A Case of Double Cancer (Pancreatic and Ovarian Adenocarcinomas) Diagnosed by Exfoliative and Fine Needle Aspiration Cytology

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Abstract

A case of double cancer (pancreatic and ovarian adenocarcinomas) in a woman suggested by exfoliative and fine needle aspiration (FNA) cytology is reported. Exfoliative cytology, including immunohistochemical findings of the biliary juice and those of clinical image examinations indicated tubular adenocarcinoma of the pancreatic body. FNA cytologic findings with immunohistochemical observation and those of ultrasound examination showed mucinous adenocarcinoma of the right ovary. As a rare event, pancreatic cancer metastasized to ovarian carcinoma.


Key words: Double cancer—Pancreatic adenocarcinoma—Ovarian adenocarcinoma—Cytology

Introduction

The incidence of pancreatic cancers has shown a tendency to increase in Japan as well as in the Western world. Generally, pancreatic cancers have a poor prognosis. Most of them are usually unresectable when the tumors are detected11 since early diagnosis of the tumor is difficult. A variety of approaches for an early diagnosis of pancreatic cancers has been employed.2-5 In particular, exfoliative or fine needle aspiration (FNA) cytology is increasingly utilized as an important diagnostic tool in detecting the tumors. The first report describing the diagnosis of tumors by needle puncture and aspiration cytology appeared in the 1930s.6 Since then, FNA cytology has been developed as a quick, economical accurate technique leading to the diagnosis of neoplasm in several organs including the pancreas. FNA cytology is also used to detect malignancy, especially of ovarian neoplasm as reported previously.7

We came across a case of double cancer (moderately differentiated tubular adenocarcinoma of the pancreatic body and mucinous cystadenocarcinoma of the ovary) suggested by exfoliative and FNA cytology. As a rare event, the pancreatic cancer metastasized to another already existing ovarian cancer. The results of the cytological findings were accurately confirmed immunohistochemically.

Case Report

A 49-year-old Japanese woman, who had had a normal menstrual pattern and undergone two normal deliveries, complained of epigastralgia and lumbago and was admitted
Fig. 1. Enhancement CT of the pancreatic level. A large tumor mass is located in the pancreatic body.

Fig. 2. Ultrasonography of the lower abdomen. A large cystic lesion is present in the right ovary.

to the Department of Internal Medicine, Tokai-Chuo Hospital, for examination on September 27, 1986. On admission, an abdominal ultrasound (US) examination and computed tomography (CT) revealed a malignant tumor mass in the body of the pancreas with dilatation of the intra- and extrahepatic bile ducts (Fig. 1). Examination of endoscopic retrograde cholangiopancreatography (ERCP) and a high titer of CA 19-9 (120 × 10³ U/ml) were in agreement with the US and CT findings. A cytologic examination of biliary juice obtained by means of percutaneous transhepatic cholangiography drainage (PTCD) indicated duct cell adenocarcinoma of the pancreas. The patient received chemotherapy (Picrobanil, 5-Fluorouracil and Mitomycin C), but anti-cancer drugs were generally ineffective. In December 1986, an abdominal US examination revealed a cystic mass in the right ovary (Fig. 2). FNA cytology of the cystic lesion was performed. The aspirated material was a viscous and gelatinous fluid. The cytological diagnosis was mucinous cystadenocarcinoma. In spite of a variety of therapies, the patient died on January 18, 1987, and autopsy was performed 12 hours after death.

The color of the whole body was yellowish due to jaundice. Approximately 1,500 ml of cloudy reddish-yellow ascites were present. A tumor mass, approximately 5 cm in diameter, was seen in the body of the pancreas. Invasion or metastasis of the tumor was present in the common bile duct, gall bladder and liver. A number of small nodules of diameter 0.5–1 cm were seen in the lungs, diaphragm, pericardia sac and the pouch of Douglas. Two submucosal tumors, of approximate size 2 and 3 cm, were also present in the stomach. A large ulcer, which was 5 cm in diameter, was present in the sigmoid colon. The lymph nodes of the para-pancreas and ascending colon were enlarged. The cut surface of the pancreatic tumor was variegated, of a grayish color containing yellowish areas of necrosis and red ones of bleeding. There was another large cystic tumor mass, approximately 20 × 15 × 8 cm in size, in the right ovary. The surface was yellowish and smooth. On the cut surface of the tumor, there were various sizes of cysts having a viscous and gelatinous content. At places, intracystic hemorrhage was observed. The left ovary revealed no significant changes, macroscopically. There were small
Fig. 3. Cytology of the PTCD-biliary juice. The overlapping of neoplastic cells is prominent. Papanicolaou stain, × 1,000.

