords

Early Puberty, Secondary Sexual Characteristics, Stature

1. Introduction

Early puberty or precocious puberty (PP) is not uncommon. It is defined by the development of secondary sexual characteristics before age 8 in girls and before age 9 in boys. In the West, one to five children out of 100,000 are concerned predominantly female [1]. The etiological features of early puberty are numerous. Early central puberty occurs more often in girls than in boys. They are more frequent among adopted girls from developing countries [2]. In girls, they are more frequently idiopathic (80% of cases), whereas neurogenic causes are more common in boys (60%). We must distinguish central early puberty involving pulsatile Gonadotropin-Releasing hormone (GnRH) secretion due to premature activation of the hypothalamic-pituitary axis, early peripheral puberty due to secretion of sexual steroids by the gonads or adrenals. The central origin of early puberty is demonstrated by elevated basal pituitary gonadotrophins and/or stimulation by Luteinizing Hormone Releasing Hormone (LHRH). It is the response to the LHRH test which is the key to the diagnosis of central early puberty: LH peak greater than 5 IU/L. LH/FSH peak ratio > 0.66 [3]. Little work has been done on the issue in sub-Saharan Africa. However some show association with sexual infections [4].

2. Objective

Examine the etiology and clinical characteristics of early puberty in a cohort of Ivorian children.

3. Methods

We conducted a cross-sectional study between 2015 and 2017 from all cases of children admitted to early puberty in the unique Endocrinology Service of Ivory Coast. Patients in whom the diagnosis of PP was suspected or posed by the pediatrician or general practitioner were referred to us for management.

The data on sex, age, height, weight, body mass index, health history have been collected. The diagnosis of PP is based on evaluation of secondary sexual characteristics according to Tanner stage [5], the acceleration of the growth rate, the advance of bone maturation according to the Atlas of Greulich and Pyle [6], and the pituitary-gonadal biological activation, including levels of LH and FSH, estradiol. Pelvic ultrasound and computed tomography (CT) or magnetic resonance imaging (MRI) of the brain were made to find specific etiology. No attemps were done to identify any gene mutations like KISS1, MSRN3 because of non availability. Neurosurgery has been performed to treat harmatoma and gonadotrophin releasing hormone agonist used to slow down pubery and improve the adult weigh as possible although is cost remained prohibitive in our country.

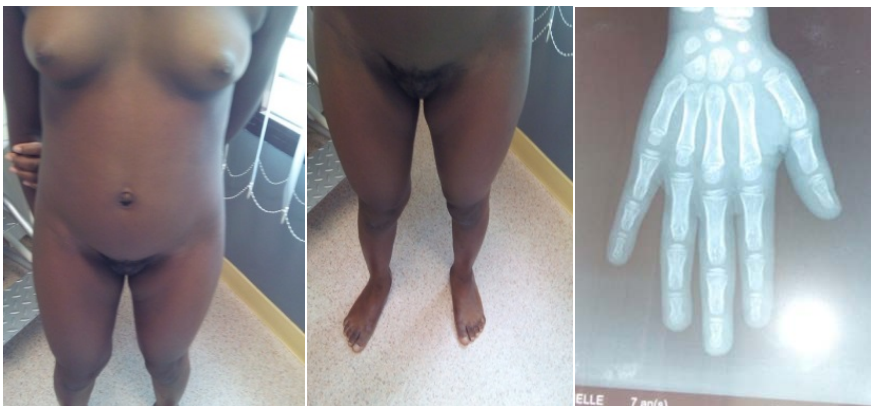
4. Results

Eight patients had been identified and were all females with age at consultation varies from 7 years 3 months (2 years 9 months to 11 years) and age of onset of

Table 1. Main characteristics of patients with early puberty.

	1	2	3	4	5	6	7	8
Age (years)	2 ys 9 months	6 ys	7 ys	7 ys 6 months	7 ys 11 months	8 ys	11 ys	7 ys 8 months
Beginning of signs (years)	2	5	6	5	6	7	6	6
Physical examination								
SP	S2P2	S3P3, menarche	S4P4	S4P4 Figure 1(a), Figure 1(b)	S4P3, menarche	S3P3	S3P2	S3P3
Weight (kg); Height (m)	9.8; 0.86	28; 1.30	31; 1.24	36; 1.37	37; 1.39	34; 1.37	75; 1.56	43; 1.4
BMI: Overweight: 85 < BMI < 95;Obesity ≥ 95	<85	<85	<85	<85	<85	<85	Obesity	Overweight
Biology								
FSH (UI/L)	3	0.06	5	4.8	5.2	3.2	-	-
LH(IU/L)	2.5	0.01	4	12	3.5	2.7		
E2(pg/ml)	0.1	46	0.3	1	4	5	-	-
Imaging								
Bone age (years)	5	7	10	11 Figure 1(c)	11	12 1/2	13	11
Pelvic Ultrasonography/	-	Left ovarian cyst	-	-	-	-	-	-
MRI/CT Scan	Microcephalia by Encephalitis	-	-	-	Hamartoma	-	-	-
Etiology	SCPP	PPP	ICPP	ICPP	SCPP	ICPP	ICPP	ICPP
Treatment	-	Decapeptyl	Decapeptyl	Decapeptyl	Neurosurgery	Decapeptyl	Decapeptyl	Decapeptyl

