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The development of hypertrophic pyloric stenosis in a patient with prostaglandin-induced foveolar hyperplasia

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Abstract *Background.* Hypertrophic pyloric stenosis (HPS) has been described in association with several obstructive antropyloric lesions including idiopathic foveolar hyperplasia (gastric mucosal hypertrophy), feeding tubes, eosinophilic gastroenteritis, and hypertrophic antral polyps. Non obstructive antral webs have also been described with HPS.
Patient and methods. We present a case of gastric-outlet obstruction in association with HPS, namely, prostaglandin-induced foveolar hyperplasia. This entity has been previously described, but rarely in association with HPS. We report a female infant requiring prostaglandin therapy for pulmonary atresia who developed dose-related prostaglandin-induced foveolar hyperplasia and symptoms of progressive non-bilious vomiting.
Results. Intially, ultrasonography demonstrated evidence of antral mucosal hypertrophy as the cause for gastric-outlet obstruction. The patient subsequently developed progressive thickening of the antropyloric muscle, resulting in sonographic appearances of hypertrophic pyloric stenosis. Pyloromyotomy was eventually required for treatment of HPS.
Conclusion. A common denominator of most of the above-described entities is thickening and/or hypertrophy of the antral mucosa. We suggest that the antropyloric musculature may hypertrophy in an effort to overcome the gastric-outlet obstruction caused by the adjacent thickened antral mucosa. In other words, these entities may represent examples of "secondary" hypertrophic pyloric stenosis.

Case report

A 3.7-kg girl, the product of a 38-5/7–week gestation complicated by pregnancy-induced hypertension, presented at birth with cyanosis, a room air O_2 saturation of approximately 80 % and a grade 3/6 systolic murmur at the left sternal border. A cardiac echo showed pulmonary atresia with intact interventricular septum. On the 5th day of life, after obtaining Hospital Investigational Review Board approval, a transcatheter retrograde radiofrequency perforation of the pulmonic valve using a 2 Fr catheter was performed [1]. Prostaglandin therapy was started on the 1st day of life, and intermittently administered for a total of 14 days (6 days at 0.05 μg/kg per minute and 8 days at 0.1 μg/kg per minute) with a total dose of 5994 μg. Over the next 4 weeks, the patient developed symptoms of progressive nonbilious vomiting. An ultrasound on day 32 of life showed this to be caused by antral mucosal hypertrophy (Fig. 1 a). At this time the antropyloric musculature was asymmetrically prominent, ranging from 2.0 mm to 3.1 mm from mucosa to serosa (Fig. 1 a, b). An upper GI series, also performed at 32 days of life, demonstrated elongation and narrowing of the pyloric channel (Fig. 1 c). Marked gastroesophageal reflux (GER) was present above the level of the clavicles on several occasions. Over the next 11 days, the pyloric musculature became progressively thickened, measuring 3.6 to 4.0 mm, consistent with the appearance of HPS (Fig. 2 a, b). At surgery, there was a typical large olive, and pyloromyotomy was performed. The patient's symptoms of vomiting slowly regressed over the following several weeks, though antral mucosal hypertrophy still persisted (Fig. 3). Eventually, sonographic thinning of the antral musculature was noted. Blood eosinophil levels were normal throughout the patient's hospital admission.

