Original articles

Acute duodenal ulcer

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SUMMARY A series of 31 infants and children with acute duodenal ulcer verified by endoscopy was studied over an eight year period. Eighteen (58%) of them were under 2 years of age. The most common symptom was upper gastrointestinal bleeding (n=27, 87%). Twenty nine patients (94%) had a preceding illness characterised by diarrhoea, upper respiratory tract infection, or fever, which was not necessarily treated with antipyretic drugs. Initial endoscopy showed that ulcer lesions were solitary in 14 patients and present on the anterior wall (n=11), posterior wall (n=2), or both (n=1). Multiple ulcers were found in 17 patients, and present in the bulb with (n=6) or without (n=11) extension into the second part of duodenum. The most conspicuous finding was the irregularly shaped ulcers seen in eight young children with similar clinical and endoscopic features. Sixteen patients were re-endoscoped one to two weeks after the initial examination; the ulcers had entirely disappeared in 13, and there were only small residual ulcers in three. Thirty patients were treated medically and only one (with uncontrollable haemorrhage) required operation. Most patients were symptom free two to six years after the initial diagnosis.

Our results suggest that young children may develop acute duodenal ulcers after viral illnesses whether or not they are treated with drugs, mainly antipyretics. This kind of acute duodenal ulcer usually heals quickly irrespective of the morphology, site, and number of ulcers.

Acute peptic ulcer in infancy and childhood occurs in many diseases; these include spontaneous ulceration in neonates, Cushing's ulcer in diseases of the central nervous system, 'stress' ulcer, and drug induced ulcer—for example, after taking steroids.¹ A review of published reports showed that most acute peptic ulcers in infancy and childhood were diagnosed by barium meal study, or at laparotomy, or even necropsy.¹⁻⁷ Radiographic studies may fail to show an acute duodenal ulcer because it is usually superficial, either causing no deformity of the duodenal wall or located on the anterior wall of the bulb.⁸ On the other hand, there may be false positive results if the duodenal bulb is spastic or irritable during a barium meal study.⁹ These problems are virtually non-existent with endoscopy, which has replaced barium examination during the last decade and is now the examination of choice in infants and children with gastrointestinal diseases.¹⁰⁻¹² The evolution of endoscopic features during the course of acute duodenal ulceration in childhood, however, has to our knowledge never been described. Additionally, so that we may better understand the pathogenesis of acute duodenal

ulcer, more clinical information is needed. We began to use endoscopy in children under 6 years of age in this large referral hospital in 1977,¹¹ and since then we have identified 31 patients with acute duodenal ulcer, which was clearly a different entity from chronic duodenal ulcer. This paper investigates the clinical and endoscopic features seen at the initial visit and during follow up in these 31 patients.

Patients and methods

Thirty one children (24 of whom were boys), aged 2 days to 14 years, were seen in the department of paediatrics at the National Taiwan University Hospital between September 1978 to December 1986 and identified at endoscopy as having acute duodenal ulcers. Their clinical details including sex, age, symptoms and signs, preceding illnesses and drugs, associated diseases, and family history were recorded. All the patients underwent panendoscopic examination at the time of presentation. Follow up endoscopy was undertaken in 16 patients one to two weeks after the initial diagnosis. The endoscopes used were the Olympus GIF-P₂ or GIF-XP. Patients

were asked to fast for eight hours before endoscopy and premedication consisted of pethidine (2 to 2.5 mg/kg) and hyoscine butylbromide (0.4 to 0.5 mg/kg) by intramuscular injection 20 to 30 minutes before the procedure. For uncooperative patients, diazepam (0.5 to 1.0 mg/kg) was given intravenously before the examination.

Patients who had recurrent or long standing digestive symptoms (more than one week) or who had initial endoscopic features showing convergent folds, deformity of the duodenal bulb, or other signs suggestive of chronic ulceration were excluded from the study.

