Perivascular Cuffing as the Sole Imaging Finding of Pancreatic Cancer

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ABSTRACT

Background: Perivascular cuffing as the sole imaging manifestation of pancreatic ductal adenocarcinoma (PDAC) is an under-recognized entity.

Objectives: To present this rare finding and differentiate it from retroperitoneal fibrosis and vasculitis.

Methods: Patients with abdominal vasculature cuffing were retrospectively collected (January 2011 to September 2017). We evaluated vessels involved, wall thickness, length of involvement and extra-vascular manifestations.

Results: Fourteen patients with perivascular cuffing were retrieved: three with celiac and superior mesenteric artery (SMA) perivascular cuffing as the only manifestation of surgically proven PDAC, seven with abdominal vasculitis, and four with retroperitoneal fibrosis. PDAC patients exhibited perivascular cuffing of either or both celiac and SMA (3/3). Vasculitis patients showed aortitis with or without iliac or SMA cuffing (3/7) or cuffing of either or both celiac and SMA (4/7). Retroperitoneal fibrosis involved the aorta (4/4), common iliac (4/4), and renal arteries (2/4). Hydronephrosis was present in 3/4 of retroperitoneal fibrosis patients. PDAC and vasculitis demonstrated reduced wall thickness in comparison to retroperitoneal fibrosis (PDAC: 1.0 ± 0.2 cm, vasculitis: 1.2 ± 0.5 cm, retroperitoneal fibrosis: 2.4 ± 0.4 cm; P = 0.002). There was no significant difference in length of vascular involvement (PDAC: 6.3 ± 2.1 cm, vasculitis: 7.1 ± 2.6 cm, retroperitoneal fibrosis: 8.7 ± 0.5 cm).

Conclusions: Celiac and SMA perivascular cuffing can be the sole finding in PDAC and may be indistinguishable from vasculitis. This entity may differ from retroperitoneal fibrosis as it spares the aorta, iliac, and renal arteries and demonstrates thinner walls and no hydronephrosis.

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KEY WORDS: pancreatic ductal adenocarcinoma (PDAC), perivascular cuffing, retroperitoneal fibrosis, vasculitis

Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy, graded as the fourth leading cause of cancer-related death in the Western world [1-3]. The 5-year survival rate is 8–12% and most patients are diagnosed with distant metastasis (52%) [1,4].

Retroperitoneal fibrosis comprises a range of diseases characterized by proliferation of fibro-inflammatory tissue with potential to obstruct retroperitoneal structures [5-7]. Two-thirds of retroperitoneal fibrosis cases are idiopathic. The rest are secondary to drug use, infections, radiation therapy, major trauma, abdominal surgery, retroperitoneal hemorrhage, and proliferative diseases. Neoplasms account for 10% of all cases of secondary retroperitoneal fibrosis [7-9]. Computed tomography (CT) and magnetic resonance imaging (MRI) are used for noninvasive diagnosis of this disease [9-14].

Vasculitis encompasses a diverse group of conditions characterized by inflammation and necrosis of vessel walls. The extent of the disease and clinical symptoms depend on the size of vessels affected, location, and histological features [15]. Various vasculitides may involve the mesenteric vessels with either local or diffuse pathological changes. CT is commonly used as the initial study of choice [16-18].

Perivascular cuffing as the sole imaging manifestation of PDAC is an under-recognized entity. We present this rare diagnostic entity and differentiate it from retroperitoneal fibrosis and vasculitis.

PATIENTS AND METHODS

Patients were retrospectively identified using a computerized search in our department's radiological information system (RIS) (January 2011 to September 2017). Search terms included *pancreatic adenocarcinoma*, *pancreatic tumor*, or *pancreatic mass*, *retroperitoneal fibrosis*, *vasculitis*, and *aortitis*.

CTs were performed on three machines (Philips Brilliance 256, Philips Brilliance 64 [Netherlands], or GE Discovery 64 [MXR Imaging, Inc., USA]). CTs were acquired with a slice thickness of 2.5 mm. Patients were scanned in the supine position from the cranial to the caudal direction at end-inspiration. A dose of 100 ml Omnipaque (Iohexol 350 mg/ml up to 2 ml/

kg, GE HealthCare Technologies Inc., USA) was injected with an automated injector at a rate of 2–3 ml/s. Axial images were reconstructed using standard algorithms.

Two board certified radiologists analyzed all images and recorded the following imaging features: vascular anatomic site, wall thickness (cm), length of vasculature involvement (cm), and presence of extra-vascular findings. For each patient, measurements were performed on the first available CT scan with the finding. The radiologists were not blinded to the clinical entities.

Institutional review board approval was granted for this study and informed consent was waived.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize the study's characteristics. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 20 (SPSS, IBM Corp, Armonk, NY, USA). P-value < 0.05 was considered statistically significant. The Mann-Whitney U test evaluated differences in wall thickness and length of vascular involvement between the three evaluated groups.

RESULTS

Fourteen patients with abdominal perivascular cuffing were retrieved, three patients were diagnosed with celiac and/or superior mesenteric artery (SMA) perivascular cuffing as the sole finding of surgically proven PDAC. None of the patients in the PDAC group demonstrated a pancreatic mass in imaging studies conducted. Seven abdominal vasculitis patients and four retro-

peritoneal fibrosis patients were included.

