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Helicobacter pylori and Infantile Hypertrophic Pyloric Stenosis: Is There a Possible Relationship?

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ABSTRACT

Background: Recently, it has been suggested that *Helicobacter pylori* might be a cause of some cases of infantile hypertrophic pyloric stenosis (IHPS) in infancy on the basis of its epidemiologic and clinical features. We performed this study to evaluate the possible relationship between IHPS and *H. pylori*.

Design: In consecutive infants with IHPS, we performed upper gastrointestinal endoscopy with biopsy before pyloromyotomy. The endoscopic appearance of the pylorus was noted to validate endoscopic features of IHPS.

Results: Sixteen infants, 15 male, 14 white, mean age 42 days, range 21 to 104 days, were studied. The index case had chronic active gastritis on biopsy with organisms suspicious for *H. pylori*. Four others had chronic active gastritis, six more had focal or mild chronic gastritis, five were normal, and none had *H. pylori* on histology or immune histochemical staining in selected cases. All patients had negative rapid urease test. Most common endoscopic findings of IHPS were thickened prominent asymmetric pyloric folds and pin-hole pylorus that could not be intubated by the pediatric endoscope.

Conclusion: *H. pylori* was not specifically identified in our patients with IHPS. The presence of *H. pylori*-like organisms in the gastric mucosa in our index case and finding of chronic active gastritis in several others may indicate the possibility of an acquired infectious etiology for IHPS. ***JPGN 42:262–264, 2006.*** **Key Words:**

INTRODUCTION

Infantile hypertrophic pyloric stenosis (IHPS) was described in 1717 by Blair (1) and by Hezekiah Beardsley 1788 (2). It is generally considered a congenital anomaly with polygenic inheritance modified by sex. Its reported incidence is 2 and 9 per 1,000 live births with a male to female ratio of 6:1 (1–3). It usually presents with projectile nonbilious vomiting after 3 weeks of age, although in up to 20% of patients, symptoms may start at birth (4). In spite of advances in diagnosis and management, it still carries a mortality rate of up to 0.5% and a recurrence rate of 1% to 3% (5).

Helicobacter pylori, a gram-negative coccobacillus, was first described as a cause of gastritis and peptic ulcers in 1984 by Marshal et al. (6,7). Subsequent evidence has implicated it in the pathogenesis of duodenal ulcers, gastric ulcers, and some types of gastric malignancies (6,8).

We identified one infant with suspected *H. pylori* gastritis that occurred before he was diagnosed with IHPS. We became curious about a possible role for *H. pylori* in the pathogenesis of IHPS. In 2000, Paulozzi (9) suggested that the epidemiologic characteristics of IHPS appeared to fit an acquired infectious disorder rather than a true congenital condition. He suggested that *H. pylori* might be a pathogen in this setting and suggested serologic testing of affected infants as a way to validate his hypothesis. Unfortunately, there are significant limitations to the use of serologic markers in establishing the diagnosis of active infection with *H. pylori* gastritis, particularly in the neonate. In its position statement, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition recommends against serologic testing for the diagnosis of *H. pylori* infection in children, particularly in developed countries (10).We determined to investigate the possible correlation between IHPS and *H. pylori* gastritis.

METHODS

The protocol for this study was approved by the institutional review boards of the University of Oklahoma and Saint Francis Hospital. We prospectively enrolled patients from birth to 6 months of age with IHPS from January through December 2004. After the diagnosis of pyloric stenosis was

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confirmed by ultrasound or upper gastrointestinal (GI) barium study, and before pyloromyotomy, informed consent was obtained for the performance of upper endoscopy with biopsy to be performed under the same anesthesia as the scheduled pyloromyotomy. We excluded infants with other acquired or congenital GI anomalies or malformations.

