Correlat ion of human growth hormone hgh),somatomedin-c (sm-c)thyriod stimulating hormone (tsh)thyroxinf (t4)and prolactin (prl)in children with growth failure using Amicrocmputer

Azza .M.A.M Abul-Fadl

SUMMARY & CONCLUSIONThis study consisted of 26 cases qf children presenting With shortstature and nine control cases from the D.E.M.P.O. Clinic in the CairoUniversity Children's Hospital. The followin" is a summary of its mostprominent findings :-1. Growth delay was the commonest cause of understature forming about35% of the overall cases, 66.7% of whom were males and 33.3% werefemales. Fifty percent of the males in the study were growth delayedand only 20% of the females were so diagnosed.2. Growth hormone deficiency (GHD) formed 19% of Egyptian childrenpresenting with short stature in our clinic of whom 80% were males and20% were females. whereas 25% of the males in the study were GHDand only 10% of the females were GHD.3. Juvenile primary hypothyroids formed about 12% of the cases andwere all females.4. The remainder of the cases comprising the miscellaneous groupconsisted of a Laron dwarf, an end organ unresponsiveness to somatomedin,la Mauriac syndrome, a Russell-Silver syndrome a query case of prolactininsufficiency, a hypogonadal short prepubertal boy and two cases withfamilial short stature with superimposed growth delay.5. Stature was most severely affected in the Laron dwarf, being farbelow -4 SO from the mean (of French standards). Patients with GHD were4 SO below the mean, patients with thyroid failure were 3 SO below themean and those with growth delay ranged from -2 SO to -4 SO below themean. So that the extent of height deficit correlated with the extentto which the hormone affected was involved in skeletal growth. Thisindicates that skeletal (linear) growth is primarily controlled by SMfollowed by GH and last but not least thyroid hormones. Growth delay,being due to the interaction of a multiplicity of factors including sometransient hormonal disturbance and consisting of a heterogenous groupof delayed children. showed this wide range in height deficit among thegroup.6. Underweight was common in all the cases. mainly below the mean(mostly -3 SO). Skinfold thickness was normal in the GHD group, butmarkedly affected in the growth delayed one, reflecting probably thedegree of malnutrition, and hence the role played by the latter in the335pathogenesis of growth delayed children.Z. The combination of estimation of SM activity together with a combinedhypothalamo-pituitary function test (ITT + TRH) proved to be verysuccessful in the diagnosis of our cases. The ITT test was simple andrapid to

perform, required minimal personnel and minimal handling ofthe patients, and has minimal side-effects, was considerably cheapcompared to other tests, and hence very convenient to use in developingcountries such as Egypt.8. Aetiologically; GHD was due to perinatal insult. idiopathic andlor hereditary. Hypothyroidism was due to late decompensation in acongenital disorder and autoimmune thyroiditis. Growth delay was dueto a combination of hereditary. environmental and social factors.Malnutrition and parasitism played a major role in pathogenesis.9. The growth delayed group fell into two well defined categories; amuscular variety in which hereditary factors predominated and a leanvariety in which nutritional and parasitic factors played a major role.Growth delay was difficult to differentiate from conditions such asfamilial short stature, hypogonadism and cases with transient GHD.10. We have described three peculiar cases of short stature:- The firstwas a GHD male Russell-Silver who did not respond to GH therapy, had alean body appearance. was dysmorphic and cryptorchoid. The second wasa male with slow growth in the first two years of life, no organicdisorder and hypothalamo-pituitary function tests suggestive of diminishedprolactin reserve. The third case was a female with dysmorphic features.infantile body proportions. stunted growth and high bioassayable SM activityand very much resembling a case described by Lanes et al (1980). Thedefect being probably due to a cellular insensitivity to somatomedin.11. We have also detected two cases with an enlarged sella turcica.The first case was a juvenile hypothyroid ~nd the second was a Lorondwarf. The enlarged sella was due to hyperplasia of the cellssecreting thyrotropin - in the first case - and to GH _ in the secondcase - secondary to thyroxine and somatomedin deficiency respectively.The second part of the study consisted of analysing hormonalinterrelationships. Positive conclusive data included briefly thefollowing:---- - ---- --- -------3361. Peak responses of growth hormone (GH) were higher in girls thanboys in the pubertal age period.2. The peak response and the degree of response of GH to insulininduced hypoglycaemia was the same in the late childhood andpubertal age periods and double that seen in early childhood.3. Very high peak GH responses were observed in some patients of thelean variety of growth delay indicating some type of peripheralresistance to GH. Partial GH responses were present in patients ofthe muscular variety of growth delay indicating a transient typeof GHD in these children.4. Somatomedin (SM) activity was observed to increase with age in themale control group of this study.5. Bioassayable 8M activity measurement in the growth delayed groupgave a wide range of values varying from marked inhibition «0.1units/nU) to values of 1.8 unitsknl, giving a fair idea of thestate of the growth conditions in the child at that particular time.SM activity gave a flat response in the prepubertal GHD patients anda marginally low 8M activity in one of the hypothyroid patients.6. There was a significant correlation between the basal SM activityand the degree of response of GH during an ITT that increased withage in the cases of the study as a whole.7. Patients with GHD and hypothyroidism showed a significant correlationbetween the degree of GH response in an ITT and the basal SM activity.Patients with hypothyroidism also showed a significant correlationbetween their basal 8M activity and peak GH response during an ITT.The correlation coefficient was high in patients with hypothyroidismindicating that 8M deficiency in these patients is related