The most common indication for performing the imaging study was abdominal pain (10/14 patients: 3/3 in the PDAC group, 3/7 in the vasculitis group, and 4/4 in the retroperitoneal fibrosis group). Abdominal pain was accompanied by weight loss in five patients (2/3 in PDAC group, 3/4 in retroperitoneal fibrosis group). Back or flank pain was described by 4/14 patients (2/4 in the retroperitoneal fibrosis group, 2/7 in the vasculitis group). Other presenting symptoms are presented in [Table 1].

Diagnoses of all the vasculitis cases (6/7), except one due to loss of follow, were made by integration of clinical presentation, laboratory findings, imaging features, response to treatment, and rheumatology board discussions. One of the cases was also confirmed via tissue diagnosis (1/7).

Patients in the vasculitis and retroperitoneal fibrosis groups showed elevated levels of acute-phase reactants to variable degree of severity and in some cases positive autoantibodies or mildly elevated complement components. None of the patients, including the PDAC patients, demonstrated elevated levels of the tumor marker CA19-9 at the time of imaging.

All three groups exhibited circumferential soft tissue perivascular cuffing. In the PDAC group, involvement of both the celiac and proximal-SMA were seen in one patient, while celiac or mid-SMA involvement were seen in each of the other two patients [Figure 1].

Vasculitis patients showed aortitis accompanied by iliac or SMA involvement (2/7), isolated involvement of celiac (2/7), isolated aortitis (1/7), mid-SMA (1/7) [Figure 2] or celiac

Figure 1. Computed tomography of 55-year-old male who presented with abdominal pain and weight loss. Computed tomography, ultrasound, endoscopic ultrasound, and magnetic resonance imaging were negative for a mass.

Computed tomography revision: soft tissue infiltration surrounding the superior mesenteric artery

Laparoscopy confirmed pancreatic cancer

[A] Axial plane   [B] Sagittal plane

Figure 2. Computed tomography (CT) of a 71-year-old female, who presented with abdominal and back pain. CT demonstrated perivascular cuffing of the superior mesenteric artery. Treated for vasculitis. Magnetic resonance imaging 6 months post-discharge showed resolution of imaging findings.

Table 1. Clinical features of cohort population

Group	Age in years	Clinical presentation	Pertinent available laboratory exams	Follow-up in months	Disease course and procedures	Patient outcome
PDAC	55	abdominal pain, weight loss, heartburn	amylase 72 IU/l	52	CT, US, EUS, MRI (11/2010-1/2011) negative for a mass. Laparoscopic investigation with intra-surgical US confirmed presence of tumor, followed by a Whipple procedure (02/2011) and chemotherapy	Died due to PDAC
	72	abdominal pain, constipation	CA 19-9, CEA normal	19	CT, PET CT (11/2015-1/2016) negative for a mass (5/2016) Pulmonary nodule, biopsy was taken confirming PDAC pathology, followed by chemotherapy	Died due to PDAC
	55	abdominal pain, weight loss	CA 19-9, CEA normal, CRP normal, IgG4 normal	16	CT, MRI negative for a mass (9-12/2016). EUS+FNA X2 (latest 5/2017) negative for malignancy. Explorative laparoscopy (7/2017) with tissue sampling surrounding celiac axis confirmed unresectable PDAC. Chemotherapy	Died due to PDAC
Vasculitis	65	back and left flank pain, radiating to groin	WBC 11K, ESR 50, c-ANCA +3	22	Primarily treated as UTI with no relief of symptoms. PET CT on later course of disease demonstrated uptake in lungs and kidneys lesions. Lung lesion biopsy Wegener granulomatosis	Lost to follow-up
	74	History of prostatic cancer with radiation treatment left lower limb swollenness, DVT ruled out	CRP 55.4 mg/l, negative IgG4	12	Family history of autoimmune diseases, including SLE, SAPHO, aortitis. Steroids treatment was initiated, later followed by methotrexate, with good response. Symptoms relapse with treatment discontinuation	Lost to follow-up
	57	Anemia	none	24	Multiple rectal varices on colonoscopy. CT referral to rule out portal vein thrombosis	Lost to follow-up
	71	Right knee monoarthritis, concomitant facial and forearms rash, fever	CRP 106.1 mg/l, elevated liver enzymes, positive ANA, mild rise in C4 41.4 mg/dl, positive anti cardiolipin	18	Steroids treatment was initiated, with good response	Continues follow-up
	65	abdominal pain, nausea, vomiting	WBC 18K, CRP 46.1 mg/l, mildly elevated C3, C4, hemoglobin 9.4 g/dl	18	Initially treated as acute cholecystitis, no relief of symptoms. CT features compatible with vasculitis. Symptoms improved during admission	No recurrence of symptoms
	71	abdominal and back pain	WBC 11K, CRP 72.9 mg/l	20	Symptoms improved during admission. MRI conducted 6 months post-discharge demonstrated resolution of imaging findings	No recurrence of symptoms
	83	abdominal pain, diarrhea. Crohn's disease patient	WBC 6K, CRP 29.5 mg/l	54	Episodic abdominal pain concluded unrelated to underlying Crohn's disease. Improvement under steroids. CT features compatible with vasculitis were consistent during follow-up	Continues follow-up
Retro-peritoneal fibrosis	59	abdominal pain, weight loss	WBC 9K, CRP 100.3 mg/l, negative IgG4, elevated C3 197 mg/dl (top -180)	22	Improvement under steroids treatment	Continues follow-up
	31	abdominal and back pain, weight loss	WBC 18K, CRP 156.7 mg/l, mildly elevated d-dimer 436ng/ml	30	Improvement under steroids treatment, later changed to DMARD (mabthera). Later diagnosed with concomitant ankylosing spondylitis	Continues follow-up
	49	abdominal pain, weight loss, lower limb pain, erectile dysfunction	ESR 100, ANA positive, mildly elevated C4 64 mg/dl	28	Improvement under steroids treatment, later changed to DMARD (Imuran+ methotrexate, followed by mabthera)	Continues follow-up, occasional relapses
	79	Abdominal and back pain	WBC 8K, CRP 10.3 mg/L	72	RPF proven by biopsy	Continues follow-up