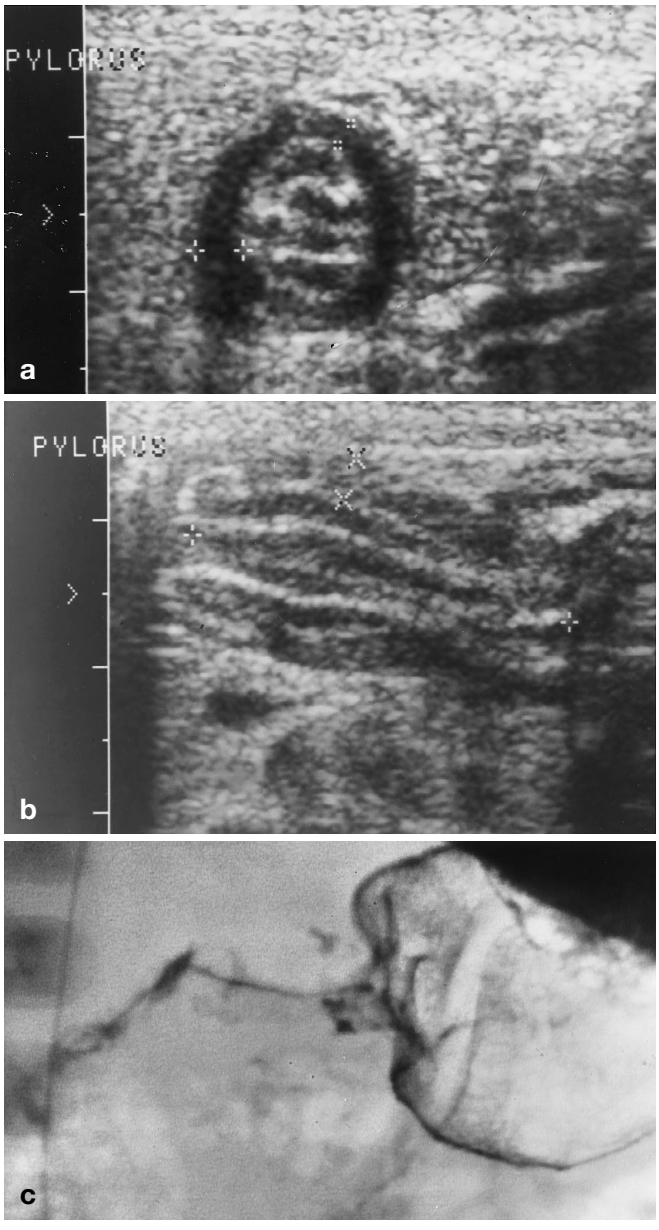


Fig. 1a Transverse image from an ultrasound of the antropyloric region on day 32 shows mild asymmetric thickening of the pyloric muscle (2.1 to 3.1 mm in thickness), which was not thick enough to make a sonographic diagnosis of HPS. Marked antral mucosal thickening is demonstrated as layers of wavy hyperlucency and hypolucency, prior to the development of HPS. **b** Longitudinal image from an ultrasound of the pylorus on day 32. The pyloric musculature measures 2.9 mm in width (between diagonal cursors), and 26 mm in length. **c** Spot film from an upper GI series on day 32 demonstrates elongation and narrowing of the pyloric channel, which was due more to mucosal hypertrophy than muscular hypertrophy when correlated with the ultrasound performed on the same date

Discussion

Neonates with cyanotic congenital heart disease often require prostaglandin (PGE) to maintain postnatal patency of the ductus arteriosus. Treatment complications are uncommon; however, prostaglandins have been shown to induce proliferation of gastric antral mucosa, caused by elongation of the gastric pits (foveolae) [2]. Occasionally, this hypertrophied antral mucosa has the potential to produce gastric-outlet obstruction in infants [2–4].

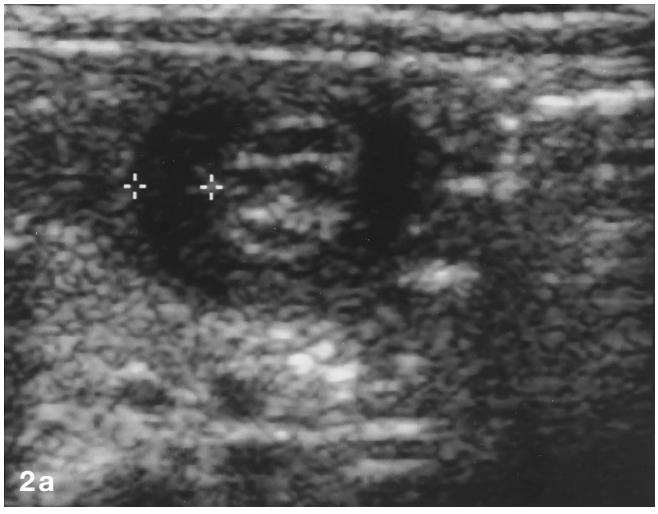
Our patient initially developed gastric-outlet obstruction from PGE-induced foveolar hyperplasia, which closely resembled the findings described by Peled [2]. In the presence of marked antro pyloric mucosal hypertrophy, the degree of which was much greater than that seen in the "antral nipple sign" described by Hernanz-Schulman [5, 6], HPS was noted to develop over the next 11 days. Following pyloromyotomy, our patient did not have complete relief of symptoms from gastric-outlet obstruction, as is nearly always seen in patients following surgical treatment for HPS. It is therefore inferred that antral mucosal hyperplasia played a significant role in the symptoms of gastric-outlet obstruction in this infant.

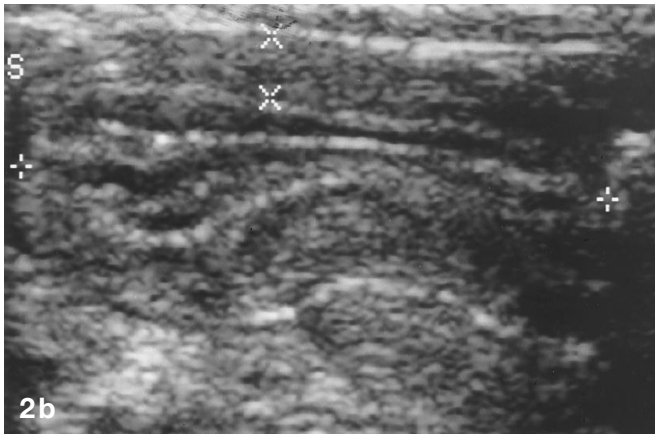
Additional associations of HPS and gastric-outlet obstructive lesions such as transpyloric feeding tubes [7], eosinophilic gastroenteritis (EG) [8–10], idiopathic focal foveolar hyperplasia [11], hyperplastic antral polyps [12], and a juxta pyloric cyst [13] have been reported.

