

CASE REPORT

Ductal Adenocarcinoma of the Pancreas with Psammomatous Calcification. Report of a Case

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ABSTRACT

Context Calcification is extremely rare in pancreatic ductal adenocarcinomas, but we may sometimes encounter focal dystrophic calcification.

Case report We herein report the case of an 83-year-old female with pancreatic ductal adenocarcinoma associated with diffuse psammomatous calcification. The calcification was preoperatively detected by computed tomography. Numerous psammoma bodies were scattered throughout the tumor. Immunohistochemical positivity of osteopontin, a non-collagenous bone-related protein, was found in the psammoma bodies.

Conclusions The possibility of pancreatic ductal adenocarcinoma should therefore be considered for a localized calcified lesion in the pancreas. Therefore, osteopontin may play a significant role in the development of psammoma bodies. Studies to elucidate the prognostic significance of psammoma bodies in pancreatic ductal adenocarcinomas are therefore recommended.

INTRODUCTION

In pancreatic disease, calcification is not uncommon in chronic pancreatitis, pseudocysts, serous cystic neoplasms, mucinous cystic or non-cystic neoplasms, solid-pseudopapillary neoplasms, and

endocrine tumors, but it is extremely rare in ductal adenocarcinoma [1, 2].

We herein describe a case of pancreatic ductal adenocarcinoma (PDAC) with diffuse psammomatous calcification which was preoperatively detected by computed tomography.

CASE REPORT

Clinical Summary

An 83-year-old female was admitted to Showa University Hospital for a detailed evaluation of abdominal pain and hyperamylasemia. She had been suffering from diabetes and asthma for approximately 40 years. The results of her physical examination were normal. Her laboratory data were within the normal limits except for a mildly elevated amylase level of 376 IU/L (reference range: 40-160 IU/L). Her serum calcium level was normal. Computed tomography (CT) of the abdomen did not reveal a tumor mass, but it did show a calcified hyperdense area in the uncinate process of the pancreas with dilated main pancreatic and common bile ducts (Figure 1). Coronal T2-weighted magnetic resonance imaging showed a filling defect in the main pancreatic and common bile ducts which was accompanied by the dilatation of each distal duct (Figure 2). Magnetic resonance cholangiopancreatography also showed the dilatation of the main pancreatic and the common bile ducts with a filling defect

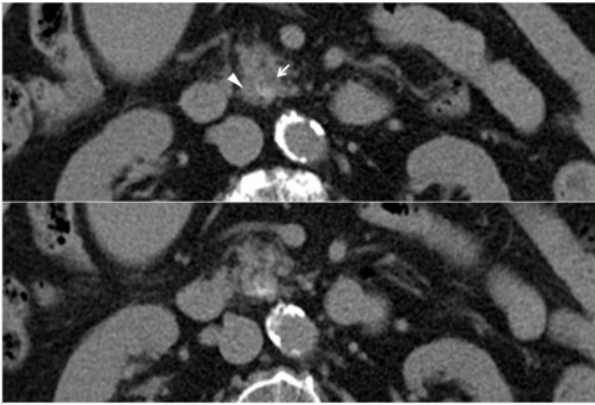


Figure 1. Computed tomography shows a calcified hyperdense area in the uncinate process of the pancreas with dilated main pancreatic (arrow) and common bile ducts (arrowhead).

(Figure 3). Bile juice cytology revealed malignant cells which were suggestive of adenocarcinoma. With a diagnosis of cancer of the head of the pancreas, a pylorus-preserving pancreaticoduodenectomy was thus performed. No recurrence has since been clinically observed during a 5-month postoperative follow-up.

Pathological Findings

A whitish invasive tumor, measuring 1.5 cm in diameter, was observed in the head of the pancreas. The tumor invaded the intrapancreatic portion of the common bile duct and caused obstruction of the main pancreatic duct; each distal duct was dilated. Histologically, the tumor consisted of a moderately to poorly differentiated invasive tubular adenocarcinoma. In addition, numerous psammoma bodies positive for von Kossa stain were scattered throughout the

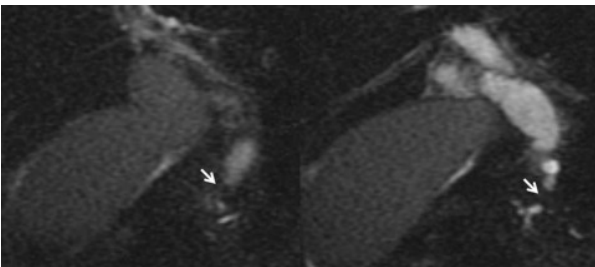


Figure 2. Coronal T2-weighted magnetic resonance imaging shows a filling defect in the main pancreatic (right, arrow) and common bile (left, arrow) ducts which is accompanied by the dilatation of each distal duct.

