Isolated short stature as a presentation of celiac disease in Saudi children

Asaad Mohamed Abdullah Assiri
Department of Pediatrics, College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia

Abstract

The aim of this study is to assess the prevalence of isolated short stature as a clinical presentation of celiac disease in Saudi Arab children and whether some of the routine laboratory tests performed to determine the cause of short stature could suggest the diagnosis of celiac disease. A total of 91 children with short stature were included in the study. Extensive endocrine and biochemical assessments, including total protein, serum albumin, calcium phosphate and alkaline phosphatase assays; renal function tests; coagulation profile; anti-endomysial antibodies and anti-tissue transglutaminase antibody, growth hormone, thyroid stimulating hormone, free-thyroxin, thyrotropin releasing hormone (TRH), insulin-induced hypoglycemia, and a small bowel biopsy. Histological evidence of CD was reported according to the Oberhuber classification, confirming the diagnosis of celiac disease. Five children had mild villous atrophy according to this classification (Type 3A), and they were considered to have potential celiac disease. Seventy-six children had normal intestinal biopsies. Therefore, the prevalence of celiac disease among Saudi children with short stature was 10.9%, and 4.3% of the children were diagnosed as having potential celiac disease. After confirming the diagnosis of celiac disease, all children were kept on a gluten-free diet and all of them showed improvement in their growth rate. We concluded that celiac disease is a very important cause of short stature in children without gastrointestinal complaints in Saudi Arabia. We highly recommend anti-tissue transglutaminase and anti-endomysial antibody screening tests, and a small bowel biopsy to confirm the diagnosis of celiac disease irrespective of the results of the antibody assays, in children with short stature in Saudi Arabia. Once the diagnosis is confirmed, children should be kept on a gluten-free diet so they can catch up on their growth early before they develop permanent short stature.
Type 3A according to this classification, and were considered to have potential CD (Group 2; N=5). Therefore, the prevalence of well-diagnosed CD among children of short stature in this study was 10.9% while 4.3% was diagnosed as having potential CD.

CD in our study affected six males and four females, thus the prevalence was equal in males and females. The mean values for chronological age, height, weight, bone age, as well as pubertal stage were not significantly different between patients with CD and non-celiacs (P>0.05). The results of serum calcium, phosphate, alkaline phosphatase, total protein, albumin assays, and hormonal tests were also not significantly different. Tests for celiac antibodies (anti-endomysial and anti-tissue transglutaminase) were done for all the patients and were strongly positive for ten children, who were confirmed histologically to have CD, Type 3C. Five patients were IgG positive for anti-endomysial antibody, shown historically to be Type 3A.

All children diagnosed to have CD and potential CD were kept on a gluten-free diet. Patients were follow-up every six months and showed improvement in growth rate. Four of them had complete catch-up in growth after one year on a gluten-free diet (Table 2). The z-score for height before diagnosis was 2.1401±1.67487 while it was 1.8414±1.83677 one year after starting the gluten-free diet.

Table 2 shows age, gender, serology, histology, and height of children at the initial presentation and on follow-up of height one year on a gluten-free diet, as a z-score.

Table 1. Selection criteria.

| Age (years) | Gender | Serology | Histology | Ht1 (cm) | Ht1 z-score | Ht2 (cm) | Ht2 z-score |
|------------|--------|----------|-----------|----------|-------------|----------|-------------|
| 4.5        | M      | ++       | Type 3C   | 100.00   | -0.74439    | 114.50   | -0.15562    |
| 11         | F      | ++       | Type 3C   | 126.00   | 1.67487     | 134.00   | 1.83677     |
| 6.5        | M      | ++       | Type 3C   | 106.00   | -0.18610    | 112.80   | -0.32931    |
| 5          | F      | ++       | Type 3C   | 98.00    | -0.93048    | 110.00   | -0.61540    |
| 10         | F      | ++       | Type 3C   | 117.00   | 0.83744     | 125.00   | 0.91721     |
| 10         | F      | ++       | Type 3C   | 117.00   | 0.83744     | 125.00   | 0.91721     |
| 5          | M      | ++       | Type 3C   | 102.00   | -0.55829    | 125.00   | -0.61540    |
| 4          | M      | ++       | Type 3C   | 102.00   | -0.55829    | 110.00   | -0.61540    |
| 7          | F      | ++       | Type 3C   | 85.00    | -2.14011    | 98.00    | -1.84149    |
| 7          | F      | ++       | Type 3C   | 107.00   | -0.93050    | 115.00   | -0.10453    |
| 9          | M      | +        | Type 3A   | 113.00   | 0.46524     | 120.00   | 0.40634     |
| 6          | F      | +        | Type 3A   | 104.00   | -0.37219    | 110.00   | -0.61540    |
| 8          | M      | +        | Type 3A   | 110.00   | 0.18610     | 107.00   | -0.92192    |
| 12         | F      | +        | Type 3A   | 119.00   | 1.02353     | 127.00   | 1.12155     |
| 12         | F      | +        | Type 3A   | 119.00   | 1.02353     | 127.00   | 1.12155     |

Z-score: 2.1401±1.67487, 1.8414±1.83677.

1. At the initial presentation. 2. Follow-up of height after one year on a gluten-free diet. Histology according to the Osterberg classification: (+), positive; (−), negative; ++, anti-tissue transglutaminase; +, anti-endomysial IgG.

