

## Case report

# Peptic ulceration and phenylketonuria: a possible link?

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**SUMMARY** We report five cases of peptic ulceration in patients with classical phenylketonuria and suggest that there may be a causal relationship between the two conditions.

Peptic ulceration is a relatively uncommon disorder of children and young adults.<sup>1</sup> Of the 180 patients with phenylketonuria (PKU) in Northern Ireland who have been diagnosed since 1954, five are known to have developed peptic ulceration which presented between 11 and 25 years of age. Two presented with haematemesis, one with perforation, one with melaena and one with abdominal pain and vomiting. None was on a strict diet at the time of presentation and plasma phenylalanine concentrations were high. Four were not receiving supplements of amino acids.

### Case histories

#### PATIENT 1

This mentally retarded woman lives at home and attends a day centre. Phenylketonuria was diagnosed when she was 10 months old. At the age of 21 years she was admitted to hospital with haematemesis requiring blood transfusion. There was a history of epigastric pain at night for 12 months and vomiting for six months. At the time of her admission she was on a protein restricted diet and an amino acid supplement as treatment for her PKU. On barium meal there was considerable increase in the amount of resting juice, with deformity, spasm and a small ulcer crater in the duodenal cap.

#### PATIENT 2

Phenylketonuria was diagnosed at eight months in this female patient because an older sibling had the

same condition. At the age of 11 years she was admitted to hospital with a two day history of central abdominal pain which had become severe one and a half hours before admission. There was a history of intermittent abdominal pain for many years. At this time she was on a normal diet, protein restriction having been discontinued at the age of nine years.

At operation she was found to have a perforated lesser curve gastric ulcer which was closed.

#### PATIENT 3

This mentally retarded man is a brother of patient 2. He was over two years old when PKU was diagnosed. At the age of 25 he was admitted to hospital with haematemesis severe enough to require blood transfusion. There was a nine month history of vomiting and weight loss. At the time of admission he was on a normal diet. Barium meal revealed that he had pyloric stenosis secondary to peptic ulceration, and a small hiatus hernia. He was treated surgically by vagotomy and gastroenterostomy, when the pyloro-duodenal junction was noted to be scarred.

#### PATIENT 4

This woman is of low intelligence although PKU was diagnosed at the age of six weeks. When 16 years old she complained of intermittent central abdominal pain and vomiting. At that time she was on a normal diet. Barium meal showed the duodenal cap to be grossly deformed, and a large ulcer crater was present.

#### PATIENT 5

Phenylketonuria was not diagnosed until this mentally retarded male patient was 13 months old.

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At the age of 20 years he was admitted with a history of melaena and a small haematemesis. He was on a normal diet at the time of presentation. At endoscopy he was found to have linear oesophagitis and a large duodenal ulcer.

### Discussion

The true incidence of peptic ulceration is difficult to evaluate because of the lack of widely accepted criteria for diagnosis. Not all cases are investigated and it is therefore likely that the number of reported cases is much less than the actual incidence. Five to 10% of the population can expect to develop the disease at some stage during their lifetime<sup>2</sup> and 2% of adults with peptic ulcers have had symptoms since childhood.<sup>3</sup> In 1972 Robb *et al*<sup>4</sup> reported 49 cases of duodenal ulcer in children in Northern Ireland from a population of 100 000 over a 10 year period. All were under 13 years at the time of diagnosis, however, and no comparable figures are available for adolescents.

The five reported cases may therefore be no more than the number to be expected from a group of this size, and reflect a selection bias in that we are observing a total, but small, population of patients with PKU.<sup>5</sup> It is noteworthy, however, that four of the five presented with the relatively uncommon complications of bleeding or perforation. Most of the patients were born before routine neonatal screening for PKU was available resulting in delayed diagnosis and mental handicap. The true incidence of peptic ulcer disease with milder symptoms is, therefore, likely to be considerably higher. We suggest that there could be a relationship between peptic ulceration and either PKU itself or its dietary treatment. It is well known that intraluminal administration of L-amino acids can stimulate gastric acid secretion in man<sup>6,7</sup> and it is therefore possible that L-amino acid supplements used in the dietary treatment of PKU could act in the same way leading to peptic ulceration. Four of the five reported patients, however, were not receiving an amino acid supplement at the time of presentation.

L-amino acids also stimulate gastric acid secretion in man when given intravenously.<sup>7</sup> McArthur *et al*<sup>8</sup> attempted to determine whether infusion of individual amino acids stimulates gastric acid secretion in man. They found that intravenous infusions of L-isomers of phenylalanine and tryptophan stimulated gastric acid secretion both in normal subjects and after parietal cell vagotomy. Plasma concentrations of phenylalanine at which significant acid

secretion occurred were similar to those obtained after eating a steak meal ( $85 \pm 7$   $\mu\text{mol/l}$ ) and were therefore considerably lower than those in PKU patients. Acid secretion tended to plateau with increasing dosage of intravenous phenylalanine. It has also been reported that mixed L-amino acid solutions used in the treatment of hepatic encephalopathy can, by stimulating gastric acid secretion, enhance gastric mucosal damage and lead to upper gastrointestinal haemorrhage.<sup>9</sup>

All five of our patients were on relaxed or normal diets when they presented with their ulcers and only one patient was taking an oral amino acid supplement. All had the classical form of phenylketonuria with plasma phenylalanine concentrations greater than 1200  $\mu\text{mol/l}$  (normal range 26–74  $\mu\text{mol/l}$ ). We therefore suggest that raised plasma phenylalanine concentrations secondary to phenylalanine hydroxylase deficiency lead to increased gastric acid secretion which in some patients will result in peptic ulceration. Vomiting which was formerly a common presenting symptom in untreated and inadequately treated PKU patients, could possibly be explained by the same mechanism.

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