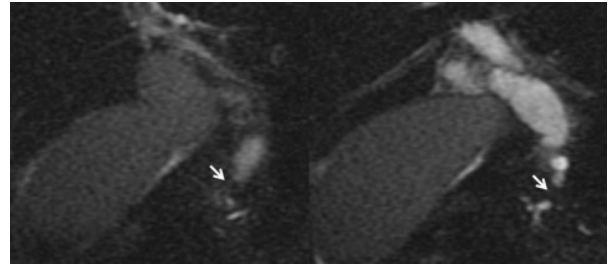


Figure 3. Magnetic resonance cholangiopancreatography shows the dilatation of the main pancreatic and common bile ducts with a filling defect (arrow).

tumor (Figure 4). Some of the psammoma bodies were found in the lumen of the tumor glands and others in the stroma. The localization of the psammoma bodies appeared to correspond to the distribution of the infiltrating cancer cells. There were co-existing intraductal neoplastic changes (PanINs), but they were not associated with the psammoma bodies. The calcification was localized in the tumor, and was not found in the surrounding pancreatic tissue. The cancer cells showed scirrhous and ill-demarcated invasion, as do most PDACs, but no lymph node metastases were found, and the surgical margins were free of any tumor. Immunohistochemically, the tumor cells were positive for CK7, MUC1, CA 19-9 (weak), CEA and p53, and negative for MUC2 and chromogranin A. A strong positivity for osteopontin was found in the psammoma bodies, but not in the tumor cells or macrophages.

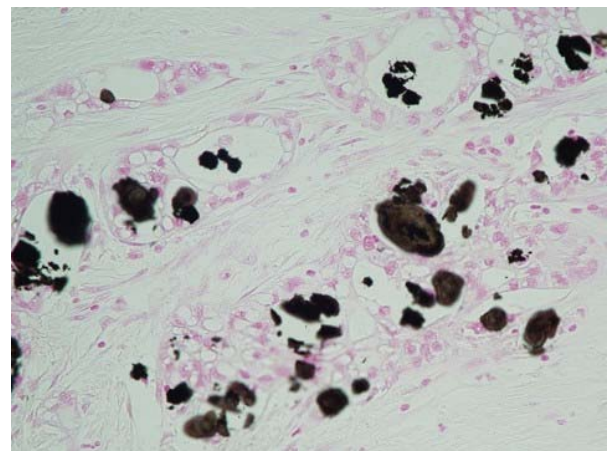


Figure 4. Histological finding of tubular adenocarcinoma of the pancreas shows psammoma bodies positive for von Kossa stain in the lumen of the tumor glands.

DISCUSSION

Calcification is extremely rare in PDACs [1, 2] and, hence, is not typically characteristic of PDAC. However, we may sometimes encounter focal amorphous dystrophic calcification in mucin pools, necrotic areas or stroma within tumors, and there have also been some case reports of PDACs with such calcification [1, 2]. Eelkema *et al.* reported calcification to be present in 2% of the PDACs studied by CT [3]. In the present case, a unique psammomatous calcification was observed throughout the tumor. Psammoma bodies are characterized by the formation of multiple, discrete, concentrically laminated, and calcareous bodies, and they are normally found in various neoplastic and non-neoplastic lesions. In neoplasms of the gastrointestinal tract and pancreatobiliary system, they are observed in small numbers of gastric, colonic, and cholangiocellular adenocarcinomas [4, 5, 6] and frequently in duodenal carcinoids but, to our knowledge, there have so far been no reports to date on their occurrence in PDACs.

