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Value of biopsy and brush cytology in the diagnosis of gastric cancer

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SUMMARY This report presents the diagnostic value of brush cytology in gastric cancer. Gastric biopsies and brush cytology were performed in 155 patients with gastric cancer and 48 with benign gastric disease. The positive rate for biopsy and brush cytology in cancer patients (including 11 cases of early gastric cancer) was 74·2% and 76·8% respectively. The positive rate of biopsy with concomitant brush cytology was 87·7%, which was superior to that of biopsy or brush cytology alone ($p<0·01$). In 29 cases of gastric cancer involving the cardiac region, 20 were biopsy positive (69%) and 22 were brush cytology positive (75·9%). Biopsy with brush cytology was positive in 27 cases (93·1%) and gave better results than biopsy alone ($p<0·01$). The positive rate of biopsy with concomitant brush cytology in Borrmann type I, II, and III lesions (89·7%) was significantly higher than in Borrmann type IV lesions (50%). In the 48 patients with benign gastric lesions, biopsy and brush cytology each provided two false positives. The study shows that the combination of biopsy and brush cytology increases diagnostic accuracy for gastric cancer.

Fibre gastroscopic biopsy and brush cytology examination under direct vision are the main methods for obtaining a preoperative diagnosis of gastric cancer. The diagnostic value of gastric biopsy is well established but the value of brush cytology is still a subject of controversy. In order to investigate the diagnostic value of brush cytology in gastric cancer, the Shanghai Gastrointestinal Endoscopy Cooperative Group has studied 203 cases of pathologically proven malignant and benign gastric lesions.

Methods

PATIENTS

In this group of 203 cases the final diagnosis was confirmed by pathological examination of surgically resected specimens, in which there were 155 gastric cancers and 48 benign gastric lesions. Gastric biopsies preceded brush cytology examinations in all 203 patients. Fibre gastroscopes used included Chinese made XW-II, Japanese Olympus GF-B_2, GIF-K, GIF-D_2, GIF-D_3. Two to nine biopsies were taken from each lesion and the specimens were fixed in 10% formalin. A nylon brush was used for cytological examination and three to five direct smears were made immediately after brushing. The smear was then fixed in 95% alcohol, stained with Giemsa's stain, and examined for the presence of carcinoma cells. Statistical comparisons were made with the use of the chi square test. P values less than 0·05 were considered to be significant.

Results

The positive rate for biopsy and the brush cytology examination in our 155 cases of gastric cancer (early gastric cancer 11 cases and advanced gastric cancer 144 cases) was 74·2% and 76·8% respectively. The positive rate of biopsy with concomitant brush examination was 87·7%, which was superior to that of biopsy or brush examination alone ($p<0·01$) (Table 1). Twenty of 29 cases of gastric cancer in the cardiac region were biopsy positive (69%) and 22 were brush cytology positive (75·9%). Biopsy with concomitant brush cytology was positive in 27 cases (93·1%), which was better than biopsy alone ($p<0·05$).

The gross morphology of the surgical specimens

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Table 1 *Results of biopsy and brush examinations in 155 gastric cancer patients*

Procedure	No. of cases	Cases with positive results (no.)	(%)
Biopsy	155	115	74·2
Brush cytology	155	119	76·8
Biopsy and brush cytology	155	136	87·7

was recorded in 103 cases of advanced gastric cancer using the classification of Borrmann. A comparison of the results of biopsy and brush examination and the different morphological types classified by the method of Borrmann, as interpreted by Schindler,[1] is shown in Table 2. Type I is a polypoid or fungating lesion, type II an ulcerating lesion surrounded by a raised wall, and type III an ulcerating lesion, limited in part by a wall but elsewhere blending into apparently normal mucosa. Type IV is a diffuse, infiltrating lesion which may be ulcerated in part. The positive rate of biopsy with concomitant brush cytology in Borrmann type I, II, and III lesions was significantly higher than in Borrmann type IV lesions ($p<0·05$).

