Gastric ulcer: is endoscopy always necessary?

Crucial to the management of gastric ulceration is the accurate distinction between benign and malignant lesions. Controversy continues over how this should be achieved, the conclusion from a recent retrospective study¹ being that all gastric ulcers should be assessed endoscopically and tissue obtained for histological diagnosis by means of multiple biopsy and brush cytology.

Good-quality double-contrast radiology of the stomach appears to permit accurate prediction of whether a gastric ulcer is benign or malignant provided that the "guideline" pattern around the ulcer crater is adequately shown.^{2,3} If this is so endoscopy could be reserved for doubtful cases rather than being a routine procedure.

Patients, methods, and results

We accepted for the study 80 patients in whom a gastric ulcer had been shown radiologically and the criteria for a benign lesion were satisfied. Patients with pyloric and prepyloric lesions and those who had undergone gastric surgery were excluded.

All barium-meal examinations were performed by consultant radiologists using a double-contrast method. In the radiological differentiation of a benign from a malignant lesion no importance was attached to the site, size, or shape of the ulcer, attention being directed to the guidelines surrounding the crater. The criteria for a benign ulcer were that the guidelines, which converge on an ulcer often from a considerable distance, had to run straight and reduce in thickness until they joined the margin of the ulcer crater.³ This is in contrast to the mucosal pattern around a malignant lesion, when the guidelines are bent, do not reduce in thickness as they approach the lesion, and often stop short of the ulcer crater³ (figure).

All the patients underwent endoscopy, carried out by a consultant physician, within four weeks of the barium-meal examination. A minimum of four biopsy specimens were taken from the edge of the ulcer (one from each quadrant when possible) and one or two specimens from the ulcer base. Further histological material was also available from those patients who ultimately underwent operation.

The age range of the 80 patients was 32-91 (mean 61) years; 53 were men and 27 women. Histological examination of the gastric mucosal biopsy specimens showed no evidence of malignancy in any of the patients studied. Twenty-one patients (26%) subsequently came to operation and histological examination of the resected specimens showed no evidence of carcinoma.

Guideline patterns indicating benign ulcer (left) and malignant lesion (right).

Comment

This prospective study was undertaken to establish whether analysis of the guideline pattern around a gastric ulcer as shown by double-contrast barium-meal examination performed by experienced radiologists permitted an accurate prediction of whether the lesion was benign or malignant. Using this criterion confident radiological diagnosis of a benign ulcer was not disproved by either endoscopic biopsy or subsequent operation with histological examination of the resected specimen.

It might be argued that some of the lesions diagnosed as benign both radiologically and endoscopically may subsequently prove to be malignant, but this was not observed during the period of the study, the longest follow-up being four years.

Although mindful of the need to diagnose gastric cancer as early as possible, we nevertheless think that when a patient has been investigated with double-contrast barium-meal examination the more invasive and time-consuming technique of endoscopy may be reserved for patients

in whom radiological assessment of whether a gastric ulcer is present is equivocal; the guideline pattern around the ulcer is not adequately shown; or the guideline pattern around the ulcer crater suggests malignancy.

The need for careful follow-up remains, however, with these two diagnostic techniques being complementary rather than mutually exclusive.

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¹ Mountford RA, Brown P, Salmon PR, Alvarenga C, Neumann CS, Read AE. Gastric cancer detection in gastric ulcer disease. *Gut* 1980;21:9-17.

² Ichikawa H. Differential diagnosis between benign and malignant ulcers of the stomach. *Clin Gastroenterol* 1973;2:329-43.

³ Scott-Harden WG. The stomach and duodenum. In: Lodge T, Steiner RE, eds. *Recent advances in radiology and medical imaging* 6. Edinburgh: Churchill Livingstone, 1979:65-77.

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Hyperoxaluria and recurrent stone formation apparently cured by short courses of pyridoxine

Calcium oxalate urolithiasis is becoming increasingly common in Britain and other developed countries. Urinary oxalate is probably more important than urinary calcium in the cause, and any way of reducing urinary oxalate concentrations therefore seems to be important. We describe here two unusual cases of recurring calcium oxalate urolithiasis with hyperoxaluria which responded remarkably to pyridoxine.

