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Direttore Nicola Picardi

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Burcu Erkan

Koç University School of Medicine, Department of Radiology

Comparative analysis of hypervascular microcystic serous cystadenoma with MRI and immunohistochemistry

PURPOSE: *Cystic tumors of the pancreas are increasingly common lesions. Unlike mucinous cystic tumors, serous cystadenomas are benign lesions and do not pose a risk of cancer. Often seen in women in the 6th and 8th decades, they are rarely seen in younger women or in male patients. Serous cystadenomas do not require surgical treatment unless they produce symptoms due to compression. Sometimes they may be misdiagnosed as cystic neuroendocrine tumors and resected because of the contrast enhancement on contrast enhanced cross-sectional studies. The purpose of this article is a translational analysis of why a cystic tumor enhances.*
MATERIAL AND METHODS: *The preoperative T2 HASTE, fat-suppressed T2 Turbo Spin Echo sequences, magnetic resonance cholangiopancreatography, diffusion weighted images, ex-vivo high-resolution T2 HASTE images of the post-operative pathologic specimen and immunohistochemical analysis with vascular marker CD31 were compared in a 58-year-old male patient with a pancreatic corpus microcystic serous cystadenoma.*
RESULTS: *The nodular lesion is observed as fluid signal in T2 weighted sequences and enhancing in postcontrast series. Ex-vivo high-resolution MRI has also revealed cysts with millimetric different sizes and septations within the lesion. Evaluation with the CD31 vascular marker showed that fibrous septa between the cysts were dense vascular and stained.*
CONCLUSION: *We show here that microcystic serous cystadenomas have intense vascularity of their septations that enhance in cross-sectional studies, especially when the cyst diameter is smaller.*

KEY WORDS: CD31, Microcystic, MRI, Serous cystadenoma

Introduction

In 2008, Laffan et al. [1] detected an incidental cystic lesion in the pancreas by 2.6% of the patient in a 2832 abdominal contrast enhanced multislice Computed Tomography (CT) scan taken with non-pancreatic causes. In 2011, Girometti et al. [2,3] performed a similar study with 3D Turbo Spin Echo (TSE) Magnetic Resonance Cholangiopancreatography (MRCP) sequence and reported incidence of incidental cystic pancreatic lesion as 44.7%. Up to now, more than twenty cystic lesions of the pancreas have been described, but most of these lesions consist of intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm, solid pseudopapillary neoplasm, and serous cystadenomas (SCA). Although it was thought that malignancy could develop very rarely in the background of the SCA in the past, Reid et al [3] in 2015 pathologically re-examined 193 SCA cases reported as malign and the rate of malignancy in SCA was found as 0%. Due to non-malignant potential the radiological differentiation of SCAs from other cystic tumors is of great importance for the protection of patient from an unnecessary surgery, especially in older age groups.

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Correspondence to: Burcu Erkan, Davutpaşa cad. No: 4, 34010, Zeytinburnu, Istanbul, Turkey (e-mail: bakpinar@kuh.ku.edu.tr)

Material and Method

A 58-year-old male patient with abdominal pain was diagnosed with a cystic lesion in the pancreas and magnetic resonance imaging (MRI) was performed for the differential diagnosis. Although the patient's complaints were believed not due to the detected pancreatic lesion, a cystic pancreatic neuroendocrine tumor and side channel IPMN probabilities were not precisely excluded and the patient was offered a biopsy of the lesion with the help of endosonography. A spleen-preserving distal pancreatectomy was performed to the patient who preferred surgery instead of advanced examination. Pre-operative T2 HASTE, fat-suppressed T2 TSE, diffusion weighted imaging (DWI), T1-weighted (W) vibe sequences before and after intravenous contrast medium administration and for research purposes, postoperative ex-vivo high-resolution T2W images were performed in 1.5 Tesla MRI (Magnetom Avanto, Siemens Medical Solutions, Erlangen). For ex-vivo images, the surgically removed distal pancreatectomy was brought to the radiology unit rapidly placed in warm saline at 37°C and scanned again with MRI, using knee coil. The lesion was then sliced for immunohistochemical study and the remaining pathological specimens were fixed with 4% paraformaldehyde solution and subjected to pathological examination.