After endoscopy, the number, size, shape, sites, activity, and surrounding reaction of ulcers were recorded. Biopsy specimens were taken from the edges of duodenal ulcers if there were any unusual endoscopic features.

All the patients were initially managed conservatively with antacids ($n=26$), cimetidine ($n=3$), or sucralfate ($n=2$). Patients were closely observed and a surgeon consulted if bleeding continued or if other complications were noted.

Follow up took place in the gastrointestinal clinic. Patients who failed to return were interviewed by telephone or letter. Information was requested concerning the frequency, duration, and characteristics of digestive symptoms after the diagnosis and treatment of acute duodenal ulceration.

Fasting serum gastrin concentrations were measured regularly by radioimmunoassay (Biodata Gastrin Kit), and the antibody used in the kit had 100% specificity for gastrin G17 and 58% specificity for gastrin G34. The results were expressed as pg/ml.

Fisher's exact test was used for statistical comparisons.

Results

Twenty four boys (mean age 3.2 years) and seven girls (mean age of 3.3 years) were studied. Eighteen (58%) were under 2 years of age, five (16%) were aged 2 to 4 years, 3 (10%) were aged 5 to 6 years, and five (16%) were aged 7 to 14 years (table 1).

A preceding fever was more common among patients under 4 years of age ($p<0.05$). Although the incidences of other preceding events were not significantly different between the age groups, diarrhoea or upper respiratory tract infection seemed to occur more often in younger patients. Among the eight patients under the age of 4 years who had previously been taking antipyretic drugs, six had taken aspirin, one had taken paracetamol, and one had taken another non-aspirin preparation; the dosages were all within the therapeutic range. Abdominal pain was much less common among younger children ($p<0.05$). Though melaena occurred more often in patients under 4 years old ($p<0.05$), haematemesis was more common in older children. Upper gastrointestinal bleeding was the most common sign, occurring in 87% of our cases. Only two patients had a family history of peptic ulceration.

Twenty nine patients (94%) had a preceding illness characterised by diarrhoea ($n=15$), upper respiratory tract infection ($n=7$), or fever ($n=20$); 14 patients had been given drug treatment before the onset of upper gastrointestinal bleeding. In two

Table 1 Clinical features in patients with acute duodenal ulcer in two age groups. Figures expressed as number (percentage)

	Patients aged 4 years or less ($n=23$)	Patients aged 5-15 years ($n=8$)	<i>p</i> Value
Sex:			
Male	18 (78)	6 (75)	>0.05
Female	5 (22)	2 (25)	>0.05
Symptoms:			
Fever	18 (78)	2 (25)	<0.05
Diarrhoea	13 (57)	2 (25)	>0.05
Upper respiratory tract infection	7 (30)	0	>0.05
Drugs:	11 (48)	3 (38)	>0.05
Antipyretics	8 (35)	1 (12)	>0.05
Others	3 (13)	2 (25)	>0.05
Family history of duodenal ulcer	1 (4)	1 (12)	>0.05
Vomiting	5 (22)	2 (25)	>0.05
Haematemesis	7 (30)	4 (50)	>0.05
Melaena	20 (87)	2 (25)	<0.05
Abdominal pain	1 (4)	4 (50)	<0.05

cases there was no preceding illness and their ulcers were diagnosed only because one had abdominal pain (a 5 year old boy) and the other had dark reddish stools (a 2 day old newborn). Investigation of those patients in hospital subsequently showed the following coexistent illnesses: salmonellosis (n=2), hypothyroidism (n=1), methylmalonic acidemia (n=1), Meckel's diverticulum (n=1), roseola infantum (n=1), oesophageal candidiasis (n=2), pharyngoconjunctivitis (n=1), Kawasaki disease (n=1), anaphylactic purpura (n=1), and tuberculous meningitis (n=1).

