

Value of exfoliative cytology in pancreatic carcinoma

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Duodenal exfoliative cytology has been used in the diagnosis of pancreatic carcinoma (Dreiling, Nieburgs, and Janowitz, 1960; Raskin, Wenger, Sklar, Pleticka, and Yarema, 1958). The present report is an attempt to evaluate duodenal exfoliative cytology in clinical practice. No deliberate attempt was made to include patients who were thought to be normal or whose diagnosis was obvious before cytological examination. The procedure was performed as a service whenever the patient's physician believed that it would assist in the management of that patient.

METHODS

PROCEDURE The patients were studied after a 14-hour fast. A double-lumen gastroduodenal tube was passed into the duodenum by the method of Raskin *et al.* (1958) and positioned at the ligament of Trietz by fluoroscopy. Duodenal drainage, uncontaminated by gastric secretion, was collected by gentle suction in Erlenmeyer flasks immersed in crushed ice. The basal secretion was collected for 20 minutes. Secretin (1.0 unit/kg) (Boots) was injected intravenously, after which four 20-minute collections were made. Each aspirate was kept immersed in the crushed ice until the end of the procedure at which time all aspirates were centrifuged separately and smears were made of the sediment. For each 20-minute aspirate two smears were made and stained according to the method of Papanicolaou.

SUBJECTS In the period between July 1963 and July 1965, duodenal intubation for cytological examination was performed in 68 patients. In two patients the examination was performed twice. Charts of 67 patients were available for examination and form the basis of this report. Each patient had been seen by at least one of the authors during their hospital stay.

RESULTS

Twenty-four of the patients studied had carcinoma of the pancreas confirmed by necropsy. Forty-three of the patients studied were felt not to have carcin-

oma of the pancreas (Table I). In 27, the absence of pancreatic carcinoma was established by necropsy or surgery. The remaining 16 patients in whom histological proof was lacking were alive and clinically free of pancreatic carcinoma at least 18 months after the cytological examination.

TABLE I

| Carcinoma of Pancreas | CYTOLOGICAL EXAMINATION OF PATIENTS WITH SUSPECTED PANCREATIC CARCINOMA | |
|-----------------------|---|----------|
| | Cytology | |
| | Positive | Negative |
| Absent | 0 | 43 |
| Present | 18 | 6 |

None of the 43 patients without pancreatic carcinoma had malignant cells in the duodenal aspirate. In two patients the clinical suspicion of carcinoma of the pancreas was strong enough for the procedure to be repeated. Both of these patients had a negative examination for malignant cells and both were proven not to have pancreatic carcinoma.

Malignant cells were obtained by cytological examination in 18 of 24 patients (75%) with pancreatic carcinoma. At the time of post-mortem examination it was difficult to determine in many cases in which portion of the pancreas the carcinoma originated. In those doubtful cases (12), if there was evidence of obstruction of the common bile duct the patient was considered to have had carcinoma of the head of the pancreas. If there was no obstruction then the patient was considered to have had carcinoma originating in the body and tail of the pancreas. Eighteen patients had carcinoma of the head of the pancreas and in 13 a positive cytological examination was obtained. Six patients had carcinoma of the body and tail of the pancreas and in five malignant cells were obtained from the duodenal aspirate. The six patients with false negative examination showed no clinical differences from the

18 with positive cytological examination. In three of the six false-negative cases, only a small amount of duodenal juice was aspirated after secretin stimulation, probably due to blockage of the main pancreatic duct by carcinoma. One false-negative examination was due in retrospect to a clear error in an observer interpretation. In the remaining two examinations no explanation could be found for the failure to obtain malignant cells after secretin stimulation.

The mean age of the patients studied with pancreatic carcinoma was older (64 years as compared to 59 years) than in those without pancreatic carcinoma. The presence of abdominal pain, back pain, weight loss, diarrhoea, or pruritis did not distinguish the group with pancreatic carcinoma from the group without pancreatic carcinoma nor patients with positive cytological examination from those with false negative cytological examination (Table II).