In order to Hematoxylin and Eosin staining, immunohistochemical analysis with endothelial marker CD31 (Dako, 1:50, M0823, Cytomation, Hamburg, Germany) for the translational research was performed to the 3μM slices of the specimen, using previously reported methodology [4].

Patient and ethics committee approval was obtained for the study (TUM 5510/12).

Results

Pre-operative, pre-contrast (Fig. 1A) and postcontrast (Fig. 1B, C) T1W and T2 HASTE (Fig. 1D), fat-suppressed T2 TSE (Figure 1E) and coronal MRCP (Fig. 1F) sequences of the lesion described in the pancreas corpus was shown. A nodular lesion (Fig. 1D, E) that is hyperintense in the T2W sequences in the pancreas corpus shows close proximity with the pancreatic duct but no clear correlation with the pancreatic duct and no dilatation of the pancreatic duct were observed in the MRCP sequences (Fig. 1D, F). The lesion does not show diffusion restriction. In contrast enhanced images contrast enhancement is seen more obvious in the arterial phase image (Fig. 1B), while the venous phase (Fig. 1C) image is also brighter than the unenhanced (Fig. 1A) sequence. The ex-vivo specimen was re-scanned to elucidate the cause of this contrast enhancement patern, which is not often seen in cystic lesions. In Fig. 2A, the details of the lesion as the microcysts with fine septations were visualized, with the increase of MRI resolution of the T2 HASTE sequence. Histological tissue sampling (Fig. 2B) through the corresponding section of the

