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Allergic eosinophilic gastroenteritis in a boy with congenital duodenal obstruction

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Eosinophilic gastroenteritis (EG) is a rare allergy-related disease, especially in early childhood. We present the case of a 1 year 4 month old boy with congenital duodenal obstruction who developed EG. That diagnosis of EG was made by a series of imaging studies and was confirmed by upper gastrointestinal (UGI) endoscopic biopsy studies which showed significant tissue eosinophilia in both mucosal and submucosal layers. No evidence of parasite segment or ova was found in the stool and biopsy specimen. Specific IgE antibodies to milk were estimated to be 2 + (CAP system). Cow's milk allergy was highly suspected but not confirmed by consecutive elimination and challenge tests since the child was too much suffered to be tested. There was partial response to the 2-week-treatment with Alfare (semi-elemental formula) and oral prednisolone 1 mg/kg/day. One month after initial examination, perforation of the stomach occurred and exploratory laparotomy disclosed stenosis of the duodenum. Congenital duodenal obstruction was diagnosed based on operative findings and previous sonographic findings. There has been only one report of EG in an infant with congenital duodenal obstruction. The nature of the relationships among cow's milk allergy as a possible etiologic factor, congenital duodenal obstruction as an predisposing factor and EG involvement at both mucosal and submucosal layers remains unclear.

Key words: Congenital duodenal obstruction, cow's milk allergy, eosinophilic gastroenteritis, tissue eosinophilia

Eosinophilic gastroenteritis (EG) is a rare and poor understood disease entity which was first described by Kaijser in 1937 [1]. Klein *et al* first described and correlated the pattern of clinical presentation of EG with the extent of the depth of eosinophilic infiltration (mucosal, muscular and subserosal layer diseases) [2]. In 1990, Talley *et al* proposed the following four diagnostic criteria for EG: (1) presence of gastrointestinal (GI) symptoms;(2) eosinophilic infiltration of one or more areas of the GI tract is demonstrated at biopsy; (3) eosinophilic involvement of any organ outside the GI tract is not present; and (4) absence of parasite infestation [3].

The clinical presentations of EG can be classified into three types. The first type is predominant mucosal layer disease, the most prevalent form of EG. The main symptoms of EG with a mucosal layer disease pattern are abdominal pain, vomiting, diarrhea, weight loss and failure to thrive. Other problems associated with this clinical pattern are iron deficiency anemia, protein losing enteropathy and malabsorption. In this subgroup of EG, approximately 50% of the patients have a past or family history of allergy (atopy, asthma and so on). Nearly 50% of these patients have food intolerance or allergy [4]. An allergic history is more common in children with EG than that in adults. The second type of EG consists of predominantly muscle layer disease, with a typical presentation of pyloric or intestinal obstruction. Associated allergic symptoms are rarely found in this patient group. The third type of EG involves subserosal layer disease. This is the rarest form of EG and typically presents with eosinophilic ascites. It is worth noting that mixed forms of these patterns may also exist.

It is believed that EG is not one but rather than several disorders that manifest similar histopathologic features with tissue eosinophilia stamping the hallmark [5]. Sampson used the term "allergic eosinophilic gastroenteritis" and classified it as IgE-related and non IgE-related [5,6]. Most cases of EG are non IgE-related and occur in adult compared to the relatively fewer cases of IgE-related EG which occurred predominately in children. In both IgE-related and non IgE-related cases,

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eosinophils are the main effector cells and may damage the GI tract directly due to the content of preformed granules [7,8].

The clinical features of the present case included severe vomiting, IDA, hypoalbuminemia and failure to thrive. This case was obviously compatible with the diagnosis of mixed type EG according to the results of biopsy although duodenal obstruction had developed prenatally. Congenital duodenal obstruction in the pathogenesis of EG has only been previously reported once [9]. The previous reported case of allergy-related EG was fed on breast milk and was presumed to be induced by allergen in breast milk. In the present case with EG, he was fed on formula milk and was suspected to be caused by cow's milk allergy. However, neither the previous reported case nor this present case fit the definite diagnostic criteria of food allergy, as three consecutive and elimination challenge tests were required for the diagnosis of food allergy. Otherwise, since the presentations of this case were so complex and complicated, as Goldman stated, cow's milk allergy alone could not explained the whole course [10].