ENDOSCOPIC FEATURES

Table 2 shows that at initial endoscopy ulcers were solitary in 14 patients, and distributed over the anterior wall (n=11), posterior wall (n=2), or both

Table 2 *Endoscopic features of 31 patients with acute duodenal ulceration*

	Single ulcer	Multiple ulcers
At initial endoscopy		
No of patients	14	17
Location of ulcers:		
Anterior bulb	11	2
Posterior bulb	2	0
Both anterior and posterior bulb	1	9
Bulb and second part	0	6
At follow up endoscopy		
No of patients	8	8
No of healed ulcers	6	7
No of small residual ulcers	2	1
Associated features		
Superficial gastritis	1	1
Haemorrhagic gastritis	2	2
Oesophageal ulcer	0	3

Table 3 *Comparison of clinical features of patients with single ulcers and those with multiple ulcers*

	No with single ulcer (n=14)	No with multiple ulcers (n=17)
Sex (M:F)	10:4	14:3
Mean (SD) age years	2.7 (4.2)	3.6 (3.5)
Symptoms:		
Fever	7	13
Diarrhoea	6	9
Upper respiratory tract infection	3	4
Drug treatment	6	8
Vomiting	1	6
Abdominal pain	1	4
Haematemesis	3	7
Melaena	12	10
Family history of duodenal ulcer	1	1
Haemoglobin concentration <80 g/l	7	4

None of the differences are significant.

(n=1). Multiple ulcers were found in 17 patients and located at the bulb with (n=6) or without (n=11) extension into the second part of duodenum. Sixteen patients were re-endoscoped one to two weeks after the initial endoscopy. The ulcers had entirely disappeared without scar formation in 13, and left as only tiny residual ulcers in three patients.

A comparison of clinical features of patients with multiple and solitary ulcers (table 3) shows that the mean age, the incidence of predisposing factors and clinical symptoms, and of a positive family history,

Figure *Endoscopic appearance in a 3 year old boy with irregularly shaped ulcers at (a) the duodenal bulb and (b) in the second part of duodenum.*

were similar in both groups. Analysis of the haemoglobin concentration at the initial presentation shows that the single ulcer group tended to have a higher incidence of profound anaemia (haemoglobin concentration <80 g/l) than the multiple ulcer group, although there were no significant differences between the two groups.

With respect to the endoscopic morphology of the ulcer lesions, eight cases with irregularly shaped ulcers were identified.

The endoscopic features of the ulcers in these patients were: that they were multiple and shallow, they varied in size from pinhead to several cm, they were well demarcated and irregularly shaped, they were distributed over the whole bulb (with or without extension into the second part), and they healed rapidly—usually within two weeks of the initial bleed (figure a and b, table 4). Patients with irregularly shaped ulcers received antipyretic drugs more often than those whose ulcers had smooth outlines: seven of eight patients with irregular ulcers received antipyretic drugs compared with two of 23 patients with smooth ulcers ($p=0.0002$). Thus the use of antipyretic drugs resulted more often in irregularly shaped ulcers, especially in those under the age of 4 years.

TREATMENT AND FOLLOW UP

Thirty patients recovered after conservative treat-

ment without complications. Only one boy aged 22 months who had multiple ulcers in the duodenal bulb developed uncontrollable haemorrhage, and finally required laparotomy, haemostasis, and pyloroplasty.

There have been no instances of recurrent ulcers in the two to six year period since the initial diagnosis.

SERUM GASTRIN CONCENTRATIONS

Gastrin analysis was performed in 11 patients. The ranges of their fasting serum gastrin concentrations were 36.2–58.5 pg/ml for two patients with solitary duodenal ulcers, 13.3–88.3 pg/ml for five patients with multiple duodenal ulcers confined to the bulb, and 26.4–69.9 pg/ml for four patients with multiple ulcers that extended from the bulb into the second part. Gastrin measurement could not be performed in the remaining patients who were either enrolled before the assay was available, or did not provide sufficient serum for analysis. The observed range of fasting serum gastrin in normal Chinese children using the same method were 40–183 pg/ml in 30 infants aged 2–6 months, 36.5–110 pg/ml in 14 infants aged 7–12 months, 20.5–140 pg/ml in 23 children aged 1–2 years, 13.7–189 pg/ml in 97 children aged 3–5 years, 12–111 pg/ml in 17 children aged 6–9 years, and 5.3–97.6 pg/ml in 32 children aged 11–15 years.