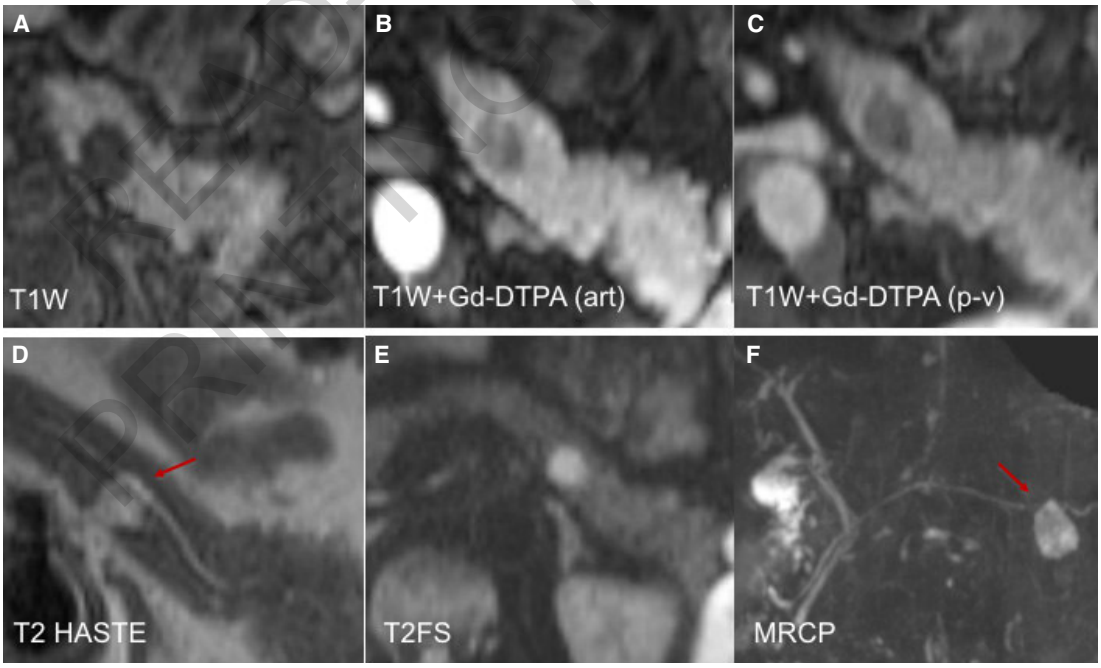

Fig. 1: Pre-contrast T1 fat-suppressed vibe sequence (A) shows a hypointense nodular lesion in the pancreatic corpus. After intravenous contrast administration hyperintensities were observed in the peripheral and central part of the lesion which is more prominent in the arterial (art) phase (B) than the portal venous (p-v) phase (C). This lesion is in fluid intensity with T2 HASTE (D) and fat-suppressed T2 TSE (E) sequences and is in close proximity to the pancreatic duct. MRCP (F) showed no direct correlation with the pancreatic duct and no ductal dilatation.

