

GROWTH AND DEVELOPMENTAL DISORDERS. HORMONALLY CONDITIONED STatural RETARDATION

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Abstract: *Hormonally conditioned statural retardation represents almost 10% of the total of growth disorders. In etiology, disorders of the following hormones are incriminated: somatotrope, somatomedins, thyroid hormones, insulin, vitamins of the D group, hypophysial and vasopressin gonadotropes. The clinical aspects of the hormonal etiology mechanism are numerous: the isolated somatotrope deficiency brings about harmonic dwarfism with normal sexual development, while the hypophysial dwarfism (due to other deficiencies in the hypophysial tropes) leads to disharmonic dwarfism with variable obesity, genital infantilism and infertility. The lack of the thyroid hormones leads to the disharmonic dwarfism with embryo-fetal anthropometric proportions, mixed-edematous infiltration, late puberty, cognitive retardation. Insulin deficiency leads to dwarfism, late osseous age and sexual maturity. Precocious puberty (due to somatotropes) produces the early closure of the growth cartilages. Its evolution starts from the small Hercule-type child to the hypostatural adult.*

Keywords: *hormonally conditioned statural retardation, growth*

Rezumat: *Retardul statural condiționat hormonal reprezintă aproximativ 10% din totalul tulburărilor serioase de creștere. In etiologie sunt incriminate deficiente ale hormonului somatotrop, somatomedinelor, hormonilor tiroiziene, insulinei, vitaminelor de grup D, gonadotropilor hipofizari și vasopresinei. Aspectele clinice ale nanismului de etiologie hormonală sunt diverse: deficitul izolat de somatotrop realizează nanism armonic cu dezvoltare sexuală normală, pe când nanismul panhipofizar (datorat și altor deficiente în tropi hipofizari), produce nanism disarmonic cu obezitate variabilă, infantilism genital și infertilitate. Lipsa hormonilor tiroiziene determină nanism disarmonic, cu proporții antropometrice de tip embriofetal, infiltrare mixedematoasă, pubertate întârziată, retard cognitiv. Deficiența insulinică induce nanism, vârsta osoasă și maturare sexuală întârziate. Pubertatea precoce (datorată somatotropilor), produce importanta accelerare a vârstei osoase, dereminând închiderea precoce a cartilajelor de creștere. Evoluția se face de la copilul cu aspect de mic Hercule, la adultul hipostatural.*

Cuvinte cheie: *retardul statural condiționat hormonal, creștere*

INTRODUCTION

The child, who is not an adult in miniature, is submitted to an ample process of morphofunctional and immunologic transformations, under genetic, hormonal, enzymatic control, as well as under the control of the nervous central system.

Hormonally-conditioned statural retardation represents almost 10% of the total of growth disorders.

1. Hypothalamo-hypophysial dwarfism and related entities.

Somatotrope hormone (STH) plays a central part in the growth control of the children, from birth to the end of puberty; it also plays a major part in anabolism control during life. It is responsible for the tissue construction through the stimulatory action on the messenger and ribosomal DNA, RNA. The action of somatotrope is predominantly chondrogenetic, stimulating the proliferation of chondrocytes of the cartilage, having a minor osteogenetic maturation action. This is necessary for the normal growth in height. In its total absence, the linear increase is reduced with 1/3-1/2 of the normal rate. STH is not the main growth stimulator; it induces the formation of somatomedins (IGF-1, IGF-2), which occur as a compulsory intermediary in the action of this hormone on the conjugation cartilage.

The somatotrope hormone is episodically secreted under the form of frequent pulses, which are ampler during the night.

The isolated somatotrope deficiency accomplishes a harmonic dwarfism with normal sexual development.

Pan-hypophysial dwarfism leads, besides the somatotrope deficiency, secretion deficiency of other hypophysial tropes; the resulting dwarfism being a disharmonic one, with a certain degree of obesity, genital infantilism and infertility.

Laron dwarfism is brought about by a deficiency of receptors for somatotropes with the incapacity of generating IGF-I. Somatotrope concentration is normal or increased, while IGF-I is reduced. Clinically: short stature, reduced growth speed, hypoglycaemia, excessive subcutaneous fat, late skeletal maturation, delayed puberty, blue sclerae.

2. Hypothyroidism

Thyroid hormones increase the reactivity of the

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growth cartilages upon the action of somatotrope, enhancing its stimulating action.

It stimulates both the growth and the maturation of the cells of the growth cartilage, the predominant action being the osteogenetic one. The delay in the skeleton maturation assessed through the marked delay of the osseous age is the characteristic of the thyroid deficiency mechanism.

The total absence of the thyroid hormones determines a closure almost complete of the linear growth. They play an essential part in the osseous growth and maturation, as well as in the maturation of the central nervous system. The congenital and the acquired mixed-oedema, untreated for a sufficient period of time manifest through a serious affection of the statural growth and of the segmentary proportions. The damage of the growth regulation system in this disease is quite reduced. STH values and dynamics are normal, the levels of IGF are discrete and constant, in spite of the osseous age which is extremely low – the witness of a considerable slowness of the nutritional activity at bone and cartilage level. There is a series of suspected anomalies, such as those of the growth hormone-independent, post-receptors anomalies, especially of the recovery of the receptors of different growth factors during the lysosomal manipulation. The treatment with human growth hormones does not lead to growth and the treatment with sexual steroids stimulates only the osseous age.

