Clinical characteristics of double pylorus

Tsung-Hui Hu, MD, Tung-Lung Tsai, MD, Chia-Chang Hsu, MD, Sheng-Nan Lu, MD, Michael Hsiao, DVM, PhD, Chi-Sin Changchien, MD
Taiwan, Republic of China

Background: Double pylorus can occur as either a congenital abnormality or an acquired complication of peptic ulcer disease. There has been no report of long-term follow-up of a large series of patients treated for double pylorus. The objective of this study was to determine the course of double pylorus in 20 patients by serial endoscopic examination.

Methods: Among 102,958 endoscopic examinations conducted from 1987 to 1999, a diagnosis of double pylorus was made in 20 patients, 18 of whom were followed from 2 months to 10 years. The demographics, clinical presentations, and outcome, as well as endoscopic patterns of double pylorus, were retrospectively reviewed. The rates of ulcer recurrence and symptoms were estimated and compared.

Results: Most fistulous rings were located on the lesser curve of the gastric antrum (75%). Evolution from an original ulcer to fistula was observed in 9 patients. The fistula disappeared in 1 patient, remained open in 12, and converged with the normal pyloric ring in 5 patients. One or more associated systemic diseases and extensive treatment with various drugs were noted in 12 patients. Eradication of *Helicobacter pylori* in infected patients resulted in a lower percentage of patients with symptoms (36% vs. 100%) and ulcer recurrence (55% vs. 100%) compared with uninfected patients, but the differences were not statistically significant.

Conclusion: In this study, fistula closure did not occur in the majority of patients. Associated systemic diseases and extensive use of medications might be important factors in persistence of double pylorus. Eradication of *Helicobacter pylori* was not beneficial in terms of relief of symptoms, prevention of ulcer recurrence, and fistula closure. Surgical intervention should be considered for patients with refractory symptoms, recurrent ulcers, and other complications.

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Double pylorus (DP), a form of gastroduodenal fistula, consists of a short accessory canal from the distal stomach to the duodenal bulb such that the gastric antrum and bulb become connected by 2 openings separated by a septum or bridge. The fistula usually arises from the lesser curve of the gastric antrum and enters the superior aspect of the duodenal bulb. In most cases, DP is an acquired complication of ulcer disease. However, some cases have been reported in which DP was evidently a congenital anomaly.1-5 The first case of DP was detected endoscopically.6 To date, there have been sporadic reports of more than 100 cases. Most patients responded well to medical treatment regardless of whether the fistula was open or closed.

However, about 20% of the patients underwent surgery because of refractory symptoms or other complications.3,5,7,8 There is no long-term follow-up study of DP.3,5,7-9 The association of DP with other systemic diseases8,9 and *Helicobacter pylori* infection9 is not well characterized. The clinical findings were reviewed in 20 patients with DP identified from among 102,958 endoscopic procedures performed over a period of 12 years. The pathogenesis of this disease and the effect of *H pylori* eradication therapy are also discussed. The aims of this study were to provide further insight into the pathogenesis of DP and to develop a treatment strategy for this condition.

PATIENTS AND METHODS

Twenty patients with a diagnosis of DP were treated from 1987 to December 31, 1999. The presence of a fistula was documented by endoscopy in all patients. Of these 20 patients, 18 were followed for periods ranging from 2 months to 10 years. During follow-up, the following procedures were performed on each of the 18 patients. First, snare biopsy specimens were obtained from the original gastric ulcers or ulcers along the fistulous tract to exclude associated diseases. Second, 11 patients with *H pylori* infections, verified by Giemsa stain or a rapid urease test, were treated with triple therapy (either colloid bismuth, metronidazole and tetracycline for 2 weeks, or omepra-
zole, amoxicillin, and clarithromycin for 1 to 2 weeks) to eradicate the infection. Third, associated systemic diseases and medication histories were obtained from patient records. Fourth, each patient was treated with an H2 receptor antagonist or proton pump inhibitor for a 3-month period. Courses of treatment were repeated if an ulcer recurred. Fifth, more than one endoscopy was performed after the diagnosis of DP. Clinical presentations and laboratory data were recorded at each follow-up appointment. By using this information, patient ages, gender distribution, clinical presentations, endoscopic patterns, response to treatment, and clinical outcome were reviewed and analyzed retrospectively.