Table 4 Clinical and endoscopic features of eight patients with irregularly shaped ulcers in the duodenum

	Case No							
	1	2	3	4	5	6	7	8
Age	1 year 10 months	1 year 2 months	3 years 10 months	1 year 4 months	2 years	11 months	4 months	10 months
Sex	Female	Male	Male	Male	Male	Male	Male	Male
Prodromal symptoms:								
Fever	Moderate	High	High	Mild	None	High	High	High
Vomiting	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Diarrhoea	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Conjunctivitis	No	No	Yes	No	No	No	No	No
Cough and rhinorrhoea	No	No	Yes	No	No	Yes	No	No
Haematemesis	No	No	Yes	No	Yes	Yes	Yes	Yes
Tarry stool	Yes	Yes	Yes	Yes	No	No	No	Yes
Duration between onset of symptoms and upper gastrointestinal bleeding (days)	2	3	2	1	7	3	2	1
Receiving antipyretic drugs	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Haemoglobin concentration on admission (g/l)	90	65	122	55	120	128	70	110
Location of ulcers:								
Anterior wall	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Posterior wall	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Second part	Yes	No	Yes	Yes	Yes	No	Yes	No
Associated illness	None	None	Pharyngo- conjunctivitis	Salmonella enteritis	None	Oesophageal ulcer	None	Roseola infantum
Histological appearance of biopsy specimen	Duodenitis and erosion	Not done	Duodenitis and erosion	Duodenal ulcer	Duodenitis and erosion	Duodenitis and erosion	Not done	Not done
Blood transfusion	Yes	Yes	No	Yes	No	No	Yes	No

Discussion

There were 29 patients (94%) in whom a preceding illness such as fever, upper respiratory tract infection, or gastroenteritis were present. In addition, 12 patients (39%) also had various associated underlying diseases of differing severity as predisposing factors. This suggests that most of the acute duodenal ulcers in the series were secondary, with a preceding illness or identifiable underlying diseases which acted as a non-specific stressful episode and potentially predisposed to the acute type of ulcer development. No methods exist, however, to quantify this stress, and it could be argued that in some of the cases, acute duodenal ulcers may have been directly related to infection. Supporting evidence may be in that *Candida albicans* was isolated from oesophageal ulcers in two patients who had apparently similar ulcers in both duodenum and oesophagus. Thus the relation between infection and acute duodenal ulcer may be analogous to that between antral gastritis and *Campylobacter pylori*, which is interesting, but still controversial. Catastrophic predisposing factors such as trauma, sepsis, operation, burns, or diseases of the central nervous system (except the one case of tuberculous meningitis) were rarely seen in this series, because patients in these categories were too ill to permit endoscopic evaluation. This is different from previous reports mostly from surgical units whose patients required surgical intervention.¹⁻⁴

Other predictive features such as age and sex as well as the commonest symptoms are in agreement with those of earlier studies.^{1-3 5} Recent observation in our children with chronic duodenal ulcers has shown that 60% of the patients had family members affected by peptic ulcer diseases.¹³ It is consistent with a previous study on predisposing factors in childhood duodenal ulcers.¹⁴ Lack of positive family history in this series probably reflects that genetic predisposition plays little part in the pathogenesis of acute duodenal ulcers. Most of our patients also lived in urban areas or other neighbourhoods with high population density. They were theoretically more likely to be infected by various viral agents than those in rural areas, resulting in febrile illness and predisposing to the development of acute duodenal ulcers. We were unable, however, to conclude that there is geographic predisposition in acute duodenal ulcers because a nationwide survey for peptic ulcer diseases has not yet been performed. On the other hand, we see fewer cases of acute duodenal ulcers than previously, probably because paracetamol is used more and aspirin is used less.