Discussion

This series shows a significant number of cases of CD and potential CD (10.9% and 4.3%) among Saudi children with short stature, who do not have underlying causes for their short statures. The prevalence of CD in children with short stature has been studied in different regions of the world. It ranged from 0.05-59.1% depending on the region of the study.3-5 In reviewing the literature we found no single parameter suggestive of CD in children with short-stature.6 3-10 This supports our data in this study.

None of the biochemical and hormonal measurements was positive in our patients. The pathogenesis of short stature as a monosymptomatic manifestation in children with CD is not known. A review of the literature showed that there are reasons to suggest that nutritional deficiencies can result in growth failure associated with changes in hormonal status. The hormonal abnormalities in these data included low levels of insulin-like growth factor-1 (IGF-1), which occurs after prolonged exposure to gluten, and poor growth hormone release in stimulatory tests.11 Other endocrine abnormalities that can occur in CD included secondary hypopituitarism probably caused by severe malnutrition and mainly found in longstanding CD, hypogonadism and delayed puberty, reversed insensitivity to androgens, elevated plasma testosterone, free testosterone index, and raised plasma luteinizing hormone.12-17 All children included in our study had no gastrointestinal symptoms or malnutrition and GH and thyroid hormone secretion were normal.

The ultimate adult height will improve if the treatment of CD is started early; however, there will be a slight negative effect of the disease on growth.18 Most of our children in this study who were followed up after one year showed an increase in their heights. Height and weight velocities had their maximum rates during the first year after initiation of the gluten-free diet, but the catch-up growth was incomplete over three years, the final height seemingly influenced mainly by familial characteristics.19

We concluded that CD is prevalent among Saudi children with short stature. The fact that there was no difference between CD and non-CD clinical, biochemical, and hormonal tests indicates that it is important to do anti-endomysial and anti-tissue transglutaminase antibody tests to investigate all children with short stature for CD. In addition, it is important to do a small bowel biopsy for children with short stature, irrespective of the result of celiac serology, in Saudi Arabia and all over the world.

References

1. Bonamico M, Sciré G, Mariani P, et al. Short stature as the primary manifestation of monosymptomatic celiac disease. J Pediatr Gastroenterol Nutr 1992;14:12-6.
2. Corera Sanchez M, Vilate Carrasco A, Igea J, et al. Celiac disease and short stature. An Esp Pediatr 1992;37:304-6.
3. Rossi TM, Albini CH, Kuma V. Incidence of celiac disease identified by the presence of serum endomysial antibodies in children with chronic diarrhea, short stature in Insulin Dependent Diabetes. J Pediatr 1993;123:262-4.
4. Farrell RJ, Kelly CP. Celiac sprue. New Engl
5. Verkasalo M, Kuitunen P, Leisti S, et al. Growth failure from symptomless celiac disease. A study of 14 patients. Helv Paediatr Acta 1978;33:489-95.
6. Anonymous. American Gastroenterological Association medical position statement: celiac sprue. Gastroenterology 2001;120:1322-5.
7. Anonymous. Revised criteria for diagnosis of celiac disease. Report of Working Group of European Society of Paediatric Gastroenterology and Nutrition. Arch Dis Child 1990;65:909-11.
8. Oberhuber G, Granditsch G, Vogelsong H. The histology of celiac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol 1999;11:1185-94.
9. Greulich WW, Pyle SI. Radiographic atlas of skeletal development of the hand and wrist. 2nd edn, Stanford University Press: Stanford, California, 1959.
10. Tanner JM. Growth at adolescence with a general consideration of the effect of hereditary and environmental factors upon growth and maturation from birth to maturity. 2nd edn, Blackwell Scientific Publications: Oxford, 1962.
11. Wales JKH, Wit J-M, Rogol AD. Pediatric Endocrinology and Growth. 2nd edn, Saunders Scientific Publications: Oxford, 2002.
12. Groll A, Candy DC, Preece MA, et al. Short stature as the primary manifestation of celiac disease. Lancet 1980;2:1097-9.
13. Knudtazon J, Fluge G, Aksnesl L. Routine measurements of gluten antibodies in children of short stature. J Pediatr Nutr 1991;12:190-4.
14. Bomanico M, Ballati G, Mariani P, et al. Screening for celiac disease: the meaning of low titre of anti-gliadin antibodies (AGA) in non-celiac children. Eur J Epidemiol 1997;13:55-9.
15. Eichler I, Frisch H, Granditsch G. Growth failure and skin insulin-like growth factor (IGF-I) in childhood celiac disease. Klinische Wochenschrift 1991;69:825-9.
16. Cacciari E, Salardi S, Lazzari R, et al. Short stature and celiac disease: a relationship to consider even in patients with no gastrointestinal tract symptoms. J Pediatr 1983;103:708-11.
17. Gemme G, Vingolo M, Naselli A, et al. Linear growth and skeletal maturation in subjects with treated celiac disease. J Pediatr Gastroenterol Nutr 1999;29:339-42.
18. Bosio L, Barrera G, Mistura L, et al. Growth acceleration and final height after treatment for delayed diagnosis of celiac disease. J Pediatr Gastroenterol Nutr 1990;11:324-9.