Nonparametric statistical methods were used for the summary statistics. The ages, duration of symptoms, and follow-up were reported as a median with an interquartile range. The final status of fistulas after treatment was presented with descriptive statistics because of the small number of patients. The Kaplan-Meier method and the log rank test were used to estimate and compare the rates of ulcer recurrence and clinical outcome after treatment with 

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S/S, Symptoms and signs; P, pain; B, bleeding; Pre-ulcer, pre-existing ulcer; Location, location of fistula; LC (GC), lesser (greater) curve side; ANT (POST), anterior (posterior) wall; HPT, Helicobacter pylori therapy; Re-ulcer, recurrent ulcer; CVA, cerebral vascular accident; DM, diabetes mellitus; CFR, chronic renal failure; COPD, chronic obstructive pulmonary disease; H/T, hypertension; F/U (M), duration of follow-up (months).

RESULTS

Table 1 shows the multi-parameter clinical database for the 20 patients with DP. Data for 18 patients were available for analysis; follow-up data were not available for patients 5 and 20. Overall, 14 of the 20 patients were men and 6 were women (ratio 2.3:1). The age at diagnosis ranged from 33 to 74 years (median 63 years, interquartile range 7 years). Twelve of the 20 patients (60%) presented initially with peptic ulcer hemorrhage and 8 (40%) with epigastric discomfort or dyspepsia. The duration of symptoms before treatment varied from 7 days to 14 months (median 60 days, interquartile range of 75.5 days).

Various fistula patterns were evident at endoscopy (Fig. 1). Seventy-five percent of the fistulas were located on the lesser curve of the gastric antrum (15/20), followed by the posterior wall (2/20), greater curve (2/20), and anterior wall (1/20). Ulcers were identified before the formation of fistulas in 9 patients (3 duodenal, 6 gastric ulcers). The time for transition from ulcer to fistula ranged from 1 to 36 months (median 6 months, interquartile range 11.5 months). Pre-existing ulcers were always deep, penetrating, and situated near the pylorus (Figs. 1-3). Patients in whom DP was diagnosed at the first endoscopic examination, and in whom there was therefore a lack of evidence of pre-existing ulcer, usually had co-existing ulcer(s) along the fistulous tract. The gastroduodenal fistula was observed to eventually close in only 1 patient (5.5%). It remained open in 12 patients (67%) (Figs. 1 and 4) and converged with the normal pyloric ring to form a single large opening in 5 patients (27.5%) (Figs. 2 and 3). The proportions of patients with symptoms were as follows: 0% (closed fistula), 66% (patent fistula), and 60% (large single opening). The convergence of the fistula and pylorus to form a single large opening usually developed as a result of
destruction of the septum, which resulted from ulceration within the fistulous tract (Figs. 2 and 3). Bile regurgitation and lack of peristasis were found in the nonphysiologic pylorus (data not shown).

Eleven of the 20 patients were infected with *H pylori* and were treated with triple therapy as explained in the Patients and Methods section. In the remaining 9 patients, 2 were lost to follow-up and 7 were free of *H pylori* infection during follow-up. Among patients treated for *H pylori*, the fistula closed in 1 (9%), remained open in 7 (64%), and fused with the normal pyloric ring in 3 patients (27%). Furthermore, the overall ulcer recurrence rate and proportion of patients with symptoms were 55% and 36%, respectively. In contrast, no fistulas closed (0%), 5 remained open (71%), and 2 fused (29%) in patients without *H pylori* infection. All patients without *H pylori* infection had ongoing symptoms and ulcer recurrence at the end of follow-up. Because of the small number of patients and variable length of follow-up, the differences between the 2 groups (infected versus noninfected) was not statistically significant (*p* = 0.98 for ulcer recurrence rate and *p* = 0.42 in symptomatic rate).