SP: Tanner classification, BMI: Body Mass Index, FSH: Follicle Stimulating Hormone, LH: Luteinizing Hormone, E2: oestradiol, MRI: Magnetic resonance imaging.



(a) (b) (c)

Figure 1. Child KS 7 years 6 months; P4 S4 (Tanner) and bone age to 12 and a half years. (a) Tanner S4; (b) Tanner P4; (c) bone age to 12 years.

signs 5 years 6 months (1 to 7 years). Clinical and laboratory examinations of our patients were classified into two categories, central PP (7 cases) and peripheral PP (1 case). Among the 7 cases of central PP 5 in which brain imaging and ultrasound were normal adrenals and ovaries did not show any abnormality were classified idiopathic (ICPC). Among the other 2 SPPC one had sequelae of encephalitis with microcephaly and the other hypothalamic hamartoma. Only one of the girls was diagnosed as peripheral PP (PPP) related to a left ovarian cyst. The 6 cases of ICPP were treated with GnRH agonist, the patient with a hamartoma had been surgically treat while microcephaly had no treatment due to lack of financial means. The main characteristics of the patients are listed in Table 1.

5. Discussion

Precocious puberty is more frequent in girls [7]. All our patients were females and the youngest was under 3 years of age. The youngest child with early puberty reported in the literature was 6 months old [8].

In etiological aspects, PP has a multitude causes (**Table 2**) [9]. CPP is dominant and is most often idiopathic related to genetic factors (family), epigenetic (migration) or environmental (nutritional, endocrine disorders) [9]. The ICPP concerns 6/8 of our cohort. Estimates of the frequency of central nervous system pathology causing CPP vary widely. In girls, estimation of idiopathic CPP range from 69% to 98%, compared with 0% to 60% in boys.

In family ICPP there is central obesity as reported by Chen in China especially in women (38.9%) [10]. Hypothalamic hamartoma is an uncommon cause of central precocious but has a significant importance [11] [12] and is often revealed by an epileptic seizure; we found one case with gelastic epilepsy and delayed psychological development. She presents vaginal bleeding during hospitalization in neurosurgery. Other neurological causes may be involved [9] including encephalitis leading to microcephaly in our patient. The cause of PPP is cyst or ovarian tumor, adrenal tumor, congenital adrenal hyperplasia, and Mc Cune-Albright syndrome. Our PPP patient with an ovarian cyst had elevated estradiol and decreased LH and FSH.

In addition to the development of secondary sexual characteristics, puberty is associated with a rapid growth rate and bone maturation leading to a decrease of global final height [9]. This disorder may cause psycho-sociological problems especially in girls [13]. In Africa, particularly in the Republic of Congo, early puberty is perceived among girls as a risk of early sexuality, with corollary early marriage and pregnancy. To combat a PP in girls, family use several practices.

Table 2. Etiology of early puberty.

Central precocious puberty
idiopathic, International Adoption
Tumors of the central nervous system:
Hypothalamic Hamartoma, Chiasma glioma, Hypothalamic Astrocytoma
Syndromes: Neurofibromatosis, tuberous sclerosis, Silver-Russel
Activating mutation of the kisspeptin receptor
Correction/Treatment of Prolonged Exposure to Sexual Steroids
Peripheral precocious puberty or early pseudo-puberty
In the girl
Ovarian or Adrenal Tumor, Mc Cune Albright Syndrome
In the boy
Testicular tumors (Leydig cells) or adrenal cells or hCG cells
Testotoxicosis linked to an activating mutation of the LH receptor (familial)
For both sexes
Congenital adrenal hyperplasia

For mammary gland, it is often recommended regular palpation by a male subject of the family up to "disappearance" or compression by bandages. When it is more developed, the girl is inflicted with blows of a spatula, which may be moderate strength to extreme violence. For the hair hot water baths regularly is used [14]. However, when diagnosed and treated earlier is started properly progresses to slowing puberty improving final height in patients [15].

6. Conclusion

The authors advocate the sensitization of the populations in order to make early diagnosis and treatment. However MRI is inaccessible and gonadotrophin releasing hormone which is indicated to slow puberty and improve final height has excessive cost.

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