Case Report

This 1 year 4 month old boy visited our out-patient department in August 1999 because of severe vomiting. Initial examination revealed dehydration and failure to thrive and he was admitted for treatment.

Review of his birth history, past history and developmental milestones showed that he was delivered at term with a birth body weight of 3000 g. He had been admitted to the neonatal intensive care unit shortly after birth because of massive cephalohematoma. Prenatal sonography had disclosed double bubble sign at the upper abdominal quadrant. Postnatal abdominal sonography was also performed but no information had been recorded. Five days after the admission, he was discharged without any apparent neurological sequelae. However, frequent regurgitation was noted several weeks later and this symptom recurred episodically. No further GI investigations other than prenatal and postnatal sonography had been performed prior to visiting our clinic.

On admission to our hospital, body weight was 7.6 kg and height was 72 cm, both of which are far below the third percentile. Other physical examinations revealed anemic conjunctiva and slight periorbital edema. Moderate to severe abdominal distension was a prominent clinical feature at that time.

The extent of eosinophilia (from 43% to 8%) accompanying leukocytosis (over 20000/mm^3) and moderate microcytic anemia (hemoglobin = 7.8 g/dL) varied during the course of hospitalization. C reactive protein (CRP) was within normal limits (between 0.78 mg/dL and 0.39 mg/dL). At the same time, erythrocyte sedimentation rate (ESR) was 1 mm/h (Westergren method) and IgE was 323 IU/mL. Guaiac test of stool was 1+ and parasite ova were not found in several stool exams of the boy and his pet dog.

Series imaging studies including plain abdominal film, abdominal sonography and an upper GI (UGI) series disclosed prominent thickening of the gastric fold and a severely distended duodenum (Fig. 1). Partial obstruction of duodenum near the junction between the third and the fourth portions was suspected. Allergic EG or parasite infestation were mostly suspected. Because of the possible need for biopsy to this tentative diagnosis or to undergo surgery, he was referred to Koahsiung Veterans General Hospital.

On arrival, total eosinophil count (TEC) had reached 1420/mm^3 despite 1 week of starvation and elimination diet. Specific IgE (CAP system) showed 1.50 KU/L (equal to class 2) for milk and 0.47 KU/L (equal to class 1) for egg white. Albumin was relative low (3.3 g/dL). Imaging studies including abdominal computerized tomography (CT) showed the same findings as in our hospital. UGI endoscopy was performed and showed severely inflamed, thickened and edematous gastric and duodenal mucosa with one 0.5 cm active ulcer over the angularis (Fig. 2). However, no mass lesion within the GI tract was seen. Biopsies at the ulcerative area, gastric body and obstruction site of the duodenum were done and they all showed severe tissue eosinophilia (all equal to Whingtinton histologic grading 4+) in both mucosal and submucosal layers (Fig. 3,4). No evidence of parasite infestation was found. Mixed type EG was thus diagnosed. It was too suffering for an severely ill 1 year 4 month old boy to perform three consecutive elimination and challenge tests aiming at cow's milk. So, by definition, we could not confirmed but just highly suspected that food allergy was the etiological factor of his condition.

Semi-elemental milk diet with Alfare and oral prednisolone (1 mg/kg/day) were given. After 2 weeks of treatment, severe vomiting and appetite improved (reached 200 cc/meal), and TEC fell to 80/mm^3. Follow-up UGI endoscopy showed little inflammation or edematous mucosa although ulcer still existed and obstruction lesion did not resolve completely. Due to parental request, he was discharged temporarily without laparotomy to determine whether congenital obstruction existed or not.