Fig. 4. FNA cytology of the right ovarian tumor. Atypical cells form small clusters. The arrangement of the neoplastic cells is relatively plane. Papanicolaou stain, × 1,200.

Fig. 5. Histology of the pancreatic body at autopsy. Atypical small ducts are present. Hematoxylin and eosin stain, × 360.

Fig. 6. Immunohistochemical staining for CA 19-9 showing positive reaction in the cytoplasms of pancreatic neoplastic cells. PAP method, × 720.
Fig. 7. Histology of the right ovarian tumor at autopsy. A large cyst covered with mucin-producing neoplastic cells is seen. In the stroma, small ducts of metastatic neoplastic cells are also observed. Hematoxylin and eosin stain, × 180.

Fig. 8. Immunohistochemical staining for CA 19-9 indicating positive granules in the metastatic cells of the ovarian stroma and negative reaction in the cells of cystadenocarcinoma. PAP method, × 360.
nODULES IN THE RIGHT LOBE OF THE THYROID AND IN THE BODY OF THE UTERUS. THE LIVER WAS ENLARGED AND CIRRHOTIC.

**Cytological Findings**

All cytologic materials were prepared routinely and stained by the Papanicolaou method and the periodic acid-Schiff (PAS) reaction. Immunocytochemical staining for CA 19-9 (COI S.A., France) was performed by the peroxidase-antiperoxidase (PAP) method.

1) **Biliary juice cytology by means of PTCD.** A number of tumor cells varying in size were found together with neutrophils, erythrocytes and cell debris. Most of the neoplastic cells were present in large clusters (Fig. 3). Glandular patterns were seen in the clusters. The overlapping of the neoplastic cells was prominent. The tumor cells were oval or round and showed positive for the PAS reaction. The nuclei were peripherally located in the cytoplasm and the nuclear membrane was irregular in thickness. Immunocytochemical staining of the neoplastic cells was weakly positive for CA 19-9. The cytological diagnosis was duct cell adenocarcinoma of the pancreas.

2) **FNA cytology of the right ovary.** The background of the cytologic smear was dirty with the presence of neutrophils, histiocytes and cell debris. Small clusters of the loosely packed clump of neoplastic cells were scattered (Fig. 4). The tumor cells with prominent vacuolization of the cytoplasm were oval in shape. The size of the neoplastic cells was smaller than that of the malignant cells found in the PTCD-biliary juice. Almost all the cells were positive for the PAS reaction in the cytoplasm. Immunocytochemical staining for CA 19-9 was completely negative for such small neoplastic cells. The cytological diagnosis was mucinous adenocarcinoma of the ovary.

**Histological Findings**

All materials were routinely prepared for histologic examination and stained with hematoxylin and eosin and reacted for PAS. Immunohistochemical staining for CA 19-9 (COI S.A., France) was also prepared by the PAP method.

In the body of the pancreas, necrosis and hemorrhage were seen. A number of atypical small ducts of neoplastic cells were surrounded by fibrous connective tissue. The malignant ducts were composed of single-layered cuboidal cells. The nuclei showed a pleomorphism (Fig. 5). The immunohistochemical staining for CA 19-9 was positive in the cytoplasm of the small neoplastic cells (Fig. 6). Thus, a histologic diagnosis of moderately differentiated tubular adenocarcinoma of the pancreas was made.

In the right ovary, there were large cysts covered with more than three layers of mucin-producing (positive PAS reaction) columnar cells (Fig. 7). The cells frequently formed papillomatous protrusions. The lumen of the cyst was packed with mucin, neutrophils and exfoliated epithelial cells. In the stroma, small atypical ducts resembling those of the pancreatic neoplasm were found (Fig. 7). Immunohistochemical staining indicated the cytoplasm of the mucin-producing columnar cells to be negative for CA 19-9. The cytoplasm of the atypical small ductal cells in the stroma, however, was positive for CA 19-9 (Fig. 8). From the above findings, the histologic diagnosis of the right ovary was mucinous cystadenocarcinoma accompanied by metastasis of the pancreatic cancer.

