

Baron reminds the reader that "risk must be weighed against benefit" and states that "although short stature may be quite unpleasant for some individuals and carry social disadvantages, it generally does not cause death, serious physical dysfunction, or probably even serious psychological dysfunction."¹ This opinion is grounded in empirical evidence.³

Baron also encourages careful evaluation of the etiology of short stature before prescribing a costly and invasive procedure to which greater than 80% of children experienced some adverse side effects. Although Cohen et al used GH therapy in children with GH deficiency as well as in children with other categories of non-GH deficient short stature, the situation may be more complex and different among the various types of patients. As an example, it is well known that decreased IGF-I levels reflect nutritional status, not necessarily GH deficits,⁴ yet no attempts were made to distinguish patients who

may have had nutritional growth retardation, nor were the body weights of the patients defined. It has been shown that a subgroup of children with idiopathic short stature show decreased weight for height,⁵ which is not typical of GH deficiency, suggesting their decreased growth and IGF-I may reflect insufficient nutrition. In such cases, lifestyle and dietary changes would be a more expedient, safer, and cost-effective treatment for the child.⁶

David E. Sandberg, PhD

References

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IGFs and Cytokines in Celiac Disease

The interesting study reported in this paper is the result of one of the few productive collaborations between pediatric endocrinologists and their gastroenterologist colleagues. This endocrine group from Parma, Italy has already published papers on the interaction of the cytokine and insulin-like growth factor (IGF) systems in Crohn's disease and cystic fibrosis. Growth failure is a well known feature of childhood celiac disease, however the precise mechanisms are not established and the possible influences of pro-inflammatory cytokines have not been well explored. The patients studied had "atypical" celiac disease, ie, they presented after the classical period of infancy. These patients were not extremely short at diagnosis but BMI SDS was decreased and both height and BMI increased significantly after treatment with a gluten-free diet.

Baseline values of IGF-I were reduced compared to controls ($P < 0.05$) and interleukin (IL)-6 and tumor-necrosis factor (TNF)- α values were significantly elevated. IGF binding protein (IGFBP)-2 acts as an acute phase protein and, as reported in inflammatory bowel disease and childhood malignancy, values were elevated in affected subjects compared to controls. On treatment with a gluten-free diet, IGF-I and IGFBP-3 normalized and IL-6

and TNF- α decreased significantly. This study provides indirect evidence that cytokines may be involved in the abnormalities in the IGF system and when mucosal inflammation is suppressed, as occurs with treatment of celiac disease, and leads to the increases of IGFs and IGFBP-3 which facilitate normalization of linear growth.

Street ME, Volta C, Ziveri MA, et al. Changes and relationships of IGFS and IGFBPS and cytokines in coeliac disease at diagnosis and on gluten-free diet. Clin Endocrinol (Oxf). 2008;68:22-8.

Editor's Comment: *The celiac disease debate remains as to whether it is improvement in nutrition or suppression of inflammation which drives the recovery of growth. Both factors probably contribute, however as shown in Crohn's disease,¹ suppression of inflammation can independently result in increase of serum IGF-I, therefore the contribution of active inflammation may be subtle, but should not be discounted.*

Martin O. Savage, MD

Reference

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Aortic Dilatation and Dissection in Turner Syndrome

The cardiovascular phenotype in Turner syndrome (TS) is largely defined on clinical signs such as aortic valve abnormalities and aortic coarctation. Investigation in asymptomatic patients has revealed a far more complex phenotype. Combined echocardiography and MRI have shown that up to 75% of adult women with TS have significant cardiovascular abnormalities. In parallel there have been reports of a high rate of aortic dissection in

TS and dilation of ascending aorta could be among predisposing factors. It is still unknown whether aortic dilatation precedes dissection in these patients and what specific diameter predicts impending deterioration.