Latchaw et al. [7] described three cases of HPS developing in older infants (3–4 months) who had long-standing transpyloric feeding tubes (3, 4, and 12 weeks' duration), and suggested that the late presentation of HPS may have been directly related to the presence of the partially obstructing feeding tubes. A mechanism for the development of HPS in these patients was not hypothesized.

Blankenberg et al. [8] presented a case of a vomiting 25-day-old girl who had eosinophilic infiltration of the lamina propria and submucosa, diagnosed as eosinophilic gastroenteritis. Upper endoscopy at first demonstrated asymmetric thickening of the pyloric musculature, that soon developed into HPS, requiring pyloromyotomy. The authors postulate the development of HPS may in part be caused by the degree and duration of an allergic gastroenteropathy.

Hümmer-Ehret et al. [9] report on two girls (3 weeks and 5 months of age), who presented with vomiting. After a presumptive diagnosis of HPS was made by sonography, pyloromyotomy was performed on each patient, but the symptoms of gastric-outlet obstruction did not regress. Eosinophilic gastroenteropathy was then diagnosed based on a retrospective review of sonograms that showed mucosal and submucosal hypertro-





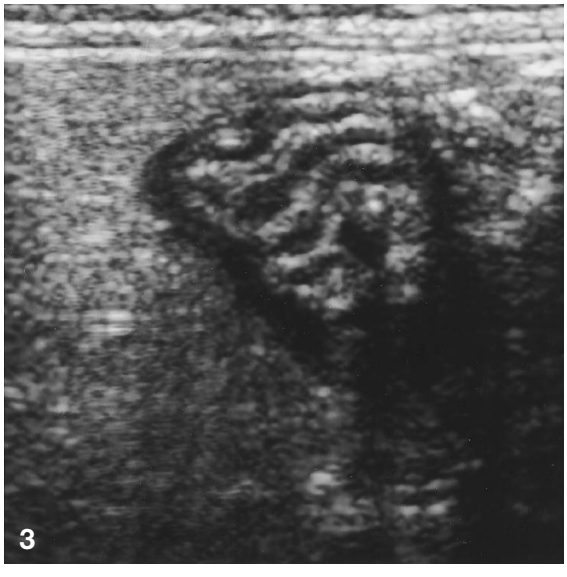


Fig. 2a Transverse sonogram of pylorus on day 43, demonstrating increased thickening of the pyloric muscle to 3.9 mm in width. **b** Longitudinal sonographic image of the pylorus on day 43, demonstrating progressive thickening of the pyloric muscle, measuring 3.6–4.0 mm in width (between diagonal cursors)

Fig. 3 Transverse sonogram of antrum performed on day 63 shows normal antral muscle thickness with a persistent wavy pattern of heaped-up mucosa, consistent with foveolar hyperplasia

phy, muscular hypertrophy, as well as blood eosinophilia, that responded well to steroid therapy.

Snyder et al. [10] report two 6-week-old patients with pyloric stenosis and histologic evidence of eosinophilic gastroenteritis. A gastric antral biopsy in one of the patients exhibited eosinophilic infiltration of the lamina propria, as well as marked elongation of the gastric foveolae (pits), which is seen in prostaglandin-induced foveolar hyperplasia. Although no definite link between HPS and EG was identified, because of the previously described association of EG with protein intolerance the authors hypothesize that HPS in a subgroup of infants may be related to intolerance to ingested protein. They reviewed the charts of 47 patients with HPS who underwent pyloromyotomy over 1-year period at their institution, and retrospectively found elevated eosinophil counts in approximately $^1/_3$ of patients.

Holland et al. [11] describe a 13-week-old infant who presented with nonbilious vomiting caused by HPS. Idiopathic focal foveolar hyperplasia (FFH) was also eventually diagnosed with histologic evidence of an eosinophilic infiltrate in the lamina propria. The authors contend that FFH is a different entity from eosinophilic gastroenteritis (EG).

Kim et al. [12] describe a case of HPS in association with a hyperplastic antral polyp. They speculate that the coexistence of the two entities is most likely coincidental; however, they suggest it is possible that HPS could have developed by the underlying hyperplastic antral polyp prolapsing into the pyloric channel causing a chronic gastric-outlet obstruction.

Hanquinet et al. [13] describe four cases of unusual ultrasonographic findings in the antropyloric region, and gastric-outlet obstruction. They report sonographic evidence of hypertrophied pyloric musculature in association with a solid mass in the pyloric channel, pyloric mucosal hypertrophy in two cases, and a double juxtapyloric cyst with an ulcer. The authors suggest that such obstructive antral abnormalities may actually cause "mild and progressive pyloric hypertrophy."

In summary, we note that there is a definite association, albeit rare, between HPS and other gastric-outlet obstructive lesions, including our case of prostaglandin-induced foveolar hyperplasia, with most of these

disease entities demonstrating mucosal hypertrophy or mucosal abnormalities of the gastric antrum. While the true cause of hypertrophic pyloric stenosis remains elusive, and is most likely multifactorial, we speculate that in many of the cases discussed HPS may have developed in an attempt to overcome the adjacent gastric-outlet obstruction, and that these cases may represent examples of secondary hypertrophic pyloric stenosis.

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