Clinically, the stature is short, disharmonic with embryo-fetal anthropometric sizes. Vertex-pube/pubesol relation is high. Slowing down the stature growth is the most precocious sign.

Mixed-edematous infiltration is present, as well as carotenoderma, cold intolerance, constipation, school difficulties, delayed puberty in most of the cases.

3. Desequilibrium insulin-dependent diabetes mellitus

Insulin has a strong anabolizing action, besides its effects on the glucidic metabolism. It stimulates the proteic synthesis and cell division. The close structural relations of insulin with the somatomediens groups, as well as its capacity to be fixed on the IGF-1 receptors, may explain its effects on growth. Even in small quantities, insulin has its own action on the stimulation of growth. The excessive growth of children with diabetic mothers may be the consequence of the high plasmatic level of insulin in foetus

Insulin deficiency may decrease the growth speed through complex metabolic disorders. In the diabetes controlled through diet and insulin therapy, possibly associated with malnutrition, peptidic inhibitors of the somatomedines effect on the specific receptors of growth cartilage and brain may occur in serum, slowing down the stature growth, SHS increase in serum and the self-aggravation of the metabolic control of diabetes. The nature of these peptidic inhibitors is not clarified.

Infant insulin dependent diabetes mellitus, having a long enough evolution, as well as variations, both of the insulin necessary and of its satisfaction registers dwarfism and late osseous age. Sexual

maturation is late, too. The long term improvement of diabetes control (diet, insulin therapy) usually brings about the acceleration of the growth, as well as the IGF increase in serum. The decrease of the growth speed is more obvious in the nutritional complications of the diabetes mellitus.

Mauriac syndrome is characterized through statural retardation, hepatomegaly, delayed in osseous maturation and puberty, obesity with facio-truncular predominance, facies rotund cushingoid.

Nobecourt syndrome includes dwarfism and loss of weight. The child is thin, with small waist, large liver, delayed osseous maturation and puberty, psychical instability and difficulties in insulin administration.

4. Statural retardation as a result of primary or iatrogenic hypercorticism.

Corticosteroid hormones have an inhibiting action on the growth hormones. Excessive glucocorticoids have anti-anabolic and catabolic effect, inhibiting the STH release, erythroblasts differentiation and the production of the organic osseous matrix. Endogen or exogen excess of cortisone stimulates the proteic catabolism and the decrease of the muscle force in the proximal muscles, increases the peripheral resistance to insulin with the alteration of glucose-tolerance; it determines central obesity, blood pressure, hirsutism, red cutaneous striations, osteoporosis, psychiatric syndromes: depression, irritability, insomnia. Clinically, the classical triad in children is the following: obesity, hirsutism and the slowing down of the linear growth (due to the association of glucocorticoids secretion with the excessive secretion of suprarenal androgens).

The children who have been treated with corticoadrenal steroids for a long period of time present a delay in their growth, which may lead up to dwarfism.

5. Statural retardation in the context of precocious puberty osteogenetic maturation action.

Precocious puberty is defined by the occurrence of the secondary sexualization signs before the age of 8 in girls and 10 in boys. An important acceleration of the osseous age is produced, bringing about the precocious closure of the growth cartilage. The evolution is made stating from the small Hercule type child up to the hypostatural adult.

The real (complete) precocious puberty occurs under the influence of the hypophysial gonadotropes, which lead to the excessive and premature production of estrogens or androgens. The final waist of these children is smaller than the average, although because of the puberty increase jump, the children are higher than their generation, at some point in time.

The real precocious puberty is isosexual, central and GnRH dependent. A precocious pulsatile secretion is launched, which is dependent of the gonadoliberin pulses.

Precocious pseudopuberty

Precocious sexualization is incomplete, isosexual, but gonadotropes and somatoliberin independent, consisting in the occurrence of at least two

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puberty alterations according to the genetic and phenotype sex, unaccompanied by gonadotropes puberty pulsations. It results from the excessive sexual hormones, produced by ovarian, testicular, suprarenal tumours, without the intervention of the hypophysial gonadotropes hormones or of other origins, such as the gonadotropes secreting extrahypophysial tumours

Within precocious pseudopuberty, the puberty sexualization without agamatogenesis can be distinguished from the puberty sexualization with spermatogenesis or with ovulation.

6. Statural retardation through the deficiency of the D hormovitamins.

In this situation, the statural retardation occurs through the metabolic disorders, induced by the deficiency of the D vitamins. At bone level, there are specific receptors for dihydroxycolecalciferol that promotes the chondrocytes differentiation and regulates the type II collagen production, leading to the maturation of the osteoblasts. For the skeleton mineralization, large quantities of calcium and phosphorus are necessary at the level of the mineralization sites.

D2 vitamin increases calcium and phosphorus absorption at intestinal level.

Rickets affect the growing skeleton, as the mineralization abnormalities intersect both the bone and the cartilaginous matrix of the growth plate.

Clinically, skeleton deformations can occur, as well as predisposition to fractures, muscular hypotonia and growth disorders.

7. Growth retarding in the context of the diabetes insipidus.

Central diabetes insipidus through vasopressin deficiency and renal diabetes insipidus through receptor deficiency may bring about dwarfism. The explication is the reduction of the caloric contribution due to polydipsia and to the existence of certain complex metabolic disorders.

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