One month later, he was sent for emergent surgery due to perforation of the stomach over the region of the

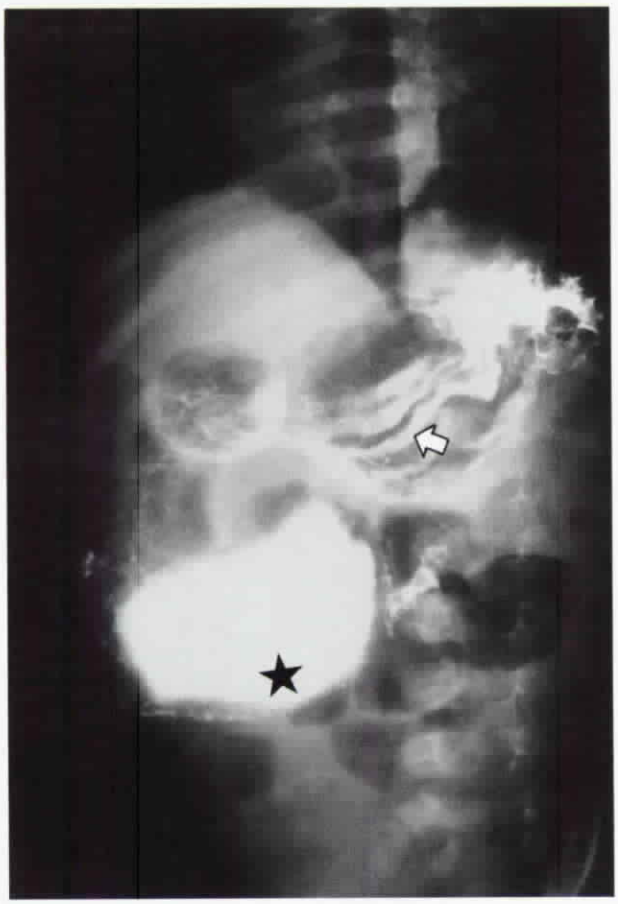

Fig. 1. An UGI series shows prominent thickening of the gastric folds (arrow) and severe distension of the duodenum (star) with obstruction level over the junction between the third and fourth portions.

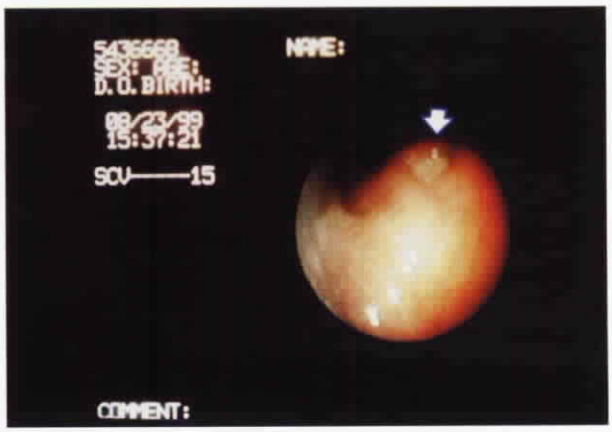

Fig. 2. An UGI endoscopic appearance shows a 0.5 cm active ulcer (arrow) over the angularis of the stomach.

previous ulcerative lesion. Intraoperatively, stenosis of duodenum was still found over the junction between the third and fourth portions and duodenal-jejunal bypass was done. Congenital stenosis of the duodenum was diagnosed. His condition stabilized after this complicated course.

Discussion

Eosinophilia in children is commonly associated with allergic disease or parasitic infestation. Marked eosinophilia is also associated with drug hypersensitivity, eosinophilic leukemia, lymphoma, some collagen vascular diseases (e.g. scleroderma, dermatomyositis), idiopathic hypereosinophilic syndrome and EG. Most cases of EG including the present case are diagnosed incidentally and often manifest severe or long lasting GI symptoms that prelude a definite diagnosis. Thus, extensive GI tract evaluations including UGI endoscopy should be done when marked eosinophilia associated with GI symptoms are found.

