Duodenal ulceration: review of 110 cases

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SUMMARY This paper describes 110 cases of childhood duodenal ulcer, which were diagnosed over 26 years: 63 were diagnosed by barium meal examination; 47 by upper gastrointestinal endoscopy. The mean age at diagnosis was 11.2 years, with symptoms reported in 46% before 10 years and in 15% before 6 years of age. There was often a considerable delay in diagnosis, particularly in the younger age group. Nocturnal pain (61%) and a close family history of duodenal ulcer disease (62%) were the most valuable pointers to the diagnosis. Fifteen children had required surgery for persistent symptoms. Thirty four had received treatment with an H₂ receptor antagonist, and all but four had had a satisfactory initial response. Seventy per cent relapsed within six months of discontinuing treatment, and long term maintenance treatment may therefore be necessary.

Recurrent abdominal pain is a common disorder in childhood, and it is well known that an organic disorder can be identified in only a minority of cases.¹ None the less, a small but significant number of these children have a peptic ulcer, usually in the duodenum.

The introduction of fiberoptic endoscopy to paediatric practice has permitted direct and accurate diagnosis of peptic ulcer.²⁻³ The development of the H₂ receptor antagonists has facilitated medical management and so increased the importance of early diagnosis.

In the past 26 years a large number of cases of duodenal ulceration in childhood have been seen in the Newcastle area. In this report we review the experience gained in the diagnosis and management of these children. We suspect that the diagnosis may often be delayed, if not completely overlooked, especially in young children.

Patients

The case histories of 110 children with primary duodenal ulceration were reviewed. All had been seen in the 26 years between 1960 and 1985. They had attended either the Royal Victoria Infirmary, Newcastle upon Tyne, or the Queen Elizabeth Hospital, Gateshead, and each patient had been assessed personally by one of the authors.

Between 1960 and 1972 63 cases were diagnosed by barium meal examination. The diagnosis was accepted only if an ulcer crater could be shown, or if

there was pronounced deformity of the duodenal cap and strong clinical evidence of active ulcer disease, such as haematemesis or melaena. Between 1973 and 1985 a further 47 cases were diagnosed by upper gastrointestinal endoscopy.

Results

Sex incidence. Of the 110 children, 87 were male and 23 female, a ratio of 3.8:1. This predominance of males agrees with that reported in other series.⁴⁻⁶

Socioeconomic groups. Cases were found in all socioeconomic groups, and when compared with the local population distribution, no excessive preponderance within any one group could be identified.

Family history. In 62% at least one first or second degree relative had had confirmed duodenal ulcer disease. The diagnosis had been established in all by radiology, endoscopy, or at surgery. The family incidence was sometimes highly impressive—for example, in the case of one boy two male siblings and the father were affected.

Age at onset of symptoms and at diagnosis. The mean age at diagnosis was only 11.2 years, and the children ranged from 4 to 15 years. Interestingly, symptoms were reported to have been present in 46% before the age of 10 and in 15% before 6 years of age. The mean interval from the reported onset of

symptoms to the time of diagnosis was 1.8 years. When symptoms began in early childhood the delay in diagnosis was likely to be considerably longer (Table 1): thus in those who were symptomatic by 6 years the mean interval to diagnosis was 4.8 years.

Clinical features (Table 2)

Abdominal pain occurred in 90% of cases and was a main presenting feature in 88%. In 48%, however, it was not suggestive of ulcer dyspepsia. The pain was located in the epigastrium in only 51% of cases, while in 36% it was maximal in the central abdomen. A temporal relation to meal times was described in only 52% of the cases. Periodicity was a common feature, being present in 71%. Nocturnal pain was present in 67 patients (61%). If those who presented with gastrointestinal bleeding are excluded, whom, it is presumed, would have already been investigated, 80% of the remainder had nocturnal pain.

Change in appetite was not a notable feature. Episodes of vomiting had occurred in 39%, but on each occasion this was accompanied by pain, and all had had previous episodes of pain.

Epigastric tenderness was not usually a striking feature. Some degree of tenderness was noted in 54%, but its absence may relate to the state of activity of the disease at the time of examination.

A third of the children had an episode of haematemesis or melaena. Interestingly, this did not necessarily occur early in the illness; more than half had had symptoms consistent with peptic ulcer

disease for at least a year before the episode of bleeding. As a presenting symptom upper gastrointestinal bleeding accounted for 36% of new cases in the 1960s. This figure had fallen to 15% by 1979, almost certainly as a result of the policy of investigating larger numbers of children with abdominal pain. No child in this series suffered a perforation of their ulcer.

Two children have died; one as a result of an accident and one with Zollinger Ellison syndrome.

Investigations

Radiology. Of the 63 cases diagnosed by barium meal examination, two thirds had a demonstrable ulcer crater. The remaining third had severe distortion of the duodenal cap, together with the clinical features mentioned previously.