After induction of general anesthesia and before pyloromyotomy, upper GI endoscopy was performed and biopsies of gastric mucosa obtained. The endoscopy also served to confirm the presence of hypertrophic pyloric stenosis and helped to validate our previously described endoscopic criteria for this diagnosis (11). Two gastric biopsies were obtained from the antrum. Rapid urease test was performed on a third antral biopsy. The biopsies were evaluated by an experienced pathologist with expertise in GI pathology. Gastritis was classified according to the updated Sydney classification (12,13). Tissue was examined after Giemsa staining. Biopsies showing chronic active gastritis underwent additional immune histochemical staining for *H. pylori*. No other viral or bacterial studies were performed.

RESULTS

Two infants with pyloric stenosis were evaluated by endoscopy before the study was planned, and we included their data with the rest of the group. Our index case had biopsy evidence of chronic active gastritis with predominantly lymphocytic infiltration and *H. pylori*-like organisms in the gastric mucosa. This was the finding that triggered interest in a possible relationship between IHPS and *H. pylori* infection. He was evaluated at 6 weeks of age by endoscopy upon presenting with hematemesis before any radiologic studies. In addition to hemorrhagic gastritis, he appeared to have pyloric stenosis that was later confirmed and treated surgically.

The second case had pyloric stenosis that was missed on a previous upper GI barium radiograph. The diagnosis of IHPS was made during endoscopy and confirmed surgically. His gastric biopsy revealed chronic active gastritis, but no *H. pylori* organisms were identified, and the rapid urease (CLO) test was negative.

Fourteen more infants with IHPS were then prospectively enrolled over 12 months and underwent endoscopy with gastric biopsy just before surgical repair. There were 13 boys, 13 white patients, and the mean age of the group was 42 days (range 21–104). All gastric biopsies were reviewed by the same pathologist. Chronic active gastritis was seen in the biopsies of three infants, focal mild gastritis was seen in six, and five were normal. No *H. pylori*-like organisms were identified, and all had negative CLO tests. In all cases with chronic active gastritis, sections were stained immunohistochemically for *H. pylori*. None were positive. None showed eosinophilic gastritis.

Endoscopic findings of pyloric stenosis in our patients included thickened prominent asymmetric pyloric folds, a pin-hole pyloric orifice that could not be intubated with a pediatric endoscope (as seen in the photograph), retained barium in the gastric lumen consistent with delayed gastric emptying, and hemorrhagic gastritis and erosions. These findings established the diagnosis of pyloric stenosis in the second case when it was missed by radiologic studies.

DISCUSSION

Pyloric muscle hypertrophy is not present during the newborn period in infants who later develop IHPS (14). That IHPS is a congenital abnormality has been challenged by Rollins et al. (15). The elapsed time of several weeks between birth and the development of anatomic changes and symptoms would suggest an incubation period of some kind may be necessary before the condition develops. The increased incidence of IHPS in bottle-fed compared with exclusively breast-fed infants and in lower socioeconomic classes suggests an acquired infectious rather than a congenital etiology (9). The presence of *H. pylori*-like organisms in gastric mucosa of our index case posed the intriguing question of a relationship between *H. pylori* gastritis and IHPS. Furthermore, the chronic active gastritis noted in five cases also suggested an infectious etiology.

H. pylori gastritis has been reported in newborn babies and infants (16,17). By prospectively following a cohort of infants and their mothers from birth to 5 years of age, Konno et al. (18) found that mother to child transmission is the most common cause of intrafamilial spread of *H. pylori*. In spite of the higher prevalence of *H. pylori* gastritis in developing countries, however, there is not an increase in the incidence of IHPS in these settings. In developing countries, exclusive breastfeeding is common, but it remains to be established whether breast milk antibodies have any protective role against the development of IHPS. Lack of a clear genetic marker for IHPS is consistent with an infectious etiology. However, the male predominance and the frequently positive family history are not consistent with an acquired etiology.