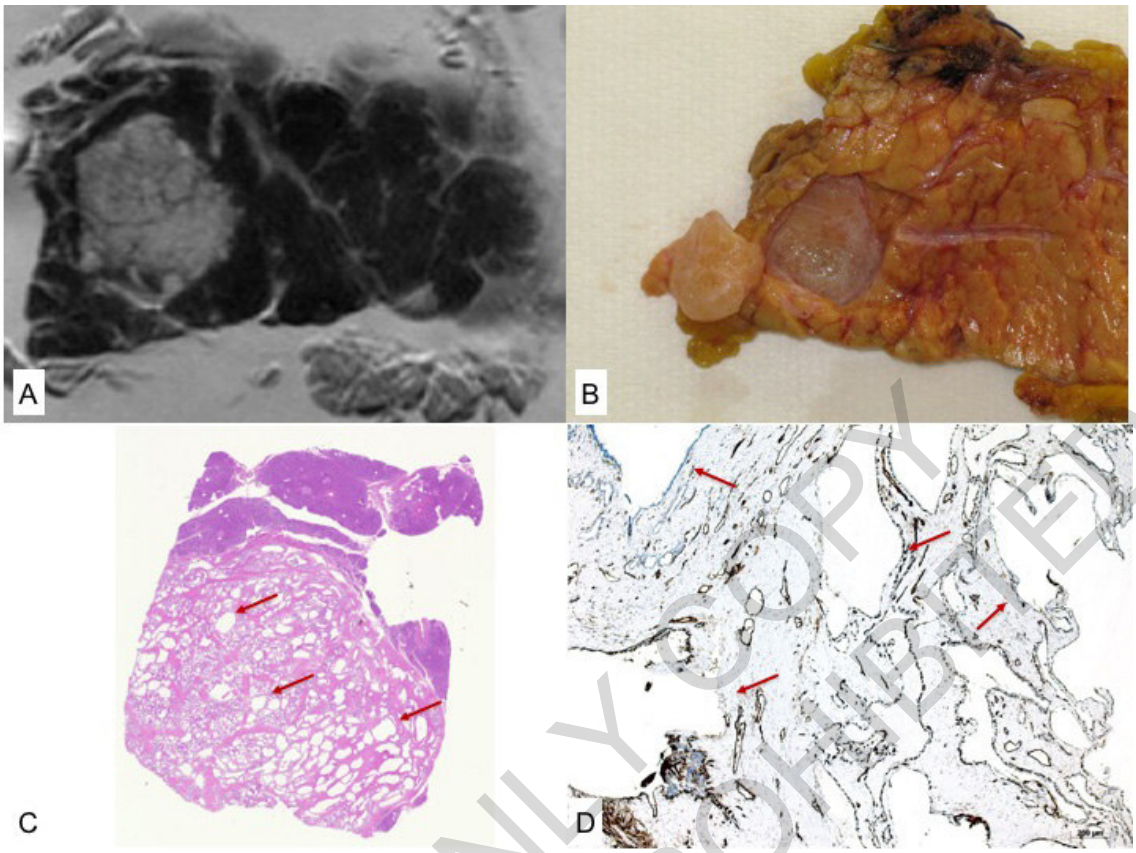

Fig. 2: Ex-vivo high resolution T2 HASTE image (A) clearly shows septations and milimetric cysts in the lesion. (B) Macroscopic section of specimen shows lesion and pancreatic duct adjacent to it. Hematoxylin Eosin staining (C) and immunohistochemical evaluation with CD31 (D) reveals large number of cysts lined with epithelium (arrows) and fibrous septa between them.

same location and hematoxylin and eosin staining (Fig. 2C) from this level show microcysts and fine septations between them. SCA diagnosed as histopathologically. Immunohistochemical analysis with CD31, a dye, specific for endothelial cells, shows that the fibrous septa between large number of cystic structures (Fig. 2D) are highly vascularized (Fig. 3A, arrows). When the solid components of the lesion were examined, areas of vascularization were found more intense (Fig. 3B).

Discussion

The purpose of this translational study is the radiological and immunohistochemical analysis of why microcystic SCAs are seen as hypervascular in contrast enhanced images.

SCAs are benign pancreatic tumors composed of numerous small cysts. There are various morphological nomenclatures in the literature. It is basically called inversely of the diameter and the number of cysts. It may subgrouped as oligocystic, microcystic, mixed (microcysts and oligocysts) and solid forms as well as policystic, honeycomb and oligocystic forms. Basically, there are different morphological forms of cysts depending on whether they are medium-large (oligocystic), small (microcystic) or microscopic (solid) sizes [3].

At the end of the 1980s, as the cross-sectional radiologic imaging did not reach its present resolution, hypervascularity of these lesions was revealed with conventional angiography and the differential diagnosis from pancreatic neuroendocrine tumors was remained a problem since it can show similar enhancement patern [5]. In CT, the cystic component could not be detected in the microcystic form. As MRI takes its place in abdominal imaging, it became easily diagnosed as the finding of typical honeycomb appearance with the cysts and septa were selected in the T2-weighted sequences [6]. In particular, solid forms of SCA with microscopic cysts, which can not be distinguished radiologically, still presents a diagnostic challenge for radiologists.

SCAs are seen in middle-aged (median age 65) and often in women. The close relation with the adjacent pancreatic duct suggests IPMN and contrast enhancement in the arterial phase suggests pancreatic neuroendocrine tumor in the differential diagnosis [7]. In addition, pancreatic cystic metastases are rarely described in the literature [8].

Nowadays the relationship with the pancreatic duct can usually be evaluated by MRCP. There is no visible con-