Endoscopy. From 1973, all cases were confirmed by endoscopic examination. From 1979, a deliberate change was made in the policy for selecting patients for investigation: in addition to those with a typical history suggesting peptic ulcer disease, and those with a history of gastrointestinal bleeding, children with recurrent abdominal pain who had had a history of nocturnal pain or a close family history of ulcer disease were also endoscoped. This change in policy resulted in a three-fold increase in the number of endoscopies performed annually; but the number of duodenal ulcers detected also increased by a factor of three (Table 3). Fifteen per cent had multiple ulcers; duodenitis was present in 50%; 70% had obvious duodenal deformity and this was often severe and associated with scarring, suggesting long standing disease.

Acid secretion studies. Studies of acid production had been performed in 26 children. In seven of these betazole was used and in the remainder pentagastrin. Both of these agents produce comparable levels of acid secretion.⁷ Maximal acid output varied between 0.05 and 1.17 mmol H⁺/kg/hour (mean of 0.52). No control studies had been carried out. A study on 20 normal children aged between 2 and 12 years using pentagastrin reported a mean maximal

Table 1 Relation between reported age at onset of symptoms and delay in diagnosis

Delay in diagnosis	Percentage of cases			
	<1 year	1-2 years	3-5 years	>5 years
Age at onset: (years)				
2-5 (n=17)	0	20	30	50
6-9 (n=43)	7	41	48	4
10-13 (n=50)	42	44	14	0

Table 2 Clinical features

	Total No(%)		Total No(%)
Abdominal pain	99(90)	Vomiting	43(39)
Periodicity	78(71)		
Nocturnal pain	67(61)	Haemorrhage	36(33)
Tenderness	59(54)		
Dyspepsia	57(52)	Perforation	0(0)

Table 3 Effect of changing selection criteria for endoscopy

	1973-78	1979-85
No of patients endoscoped	54	189
No of endoscopies/year*	9	27
No of duodenal ulcers detected	9	38
No of duodenal ulcers/year*	1.5	5.4
% of positive examinations	20	20

*Average number

acid output of 0.372 (SD=0.089) mmol H⁺/kg/hour.⁸ Nine of the 26 investigated here had results greater than 2 SD above this control mean.

Treatment

Until H₂ receptor antagonists were introduced children were treated by various dietary manipulations, antacids, and, in a few cases, propantheline or carbenoxolone sodium. Thirty four children had been treated with either cimetidine (25 mg/kg/day), or latterly ranitidine (150 mg twice daily) for eight weeks. Thirty (88%) had responded clinically to this initial course of treatment. As 70% relapsed within six months of discontinuing treatment, however, those who seemed to have had peptic ulcer disease for a prolonged period, judged by the history or the finding of severe scarring and deformity on endoscopy, were given an additional six month course of nocturnal maintenance treatment. Nevertheless, longer periods of maintenance were needed by some children. One boy received a total of four years of treatment. No child suffered any side effects.

Fifteen patients are known to have had surgery (Table 4). One of these was the patient with Zollinger Ellison syndrome. He was diagnosed

before cimetidine had been introduced. Despite surgery, he succumbed to his illness. Of the remaining 14, two were lost to follow up in our department soon after surgery and no information is available on their subsequent course.

Ten patients were followed up for between two and 15 years postoperatively. Two of these, having failed to benefit from an initial vagotomy and pyloroplasty, required a second and more radical acid reducing procedure (partial gastrectomy). Another had a recurrence of his disease at the age of 23, seven years after surgery. Seven of these 10 had remained asymptomatic when last seen.

Follow up

Only 15 of the 110 children were followed up for more than 10 years in the paediatric department, and half of these continued to complain of symptoms when last seen. The long term outcome of the patients in this series is the subject of a study currently in progress.

