SHORT REPORTS

Value of brush cytology in diagnosis of gastric cancer

Multiple biopsies and brush cytology of gastric mucosal lesions can be performed with the fiberoptic endoscope. Though biopsy is used routinely, cytological examination of smears made from the gastric brushings has not been widely used. In a prospective study we assessed the relative value of brush cytology, multiple biopsy, and endoscopic and radiological appearances in the differentiation of benign and malignant gastric lesions in routine clinical practice in a district general hospital.

Patients, Methods, and Results

Patients admitted to the study had either radiological evidence of a gastric lesion or a gastric lesion visualized at endoscopy after a negative finding on barium meal examination. Forward- or side-viewing gastroscopes were used. If a gastric ulcer was present at least four biopsy specimens were taken. The abnormal mucosa was then brushed and eight smears were made on consecutively numbered slides and fixed immediately in 95% alcohol. Smears were stained with Papanicolaou stain and examined sequentially. The cytologist and histopathologist were given the same clinical information about the patient, which included the endoscopist's opinion on the nature of the lesion. The results of endoscopy and histopathological and cytological examinations were independently recorded as benign, suspicious, or malignant.

Altogether 134 patients with gastric lesions were admitted to the study. In 34 of the patients the diagnosis of gastric cancer was finally established either by histopathological examination of the resected specimen or by appearances at laparotomy in inoperable cases. The 100 patients with lesions judged to be benign have remained well for at least one year. Barium meal diagnosed malignancy correctly in 20 of the 34 patients (59%), gastroscopy in 30 (88%), biopsy in 21 (62%), and cytology in 28 (82%). The table summarizes the results of the other tests in the 14 patients in whom the x-ray film raised no suspicion of malignancy. Cytology confirmed the endoscopic diagnosis in 10 patients and in three patients was the only investigation that gave a positive result. In the 100 patients with benign gastric lesions barium meal indicated malignancy in 15. In eight no evidence of malignancy was found at endoscopy, biopsy, or brush cytology. The other seven patients were also suspected of having cancer at endoscopy but both biopsy and brush cytology were negative. Five patients with negative x-ray and biopsy findings had suspicious cytological results and in four of them cancer was also suspected at endoscopy. Partial gastrectomy in three and follow-up in two patients showed no evidence of malignancy. The diagnosis of malignancy was established after scanning only the first four smears in all except one case. There were no untoward clinical effects after the brushing of gastric lesions.

Discussion

All except one of the cancers in this series were diagnosed by endoscopy and cytology, which gave a 97% diagnostic rate. This contrasts with the disappointing results of gastric washings.^{1 2} Though brush cytology is easy to perform it may cause problems of interpretation, which are illustrated by the five patients in the benign group with suspicious cytological results.

The difficulties posed by the appearance of regenerating cells from the ulcer edge, which may be indistinguishable from malignant tissue, are well known.^{3 4} On the other hand, combined negative biopsy and cytological findings with suspicious radiological and endoscopic appearances prevented laparotomy in six patients. Gastric biopsies did not give any false positive results, and the high false negative rate was due to the failure to sample the malignant site, which may have been due to the small number of specimens taken.

Brush cytology is technically easier and cheaper to process than

multiple biopsy and deserves widespread evaluation in the diagnosis of gastric cancer.

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Malignant hypertension with irreversible renal failure due to oral contraceptives

Three observations of malignant hypertension while a patient was taking oestro-progesterones have been reported.¹⁻³ This further case calls attention to the much discussed role of this contraceptive in the onset of obstructive arteriolitis leading to an elevated renin secretion with hypertension and renal failure.

Case report

A 27-year-old married woman was admitted to hospital on 16 September 1970 with malignant arterial hypertension. She had no history of proteinuria, hypertension, or renal disease. She had always been normotensive until her first pregnancy in 1964. This was normal. Her blood pressure did not exceed 120 mm Hg systolic. Two months after the delivery she began taking oestro-progesterone. She was given Enidrel R (Norethynodrel 4.925 mg, mestranol 0.075 mg) for a year and a half and then Ovariostat (lynestrenol 2.5 mg, mestranol 0.075 mg). Her blood pressure was not measured until two years later—180 mm Hg systolic. The patient discontinued the contraceptive in February 1969. One month later she became pregnant, her systolic pressure was 120 mm Hg, and she gave birth at term to a 2300-g boy. Proteinuria was not evident and her blood pressure never exceeded 120/80 mm Hg.

Four months after the second birth the patient started taking oestro-progesterone again—Ovariostat. But she developed intense headaches and in August her doctor found her blood pressure to be 270/150 mm Hg. The patient entered hospital three weeks later when her blood pressure was 250/160 mm Hg. There was left ventricular hypertrophy. Renal failure was confirmed and creatinine clearance was 32 ml/min. An investigation showed

Results in 14 Patients with Gastric Cancer and Negative Barium Meal Results

Case no.:	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Endoscopy	-	-	-	-	+	++	++	++	+	+	+	++	++	++
Biopsy	-	-	-	-	+	+	+	++	++	++	++	++	++	++
Brushing	-	++	++	+	++	++	++	+	+	++	++	++	++	++

- = Negative. + = Suspicious. ++ = Malignant.

no cause for this hypertension: urinary output of catecholamines was normal; the arteriography demonstrated renal arteries of normal calibre; the nephrogram showed no parenchymous anomaly. Nevertheless, with a normal salt-free diet she demonstrated low serum potassium (between 2.7 and 3.1/l) (2.7 and 3.1 mEq/l). She was prescribed 300 mg of spironolactone, 20 mg of furosemide, 750 mg of methyldopa per day, and strict bed rest. But the salt-free diet was not strictly followed.