Eosinophilic infiltration in the gut may be normal and vary in different gut regions. Whintington *et al* proposed a grading system for tissue eosinophilia in the gut [11]. Generally speaking, eosinophilia is diagnosed if over 10 eosinophils are seen in one high power field and the proposed grading is 10 to 20 (1+), 20 to 50 (2+), over 50 or aggregates of 10 (3+), extremely abnormal (4+). However, in selecting areas for biopsy in diagnostically difficult cases, a lesion site, especially one in the stomach, is preferential because eosinophil distribution varies in the gut of the normal population, except in the stomach [12,13]. Most other reported causes of eosinophilia in differential diagnosis, including cow's milk allergic gastroenteropathy, did not present with significant tissue eosinophilia in the gut [10]. However, in the present case, severe tissue eosinophilia was encountered. That is why EG but not cow's milk allergy alone is the most suitable diagnosis. Whether cow's milk allergy associated gastroenteropathy existed in the present case remains uncertain since specific IgE alone is only suggestive of food allergy and specific tests could not be performed. As Sampson *et al* stated, definite diagnosis of food allergy associated gastroenteropathy should include double-blinded placebo-controlled food challenge (DBPCFC) or three consecutive elimination and challenge tests [6,14,15]. However, the severity of illness in our patient prohibited the performance of these tests to complete the diagnosis.

Whether congenital duodenal obstruction plays a role in the pathogenesis of EG remains unclear. Olson *et al* proposed that stasis caused by congenital obstruction of the bowel may predispose to antigen penetration and thus to early formation of EG [8].

