

## Idiopathic Hypertrophic Pyloric Stenosis in Identical Twins

Ju-Bei Yen, MD; Man-Shan Kong<sup>1</sup>, MD; Wan-Jao Wu, MD;  
Chen-Sheng Huang<sup>2</sup>, MD; Kuei-Wen Chang<sup>1</sup>, MD

Idiopathic hypertrophic pyloric stenosis (IHPS) was thought to be a congenital disease traditionally, even though several published reports assumed IHPS was an acquired disease. The pathogenesis and inheritance patterns of IHPS are not fully understood. Except for the familial recurrence of IHPS, concordance of IHPS in monozygotic or dizygotic twins was also noted, but occurrence in female twins is rare. From July 1992 through June 2000, 130 patients were diagnosed with IHPS in our hospital including one pair of female twins. We present the finding in the twins and review the associated articles about the pathogenesis and inheritance patterns of IHPS. (*Chang Gung Med J* 2003;26:933-6)

**Key words:** pyloric stenosis, twins.

Idiopathic hypertrophic pyloric stenosis (IHPS) is the most common cause for abdominal operation during infancy. However, its pathogenesis and inheritance patterns are not fully understood. Hypochloreaemia and metabolic alkalosis usually develop in patients with IHPS<sup>(1)</sup> and hyperbilirubinaemia may be noted.<sup>(2)</sup> Familial recurrence<sup>(3)</sup> and concordance of IHPS in monozygotic or dizygotic twins<sup>(4)</sup> have been noted, but the prevalence in male twins is much higher than in female twins.<sup>(5)</sup> Herein, we present one set of female twins who were both affected with IHPS. We also reviewed the associated literature.

### CASE REPORT

The female twins were born to a G2P2 mother at gestational age of 36 weeks. The birth body weight (BBW) and birth body height (BBH) of twin A were 2908 g and 52 cm, respectively. The BBW for twin B was 2902 and the BBH was 48.5 cm. Meconium passage was noted on the first day of life but jaundice did not develop. Since the 6th week of

life, they both suffered from postprandial nonbilious vomiting. Physical examination revealed low activity levels, dry lips, and sunken eyes. No other abnormalities were noted and no abdominal masses were palpable. Their hemograms were within reference ranges. Biochemistry study of twin A revealed high serum level of aspartate aminotransferase (AST, 131 U/L), and low levels of sodium (Na, 132 meq/L) and chloride (Cl, 91 meq/L). Laboratory data of twin B showed the similar data including AST, 95 U/L; Na, 132 meq/L; and Cl, 96 meq/L. Plain abdominal radiographs were unremarkable. Ultrasonography showed a hypoechoic target about 2.1 cm in length, 0.6 cm in thickness and 1.7 cm in diameter in the epigastric area of abdomen in twin A. A hypoechoic target about 2.1 cm in length, 0.6 cm in thickness and 1.6 cm in diameter in the right upper quadrant of abdomen was shown in twin B. IHPS was diagnosed. After intravenous hydration, they underwent Fredet-Ramstedt's pyloromyotomy. Regular formula was fed to the patients the day after surgery and they were discharged on the 4th day after surgery. No family history of IHPS of the two cases was found.

From the Department of Pediatrics, Chang Gung Memorial Hospital, Chiayi; <sup>1</sup>Department of Pediatrics, <sup>2</sup>Department of Pediatric Surgery, Chang Gung Children's Hospital, Taipei.

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Address for reprints: Dr. Ju-Bei Yen, Department of Pediatrics, Chang Gung Memorial Hospital, 6, West Chia-Pu Road, Putz City, Chiayi, Taiwan 613, R.O.C. Tel.: 886-5-3621000 ext. 2765; Fax: 886-5-3623002; E-mail: irishcorners@yahoo.com.tw

## DISCUSSION

Idiopathic hypertrophic pyloric stenosis (IHPS) is the most common cause for abdominal operation during infancy. The overall incidence was about three cases in 1000 live births with a sex ratio (male to female) of five to one.<sup>(3)</sup>

Clinically, patients with IHPS presented with nonbilious vomiting from the fourth to sixth weeks of life with progression.<sup>(6)</sup> Visible gastric peristalsis and a palpable mass in the epigastric area may be observed.<sup>(1)</sup> Laboratory studies revealed metabolic alkalosis and sometimes hypochloremia.<sup>(1)</sup> Hyperbilirubinemia might be documented in patients with IHPS, but no confirmed pathogenesis has been proven.<sup>(2)</sup> In our cases, hypochloremia and elevated levels of serum aspartate aminotransferase were noted. This is interesting as no reported cases in the literature had mentioned liver dysfunction in patients with IHPS, except for the increased level of serum bilirubin.