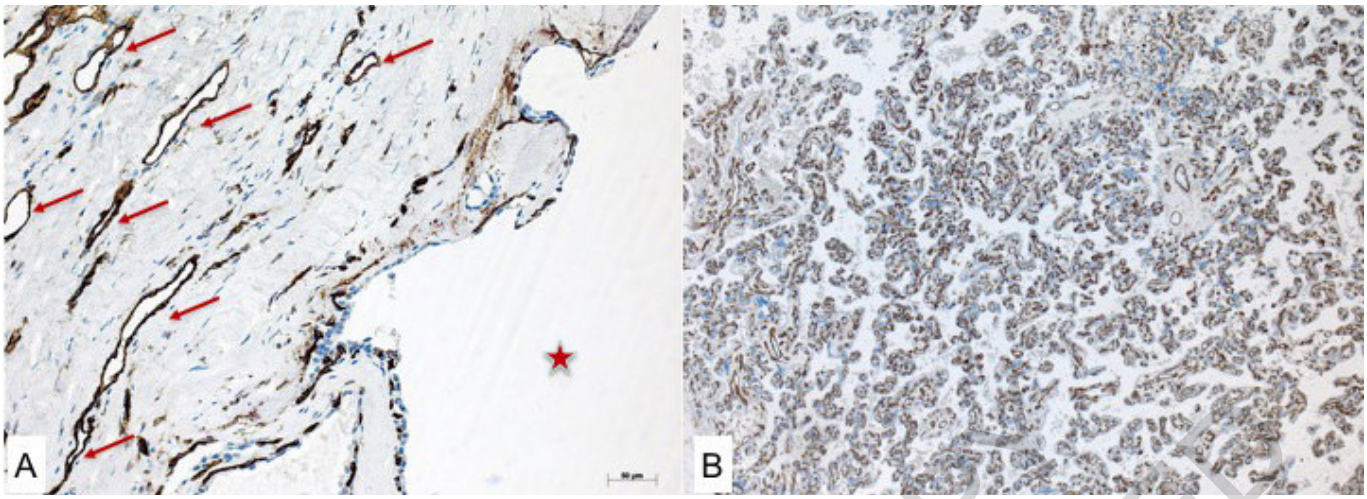

Fig. 3: (A) Immunohistochemical examination with CD31 is revealed vascular structures (arrows) colored as brown with CD31 are observed in fibrous tissue adjacent to cyst (star) on magnified image. (B) Intensive vascularity of the solid section is observed.

nection between the cyst and the pancreatic duct in SCAs.

In SCA, cysts are lined with glycogen-rich epithelium and separated by fibrous septa [9]. The retraction of the fibrous tissue may form a central scar, which can be calcified. This study with the evidence of immunohistochemical staining showed that the fibrous tissue is dense vascular (Fig. 3). Hypervascularity in contrast enhanced MRI sequences is also the result of this vascularity. Another important finding of this study is that the visibility of microcysts and septa are increased when high resolution images are performed. As the MRI resolution increases, accurate diagnosis of serous cystadenomas, which are composed of solid microscopic cysts, will be possible.

Conclusions

We show here that microcystic serous cystadenomas have intense vascularity of their septations that enhance in cross-sectional studies, especially when the cyst diameter is smaller.

Acknowledgement

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Riassunto

I tumori cistici del pancreas, sempre più comuni, e a differenza di quelli mucinosi, i cistoadenomi sierosi sono lesioni benigne e non presentano un rischio di cancro. Spesso visti nelle donne tra i 60 e gli 80 anni, raramente si incontrano in donne più giovani o nei pazienti maschi. I cistoadenomi sierosi non richiedono un trattamento chirurgico a meno che non producano sintomi dovuti alla compressione. A volte possono essere diagnosticati erroneamente come tumori neuroendocrini cistici e resecati a causa del potenziamento del contrasto negli studi trasversali potenziati dal contrasto. Lo scopo di questo articolo è un'analisi del perché un tumore cistico migliora.

Sono state messe a confronto T2 HASTE, sequenze T2 Turbo Spin Echo soppresse di grasso, sequenze colangiopancreatografiche di risonanza magnetica, immagini ponderate per diffusione del preoperatorio, con le immagini T2 HASTE ad alta risoluzione ex vivo del campione padel tologico post-operatorio e analisi immunoistochimica con marcatore vascolare CD31 in un paziente di 58 anni con un cistadenoma sieroso microcistico del corpo pancreatico.

La lesione nodulare è stata osservata come segnale fluido in sequenze ponderate T2 e potenziamento in serie post-contrasto. La risonanza magnetica ad alta risoluzione ex vivo ha anche rivelato cisti con dimensioni e settazioni millimetriche diverse all'interno della lesione. La valutazione con il marker vascolare CD31 ha mostrato che i setti fibrosi tra le cisti erano densi vascolari e colorati.

In conclusione si dimostra in questo caso che i cistadenomi sierici microcistici hanno un'intensa vascolarizzazione delle loro settazioni che si intensifica negli studi trasversali, specialmente quando il diametro della cisti è più piccolo.

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