mainlyto the secretory status of GH in this dis~ase While in patients withGHD, 8M activity is under the net control of other hormones,especially that thyroid hormones are secreted normally in thesepatients.8. In the growth delay group the disruption of the normally presentcorrelation between basal SM activity and the degree of responseof GH to ITT indicates a disturbance in growth in these patientsand may be a diagnostic feature for this condition.9. Basal and peak TSH levels decreased with age in the cases of thestudy as a whole. On analysing the sex differences during puberty,-'--3317males showed the progressive decline in the basal and peak levels.while in females the degree of response of TSH to TRH wassignificantly higher in girls in puberty than in boys of the sameage group. Also there was a highly significant correlationbetween the basal and peak TSH values that increased with age.Furthermore it was the female sex that evidenced this correlation.males showed a weaker correlation only at puberty. Basal andpeak responses of TSH were negatively correlated with the basallevels of thyroxine only in females prepubertally. from thestudy of basal. peak and degree of responses of TSH to TRH andbasal T4 in hypothyroid patients. it was deduced that the mostuseful diagnostic tool in detecting hypothyroid patients is thebasal TSH levels.10. Under physiological states there is no evident correlation betweenbasal GH. TSH and T4 in relation to age and sex. In hypothyroidismGH peak levels were reduced. On the other hand thyroid functionin patients with GHD is not entirely normal.11. The type of prolactin secretory response during the combined ITTand TRH test was analysed and correlated with other hormones. thefollowing was observed:-The PRL responses to the TRH+ ITT test observed fell into sixdistinct patterns. namely. the normal. the persistently elevated.the exaggerated. the delayed and the poor responses. On analysingthe responses in relation to age. sex and in relation to otherhormones the following was observed:-1. There were no sex differences in the PRL responses which tended tobe increasingly'hormal" with age.2. Lowered.absent or inhibited 8M activity was associated with raisedor normal PRL responses. indicative of some positive interrelation.whether direct or indirect. between both hormones.3. High PRL responses were a common finding in cases with poor GHresponse but not vice versa. While a poor PRL response was notaffected or associated with the abnormal GH response and was foundto be an independent finding. It was also common to find delayedresponses of PRL when the GH response was delayed but not vice versa.------- ----- -----._---338It was concluded that the high PRL response in the cases with poorGH response may enable us to differentiate between isolated GHDofpituitary origin and that of hypothalamic origin. as PRL responseswill be raised in the former not in the latter. Also that isolatedPRL deficiency is a primary condition independent of other pituitaryhormones and should be taken into account when diagnosing multiplepituitary hormone deficiency. Finally that the delayed responsesof PRL in a ,TRH + ITT test are due to the response of PRL tohypoglycaemia and is usually higher because of the priming effectthe TRH has on the PRL secreting cells.4. Persistently elevated PRL responses were characteristic tohypothyroidism whether primary. secondary or tertiary,probably relatedto the modality in which TRH is secreted. Hence PRL and TSH areregulated independently from one another.Last but not least. by analysing our control group and comparing itwith our delay group we were able to identify a new entity of delay.namely. the

marginal growth delay. which have some endocrine featuresin common with the delay group but are clinically normal.