Patients and results

Both patients were studied mainly as outpatients with normal activities and diet. Their short admissions to hospital did not seem to alter urinary composition. Urinary oxalate and glycolate concentrations were measured by enzymatic techniques.^{1,2}

Case 1—This 42-year-old man had suffered painless haematuria in 1948, when an intravenous urogram showed slight left hydronephrosis. He suffered further haematuria in 1949 and 1952 and renal colic in 1959, 1963, and 1972 and subsequently every few months. Several stones were removed from the right ureter by Dormier basket. One was analysed and showed calcium, phosphorus, and oxalate. Investigations at the General Hospital, Northampton, showed normal plasma and 24-hour urinary calcium concentrations. He continued to pass small stones and in March 1977 was referred to our hospital. The dietary history was unremarkable except for his consumption of one to two pints of milk a day and a low intake of oxalate-rich foods, except strawberries in season. There was no family history of urinary stones. Physical examination showed nothing abnormal; 24-hour urinary concentrations were normal except for oxalate (0.78 and 0.83 mmol (70 and 75 mg)) and glycolate (0.79 mmol (60 mg)) (upper limits of normal 0.45 and 0.36 mmol respectively (41 and 27 mg)). Pyridoxine 200 mg twice a day was started in April 1977 but stopped in August after urinary oxalate and glycolate concentrations returned to normal. His further progress is shown in the figure. He passed a 10-mg stone in June 1977 and gravel in December 1977 but since then has had no recurrence of hyperoxaluria or symptoms of stone.

Case 2—This 26-year-old woman suffered haematuria in 1973 and stones were removed from her right kidney in April 1974. Hypercalciuria was treated with cellulose phosphate until September 1977, when this was changed to hydrochlorothiazide. Despite this treatment she had passed a further 10 to 12 stones by September 1978. She was admitted to our hospitals in November 1978, after several weeks off thiazide. She was 180 cm tall and weighed 68.4 kg. There was no skeletal asymmetry. Her plasma concentrations were normal, as were 24-hour urinary excretions, except for calcium (11.8 and 16.9 mmol (472 and 676 mg)), oxalate (0.61 and 0.69 mmol (55 and 62 mg)), and glycolate (0.80 and 0.84 mmol (61 and 64 mg)). The lowest pH levels after two ammonium chloride urine acidification tests were 5.71 and 5.33. One of her brothers had normal urinary oxalate concentrations (0.21 mmol/24 h (27 mg)). Pyridoxine was started in November 1978 and stopped in January 1980. She passed two stones in May 1979 (27% calcium

oxalate, 10% magnesium ammonium phosphate, and the remainder calcium phosphate), but she has apparently made no more. Biochemical progress is shown in the figure.

Biochemical progress of two patients with hyperoxaluria treated with pyridoxine.

Conversion: SI to traditional units—Glycolate: 1 mmol/24 h $\approx$ 76.1 mg/24 h. Oxalate (anhydrous): 1 mmol/24 h $\approx$ 90 mg/24 h. Calcium: 1 mmol/24 h $\approx$ 40 mg/24 h.

Comment

Both patients showed hyperoxaluria that was clearly metabolic in origin since urinary glycolate excretion was also raised. The known causes for raised excretion of these acids are primary hyperoxaluria, pyridoxine deficiency, excess glycine load, and ethylene glycol intoxication. None of these fits the facts in these cases. The last two are obviously excluded, and there was no other evidence of pyridoxine deficiency (anaemia, convulsions). Nevertheless, some young women apparently exist on a low pyridoxine intake and show subclinical pyridoxine deficiency.³ So simple an explanation for hyperoxaluria seems unlikely in the second case, however, because of the finding of renal tubular acidosis, which has been described before in combination with hyperoxaluria.⁴ Primary hyperoxaluria is excluded by four facts. Firstly, in this condition urinary oxalate excretion is considerably higher than in these cases. Secondly, urinary glycolate excretion in primary hyperoxaluria is lower than urinary oxalate excretion. Thirdly, in primary hyperoxaluria the response to pyridoxine lasts only as long as the vitamin is given and immediately relapses on stopping it. These two patients did not relapse even after long periods of time. Fourthly, primary hyperoxaluria requires high doses of pyridoxine whereas in case 2 a remarkably low dose was effective.

It seems necessary to postulate a new cause of hyperoxaluria. There may have been a slightly increased requirement for pyridoxine, possibly induced by extraneous factors. The second patient had been taking oral contraceptives, a known cause of biochemical abnormalities, as found in pyridoxine deficiency,⁵ while the first patient had been an agricultural worker and might have been exposed to a pyridoxine antagonist. Whatever the cause of the hyperoxaluria the outcome was fortunate, with an apparently permanent remission on pyridoxine.