Metastases, or invasions, of the pancreatic cancer were found in the lungs, common bile duct, gall bladder, liver, stomach, sigmoid colon, ovaries, diaphragm, pericardial sac, pouch of Douglas and the lymph nodes of the para-pancreas and ascending colon.

No metastasis or invasion of the right ovarian cancer, however, were found anywhere. Besides the above histologic findings, liver cirrhosis and tubular necrosis of the kidneys were present. Uterine leiomyoma and follicular adenoma of the right thyroid were also present. The cause of death was
Discussion

In the present case, double cancer (pancreatic duct cell adenocarcinoma and mucinous cystadenocarcinoma of the ovary) was diagnosed by exfoliative and FNA cytology, and confirmed histologically and immunohistochemically at autopsy. Although the occurrence of double cancer in different organs is not so rare, it is clinically difficult in a patient already suffering from the first cancer to confirm another primary cancer of a different organ by means of cytology before surgery or at autopsy. In the present case, double cancer could be presumed by the cytomorphologic distinction of exfoliative and FNA cytology.

In the present case, the pancreatic cancer metastasized to mucinous adenocarcinoma of the right ovary. In general, pancreatic body or tail carcinoma commonly metastasizes to the stomach, spleen, adrenal gland, kidney and colon. Metastases of a cancer to another coexisting tumor in the same individual are extremely rare.\(^8\) To our knowledge, the present report is the first case of a pancreatic cancer metastasizing to an ovarian cancer. Immunohistochemically, the atypical cells derived from the pancreatic cancer were strongly positive for CA 19-9; however, the malignant cells of the ovarian cancer were completely negative. Since both carcinomas of the pancreas and ovary were adenocarcinomas, immunohistochemical staining for CA 19-9 was useful in distinguishing the atypical cells from the pancreatic carcinoma from those of the ovarian carcinoma.

It is difficult to diagnose pancreatic cancer before an apparent onset of clinical symptoms since the organ can not be well observed through any endoscope, and the distinction between malignant neoplasms and inflammatory diseases of the organ is not easy to distinguish by various methods including cytology. Cytologic examination of the pancreas has an important role to play in the preoperative diagnosis of malignancy. Many investigators have reported the use of ERCP with or without using cytology.\(^9,10\) In pancreatic head cancer, the combined use of cytology and duodenal biopsy has been reported previously.\(^5\) The rate of correct diagnosis using such a method was over 80%. Most tumors, however, were already inoperable at the time of the diagnosis. Furthermore, in cancer of the pancreatic body or tail, the correct diagnostic rate with the same method was much lower.\(^5\)

For early diagnosis of pancreatic cancer, it is necessary to obtain cytologic material directly from the tumor. Percutaneous FNA cytology under CT\(^11\) or US\(^12\) guidance would be effective in the early diagnosis of pancreatic malignancy. In the present case, we did not use such methods. PTCD-biliary juice cytology, however, was good enough to diagnose the pancreatic neoplasm, since the tumor was already advanced.

FNA cytology has also been used for the detection of female pelvic tumors. The ovary is now one of the most popular organs for cytodiagnosis, because a variety of primary benign and malignant tumors develop in the ovary and a number of nongynecologic malignant tumors, such as malignant lymphoma and metastatic carcinomas, also involve the ovary. It has been postulated that should the tumor be cystic, preoperative FNA cytology would not be adequate; there would be the fear of a possible spillage of tumor cells into the peritoneal cavity following perforation of the cyst.\(^13\) FNA cytology of ovarian tumors including cystic neoplasms, however, is neither more troublesome nor more complicated than the well-established cytologic biopsy of the prostate.\(^14\) In the present case, the patient was inoperable, and in a poor general condition at the time when the ovarian tumor was detected. Even although the ovarian tumor is cystic, FNA cytology can be performed without complications in order to select the appropriate mode of therapy. On preparing an adequate cell sample, the diagnostic accuracy of pelvic
PANCREATIC CANCER METASTASIZED TO OVARY

FNA cytology was shown to be 90–95%. Furthermore, the purpose of FNA cytology is not for screening, as for exfoliative smears from the uterine cervix, but for the histological micro biopsy.

References