The true pathogenesis of IHPS is still not clearly understood. The theory of that IHPS is congenital could not be supported by the autopsies of stillbirths.<sup>(7)</sup> Rollins et al. considered that IHPS was an acquired condition according to the experience in the US of 1400 consecutive newborns.<sup>(8)</sup> Histologic studies of IHPS patients revealed that the circular muscle of the pylorus becomes grossly thickened,<sup>(9)</sup> and immunohistochemistry study results revealed that nitric oxide synthase activity (NOS) was deficient in the enteric nerve fibers in the hypertrophic circular musculature in some IHPS patients.<sup>(10)</sup> NOS deficiency was thought to be the most likely cause of the pylorospasm in IHPS.<sup>(10)</sup> Kusafaka and Puri confirmed that NOS deficiency was caused by reduced expression of the neuronal NOS gene at the messenger RNA level.<sup>(11)</sup> In addition, few cases of IHPS in patients with ovarian dysgenesis have been noted.<sup>(12)</sup>

Several features of the genetic transmission of IHPS have been observed, including (1) male predominance,<sup>(3)</sup> (2) high incidence in the offspring of affected parents,<sup>(3,13)</sup> (3) high incidence in the relatives of affected patients,<sup>(3,13)</sup> and (4) high incidence of IHPS in twins compared with the general population.<sup>(3)</sup> Nevertheless, the inheritance pattern is still not confirmed. Carter and Evans assumed that IHPS was inherited as a dominant type whose clinical expression was affected by the sex and the critical

number of genes for IHPS of the individuals,<sup>(3)</sup> and this inheritance model was generally considered to be the most appropriate for IHPS. According to the reports in the literature, IHPS was induced by prostaglandin therapy for maintaining the patency of the ductus arteriosus.<sup>(14)</sup> Therefore, environmental factors should be considered in IHPS and this may explain why the prevalence of IHPS was high in the families of the involved patients.

The prevalence of IHPS in twins was higher than that in the general population, especially in monozygotic twins.<sup>(4)</sup> Metrakos reviewed reports of IHPS in 132 pairs of twins where at least one member of each pair was affected, and only three sets had both female affected compared with 31 sets where both males were affected.<sup>(5)</sup> Thus, it seems the male predominance exists in the twins as well. Discord in the development of IHPS in identical twins was also noted.<sup>(4,5)</sup> Thus, environmental effects or other factors on the gene expression should be considered. As for our patients, there was no family history of IHPS. They were identical twins, and we assumed their condition might be gene-related. Van der Horst et al. reported one set of female twins with X/XX mosaicism,<sup>(15)</sup> and it was a pity that no further chromosome study was performed for our patients.

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## 雙胞胎的原發性肌肉肥厚型幽門狹窄

顏如貝 江文山<sup>1</sup> 吳宛昭 黃振盛<sup>2</sup> 張魁文<sup>1</sup>

原發性肌肉肥厚型幽門傳統上認為它屬於先天性疾病，但有些文獻認為它可能是後天的疾病。它的致病機轉及遺傳模式目前仍不十分明瞭。原發性肌肉肥厚型幽門狹窄會在同一家族內重複發生，而在雙胞胎身上的發生機率亦較一般人口高，但女性雙胞胎兩人均罹患的機率卻極低。本院從西元1992年7月到2000年6月共診斷出130位原發性肌肉肥厚型幽門狹窄的病患，其中有兩位為女性雙胞胎。我們藉由此特殊病例來介紹原發性肌肉肥厚型幽門狹窄可能的遺傳模式及相關文獻。(長庚醫誌 2003;26:933-6)

**關鍵字：**幽門狹窄，雙胞胎。

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長庚紀念醫院 嘉義院區 小兒科；長庚兒童醫院 台北院區 <sup>1</sup>兒童內科部，<sup>2</sup>兒童外科部

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索取抽印本處：顏如貝醫師，長庚紀念醫院 小兒科。嘉義縣朴子市嘉朴路西段6號。Tel: (05)3621000轉2765; Fax: (05)3623002; Email: iriscorners@yahoo.com.tw