More than half of the patients with DP (12 patients, 60%) had associated systemic diseases including chronic obstructive pulmonary disease (4 patients), chronic renal insufficiency (4), hypertension (3), gouty arthritis (3), diabetes mellitus (2), cerebral vascular disease (2), ureteric stone (1), and hyperthyroidism (1). Patients with these associated diseases usually had a long history of treatment with multiple drugs including corticosteroids (prednisolone), nonsteroidal anti-inflammatory drugs (NSAID); indomethacin, piroxicam, naproxen, and ibuprofen), anti-platelet agents (aspirin), and bronchodilators (theophylline). Among the 9 patients with pre-existing ulcers, 2 had been treated with corticosteroids intermittently for lung disease, and 2 other patients had been treated with NSAIDs for gouty
arthritis during the period in which there was progression from an ulcer to the formation of a fistula. In addition, the 2 patients with cerebral vascular diseases had been treated with aspirin for 4 months and 1 year, respectively, before the diagnosis of DP. Furthermore, all 4 patients with chronic lung diseases in whom corticosteroids were intermittently administered had recurrent ulcers develop. Of the 3 patients with gouty arthritis and the 1 with ureteric stone, 2 had been treated with NSAIDs intermittently for 7 and 12 months, respectively, before their ulcers recurred. None of these patients had abnormal serum calcium or gastrin levels. Thus, the formation of fistula and ulcer recurrence seemed to be closely related to the use of various ulcerogenic medications.

Thirteen of 18 patients (13/18, 72%) had recurrent ulcers after the initial treatment (Figs. 1C, 1D, 2C, and 4D). The duration of time to ulcer recurrence ranged from 2 to 60 months (median 9 months, interquartile range 8.5 months). Recurrent ulcers were located either along the fistulous tract (10/13) (Figs. 1C and 1D) or in the enlarged pylorus (3/13). Only 3 of the 13 (23.1%) patients with recurrent ulcer responded to subsequent treatment and ultimately became asymptomatic. The majority of patients (10/13, 76.9%) experienced intermittent GI symptoms and hemorrhage; 2 underwent surgery because of symptoms or GI bleeding. The other 8 patients continued with medical therapy because of patient preference or because the risk of surgery was high due to the co-existing diseases. Three died of diabetic, renal, and pulmonary complications unrelated to DP.

**DISCUSSION**

The incidence of DP is not well characterized. The prevalence is reportedly around 0.06% to 0.4% with a male-female ratio of approximately 2:1. Based on the results of the present study, the incidence of DP at endoscopy (0.02%) seems to be lower than pre-
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Previously reported. With follow-up of as long as 10 years, the present series represents the longest serial study with the largest number of cases of DP.

Although DP has a characteristic radiographic appearance on double contrast studies, the radiologic findings are sometimes misinterpreted as polyps, tumors, or large mucosal folds. In contrast, the endoscopic diagnosis of DP is straightforward. Usually, endoscopy shows a variable-sized accessory orifice with an absence of normal peristasis (Fig. 1). However, large mucosal folds may sometimes conceal smaller fistulas (Figs. 3B, 4B, and 4C). The antrum must be sufficiently distended with air to visualize the fistula within thickened gastric folds, and it may be necessary to introduce the endoscope or a biopsy forceps through the fistula into the duodenal bulb to establish the diagnosis (Fig. 3C).

Most of the fistulas were located on the lesser curve aspect of gastric antrum or duodenal bulb. For ulcers in these locations, the route of penetration, either from antrum to duodenum, or duodenum to antrum, is the shortest. The fistula and the pylorus were separated by a septum or bridge, which was also the usual location for recurrence of ulcers. The endoscopic findings were striking in 5 patients in whom the septum was destroyed by eroding ulcers to create a large single opening (Figs. 2 and 3). The enlarged opening did not close completely during peristasis and resulted in bile regurgitation. The differential diagnosis of DP is not extensive, although possible confusion with antral carcinoma has been mentioned.

DP may be either congenital or acquired. DP arose in most cases in the present series as a complication of peptic ulcer and thus these cases were considered to be of the acquired type. The hypothesis that a gastroduodenal fistula could derive from peptic ulcer was initially proposed by Rokitansky. He suggested that such a communication was creat-

Figure 3. Endoscopic views showing evolution of gastric ulcer (case 8) (P, normal pyloric ring). A, Deep ulcer (arrow) on greater curve of antrum. B, One and one-half months later gastric ulcer has progressed and penetrated to form fistula (arrow). C, Five months later, after completion of 3-month course of treatment, fistula remains patent without ulcer. Biopsy forceps has been passed through fistula into duodenum. D, Two years later septum between fistula and pylorus has disappeared to form single large opening.
ed by 2 separate ulcers, 1 in the stomach and the other the duodenum, that erode toward each other. However, most reports have failed to confirm the presence of 2 opposing ulcers as prerequisite for fistula formation. Instead, the following pathogenesis has been repeatedly demonstrated: Penetration of a peptic ulcer originating in the gastric antrum or duodenal bulb leads to the formation of adhesions between the adjacent walls of the stomach and duodenum. Subsequently, further penetration along the muscular layer results in a fistulous tract.3-5,7,18,19