¹ Hallson PC, Rose GA. A simplified and rapid enzymatic method for determination of urinary oxalate. *Clin Chim Acta* 1974;55:29-39.

² Kasidas GP, Rose GA. A new enzymatic method for the determination of glycolate in urine and plasma. *Clin Chim Acta* 1979;96:25-36.

³ Vir SC, Love, AHG. Effect of oral contraceptives on vitamin B₆ nutriture of young women. *Internat J Vit Nutr* 1980;50:29-34.

⁴ Dent CE, Stamp TGB. Treatment of primary hyperoxaluria. *Arch Dis Child* 1970;45:735-45.

⁵ Rose DP. The influence of oestrogens on tryptophan metabolism in man. *Clin Sci* 1966;31:265-72.

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Eosinophilia in patients undergoing dialysis

Over the past few years, many of our patients on maintenance haemodialysis have developed eosinophilia without apparent reason. To our knowledge, the published reports contain little information on the subject,¹ and major textbooks on dialysis do not even mention it.²

We report our experience with this phenomenon.

Patients, methods, and results

Nineteen (25%) out of 77 uraemic patients undergoing dialysis for 18 hours weekly with deionised water, RSP artificial kidneys, cuprophane coils, and polyvinylchloride tubing (all from Travenol Laboratories, Deerfield, Illinois) developed eosinophilia (>500 eosinophils/mm³). Dialysers were not reused. Mean number of eosinophils per mm³ was $1391 \pm (\text{SEM}) 319$; (range 500 to 9028). Eosinophilia appeared after an average of 20 ± 3 months of haemodialysis (range two to 35 months), and once it had appeared persisted in all patients but two, in whom the number of eosinophils returned to normal after having remained raised for six and 72 months. No cause for eosinophilia other than haemodialysis could be found in any patient. The stools of several patients with high degrees of eosinophilia were tested for ova and parasites, but results were negative. None of these patients had rashes, asthma, or other symptoms that could conceivably represent a hypersensitivity reaction related to the high eosinophil count. Nine of the 19 patients had pruritus, but this symptom was also present in 23 of the 58 patients without eosinophilia and was not significant. Age (43.5 ± 4.6 years), total duration of dialysis (61.7 ± 6.5 v 54.5 ± 4.7 months), clinical course, medications, and primary renal disease were similar in the patients with eosinophilia and those without it. Medications were basically: aluminium hydroxide, multivitamins, and—in some patients—propranolol and 25-hydroxycholecalciferol. In both groups primary renal diseases had a distribution similar to that usually seen in the general population. No patient had undergone splenectomy or had a history of malignancy, autoimmune disease, or collagen vascular disease.

Comment

This study shows that about 25% of those undergoing haemodialysis develop eosinophilia. It seems logical to assume that the raised eosinophil count is a consequence of the dialysis procedure per se if one considers that: (a) eosinophilia was not present before the start of haemodialysis and was therefore not due simply to renal failure, (b) there was little association with the diseases responsible for renal failure, (c) there was no obvious relation to any medication, (d) other causes of eosinophilia were not apparent, and (e) eosinophilia tended to persist once it had appeared, suggesting that it was somehow maintained by repetitive dialysis.

Patients undergoing haemodialysis are subject to many substances that may invoke hypersensitivity, such as heparin, plasticisers from tubing,³ particles of rubber from stoppers, etc. Any one of these substances, or a combination of them, could lead to the development of eosinophilia, and further studies are clearly needed to determine its causes.

Although serious cutaneous hypersensitivity³ and anaphylactic reactions¹ have been associated with eosinophilia in patients undergoing dialysis, our experience appears to show that eosinophilia in patients undergoing dialysis is a benign laboratory abnormality that does not necessarily result in increased morbidity. Contrary to previous reports,¹ reuse of dialysers did not seem to be implicated.

¹ Hoy WE, Cestero RVM. Eosinophilia in maintenance hemodialysis patients. *Journal of Dialysis* 1979;3:73-87.

² Drukker W, Parsons FM, Maher JF, eds. *Replacement of renal function by dialysis*. The Hague: Martinus Nijhoff, 1979.

³ Bommer J, Ritz E, Andrassy K. Necrotising dermatitis resulting from hemodialysis with polyvinylchloride tubing. *Ann Intern Med* 1979;91: 869-70.

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