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Case Report

Short Stature and Anemia in Pediatric Eosinophilic Gastroenteritis

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Abstract

A 4.5-year-old male child with short stature (-2.8 SD), who had a history of asthma and with high RAST values of IgE antibodies to specific food allergens, visited our clinic with chronic vomiting and severe anemia (Hb 4.4 g/dL). He was also noted to have peripheral eosinophilia (2,049/μL) and high serum IgE (RIST: 8,761 U/mL). With Eosinophilic Gastrointestinal Diseases (EGIDs; eosinophilic gastritis, EG and Eosinophilic Gastroenteritis, EGE) being suspected, an upper gastrointestinal endoscopy was performed, which confirmed the pathological histology of eosinophilic gastritis. His short stature was not familial but was thought to be related to EG/EGE. To determine if short stature is one of the EG/EGE-related symptoms, a literature survey was performed in Japanese pediatric EGE cases. We have analyzed 4 such cases including this case report. Probable pathological involvement of EG/EGE in the physical growth in pediatric patients was speculated because short stature improved after treatment for EG/EGE in 3 of the four cases. Further studies are required on the impaired growth in patients with EG/EGE.

Keywords: Eosinophilic Gastroenteritis; Anemia; Short Stature; Eosinophilia IgE

Introduction

Short stature is caused by familial or pathological factors. Pathological short stature is due to growth hormone deficiency or other hormonal abnormalities, skeletal dysplasia, malabsorption syndrome like Inflammatory Bowel Disease (IBD) or celiac disease in childhood [1-5]. Endocrinologically, besides growth hormone, insulin-like growth factor and its receptor (IGF-1/IDF-1R) play critical roles in skeletal growth and development [6]. Idiopathic short stature is defined in which all possible causes are excluded. Eosinophilic Gastrointestinal Diseases (EGIDs) are chronic inflammatory diseases due to the accumulation of eosinophils in the gastrointestinal tract, which cause various gastrointestinal as well as systemic symptoms. EGIDs consist of either Eosinophilic Esophagitis (EoE) or other gastritis (EG)/ gastroenteritis (EGE) in children and adults [7]. In the United States, the prevalence of EGE was the highest among children aged < 5 years, whereas EG was more prevalent among older age groups [8]. In Japan, the incidence of EG/EGE is higher than EoE [9]. In young children, the diagnosis of EGIDs could be misdiagnosed or delayed because of no routine use of the endoscopic study. In addition, pediatric EGIDs may cause short stature [10]. However, to date, the prevalence and predictors of growth failure remain undetermined at diagnosis in children with EG/EGE. We report here a case of EG in a short male child and further discuss short-stature cases associated with pediatric EG/EGE in the literature survey.

Case Report and Literature Survey

A 4.5-year-old male child with short stature (-2.8 SD), who had a history of asthma but no food anaphylaxis, visited our clinic with chronic vomiting and severe anemia. He was negative for fecal occult blood. He suffered from Kawasaki disease at 11 months of age. No family history of EGIDs. The patient was hospitalized to examine the cause(s) of chronic recurrent vomits from the age of 2 years. Laboratory data showed associated severe iron deficiency anemia (Hb 4.4g/dL) with peripheral