TABLE II
FINDINGS IN PATIENTS WITH SUSPECTED
PANCREATIC CARCINOMA

| | <i>Pancreatic Carcinoma</i> | |
|--|-----------------------------|----------------------------|
| | <i>Absent</i> | <i>Present¹</i> |
| Abdominal pain | 18/43 | 6/24 (2) |
| Weight loss | 16/43 | 10/24 (1) |
| Diarrhoea | 2/43 | 3/24 (1) |
| Back pain | 3/43 | 0/24 (0) |
| Pruritis | 1/43 | 1/24 (0) |
| Thrombophlebitis | 1/43 | 1/24 (0) |
| Jaundice | 18/43 | 18/24 (5) |
| Radiographic abnormality of second and third portion of duodenum | 29/43 | 13/24 (3) |

¹With negative cytological examination

On the basis of history, physical examination, and initial laboratory studies, 15 of 43 patients (35%) were mistakenly thought to have had carcinoma of the pancreas. Eleven of 24 patients (46%) who eventually were proven to have pancreatic carcinoma, were initially so diagnosed. In two patients the cytological examination was performed after a decision had been made to operate upon the patient for the presumptive diagnosis of pancreatic carcinoma. The examination was positive in one patient and falsely negative in the other.

Retrospectively, an attempt was made to determine the findings which caused the physician to request a cytological examination. Obstructive jaundice and/or radiographic abnormality of the second portion of the duodenum appeared to account for the majority of the requests. Pancreatitis, with or without jaundice, was the most common final diagnosis in those patients with negative cytological examinations,

TABLE III
FINAL DIAGNOSIS IN 43 PATIENTS WITHOUT
PANCREATIC CARCINOMA

| | <i>Number of Cases</i> |
|-------------------------------------|------------------------|
| Pancreatitis | 15 |
| Common duct stone | 6 |
| Non-pancreatic malignancy | 5 |
| Cirrhosis | 4 |
| Intrahepatic cholestasis | 3 |
| Congestive heart failure | 3 |
| Peptic ulcer | 3 |
| Non-gastrointestinal, miscellaneous | 4 |

and common duct stone was the second most common diagnosis.

Twenty-two of 24 patients with pancreatic carcinoma died of the disease within one year of diagnosis, and the remaining two died two and a half years after diagnosis.

DISCUSSION

The problem of early diagnosis of pancreatic carcinoma is generally recognized. Dreiling *et al.* (1960) and Raskin *et al.* (1958) have found duodenal exfoliative cytology to be a useful procedure. Dreiling *et al.* (1960) found that 78% of their patients with pancreatic neoplasm have a positive cytological examination. Recently the procedure has been criticized as being too time consuming (Rodríguez-Antúnez, Filson, Sullivan, and Brown, 1966) or as being useful only in the hands of an expert few (Sandlow and Necheles, 1966). The performance of this procedure with proper placing of the tube and preparation and reading of the slides takes about three hours in the average case. Although this may be considered time consuming it is certainly, in our opinion, worthwhile when dealing with such a difficult disease to diagnose as pancreatic carcinoma. Meticulous attention to simple details such as placing the tube and immediate preparation of slides is extremely important but requires little additional skill and can be done in any unit performing gastrointestinal cytological examinations.

The false positive diagnosis has not been a problem in our unit. At times patients may exfoliate ductal epithelial cells after secretin stimulation. These cells bear a superficial resemblance to malignant cells.

We have found duodenal exfoliative cytological examination quite useful in the diagnostic approach to patients with suspected pancreatic carcinoma. In a group of 67 such patients, a positive cytological examination was obtained in three out of four of the patients with pancreatic carcinoma. While none of our patients with carcinoma of the pancreas were

cured of the disease, the finding of malignant cells on cytological examination of duodenal contents provided a 'tissue diagnosis' in those particular patients in whom there was no possibility of a palliative operation nor hope of a curative procedure. Some patients may thus be spared a major operation for solely diagnostic purposes.

SUMMARY

Over a two-year period, 67 patients underwent exfoliative cytological examination of the duodenal contents after secretin stimulation because of a clinical suspicion of pancreatic carcinoma. Forty-three were eventually proved not to have the disease, and no malignant cells on cytological examination were found in this group. Twenty-four patients had

carcinoma of the pancreas and malignant cells were recovered in 18 by this technique. We believe that duodenal exfoliative cytology is a valuable adjunct in the diagnosis of pancreatic carcinoma.

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