The mechanism and etiology of psammomatous calcification remain controversial, but one hypothesis is that psammoma bodies arise due to the secondary accumulation of hydroxyapatite in cells undergoing degeneration. The concentrations of calcium and phosphate in the extracellular fluid are usually too low to initiate hydroxyapatite formation. However, after a crystal nidus is formed, a large calcified mass with lamination can develop [4]. In addition, there have been reports that osteopontin, a non-collagenous bone-related protein produced by tumor-associated macrophages, plays a significant role in the development of the psammoma bodies [7, 8]. In the present tumor, from the distribution of the psammoma bodies, they indeed appeared to originate from the necrotic or degenerating tumor cells (with somewhat mucous secretions). In addition, the immunohistochemical study of osteopontin showed a strong expression in only psammoma bodies. These findings indicate that osteopontin may be produced and then promptly secreted by macrophages which are

then subsequently translocated to the degenerated tumor cells, as described in previous reports [7]. Therefore, the deposited osteopontin protein may play a critical role in the following deposition of calcium phosphate which therefore results in the development of the psammoma bodies.

In this case, on imaging, the differential diagnosis included not only other types of solid tumors with calcification, but also localized calcifying pancreatitis and choledocholithiasis. In the present case, a mass lesion was not detected by CT, although it was shown by magnetic resonance imaging as a filling defect in the main pancreatic and the common bile ducts. Actually, the definitive diagnosis of PDAC was difficult to establish without a cytologic examination. This case, therefore, suggests that the possibility of a PDAC, and various approaches for its diagnosis, should be taken into consideration for a localized calcified lesion even if a tumor mass is not detected on imaging findings.

The prognostic significance of psammoma bodies in PDACs is unclear but, in our case, a radical cure was expected because of the T3N0M0R0 status in the TNM classification. In addition, the more the psammoma bodies are microscopically noted, the lower the number of viable tumor cells. In addition, ovarian serous psammocarcinomas have been reported to have a more favorable prognosis than the more common serous carcinomas [9]. In order to clarify and confirm the above findings, more studies involving similar cases of PDACs are required.

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Keywords Adenocarcinoma; Calcinosis; Osteopontin; Pancreas; Tomography, X-Ray Computed

Abbreviations PDAC: pancreatic ductal adenocarcinoma

Conflict of interest The authors have no potential conflicts of interest

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References

1. Furukawa H, Takayasu K, Mukai K, Inoue K, Mizuguchi Y, Ushio K, et al. Ductal adenocarcinoma of the pancreas associated with intratumoral calcification. *Int J Pancreatol* 1995; 17:291-6. [PMID 7642976]
 2. Kim T, Murakami T, Takahashi S, Hori M, Sakon M, Nakamori S, et al. Ductal adenocarcinoma of the pancreas with intratumoral calcification. *Abdom Imaging* 1999; 24:610-3. [PMID 10525818]
 3. Eelkema EA, Stephens DH, Ward EM, Sheedy PF 2nd. CT features of nonfunctioning islet cell carcinoma. *AJR Am J Roentgenol* 1984; 143:943-8. [PMID 6091432]
 4. Kawahara K, Niguma T, Yoshino T, Omonishi K, Hatakeyama S, Nakamura S, et al. Gastric carcinoma with psammomatous calcification after Billroth II reconstruction: case report and literature review. *Pathol Int* 2001; 51:718-22. [PMID 11696176]
 5. Nakayama H, Okumichi T, Nakashima S, Kimura A, Ikeda M, Kajihara H. Papillary adenocarcinoma of the sigmoid colon associated with psammoma bodies and hyaline globules: report of a case. *Jpn J Clin Oncol* 1997; 27:193-6. [PMID 9255277]
 6. Yamada S, Sanefuji H, Morimoto H, Harada Y, Mine S, Morimoto I, Eto S. Parathyroid hormone-related peptide producing cholangiocellular carcinoma with a marked psammoma formation. *J Gastroenterol Hepatol* 2000; 15:1442-6. [PMID 11197058]
 7. Maki M, Hirota S, Kaneko Y, Morohoshi T. Expression of osteopontin messenger RNA by macrophages in ovarian serous papillary cystadenocarcinoma: a possible association with calcification of psammoma bodies. *Pathol Int* 2000; 50:531-5. [PMID 10886734]
 8. Hirota S, Nakajima Y, Yoshimine T, Kohri K, Nomura S, Taneda M, et al. Expression of bone-related protein messenger RNA in human meningiomas: possible involvement of osteopontin in development of psammoma bodies. *J Neuropathol Exp Neurol* 1995; 54:698-703. [PMID 7666059]
 9. Gilks CB, Bell DA, Scully RE. Serous psammocarcinoma of the ovary and peritoneum. *Int J Gynecol Pathol* 1990; 9:110-21. [PMID 2332269]
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