In 48 benign gastric lesions (ulcer, 42; chronic gastritis, four; leiomyoma, one; and polyp, one), biopsy and brush cytology each yielded two false positives.

Discussion

There are major discrepancies in reports of the accuracy of the diagnosis of gastric cancer by biopsy and brush cytology.[2] Biopsy has been used as a routine examination method for the diagnosis of gastric cancer, but its diagnostic accuracy is not as high as it was considered previously.[3] Many factors influence diagnostic accuracy. The positive rate of biopsy is low in cancer of the cardiac region and in infiltrative, ulcerative, and recurrent carcinomas.[4 5] When the cancerous tissue is covered by normal mucosa or necrotic tissue, the biopsy may be too superficial. The anatomical location of the cancer may prevent multiple biopsies being taken. Stenosis of the cardiac or antral canal may also restrict access to the tumour. The distribution of the carcinomatous tissue may not be uniform and the scope for biopsy is quite limited. It is to be expected that brush cytology examination would provide additional information in these circumstances.

Table 2 *Results of biopsy and brush cytology in different gastric cancer lesions*

Morphological type*	No. of cases	Cases with positive results: Biopsy (no.)	(%)	Brush cytology (no.)	(%)	Biopsy and brush cytology (no.)	(%)
Borrmann Type I	8	8	100	6	75	8	100
Type II and III	89	67	75·3	72	80·9	79	88·8
Type IV	6	3	50	1	16·7	3	50

* Details of this classification are provided in the text.

Currently, brush cytology is not performed frequently. Kill *et al* considered that the diagnostic rate of gastric cancer could not be increased by cytology.[6] Kobayashi *et al*[7] believed that if biopsies were negative or there were marked stenosis next to the cancer, brush examination should be performed. Winawer *et al*[8] have suggested that brush cytology may improve the diagnostic rate. Although there was no apparent difference between the positive rate for brush cytology and biopsy in our 155 gastric cancer patients, biopsy with concomitant brush cytology was significantly better than either examination alone ($p<0·01$). For carcinoma of the cardiac region and some ulcerative types in which it is technically difficult to get satisfactory specimens, biopsy with concomitant brush examination was more helpful than biopsy alone. This study also shows that brush cytology can compensate for the shortage of biopsy material. Brush cytology examination is technically simple without prolonging the time of endoscopy examination.

In order to improve the positive rate of brush cytology examination, some technical considerations should be noted: (1) the site for the specimen should be appropriately selected, and if the ulcerative lesion is covered by thick slough, brushing should be performed at the margin of the ulcer; (2) the entire head of the nylon brush should be used over a wide area; (3) the brushing should be performed with appropriate force in order to include cancer cells that may be covered by mucus, necrotic tissue, or blood clot after biopsy; (4) after the brushing is completed and before the gastroscope is withdrawn, the head of the brush should be withdrawn to the tip to prevent the loss of the specimen. If it is withdrawn deeply into the channel, the specimen may be lost.[6] During the smearing of the slide, filter paper should be used to absorb excess mucus or clot adherent to the head of the brush. Smears should be done firmly in order to release the specimen hidden between the hairs of the brush. Furthermore, the cytological examination should be

performed by experienced personnel.

Biopsy and brush cytology may provide false positive results. Smithies *et al* showed that the false negative rate of biopsy is higher than that of brush cytology, and the false positive rate of cytology is higher than that of biopsy.[9] Winawer *et al* found that the false positive rate is not high in the hands of an experienced examiner.[8] Ekeda *et al*[4] reported six false positive cases which resulted from regarding atypical epithelial proliferation or newly grown epithelium as differentiated carcinoma. The pathological findings in the surgically resected specimens in our four false positives showed that three were benign gastric ulcers (two with atypical proliferation), and one was a gastric leiomyoma with an ulcer covered with newly grown epithelium.

While these findings need to be taken into account in analysing the value of biopsy and brush cytology, they do not detract from the overall value of this combined approach to diagnosis.

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