eosinophilia (2,049/μL). Serum total protein 5.8 g/dL and albumin 3.7 g/dL were slightly reduced. He showed high serum non-specific IgE (RIST; 8,761 U/mL; reference <110) and markedly high specific RAST values for various antigens, such as milk, egg white, egg yolk, wheat, rice, soy, shrimp, crab, chicken meat, pork, house dust, cat and dog sebum, etc. The serum level of baseline growth hormone was 1.07 ng/mL (<2.47) and that of Insulin-like Growth Factor (IGF)-1 was low at 16 ng/mL (32-176), respectively, when bone age was <3.2 years. *Helicobacter pylori (H. pylori)* infection status was contradictory because of the data that the urea breath test was positive, while serum *H. pylori* antibody and antigen in the stool were negative. After recovery of anemia due to packed red blood cell transfusion and Fe supplementation, he received an upper endoscopy under general anesthesia with a suspicion of EG/EGE, with the use of OLYMPUS GIF-H290Z® at the age of 4.7 years. Gastric mucosa revealed multiple linear erosion at the gastric vestibule with nearly normal esophageal and duodenal findings. Biopsies were done one in the esophagus, 3 in the stomach and one in the duodenum. Significantly abnormal histology was noted only in the stomach showing >20/HPF of eosinophils in all 3 biopsied tissues (Fig. 1). He was diagnosed with EG, though EGE could not be ruled out because neither a jejunal biopsy nor a colonoscopy was performed and treated not with food elimination, but with 0.7 mg/kg/day of oral Prednisolone (PSL) and 6mg/kg/day of suplatast tosilate, which markedly improved his symptoms. Soon after, oral cyclosporin (3 mg/kg/day) for steroid-sparing effect in case of long-term PSL use, pranlukast hydrate and methenolone acetate were also introduced. Serum IGF-1 values improved to 132 ng/mL at the age of 5.3 years and 162 ng/mL (baseline growth hormone 3.97 ng/mL) at the age of 6.3 years, respectively. Thereafter, at the age of 7.7 years, his height improved up to -2.4 SD from an initial -2.8SD; however, his bone age remained at 5.6 years. Regarding his short stature, it was not familial, so we assumed it could be one of the EG/EGE-related symptoms. To search for similar cases, a literature survey (PubMed, https://login.jamas.or.jp and https://mol.medicalonline.jp/library/) on Japanese pediatric EGIDs during 2010-2020, was performed with keywords of EGIDs, EG or EGE x pediatric or children. A total of 25 cases including this report (endoscopies were performed for the upper in 11, for the lower in one and for the combined in 13) were accumulated; with a median age of 8.0 years and an M/F ratio of 19/6, in whom nausea/vomiting was noted in 9, abdominal pain in 9, anemia in 6 (not mentioned in 5), diarrhea/bloody stool in 5 and short stature in 4 (not mentioned in 4) (11-13 Yamazaki, Doi, Sasaki, this case). Cases of short stature are summarized in Table 1. Yamazaki, et al., described a short case (-3.6 SD) at the age of 1.6 years when he was diagnosed with EGE with low serum IgG [11]. At the age of 4.4 years, short stature improved to -2.3 SD after treatment with leukotriene receptor antagonist, suplatast tosilate and PSL. The authors suspected that EGE-related malabsorption might have contributed to the physical growth disturbance. Doi, et al., reported an 8-year-old boy, in whom chronic diarrhea occurred after the beginning of wheat ingestion (at the age of 4 years) and continued for 4 years [12]. The patient was diagnosed with EGE by the lower endoscopy. His height was close to -2.0 SD. One year after treatment with food elimination, Fe, suplatast tosilate and montelukast sodium, his height remained at -2.0SD. The authors did not elaborate to comment on the role of EGE in the patient's short stature. Sasaki, et al., described a 7-year-old boy with abdominal pain, vomiting and positive fecal occult blood. The patient had multiple food allergies [13]. He was short (-2.9 SD), but not severely anemic (Hb 11.9 g/dL) and diagnosed with EGE by endoscopy. After food elimination and oral PSL, his height improved to -2.5 SD. Our case was notable for his severe iron deficiency anemia and short stature, which was thought in part due to EG and in part due to an unbalanced diet because he became a picky eater after suffering from Kawasaki disease, though we could not negate the possibility that a specific food allergy was related to his eating habits. His height improved from -2.8 SD to -2.4 SD during the 3.2 years of treatment. In all, the improvement in the patients' height was noted in 3 of 4 cases, which might have indicated the pathological involvement of EG/EGE in the development of short stature in these cases.

N	Age (Years) Gender	Symptoms	Allergy	Hb (G/Dl)	Eo (/μl)	Short Stature (Sd)	Eds	Ref
1	1.6/M	Anemia bloody stool	NA	8.9	957	-3.6	U/L	11
2	8.0/M	Food allergy	Food	NA	430	-2.0	U/L	12
3	7.0/M	Abdominal pain/ vomiting FOB	Food	11.5	2,052	-2.9	U/L	13
4	4.5/M	Short stature vomiting anemia	Asthma food	4.4	2,049	-2.8	U	CR
N; Case Number, M; Male, F; Female, Hb; Hemoglobin, Eo; Eosinophils, FOB; Fecal Occult Blood, SD; Standard Deviation, EDS; Endoscopy, U; Upper Gastrointestinal Tract, L; Lower Gastrointestinal Tract, Ref; Reference Number, CR; Current Report, NA; Not Available.								

Table 1: Four pediatric cases of eosinophilic EG/EGE with short stature.

