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ORIGINAL ARTICLE

Natural progression of premature pubarche and underlying diseases☆,☆☆

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KEYWORDS
Idiopathic premature adrenarche;
Premature pubarche;
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Abstract
Introduction: Premature pubarche (PP) is generally thought to be a benign condition, but it can also be the first sign of underlying disease.
Objective: To analyse the aetiology and the evolution of the anthropometric, analytical and metabolic risk parameters of a group of patients with PP.
Material and methods: A descriptive and analytical retrospective study of 92 patients affected by PP. Anthropometry, analyses, bone age and indicators of lipid metabolism were all evaluated.
Results: The sample included 92 patients with PP (67 female and 25 male), with a mean age of 7.1 ± 0.6 for girls and 8.3 ± 0.7 for boys. Small for gestational age was recorded in 7.7%. There was an accelerated bone age (1.20 ± 0.1 years). A total of 21 patients were classified as idiopathic (23%), 60 as idiopathic premature adrenarche (65%), and 11 with non-classic congenital adrenal hyperplasia (12%). Puberty was reached early ($11 + 0.9$ years old in boys and 9.9 ± 0.8 in girls), as was menstruation age ($11.8 + 1.1$ years old), $P < .001$. The stature finally reached was close to their genetic stature. There is a positive correlation between body mass index, blood glucose and LDL cholesterol, as well as a tendency towards hyperinsulinaemia.
Conclusions: The present study shows that PP is a benign condition in the majority of cases, but non-classic congenital adrenal hyperplasia (12%) is not uncommon. Menstruation and puberty started early and bone age was accelerated. Growth was normal, and more or less in line with genetic size. PP associated with obesity is linked with analytical variations of metabolic risks.

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PALABRAS CLAVE
Adrenarquia prematura idiopática;
Pubarquia precoz;
Hiperplasia suprarrenal congénita no clásica;
Pubertad

Evolución natural de la pubarquia precoz y posibles patologías asociadas

Resumen
Introducción: La pubarquia precoz (PP) es generalmente considerada como una enfermedad benigna, pero puede ser el primer signo de una enfermedad subyacente.
Objetivo: Analizar la etiología y la evolución de parámetros antropométricos, analíticos y de riesgo metabólico, en pacientes con PP.
Material y métodos: Estudio retrospectivo, descriptivo y analítico, de 92 pacientes afectos de PP. Se evaluaron medidas antropométricas y analíticas, la edad ósea y marcadores de metabolismo lipídico.
Resultados: Muestra de 92 pacientes (67 mujeres y 25 varones) con PP, con una edad media de $7{,}1 \pm 0{,}6$ años las mujeres y $8{,}3 \pm 0{,}7$ los varones. El 7,7% fueron pequeños para la edad gestacional. La edad ósea estaba adelantada ($1{,}2 \pm 0{,}1$ años). Veintiún pacientes fueron clasificados como PP idiopática (23%), 60 como adrenarquia precoz idiopática (65%) y 11 como hiperplasia suprarrenal congénita no clásica (12%). La pubertad se mostró adelantada respecto a la media ($11 \pm 0{,}9$ años en varones versus $9{,}9 \pm 0{,}8$ años en mujeres), así como la edad de la menarquia ($11{,}8 \pm 1{,}1$ años), $p < 0{,}001$. La talla final alcanzada es próxima a la talla genética. Existe una correlación positiva entre el Z-*score* del índice de masa corporal, la glucemia y el colesterol LDL, así como una tendencia a la hiperinsulinemia.
Conclusiones: El presente estudio demuestra como la PP en la mayoría de los casos supone una patología benigna, no siendo infrecuente la hiperplasia suprarrenal congénita no clásica (12%). Estos pacientes presentaron un adelanto puberal, de la edad ósea y de la menarquia. El crecimiento fue adecuado, alcanzando prácticamente su talla genética. La PP asociada a obesidad presenta alteraciones analíticas de riesgo metabólico.

Introduction

The term pubarche refers to the development of pubic hair, which may be an isolated event or be accompanied by axillary hair, oily skin, acne or adult-like body odour. This process is considered premature when it occurs before age 8 years in girls and 9 years in boys.[1–4] Each of these clinical features may appear in isolation in the context of physiological adrenarche, which starts at around age 6–8 years.[5] Premature adrenarche (PA) refers to the premature production of adrenal androgens and is the most frequent cause of pubarche. Its prevalence varies depending on the criteria applied for its definition and on ethnicity, and its incidence is higher in African American children.[6] There is a clear female predominance (female to male ratio, 9 or 10:1),[7] and is characterised by occurring independently of puberty. The best marker of adrenarche is dehydroepiandrosterone sulphate (DHEA-S): levels of this metabolite greater than 40–50 μg/dL are considered indicative of its onset.[1,2,5]

Premature pubarche (PP), in which pubarche is not accompanied by any other sign of puberty, marked virilization or an abnormally advanced bone maturation (≥2 years), is considered a normal variation.[5,8] However, there is debate as to whether it should be considered a separate clinical entity and included in the category of prepubertal hyperandrogenism, as affected girls may exhibit prepubertal hyperinsulinism and are at increased risk of ovulatory dysfunction, functional ovarian hyperandrogenism, dyslipidaemia and obesity in adolescence.[4,5]

Premature adrenarche and premature pubarche are not equivalent terms, even though they are sometimes used interchangeably. No unanimous criteria have been established in the literature to defined variations of normal such as idiopathic premature adrenarche (IPA) or idiopathic premature pubarche (IPP). Some authors consider that IPA should be defined exclusively by clinical criteria (development of pubic and/or axillary hair and/or increase of body odour of apocrine origin) before age 8 years in girls and 9 years in boys, after ruling out other diseases that can cause hyperandrogenism (tumours, adrenal hyperplasia).[4,7] Others define IPA based on the presence of clinical criteria combined with biochemical criteria (DHEA-S levels greater than those found in prepubertal children, with a cut-off value of 40 μg/dL), and IPP as pubarche occurring before age 8 years in girls and 9 years in boys after ruling out all other possible causes of hyperandrogenism, with DHEA-S values of less than 40–50 μg/dL.[1,2]

The exact mechanisms underlying this phenomenon are unknown, but it seems that the adipose tissue[2] and a hypersensitivity of the hair follicle to steroid hormones[4,9,10] may play a significant role in its presumably multifactorial aetiology.

We conducted a study on a group of patients with PP, analysing their clinical manifestations through adulthood and exploring the aetiology of PP and its association with anthropometric and laboratory values and metabolic risk factors.