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Case Report

Eosinophilic Esophagitis and Gastritis in Rubinstein-Taybi Syndrome

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INTRODUCTION

Rubinstein-Taybi syndrome is a rare disorder associated with mutations in the CREB-binding protein gene (1). It is characterized by broad thumbs and toes, characteristic facies, postnatal failure to thrive, and delayed development (2). These children often have chronic gastrointestinal problems, including gastroesophageal reflux, feeding difficulties, and chronic constipation (2–4). They are not reported to have an increased incidence of atopic disease. Herein is the first report, to the authors' knowledge, of eosinophilic gastrointestinal disease presenting as dysphagia in this population.

CASE 1

A white boy who had received a diagnosis of Rubinstein-Taybi syndrome in infancy was assessed by our gastroenterology service for dysphagia and possible gastroesophageal reflux at 12 years of age. He had many characteristics of Rubinstein-Taybi syndrome, including short stature, developmental delay, hypertrophic thumbs and first phalanges, and characteristic facies. He also had bilateral colobomas of the iris, inguinal hernia, bilateral cryptorchidism, and a type 2 atrial septal defect. In infancy he experienced gastroesophageal reflux and multiple episodes of aspiration pneumonia. A videofluoroscopic swallowing study revealed aspiration of liquids. Subsequently, he required a feeding gastrostomy tube and Nissen fundoplication. By 4 years of age, he was eating well, and the gastrostomy was closed. At 5 years of age, he was brought for treatment of dysphagia. A rigid endoscopy was performed, and an alimentary foreign body was found in the lower third of the esophagus. Since that time, he has undergone 5 esophageal dilatations for recurrent dysphagia and a second esophageal food impaction, all performed by surgery. No esophageal biopsies were performed during these rigid endoscopies. His medical history was pertinent for asthma treated with intermittent fluticasone during the same time period. He had no known allergies. The family history was positive for allergies (brother).

At 12 years of age, he was given omeprazole for possible gastroesophageal reflux. Despite this treatment, he continued to experience significant dysphagia with solid food during the next 6 months. The results of a barium swallow were normal. Complete blood counts were normal aside from eosinophil counts ranging from 0.8 to 1.0×10^9/L. His total immunoglobulin E was elevated at 5052 kU/L. Flexible upper endoscopy revealed a tubular esophagus, thickened esophageal mucosa, and multiple white deposits. The remaining examination results were normal. Esophageal brushings were negative for *Candida* species. Multilevel esophageal biopsy specimens revealed >50 eosinophils/HPF (40×) and eosinophilic micro-abscesses. Antral and gastric body biopsy specimens revealed significant eosinophilic infiltration. The results of duodenal biopsy were normal. Prednisone ($1\ \mathrm{mg \cdot kg^{-1} \cdot d^{-1}}$) rather than inhaled corticosteroids was given secondary to the presence of eosinophilic gastritis in addition to esophagitis. The patient experienced significant improvement of his dysphagia while receiving prednisone and was able to begin being weaned from the drug after 1 month. An assessment for allergies revealed positive results of skin prick testing for milk, soy, and wheat. Radioallergosorbent testing for milk and soy also yielded strongly positive results. A diet free of milk, soy, and wheat was implemented, and he was weaned from prednisone. During the next

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4 months he continued to do well, experiencing only 2 brief episodes of dysphagia that resolved without medical intervention.

CASE 2

A second white boy with Rubinstein-Taybi syndrome presented at 10 years of age with a 5-year history of dysphagia for solid food. He also had short stature, developmental delay, hypertrophic thumbs and first phalanges, and characteristic facies. At 9 years of age he required an emergent upper endoscopy and esophageal dilatation for esophageal food impaction. Unfortunately, esophageal biopsies were not performed during that procedure because it was performed urgently in a nontertiary medical center. His medical history included atopic dermatitis, asthma, allergic rhinitis, and chronic constipation. The family history was positive for food allergies.

