Undifferentiated Carcinoma of the Pancreas Involving Intraductal Pedunculated Polypoid Growth

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Abstract

We herein report a case of pancreatic undifferentiated carcinoma involving intraductal pedunculated polypoid growth. Duodenoscopy disclosed a congested polypoid mass protruding from the orifice of the papilla of Vater. Endoscopic retrograde pancreatography (ERP) showed a polypoid lesion in Wursung’s duct and Santorini’s duct. Pancreatic juice cytology using the cell block method revealed the presence of undifferentiated carcinoma. No extraductal invasion was detected on endoscopic ultrasonography and or intraductal ultrasonography. The patient therefore underwent pancreaticoduodenectomy. A histological examination revealed an intraductal polypoid tumor with a thin stalk without extraductal invasion. The tumor was composed of an abundant mixture of pleomorphic cells, spindle cells, giant cells, and a small amount of adenocarcinoma.

Key words: undifferentiated carcinoma of the pancreas, intraductal tumor, polypoid tumor, cell block method, pancreatic juice cytology

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Introduction

Undifferentiated carcinoma of the pancreas is defined as a malignant epithelial neoplasm in which a significant component of the neoplasm does not show any definitive trend of differentiation (1). This type of tumor, which is associated with a poor prognosis, commonly presents as a large mass, showing aggressive growth (2). Therefore, only a few cases of pedunculated polypoid forms of undifferentiated carcinoma of the pancreas without extraductal invasion have so far been reported.

Case Report

A 61-year-old man was referred to our department due to transient liver dysfunction. His serum carbohydrate-associated antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) levels were within the normal ranges. Computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) revealed an intraductal tumor and a multilocular cystic lesion in the pancreatic head (Fig. 1a). Duodenoscopy disclosed a congested polypoid mass protruding from the orifice of the papilla of Vater without mucin secretion (Fig. 2a). Endoscopic ultrasonography (Fig. 2b) and intraductal ultrasonography (Fig. 1b) demonstrated an intraductal polypoid lesion in Wursung’s duct and Santorini’s duct without extraductal parenchymal invasion.

ERP showed that the polypoid mass in Wursung’s duct and Santorini’s duct occluded the main pancreatic duct (MPD) in the periampullary area (Fig. 1c). Although a tumor biopsy was not performed in order to avoid bleeding, pancreatic juice cytology using the cell block method with immunostaining showed undifferentiated carcinoma cells (Fig. 3a, Table).

The patient underwent subtotal stomach-preserving pancreaticoduodenectomy. Macroscopically, a polypoid tumor...
Figure 1. a: MRCP revealed an intraductal tumor (arrow head) and IPMN* in the pancreatic head. b: Intraductal ultrasonography demonstrated an intraductal polypoid mass in Wirsung's duct and Santorini's duct (arrow head). c: ERP revealed an almost completely occluded MPD resulting from intraductal growth of the polypoid mass in the periampullary area.

Figure 2. a: Duodenoscopy revealed a brownish polypoid mass protruding through the orifice of the papilla of Vater. b: EUS demonstrated an intraductal polypoid mass in the MPD protruding from the orifice of the papilla of Vater (arrow head) without extraductal invasion. *Common bile duct

measuring 3.2×1.1 cm in diameter was observed to occupy the lumen of the MPD (Wirsung’s duct) and Santorini’s duct in the pancreatic head (Fig. 3b). A histological examination revealed that the tumor originated from the junction of Wirsung’s duct and Santorini’s duct with a thin stalk and protruded into the duodenal lumen via the papilla of Vater (Fig. 3c). The intraductal polypoid tumor was composed of abundant pleomorphic cells, spindle cells, and giant cells showing sarcomatous findings and a small amount of adenocarcinoma on its surface (Fig. 3d). There were findings of transition from adenocarcinoma to undifferentiated carcinoma near the surface of the polypoid lesion (Fig. 3e). This pedunculated polypoid undifferentiated carcinoma filled the main pancreatic duct without invasion via the stalk into the pancreatic parenchyma. Atypical epithelium, that is, probable epithelial spreading of the adenocarcinoma was seen in the MPD adjacent to the polypoid tumor. Immunohistochemically, the sarcomatous components were positive for vimentin and focally positive for cytokeratin, while the adenocarcinomatous components were negative for vimentin and positive for cytokeratin (Table).

In the sarcomatous components, osteoclast-like giant cells positive for histomonocytic marker CD68 were identified (Fig. 3f). We identified giant cells that were positive for CD68 as osteoclast-like giant cells.

A multilocular cystic lesion with low papillary epithelium was seen in the pancreatic head adjacent to the polypoid cancer (Fig. 3g). This lesion was diagnosed to be a gastric-type intraductal papillary mucinous neoplasm (IPMN) according to the results of immunochemistry, as shown in Table.

The patient was alive and well, without evidence of recurrence 14 months after undergoing surgery.
Figure 3. a: Pancreatic juice cytology using the cell block method showed undifferentiated carcinoma cells (Hematoxylin and Eosin (H&E) staining ×100). b: Histological mapping of the resected specimen. Cancer was identified in the area marked by the black line. No continuity was seen between the polypoid cancer and intraductal papillary mucinous neoplasm (IPMN). c: A polypoid undifferentiated carcinoma was found to be growing in the MPD with a thin stalk (H&E staining ×3). *Wirsung’s duct, **Santorini’s duct. d: A histological examination revealed a tumor composed of an abundant mixture of pleomorphic cells and spindle cells without extraductal invasion via the stalk (H&E staining ×25). e: There were findings of transition from adenocarcinoma to undifferentiated carcinoma near the surface of the polypoid lesion (H&E staining ×25). f: In the sarcomatous components, osteoclast-like giant cells were identified (H&E staining ×40). g: IPMN was seen in the pancreatic head adjacent to the polypoid cancer (H&E staining ×20).

