

## **Impaired Calcitonin Secretion in Patients With Williams Syndrome**

The Williams syndrome (WS) is characterized by prenatal and postnatal growth retardation, microcephaly, facial dysmorphism (the so-called elfin facies), congenital heart disease (most commonly, supraaortic stenosis), and mental deficiency. In a number of patients, this condition has been associated with neonatal hypercalcemia. This latter finding led to the initial description in 1952 of WS as "idiopathic hypercalcemia of infancy." In older children, metastatic calcium deposits have been found in the kidney, and osteosclerosis has been seen on x-ray in the skull and the metaphyses of the long bones.

Because the etiology of the hypercalcemia seen in WS has been debated for a number of years, the authors examined several aspects of calcium and vitamin D metabolism in five children with WS and seven age-matched controls. At the

time of this study, all patients, whose ages ranged from 2 to 14 years, had normal serum calcium concentrations. After an overnight fast, all received a 3 mg/kg bolus of calcium (as calcium chloride) and blood samples were analyzed over a one-hour period for serum calcium, parathyroid hormone (PTH), and immunoreactive calcitonin. In addition, the response of WS patients to an infusion of 200 U of synthetic human PTH was determined by measuring 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D levels. Serum calcium and phosphate concentrations were also measured at three and 24 hours after PTH administration.

Patients with WS had a delayed clearance of infused calcium when compared to the controls. No significant difference between the groups was noted in the PTH response, but the WS patients had a blunted immunoreactive calcitonin response.

Serum creatinine, phosphate, and total protein values did not differ between the two groups. Finally, the rise in 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D concentrations seen at three and 24 hours after the PTH infusion was not significantly different in patients with WS from the response reported in normal adults.

The authors conclude that delayed clearance of the exogenously infused calcium in WS patients is due to deficient secretion of calcitonin rather than abnormalities of PTH or vitamin D metabolism. In support of their conclusions, they point out that children with hypothyroidism secondary to thyroid dysgenesis have a similar delay in clearance of infused calcium and a blunted calcitonin response. These children had little or no functional thyroid tissue, and presumably lacked calcitonin-secreting parafollicular cells (C cells).

Culler FL, Jones KL, Deftos LJ: *J Peds* 1985;107:720.

**Editor's comment**—*This study provides a possible explanation for the hypercalcemia associated with Williams syndrome. The authors have shown that the abnormality in calcium metabolism seen in patients with WS and thyroid dysgenesis might both result from a common pathophysiologic mechanism, namely, a deficiency of calcitonin secretion. The pathogenesis of the calcitonin deficiency in WS and its relationship to its other clinical manifestations remain unknown. It is interesting that the calcitonin deficiency was present in these normocalcemic older children, whereas the hypercalcemia seldom manifests itself after infancy. To better understand the physiology, calcitonin secretion should be evaluated prospectively in infants with WS and concomitant hypercalcemia.*