Our experience favors this hypothesis. Half of the patients in the present study had gastric (6 patients) or duodenal ulcers (3 patients) before the formation of a fistula (Figs. 2-4). Moreover, patients in whom DP was diagnosed at the initial endoscopy usually had long-standing symptoms of peptic ulcer, suggesting that they may have had ulcers before the diagnosis of DP. In addition, the patients with DP in this study were usually older and had other systemic diseases. When these factors are considered together, DP in our patients seemed to be an acquired rather than congenital disorder.

Some patients have experienced relief of ulcer symptoms concurrent with fistula formation.4,5,7,8,20 However, others have persistent symptoms after development of a fistula.8,9,21 In the present series, the patient whose fistula closed had no further symptoms. However, 13 of 17 patients with persistent fistulas experienced ulcer recurrence at least once. Even with repeated courses of treatment with antisecretory agents (3 months in each course), the success rate for curing the ulcers was still low in our patients (3/13, 23%).

The reason(s) underlying the poor healing of ulcers in patients with DP is unclear. However, comorbid illness and the use of various medications are possible exacerbating factors. Several systemic diseases, including diabetes, chronic obstructive pul-

Figure 4. Endoscopic views demonstrating evolution of gastric ulcer (case 19) (P, normal pyloric ring). A, Large, deep ulcer (arrow) on lesser curve of antrum. B, Six months later (no treatment) ulcer (arrow) is still present and bleeding. C, With further distention by air insufflation a small fistula (arrow) is evident near ulcer. D, One year later fistula is still present and widened with ulcer along tract (arrow).
monary disease, chronic renal failure, chronic rheumatism, and systemic lupus erythematosus, have been reported to be associated with DP. In the present study, 12 patients (60%) had 1 or more systemic diseases. Furthermore, the patients with chronic lung disease and rheumatoid arthritis had taken corticosteroids and NSAIDs for long periods of time, and this may have promoted ulcer recurrence. In addition, multiple agents such as anti-platelet drugs had been used in patients with cerebral vascular disease and hypertension. Therefore, it seems rational to postulate that drug-associated ulcers play an important role in the pathogenesis of DP. These ulcers were usually large and deep. The role of medication in the production of a gastroduodenal fistula is relevant in cases of diabetes and chronic renal failure in which there is impairment of mucosal protective mechanisms.

It is not known whether the convergence of the fistula and pylorus is critical to ulcer healing. Only one similar case has been reported to date. In the present series, 3 of 5 such patients had recurrent ulcers. Thus it can be postulated that convergence might result in a nonphysiologic neopyloric ring that allows bile reflux and predisposes to ulcer recurrence.

Among the 11 patients who received triple therapy to eradicate *H. pylori*, the fistulas remained open in 7 patients, converged to form a single ring in 3, and closed in 1. Although the eradication of *H. pylori* in the infected patients resulted in a lower percentage of patients with overall symptoms (36% vs. 100%) and ulcer recurrence (55% vs. 100%) compared with uninfected patients, the differences were not statistically significant. The lack of significance could have been due to the variable lengths of follow-up and/or the relatively small number of cases.

Most patients in the present series had a refractory course. It remains to be determined whether this is due to ulcer nonhealing or the unclosed fistula. However, the refractory nature might be attributable to underlying diseases and the extensive use of medications by the patients. Therefore, it is recommended that the use of ulcerogenic medications be avoided or minimized during treatment of the ulcer. Because the patients with pre-existing ulcers often received incomplete treatment, the penetration of the ulcer and the development of a fistula may have occurred more readily. Thus, aggressive and complete antiulcer treatment should be undertaken as soon as possible. Although no significant benefit for *H. pylori* therapy was demonstrated in the present study, such therapy should still be carried out in infected patients. Based on successful outcomes in 2 patients who underwent surgery, surgery seems to be an alternative for the treatment of DP, particularly in patients with recurrent ulcer after intensive anti-ulcer therapy.

REFERENCES