Discussion

This is the largest reported series of duodenal

Table 4 Details of subjects undergoing surgical procedures

Case No	Sex	Age (years) at diagnosis	Age (years) at surgery	Indications	Surgical procedure(s)	Postoperative follow up (years)	Outcome
1	M	14	17	Recurrent pain and gastrointestinal bleeding	1 Vagotomy and pyloroplasty	2	Symptoms continued
			19	Recurrent pain	2 Partial gastrectomy		Unknown
2	M	12	14	Recurrent pain	Vagotomy and pyloroplasty		Unknown
3	M	14	14	Recurrent gastrointestinal bleeding	1 Vagotomy and pyloroplasty	3	Symptoms continued
			17	Recurrent pain	2 Partial gastrectomy	1	died (accident) at 18 yrs
4	M	8	8	Intractable pain and gastrointestinal bleeding (Zollinger Ellison syndrome)	1 Vagotomy and gastrectomy	<1	No improvement
			8	Vomiting, hypochloraemic alkalosis	2 Relief of duodenal adhesion and gastrectomy	2	Condition worsened
			10	Surgery to search for tumour	3 Unsuccessful exploration		Died shortly after surgery (hepatic ZE-tumour at pm)
5	M	10	17	Recurrent pain	Vagotomy and pyloroplasty	4	No recurrence
6	F	10	25	Recurrent pain	Vagotomy and pyloroplasty		Unknown
7	M	10	14	Recurrent pain	Partial gastrectomy	15	No recurrence
8	M	8	16	Pyloric stenosis	Vagotomy and gastroenterostomy	10	Symptoms returned 7 years after surgery
9	M	10	10	Intractable pain, melaena	Vagotomy and gastroenterostomy	5	No recurrence
10	M	11	16	Recurrent pain, melaena	Vagotomy and gastroenterostomy	7	No recurrence
11	M	12	12	Intractable pain, weight loss	Partial gastrectomy	4	No recurrence
12	M	9	12	Recurrent pain, and gastrointestinal bleeding	Vagotomy and pyloroplasty	8	No recurrence
13	M	10	18	Recurrent pain, duodenal stenosis	Vagotomy and pyloroplasty	1	No recurrence
14	M	12	14	Recurrent pain	Partial gastrectomy	1	No recurrence
15	M	11	13	Recurrent pain	Vagotomy and pyloroplasty	2	No recurrence

ulceration in childhood from a centre in Europe.^{5 6 9-11} The published series from the North American continent and Europe suggest that large paediatric centres identify, on average, about two new cases annually, and rarely more than five.¹²⁻¹⁷

Between 1960 and 1972 one of the authors (RHJ) actively sought out cases from other hospital departments in the northern region, and this accounted in part for the large numbers seen in that period; no real comparison can therefore be made between the numbers at that time and subsequently. Neither is it possible to draw any conclusions about the local incidence of the disease.

Since 1973, however, the cases were all primary referrals. This was also the period in which paediatric endoscopy was introduced. The more liberal policy adopted in 1979 in selecting patients for investigation clearly had a strong impact on the numbers as the average annual detection rate rose from 1.5 to 5.4. The simultaneous decrease in the proportion presenting with overt gastrointestinal bleeding illustrates the fact that more of those being diagnosed in recent years have presented with abdominal pain rather than a complication of ulcer disease. This is of considerable importance as studies have shown that one third of patients found to have a duodenal ulcer subsequently suffer an episode of bleeding, and with treatment the risk of this occurrence can be reduced.¹⁸

Paediatric duodenal ulcers are not, as is often assumed, only found in adolescents. The onset may be in early childhood, as was seen in this series. The young child is less likely to give an accurate description of symptoms, and this together with a reluctance to consider the diagnosis in younger patients probably explains the occurrence of the longest delays in diagnosis in this group.

It is important to realise that many of these children do not have the typical clinical pain syndrome of non-radiating epigastric pain, which begins several hours after eating, and is relieved by food, antacids, or vomiting. Many presented with recurrent central abdominal pain unassociated with meal times. The high incidence of nocturnal pain in these children, however, is important: in Apley's series of recurrent abdominal pain only 7% of 118 children were woken at night by their pain.¹

The high incidence of a family history of ulcer disease is striking. Clearly the percentage of cases with an affected first or second degree relative will depend on factors such as the number of relatives. A genetic study was carried out by RHJ, in which 44 affected children and their families were matched with 35 control families. In the families with duodenal ulcers 8.2% of first and second relatives were affected, while in the control families only

1.9% were so affected; this illustrates the real importance of genetic factors.¹⁹

The optimal management of this disorder remains to be established. Clearly the H₂ receptor antagonists are effective in inducing a remission, as has also been shown in adults. The high relapse rate following withdrawal of treatment, however, also follows the pattern reported in older patients.¹⁸ The limited information available on the natural history of duodenal ulcer disease, beginning in childhood suggests that the diathesis may quite often persist into adult life.²⁰ It may be that some patients will require protracted periods of treatment.

Considerable experience has now been gained in the use of the H₂ receptor antagonists, especially cimetidine. Healing rates, symptomatic responses, and the effectiveness of maintenance treatment with cimetidine and ranitidine seem to be similar.²¹ Some rare specific side effects have been reported with cimetidine. It has been incriminated in cerebral and hepatic toxicity in children as well as in adults.^{22 23} In male children gynecomastia may develop.²⁴ Drowsiness and confusion have not been observed with ranitidine, and unlike cimetidine, it does not block androgen receptors, and gynecomastia has not been reported.²⁴ It is important to realise that serious side effects are rare with either drug. Potential hazards must be balanced against the definite morbidity and mortality risks associated with surgery.

In conclusion, we suspect that awareness of the commonly atypical presentation of this disorder, especially in young children might result in earlier diagnosis. We wish to emphasise the importance of investigating those children with recurrent abdominal pain associated with nocturnal pain, or those who have a family history of peptic ulcer disease. Early recognition and treatment may reduce both morbidity and the incidence of complications.

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