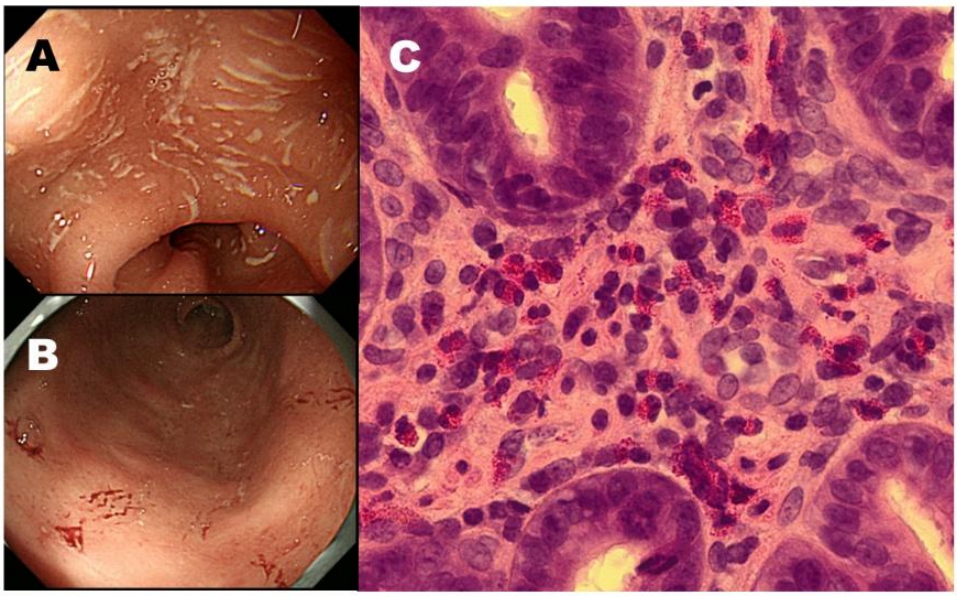

Figure 1: Findings of upper gastrointestinal endoscopy. Macroscopically. (A): Multiple linear erosions with white moss were detected in the gastric antrum; (B): Sporadic hemorrhagic erosions were noted also in the gastric body. Microscopically; (C): Infiltration of eosinophils was shown more than 20/high power field in the stomach (Hematoxylin and Eosin stain, original magnification x400).

Discussion

Our case met the diagnostic criteria of EG, which is defined by the presence of histologically marked eosinophilia in the stomach [7]. In EG/EGE, peripheral eosinophilia is usually found but is not required for the diagnosis [14]. A history of atopy, asthma and food allergies is common and clinical presentation may include vomiting, abdominal pain, diarrhea and gastrointestinal bleeding [8,15]. Our case showed a correlation between anemia and short stature; however, in the literature survey, anemia was only noted in 6/25 (not mentioned in 5) and it was stated that clinically relevant anemia is a quite rare complication in infants with EG [14]. In our case, severe anemia was thought related to multiple linear erosions in the stomach (Fig. 1), but the precise cause of erosions remains unidentified if EG alone or EG combined with other factor(s) like Helicobacter pylori infection played a role. It is thought that the management of non-EoE EGIDs is more challenging than EoE [7]. The treatment of EG/EGE is based on food elimination therapy, consisting of the removal of common food triggers. Corticosteroids like PSL are also used as first-line drug therapy [16]. Cyclosporine as an alternative to corticosteroids needs to be evaluated. We have tested if methenolone acetate is effective for catch-up growth. Previously, an elemental diet was shown effective in reversing growth failure in a white boy with growth failure (> -2S D) between 7 and 17 years of age, in whom symptoms initially developed at 6 months of age [10].

In terms of short stature in association with pediatric EG/EGE, we found three more Japanese cases in addition to this case report (Table 1). Children with IBD or celiac disease are well-recognized as representative cases that show short stature, in which chronic inflammation and malabsorption may play a major role [2,4,5]. In IBD, it was stated that male gender and prepubertal diagnosis were found to impose risk for reduced height [2]. In this study, somehow EG/EGE-related short stature was all males. Also, in IBD, growth hormone resistance associated with low serum levels of IGF-1 was observed [17]. In pediatric celiac disease, a significant negative association between the duration of gluten exposure and serum IGF-I levels was noted [18]. In our case, we obtained improved serum IGF-1 levels after treatment for EG/EGE. On the other hand, regarding the role of anemia in growth failure, chronic anemia could be responsible for short stature in celiac disease [4,5]. In our case, severe anemia also might have played a role, considering the findings of a positive correlation between Hb and growth hormone peak levels considering the study of Zhang, et al. [19].

We propose that patients with EG/EGE during childhood need to be watched for physical growth and be characterized in detail for short stature, as in IBD or celiac disease. Hopefully, EG/EGE-related delayed growth should be studied longitudinally and comparatively with patients of IBD and celiac disease. The limitation of this report is that it describes a single case report of EG

without apparent protein-losing enteropathy and discusses a very limited number of Japanese pediatric EG/EGE cases in the literature survey, indicating the necessity of future large-scale studies on EG/EGE-related short stature globally.

