

Growth in Children With Craniopharyngioma Following Surgery

Tiulpakov et al attempted to determine why some children rendered growth hormone deficient (GHD) secondary to surgery for craniopharyngioma continue to grow normally postoperatively. Twenty-five patients (14 boys, 11 girls), aged 3.8 to 18.9 years, were studied between 0.5 and 10.0 years after surgery. At the time of the study 22 were receiving thyroxine replacement, 13 glucocorticoid replacement, and 23 desmopressin for diabetes insipidus. None were receiving growth hormone (GH) or sex steroids. All children were prepubertal height. Height velocities were recorded as SDS values. Body mass index (BMI) and bone ages also were determined. Following an overnight fast, insulin-like growth factor 1 (IGF-1), IGF-binding protein 3 (IGFBP-3), IGFBP-1, and prolactin were measured. In addition, GH was measured following stimulation with oral clonidine and after 1 mg/kg GH-releasing hormone (GHRH) intravenously. Serum insulin levels were measured during an oral glucose tolerance test (OGTT).

Height SDS for chronologic age ranged from -4.7 to 0.6. However, 4 of the patients had height SDS values (-1.8 to -1.2) that were within normal limits. Height velocity for chronologic age in the patients under 12 years of age ranged from -4.5 to 8.4. BMI ranged from 14.5 to 38.3, and there was a significant correlation between BMI and height SDS ($r=0.37$, $P=0.03$), but not between BMI and height velocity SDS. Thirteen patients showed hyperinsulinemia during OGTT. Only 2 of the 25 children had significant GH responses to oral clonidine with peaks >1.0 $\mu\text{g/L}$. Maximal GH after GHRH was <5 $\mu\text{g/L}$ in all but 1 subject. Mean fasting IGFBP-1 was 104.5 ± 53.7 $\mu\text{g/L}$. Only 8 of 31 measurements of fasting IGF-1 were within normal limits. IGF-1 SDS correlated significantly with both height SDS ($r=0.77$, $P=0.0002$) and bone age SDS ($r=0.5$, $P=0.03$). Fasting IGFBP-3 levels were within the normal range for 12 subjects and correlated significantly with height SDS, but not with height velocity SDS. IGFBP-3 SDS correlated significantly with the log of the insulin area under the curve (AUC) ($r=0.56$, $P=0.002$). Basal prolactin concentrations were slightly elevated in 5 subjects. Forward stepwise regression analyses of height SDS and height velocity SDS were performed. The following variables were included in the initial model: log time after surgery;

tumor location; log BMI; midparental height SDS; log insulin AUC; log GH level after clonidine; log GH after GHRH; prolactin; IGFBP-1; IGFBP-3 SDS; and IGF-1 SDS. IGF-1 SDS was the single most important predictor for height SDS ($r=0.33$, $P=0.001$), while log time after surgery was most strongly associated (negatively) with height velocity SDS.

The authors note that the correlation between height SDS and BMI shows that obese subjects maintain a higher growth rate after surgery than nonobese patients. Hyperprolactinemia and hyperinsulinemia and normal IGF-1 were the most frequent findings in the fast-growing GHD patients. However, the correlation between log of insulin AUC and height SDS indicates that hyperinsulinemic patients maintain higher integrated growth rates after surgery compared with children with low or normal insulin. Significant correlations between the insulin AUC and IGF-1 SDS and IGFBP-3 SDS were observed. The authors concluded that the growth phenomenon in children following craniopharyngioma usually accompanied by obesity is likely to be associated with IGF-1 bioavailability, which may be modulated by insulin.

Tiulpakov AN, et al. *Clin Endocrinol* 1998;49:733-738.

Editor's comment: This study of a relatively large number of individuals provides further information concerning the growth of children following craniopharyngioma surgery. The data are particularly interesting since not all of the 25 patients grew and since a large amount of data were examined. The fact that IGF-1 SDS was the single most important predictor of height SDS is not surprising. That IGF-1 levels might be modulated largely by insulin supports clinical observations. Pediatric endocrinologists need to continue to keep careful records with regard to auxologic and hormonal changes that occur in their patients following craniopharyngioma surgery. It would be of particular interest to know whether obese children remain obese once GH therapy is initiated and what changes occur in their growth velocity during that therapy.

William L. Clarke, MD

Editorial Board

Chairman

Robert M. Blizzard, MD
Charlottesville, Virginia

Associate Editors

William L. Clarke, MD
Charlottesville, Virginia

William A. Horton, MD
Portland, Oregon

Judith G. Hall, MD
Vancouver, BC, Canada

Fima Lifshitz, MD
Miami, Florida

Allen W. Root, MD
St. Petersburg, Florida