The absence of *H. pylori* organisms even on immune histochemical stains makes it unlikely that *H. pylori* was the agent producing IHPS in our patients. Other infectious agents were not excluded and may be possible in view of the one case in which *H. pylori*-like organisms were seen and the cases with chronic active gastritis. It is also possible, however, that gastric outlet obstruction leading to continuous exposure of gastric mucosa to unbuffered acid might produce a chemical gastritis if the mucous coat of the infant stomach was insufficient.

Endoscopic diagnosis of IHPS is an increasingly recognized modality of establishing the diagnosis of IHPS since its first description by one of the investigators (11). We believe that this method of diagnosis may be of benefit when the radiologic evaluation is not conclusive. We hope this study will stimulate larger scale studies to evaluate the pathogenesis of IPHS.

REFERENCES

1. Spicer RD. Infantile hypertrophic stenosis: a review. *Br J Surg* 1982;69:128–35.
2. Donovan EJ, Beardsley H. Congenital hypertrophic stenosis of the pyloris.. *Arch Pediatr* 1958;75:359–61.
3. Jedd MB, Melton LJ, III Griffin MR, et al. Factors associated with infantile hypertrophic pyloric stenosis. *Am J Dis Child* 1988; 142:334–7.
4. Geer LL, Gaisie G, Mandell VS, et al. Evolution of pyloric stenosis in the first week of life. *Pediatr Radiol* 1985;15:205–6.
5. Benson CD. Infantile pyloric stenosis: historical aspects and current surgical concepts. *Prog Pediatr Surg* 1971;1:63–88.
6. Marshall B, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984;1: 1311–4.
7. Marshall BJ, Armstrong JA, McGechie DB, et al. Attempt to fulfill Koch's postulate for pyloric Campylobacter. *Med J Aust* 1985;142:436–9.
8. Wotherspoon AC, Doglioni C, Diss TC, et al. Regression of primary low-grade B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of Helicobacter pylori. *Lancet* 1993; 4:342:575–7.
9. Paulozzi LJ. Is Helicobacter pylori a cause of infantile hypertrophic pyloric stenosis? *Med Hypothesis* 2000;55:119–25.
10. Gold BD, Colletti RB, Abbott M, et al. North American Society for Pediatric Gastroenterology and Nutrition: Helicobacter pylori infection in children: recommendations for diagnosis and treatment. *J Pediatr Gastroenterol Nutr* 2000;31:490–7.
11. Donovan GK, Yazdi AJ. The endoscopic diagnosis of pyloric stenosis. *J Okla State Med Assoc* 1996;89:58–9.
12. Dixon MF, Genta RM, Yardley JH, Correa P. Histological classification of gastritis and Helicobacter pylori infection: an agreement at last? The International Workshop on the Histopathology of Gastritis. *Helicobacter* 1997;2(Suppl 1):S17–24.
13. Cohen MC, Cueto Rua E, Balcarce N, Donatone J, Drut R. Assessment of the Sydney System in Helicobacter pylori-associated gastritis in children. *Acta Gastroenterol Latinoam* 2000;30:35–40.
14. Van Heurn LW, Vos P, Sie G. Recurrent vomiting after successful pyloromyotomy. *Pediatr Surg Int* 1999;15:385–6.
15. Rollins MD, Shields MD, Quinn RJ, et al. Pyloric stenosis: congenital or acquired? *Arch Dis Child* 1989;64:137–8.
16. Raymond J, Bargaoui K, Kalach N, et al. Isolation of Helicobacter pylori in a six-day-old newborn. *Eur J Clin Microbiol Infect Dis* 1995;14:727–8.
17. Gottrand F, Turck D, Vincent P. Helicobacter pylori infection in early infancy. *Lancet* 1992;22;340:495.
18. Konno M, Fujii N, Yokota S, et al. Five-year follow-up study of mother-to-child transmission of Helicobacter pylori infection detected by a random amplified polymorphic DNA fingerprinting method. *J Clin Microbiol* 2005;43:2246–50.