Conclusion

In conclusion, young children with gastrointestinal symptoms associated with a history of allergic diseases, particularly food allergies, are recommended for endoscopic examination to determine if they have EG/EGE where celiac disease is not common like in Japan. In addition, detailed studies on the pathological role of EG/EGE on growth failure are required in pediatric patients. Pediatricians must assess if the patients show growth failure and evaluate endocrinological data such as growth hormone, IGF-1 and bone ages with follow-up of catch-up growth after treatment in each case of pediatric EG/EGE.

Conflict of Interests

The authors have no conflict of interest to declare.

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Consent for Publication

Written informed consent was obtained from the patient's parents.

Policy and Ethics

The work was carried out following the Declaration of Helsinki (as revised in 2013). This publication was made by ethics committee approval (Uji-Tokushukai No.2024-23).

References

1. Polidori N, Castorani V, Mohn A, Chiarelli F. Deciphering short stature in children. Ann Pediatr Endocrinol Metab. 2020;25:69-79.
2. Rinawi F, Assa A, Almagor T. Prevalence and predictors of growth impairment and short stature in pediatric-onset inflammatory bowel disease. Digestion. 2020;101:674-82.
3. Wong K, Isaac DM, Wine E. Growth delay in inflammatory bowel diseases: significance, causes and management. Dig Dis Sci. 2021;66:954-64.
4. Leffler DA, Green PHR, Fasano A. Extraintestinal manifestations of coeliac disease. Nat Rev Gastroenterol Hepatol. 2015;12:561-71.
5. Saadah OI. Short children with impaired growth hormone secretion. Do they have celiac disease? Saudi Med J. 2020;41:68-72.
6. Yakar S, Courtland HW, Clemmons D. IGF-1 and bone. New discoveries from mouse models. J Bone Miner Res. 2010;25:2543-52.
7. Chen PH, Anderson L, Zhang K, Weiss GA. Eosinophilic gastritis/gastroenteritis. Curr Gastroenterol Rep. 2021;23:13.
8. Jensen ET, Martin CF, Kappelman MD, Dellon ES. Prevalence of eosinophilic gastritis, gastroenteritis and colitis: Estimates from a national administrative database. J Pediatr Gastroenterol Nutr. 2016;62:36-42.
9. Kinoshita Y, Furuta K, Ishimura N. Clinical characteristics of Japanese patients with eosinophilic esophagitis and eosinophilic gastroenteritis. J Gastroenterol. 2013;48:333-9.
10. Justinich C, Katz A, C Gurbindo C. Elemental diet improves steroid-dependent eosinophilic gastroenteritis and reverses growth failure. J Pediatr Gastroenterol Nutr. 1996;23:81-5.
11. Yamazaki S, Ohtsuka Y, Yoneyama T. Two cases of eosinophilic gastroenteritis in children. JJACI. 2016;30;120-6.
12. Doi M, Furuichi Y, Tsuji S, Takano T. Eosinophilic gastroenteritis treated with a targeted food elimination diet. Pediatr Int. 2020;62:866-8.
13. Sasaki A, Sugimoto M, Tokaji N. Efficacy of an elimination diet in a patient with eosinophilic gastroenteritis: A pediatric case with multiple food allergies. J Med Investig. 2019;66:201-4.
14. Daidone A, Barbi E, Villanacci V, Di Leo G. Severe anaemia after gastric biopsy in an infant with eosinophilic gastritis. Ital J Pediatr. 2019;45:69.

15. Ko HM, Morotti RA, Yershov O, Chehade M. Eosinophilic gastritis in children: clinicopathological correlation, disease course and response to therapy. Am J Gastroenterol. 2014;109(8):1277-85.
16. Kinoshita Y, Ouchi S, Fujisawa T. Eosinophilic gastrointestinal diseases-pathogenesis, diagnosis and treatment. Allergol Int. 2019;68:420-9.
17. Casadonte CJL, Brown J, Strople J. Low insulin-like growth factor-1 influences fatigue and quality of life in children with inflammatory bowel disease. J Pediatr Gastroenterol Nutr. 2018;67:616-21.
18. Eichler I, Frisch H, Granditsch G. Growth failure and Insulin-like Growth Factor (IGF-I) in childhood celiac disease. Klin Wochenschr. 1991;69:825-9.
19. Zhang T, Bo Ban B, Mei Zhang M. Association between hemoglobin and growth hormone peak in Chinese children and adolescents with short stature: a cross-sectional study. Int J Gen Med. 2021;14:497-504.