The patient was readmitted one month later with persistent hypertension at 210/160 mm Hg, standing and lying down. Renal function rapidly deteriorated. The dosage was augmented combining diuretics (spironolactone and furosemide) with methyldopa and a blocking drug. This was not effective. Diazoxide was administered for a short time bringing her blood pressure up to 130/80 mm Hg lying down and 100/70 mm Hg standing. Retinal haemorrhaging receded but azotemia reached 1.80 g/l. After eight days her blood pressure rose to 180/140 mm Hg accompanied by heart failure and severe oliguria. Even though large doses of furosemide were administered diuresis was less than 100 ml/24 h and dialysis was necessary twice a week.

A bilateral nephrectomy was performed on 20 January 1971. The microscopic appearance of the kidney tissue was typical of malignant nephrosclerosis. After 10 days her blood pressure stabilized at 150/100 mm Hg. Her general condition rapidly improved and the patient was able to return home 12 days after surgery, without medication, but she had to follow a diet containing less than 2 g of Na Cl in 24 hours. When examined six weeks later her general condition was excellent with blood pressure at 140/80 mm Hg before dialysis. In November 1972 she underwent a renal graft and after 10 months her blood pressure still remained normal.

Renal vascular disease: fibrinoid necrosis.

Discussion

This case fits into the framework of hypertension due to oestro-progesterone. Authors differ about the frequency of this hypertension. Where there has been a marked increase in systolic arterial pressure it has usually remained within normal limits.⁴ These hypertension are usually benign and recovery is rapid after the contraceptive has been discontinued.⁵ Nevertheless, when oestro-progesterones are prescribed blood pressure should be carefully watched and if arterial hypertension arises, this method of contraception should be discontinued, except in special cases.

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Ocular reaction to propranolol and resolution on continued treatment with a different beta-blocking drug

A hypertensive patient treated for 20 months with propranolol developed ocular symptoms and signs similar to those described after practolol. Changing to oxprenolol was associated with remission of the ocular reaction.

Case report

In June 1973 a 48-year-old woman presented with asymptomatic, stable, uncomplicated hypertension (blood pressure 170-190/120-130 mm Hg). She had no history of allergy, rashes, or ocular disease. Treatment with propranolol twice daily, 40 mg for four weeks, 80 mg for four weeks, and finally 160 mg reduced the blood pressure to 155/105 mm Hg. This dose was continued without incident until April 1975, when the patient complained of dryness of the mouth associated with a prickling sensation of the eyes, particularly the left. She had no rash or other evidence of systemic disease. Schirmer's test showed a slight diminution of tear production in the right eye and a definite diminution in the left eye. Slit-lamp examination showed generalised hyperaemia of her conjunctivae with foci of new vascular loops in the depths of the lower fornix and areas of superficial whitening obscuring underlying vessels (fig).

Because of the effective control of her blood pressure with propranolol, and in view of the reported absence of cross-reactions,¹ she was transferred to treatment with oxprenolol in a twice daily dose of 80 mg, increased after one month to 160 mg. At this dosage her blood pressure was maintained at 155-165/100-105 mm Hg at rest. After six weeks' treatment on oxprenolol and methyl cellulose eye drops 0.5% four times daily, in both eyes, her dry mouth and prickling sensation in the eyes diminished leaving only an occasional slight burning sensation in the left eye. Further ocular examination showed regression of the conjunctival vascular loops and pale areas although tear secretion by Schirmer's test was unchanged.

Foci of new vessels (smaller arrow) and superficial pale areas (larger arrow) in lower fornix of left conjunctival sac.

Discussion

Many cases of oculocutaneous reactions to practolol have been reported,^{1,2} but only rarely in patients during treatment with other beta-adrenoceptor antagonists.³ Although rashes have been reported during treatment with propranolol,³ this patient appears to be the first one described with an ocular reaction. The lesions observed were similar to, but milder than, those observed after practolol² and receded when the patient was transferred to oxprenolol. This absence of cross sensitivity between different beta-adrenoceptor antagonists confirms the experience of others.¹ Nevertheless, in view of the circumstantial nature of the evidence in most reports, claims of specific reactions to beta-blocking drugs other than practolol must be viewed with reserve.

Generally it is important to emphasise that the development of this syndrome is extremely rare, given the very many patients under treatment with these drugs. The efficacy of beta-receptor antagonists in the treatment of ischaemic heart disease, hypertension, and dysrhythmias is beyond question and undoubtedly also they are