Further investigation revealed a normal complete blood count and normal results of 24-hour esophageal pH monitoring. A second upper endoscopy found longitudinal furrowing and a ringed appearance of the esophagus. Multilevel esophageal biopsies revealed 55 eosinophils/HPF. The results of macroscopic and microscopic examination of the stomach and duodenum were normal. Because of the severity of his symptoms, he was treated with prednisone ($1\,mg \cdot kg^{-1} \cdot d^{-1}$) for 2 weeks, followed by a gradual decrease during 6 weeks. The results of skin prick testing were positive for eggs, nuts, and apples. Radioallergosorbent testing also gave positive results for eggs. He was asymptomatic after receiving a diet free of eggs, nuts, and apples for 6 months. Subsequent recurrent solid food dysphagia was treated with swallowed fluticasone 250 μg twice daily for 1 month and then 125 μg twice daily for another month. He responded well to the fluticasone and remained asymptomatic 6 months after its discontinuation.

DISCUSSION

Dysphagia and easy choking have been reported in several children with Rubinstein-Taybi syndrome. A Canadian series of 18 children who were monitored into adulthood noted 2 men with persistent dysphagia for solids who had had feeding difficulties during infancy (4). A similar series of 45 children and adults from the Netherlands mentioned many patients with swallowing difficulties and easy choking (3). Scott et al (5) reported a 7-year-old boy with dysphagia for solids secondary to a postcricoid web, and 2 other patients were reported with vascular rings impinging on the esophagus (6,7). Eosinophilic esophagitis, a known cause of dysphagia in children and adults, has not yet been described in this population.

Eosinophilic esophagitis and gastritis are associated with many symptoms, including vomiting, dysphagia, and abdominal pain. Affected individuals frequently have a personal or family history of atopic disease. Peripheral eosinophilia and elevated immunoglobulin E are variably found (8). Endoscopy may reveal nonspecific inflammation of the esophageal and gastric mucosa. More specific features include white specks on the esophageal mucosa, a ringed appearance of the esophagus, and longitudinal linear creases (9–11). Esophageal and gastric biopsies reveal mucosal inflammatory changes, eosinophilic infiltration, and microabscesses. No absolute number of eosinophils is diagnostic of this condition, but generally, >20 eosinophils/HPF are found in the gastrointestinal mucosa of this population (8,9). These patients undergo allergy testing, and when the results are positive, restrictive diets and environmental precautions are implemented. Patients who do not respond to dietary changes usually respond to an elemental diet or corticosteroids (12).

Dysphagia and esophageal food impaction are not uncommon in eosinophilic esophagitis. In a case series of 12 children with dysphagia and >10 eosinophils/HPF in the esophageal mucosa, 6 presented with an esophageal food impaction (13). Another series of children with dysphagia demonstrated that esophageal food impaction was more common in the group with >20 eosinophils/HPF in the esophageal mucosa (14). Esophageal strictures have also been reported in children with eosinophilic esophagitis (8,10,15).

Eosinophilic disease of the gastrointestinal tract is clearly associated with atopic disease. There is no known association between the gene mutations found in Rubinstein-Taybi syndrome and eosinophilic disease of the gastrointestinal tract, nor does there seem to be an increased incidence of atopic disease in this population. Consequently, the finding of eosinophilic esophagitis in these 2 children with Rubinstein-Taybi syndrome may be secondary to chance alone. However, this association does underline the importance of a thorough investigation when children with Rubinstein-Taybi syndrome present with dysphagia or feeding difficulties.

CONCLUSIONS

The clinical presentation, endoscopic findings, and biopsy findings in these 2 patients are consistent with isolated eosinophilic esophagitis in case 2 and eosinophilic esophagitis and gastritis in case 1. The prevalence of eosinophilic disease may be underreported in this population because of the lack of endoscopic evaluation of children with Rubinstein-Taybi syndrome and dysphagia in earlier studies. Given the importance of a diagnosis of eosinophilic disease to the subsequent medical management of this condition, we suggest a full upper endoscopy with biopsies in children with

Rubinstein-Taybi syndrome presenting with persistent dysphagia or feeding difficulties.

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