Table. The Results of an Immunohistological Study of the Resected Specimen

<table>
<thead>
<tr>
<th>Antibody</th>
<th>undifferentiated carcinoma</th>
<th>adenocarcinoma</th>
<th>IPMN</th>
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<tbody>
<tr>
<td></td>
<td>cancer cells</td>
<td>osteoclast-like giant cells</td>
<td>cancer cells</td>
</tr>
<tr>
<td>Ki67 (L.I.)</td>
<td>20%</td>
<td>0%</td>
<td>20%</td>
</tr>
<tr>
<td>CK</td>
<td>f(++)</td>
<td>(-)</td>
<td>d(++)</td>
</tr>
<tr>
<td>CEA</td>
<td>(-)</td>
<td>(-)</td>
<td>a(+)</td>
</tr>
<tr>
<td>p53</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>Vimentin</td>
<td>d(+)</td>
<td>f(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>CD68</td>
<td>(-)</td>
<td>f(+++)</td>
<td>(-)</td>
</tr>
<tr>
<td>MUC1</td>
<td>f(+)</td>
<td>(-)</td>
<td>f(++)</td>
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<tr>
<td>MUC2</td>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>MUC5AC</td>
<td>(-)</td>
<td>(-)</td>
<td>f(++)</td>
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<tr>
<td>MUC6</td>
<td>(-)</td>
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L.I.: labeling index  f: focal  d: diffuse
Intraductal growth or spreading of a pancreatic tumor frequently occurs in cases of intraductal papillary mucinous neoplasm (IPMN) (3, 4) and intraductal tubular neoplasm (5, 6). Acinar cell carcinoma and undifferentiated carcinoma of the pancreas also sometimes show intraductal growth. Undifferentiated carcinoma of the pancreas usually grows expansively, sometimes compressing and penetrating the MPD wall into the lumen and forming a polypoid lesion. Three histological variants of undifferentiated carcinoma, namely, the spindle cell type, the pleomorphic cell type, and the giant cell type, have been described (1). The prognoses of patients with these three types of carcinomas of the pancreas have been reported to be very poor. On the other hand, undifferentiated carcinoma with osteoclast-like giant cells classified as a subtype of invasive ductal carcinoma in the WHO classification (1) is less invasive than ordinary ductal cell carcinoma and it may have a more favorable prognosis (2).

Recently, some cases of undifferentiated carcinoma of the pancreas involving predominant intraductal growth have been reported and have been speculated to be associated with potentially less aggressive behavior. A MEDLINE search of the literature using the keywords “undifferentiated carcinoma of the pancreas,” “giant cell carcinoma of the pancreas,” and “anaplastic carcinoma of the pancreas” between 1966 and 2011 revealed three cases of undifferentiated carcinoma involving intraductal growth and protrusion into the MPD without extraductal invasion (7-9). All three patients exhibited osteoclast-like giant cells histologically. However, the proportion of osteoclast-like giant cells was small in our case judging from the results of immunohistochemistry for CD68. The present case included a unique feature of a thin stalk. The pedunculated mass protruded through the orifice of the main pancreatic duct and might have suffered from compression by inflammation and Oddi’s sphincter. Mechanical obstruction of the common bile duct orifice by this polypoid lesion also caused transient liver dysfunction. Mechanical obstruction of the common bile duct orifice also occurred from compression by inflammation and Oddi’s sphincter.

Intraductal tubular neoplasms of the pancreas involving predominant intraductal growth have frequently occurred from the epithelium of the MPD. Naito et al. (9) studied the relationship between undifferentiated carcinoma and pancreatic ductal epithelium in seven cases, all of which contained adenocarcinomatous and sarcomatous components and three of which involved atypical epithelium (PanIN-3, described in this report) in the MPD wall. In some cases, the presence of PanIN3(atypical epithelium in the pancreatic branch) in undifferentiated carcinoma was confirmed at an early stage (10). Bergman et al. (10) documented the initial steps in the evolution of these tumors and provided evidence for their ductal origin, including their close association with PanIN3 lesions.

We speculate that, in the present case, adenocarcinoma in situ, which arose from the pancreatic ductal epithelium near the junction of Wirsung’s duct and Santorini’s duct, showed expansive polypoid growth, then invaded the surface of the polyp with sarcomatous transformation. Because invasion was seen only in the polyp itself, a better prognosis can be expected compared with that observed in patients with ordinary pancreatic undifferentiated carcinoma.

In our case, gastric type IPMN was seen near the polypoid carcinoma. Yamaguchi et al. reported that IPMN is sometimes concomitant with invasive pancreatic carcinoma (11). A search of PubMed revealed no other reports similar to the present case. However, it is not clear whether IPMN was related in any way to the development of undifferentiated carcinoma in our case.

In our previous study, intraepithelial cancer spread in the MPD was more frequently observed in pTS1 (histologically 2 cm or less in diameter) invasive pancreatic carcinoma than in pTS2 (more than 2 cm and less than 4 cm in diameter) or larger cancer (45% vs. 13%) (12), and the sensitivity of pancreatic juice cytology for pTS1 cancer was higher than that for pTS2 or larger cancer. Although, in the present case, the cancer was pTS2, pancreatic juice cytology using the cell block method (13) revealed undifferentiated carcinoma. The cell block method allows for cytological and histological evaluation with Hematoxylin and Eosin staining and immunostaining for serial sections if necessary.

We reported a case of pancreatic undifferentiated carcinoma involving intraductal pedunculated polypoid growth concomitant with IPMN.

Pancreatic juice cytology using the cell block method was useful for making a preoperative cytohistological diagnosis.

The authors state that they have no Conflict of Interest (COI).

References


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