Curci *et al*, Krasna *et al*, and Dunn *et al* have all showed that most of the acute peptic ulcers found at

necropsy and at laparotomy were solitary.^{1 15 16} This study, on the contrary, showed that multiple lesions in acute duodenal ulcers in childhood were common. Furthermore, solitary ulcers often occurred on the anterior wall of the duodenal bulb, and multiple ulcers extending from the bulb into the second part of duodenum were not rare. Indeed, fasting serum gastrin concentrations were within normal limits in the later four patients with extending multiple ulcers. This together with the lack of recurrence indicate that the Zollinger-Ellison syndrome is not a likely diagnosis in these patients. The stress or secondary ulcer is often shallow without induration, and difficult to recognise radiologically.⁵ Endoscopy provides the best visualisation of the shape, number, and distribution of acute duodenal ulcers.

Follow up endoscopy in 16 patients has shown that acute duodenal ulcers in childhood after viral illness with or without treatment with antipyretic drugs often healed within one to two weeks of the initial bleed irrespective of the morphology, size, site, and number of the ulcers. Endoscopic and clinical follow up of these patients also suggests that, in contrast with chronic duodenal ulcers, acute duodenal ulcers are usually self limiting without recurrence, and follow up endoscopy may be unnecessary. Operation has been commonly considered the treatment of choice for serious complications of acute peptic ulcer in childhood, such as uncontrollable bleeding or perforation.^{1-3 5 6} Only one of our patients required operation, and this shows the less serious problems with acute duodenal ulcers in this series in striking contrast with the serious outcome of stress ulcers often seen in other critically ill patients. Moreover, conservative management of the patients with acute duodenal ulcers was successful by short term treatment with antacids, H₂ receptor antagonists or a mucosal cytoprotector alone. No patients relapsed, which usually occurs in children with chronic duodenal ulcer once treatment has been stopped.¹³

Perhaps the most interesting endoscopic features of this series, not previously reported, is that of the irregularly shaped ulcers seen in eight patients. These patients shared common clinical features: they were infants or toddlers, they had had a viral illness with fever, antipyretics had been given before upper gastrointestinal bleeding had occurred, and they did not recur after a long period of follow up. The endoscopic lesions in these eight patients also had common characteristics, as shown in the results.

Aspirin is known to be associated with gastric ulcer, but the causal relation between aspirin and duodenal ulcer remains uncertain.¹⁷ We have recently encountered 16 patients with acute gastric

ulcers. Seven of them also had a history of taking antipyretic drugs, but none had irregularly shaped ulcers.¹³ In this series, infants with irregularly shaped ulcers often were fasted by their anxious mothers when they had acute diarrhoea. Starvation, plus a viral illness or its related stress, probably enhance the likelihood of developing acute duodenal ulcers when ulcerogenic drugs like aspirin were also given. Ament described a case with a small superficial lesion like an aphthous ulcer in the second part of the duodenum.¹⁰ Krasna *et al* and Rosenlund *et al* reported cases of childhood duodenal ulcers confined to the second part of the duodenum.^{15 18} Their cases differed from ours, who showed irregular ulcers both in the bulb and extending to the second part. As these eight and the other patients in the present series showed similar courses both clinically and endoscopically, it is premature to draw a conclusion that these irregular ulcers may implicate any particular form of acute duodenal ulcers in early childhood.

In summary, the present results are at variance with previous reports in showing that acute duodenal ulcers in childhood often appear as multiple lesions, may be irregularly shaped, and may extend into the second part of duodenum. These acute ulcers are generally benign with rapid healing, and do not relapse. Febrile illnesses of viral or other origin, often in combination with ulcerogenic drugs, frequently preceded upper gastrointestinal bleeding. The mechanisms by which these preceding events produce acute duodenal ulceration requires further study.

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