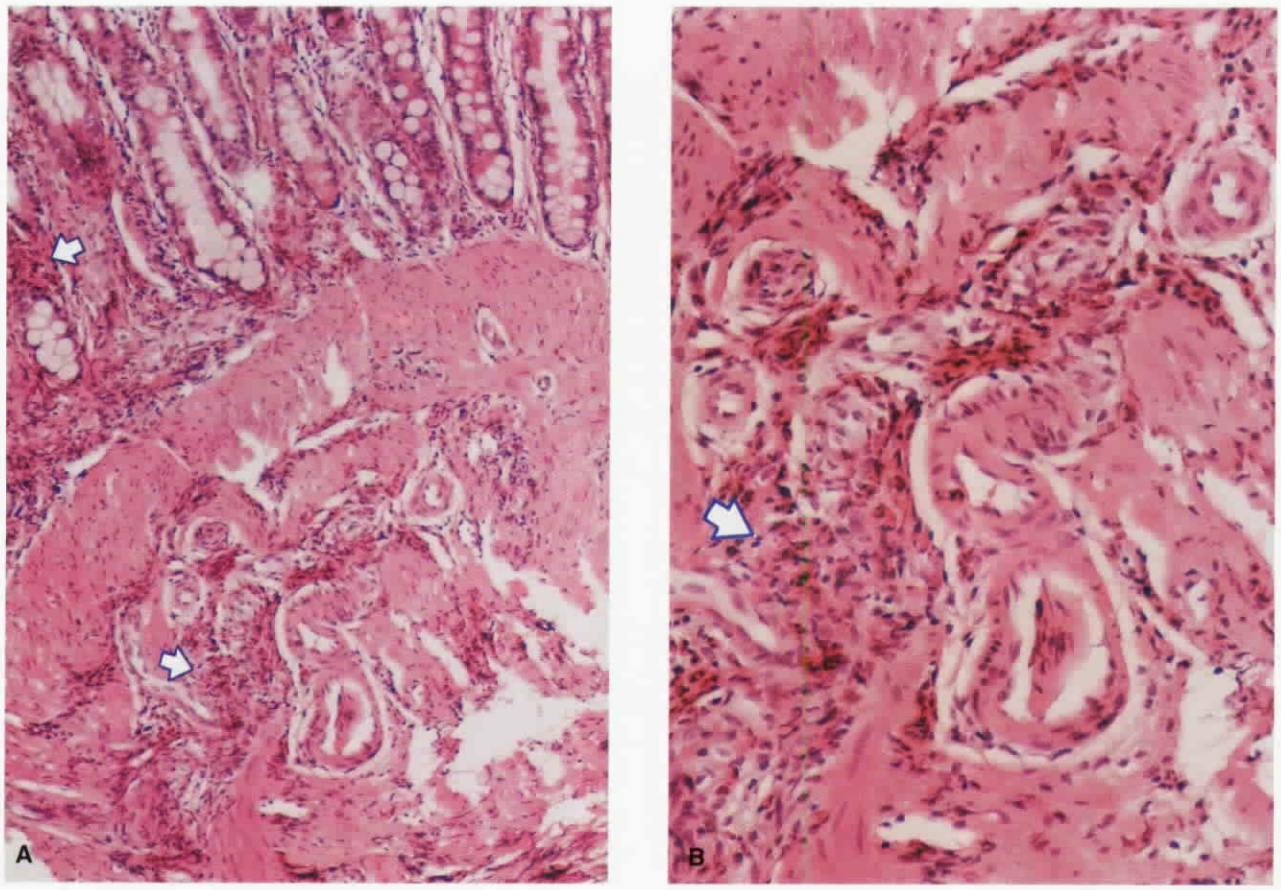

Fig. 3. Biopsy from the stomach of the patient which shows heavy eosinophilic infiltration both in (**A**) mucosal and submucosal layers (arrow), (**B**) eosinophils gathering in clusters (arrow) (H & E x 100).

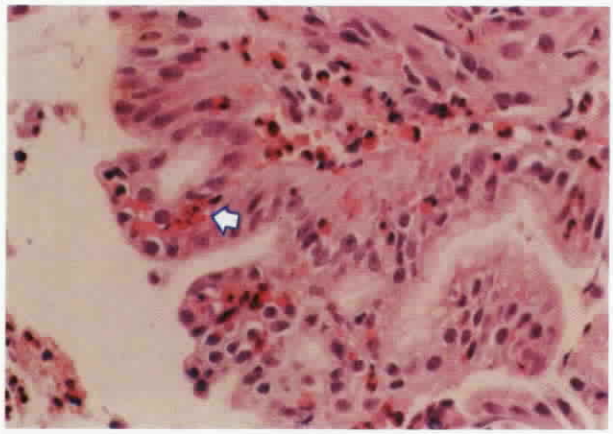

Fig. 4. Duodenal mucosa shows prominent eosinophil infiltration into the mucosal epithelium (arrow) (H & E x 400).

Another predisposing factor in the present case might have been disruption of mucosal integrity (like gastric ulcer), as mentioned by Cello [17], which could increase antigen penetration and formed a vicious cycle [4].

The procedure for correct diagnosis of EG should emphasize that parasitic infestation must be ruled out. Although our patient had a history of dog rearing, we could not find any evidence of parasitic infestation in duodenal fluid of endoscopic aspirate, biopsy specimens and stools of the boy and his dogs.

Initial management of EG includes an elimination diet and steroids. Katz *et al* [12] reported that an elimination diet alone might result in recurrence. Thus, steroid should always be used as the mainstay of treatment. Oral prednisolone (1-2 mg/kg/day) for 2 weeks is appropriate. In some cases, low dose maintenance prednisolone therapy may be needed to achieve complete control. Other approaches to treatment include the use of immunosuppressive agents, other anti-inflammatory drugs, mast cell stabilizers and surgery. Use of immunosuppressive agents such as azathioprine has been mentioned for their steroid sparing effects in some steroid dependent patients [4]. The use of sodium cromoglycate in some series also seemed to provide encouraging results [17]. The use of ketotifen has also been reported to reduce the symptoms

in some patients but its role in the treatment of EG has not yet been established [18]. Operation, as a destructive method, should always be reserved for intractable or complicated cases.

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