The purpose of this study by Matura et al was to reliably identify girls and women at risk for such acute aortic events. This study included 166 adult volunteers with TS, aged more than 18 years, who

were not selected for cardiovascular disease and a group of healthy females. Ascending and descending aorta diameters were measured by MRI at the right pulmonary artery. Average diameters were identical in both groups; however results needed to take into account a mean 20 cm difference in height between both groups. When normalized to body surface area (aortic size index) the ascending aortic diameters were significantly greater in the TS group, and close to 32% of the TS women had values >95th percentile of 2.0 cm/m². Ascending/descending aorta diameters ratios were significantly greater in the TS group. During 3 years of follow-up aortic dissection occurred in 3 women with TS. Their ascending aortic diameters ranged from 3.7 to 4.8 cm and the aortic size indices were >2.5 cm/m². This rate is almost 100 fold higher than that of normal women who are usually affected at a much later age. Unfortunately there are no prospective data to know whether dilatation of the ascending aorta preceded dissection or elongation of the transverse aortic arch—a feature more recently described in TS.

The risk for aortic dissection is greatly increased in young women with TS. Because of their small stature, ascending aorta diameters of >5 cm may represent significant dilatation. The use of an aortic size index is therefore recommended. Individuals with a dilated ascending aorta defined as aortic size index >2.0 cm/m² require close cardiovascular surveillance, and values >2.5 cm/m² indicate a high risk for aortic dissection. The authors suggested that haploinsufficiency for a pseudoautosomal gene is responsible for the linked cardiovascular and lymphatic defects in TS. In addition, it is acknowledged that this study did not provide evidence-based recommendations for the follow-up of these patients

with aortic dilatation. Further studies are also needed, like those in Marfan syndrome, to determine whether beta-blocker or rennin-angiotensin system blockade may prevent or retard aortic dilatation and if prophylactic surgery is appropriate.

Matura LA, Ho VB, Rosing DR, Bondy CA. Aortic dilatation and dissection in Turner syndrome. *Circulation*. 2007;116:1663-70.

Editor's Comment: *Recently published clinical guidelines¹ for care of girls and women with TS recommended that magnetic resonance angiography be used, in addition to echocardiography to evaluate the cardiovascular system. It was suggested that patients with defined defects be cautioned in regard to pregnancy. The present study of Matura et al provided an interesting addition of a new tool with appropriate reference data, which should help to evaluate the vital risk of aortic dissection in TS. However, prospective studies are needed which should include adolescent girls as well. The handling of the infertility issues is critical. The patients with spontaneous puberty and apparent ovarian activity should be evaluated for additional risk factors, such as systemic hypertension. The large group of infertile TS patients who have been told that assisted pregnancy can be considered in adulthood should keep in mind there is a risk of fatal aortic dissection during pregnancy. The aortic diameter should be monitored and be part of the follow-up and be taken into account in the reproductive life during adulthood.*

Raphaël Rappaport, MD

Reference

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The Late Effects on Childhood Cancer Survivors

Modern therapies and supportive care have increased the number of the childhood cancer survivors (CCS); as well, there has also been an increase in the late effects such as endocrine impairments and neuropsychological problems. These late effects often do not become clinically apparent until decades after cancer therapy. Unfortunately, over time the likelihood of medical follow-up decreases. Therefore, it is important for physicians to be aware of the late effects facing this population over their lifetime and the need to recall CCS patients for follow-up. However, where and by whom the follow-up of CCS can best be done is still a question that remains to be answered. Dickerman has set forth the recommendations for monitoring the late effects of CCS. He listed in a table both radiation-therapy site and chemotherapeutic agents along with the late effects that result from their use. These include: hypopituitarism, growth problems, hypogonadism, neurocognitive

defects, coronary artery disease, cardiomyopathy, lung fibrosis, interstitial pneumonitis, breast cancer, nephropathy, muscle atrophy, osteoporosis, and second cancers. He recommended that in addition to being followed by a primary care physician, all CCS patients should also attend a specialized late-effects clinic on a yearly basis. At that specialized clinic, CCS patients would be evaluated by a member of the oncology team and subspecialists such as an endocrinologist, psychologist and neurologist. Ideally, such clinics should be located in the same center in which the patient was initially treated and be available on or near the site of residence.

Dickerman JD. The late effects of childhood cancer therapy. *Pediatrics*. 2007;119:554-68.

Editor's Comment: *This is a very special review article which provides important information for*