ANCA = antineutrophilic cytoplasmic antibody, CEA = carcinoembryonic antigen, CRP = C-reactive protein, CT = computed tomography,
DMARD = disease-modifying anti-rheumatic drugs, DVT = deep vein thrombosis, ESR = erythrocyte sedimentation rate,
EUS = endoscopic ultrasound, MRI = magnetic resonance imaging, PDAC = pancreatic ductal adenocarcinoma, PET = positron-emission tomography,
RPF = retroperitoneal fibrosis, SAPHO = synovitis, acne, pustulosis, hyperostosis, osteitis, SLE = systemic lupus erythematosus, US = ultrasound,
UTI = urinary tract infection, WBC = white blood cell count

Figure 3. Computed tomography (CT) of a 31-year-old female, presented with abdominal and back pain and weight loss. CT demonstrated perivascular cuffing of the superior mesenteric artery **[A, C]**, aorta **[B, C]** and hydronephrosis **[B]**. Patient improved under steroid treatment. Rheumatologist surveillance diagnosed retroperitoneal fibrosis.
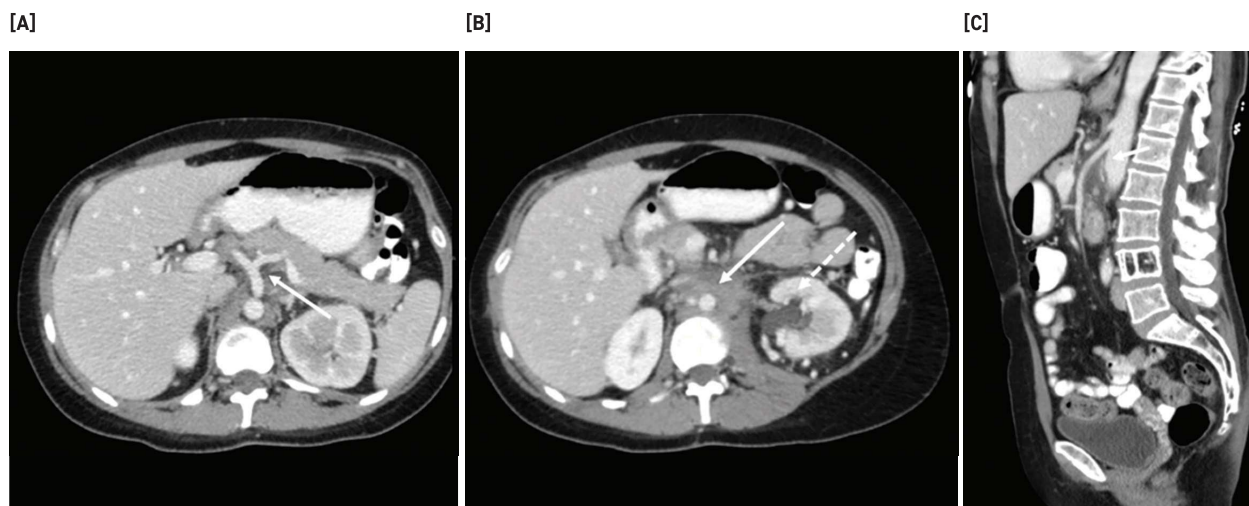
and proximal-SMA (1/7) involvement.

Retroperitoneal fibrosis involved the aorta (4/4), common iliac arteries (4/4), and renal arteries (2/4). Hydronephrosis was present in 3/4 of patients [Figure 3].

PDAC and vasculitis demonstrated reduced wall thickness in comparison to retroperitoneal fibrosis (PDAC: 1.0 ± 0.2 cm, vasculitis: 1.2 ± 0.5 cm, retroperitoneal fibrosis: 2.4 ± 0.4 cm; $P = 0.002$).

There was no significant statistical difference in the length of vascular involvement (PDAC: 6.3 ± 2.1 cm, vasculitis: 7.1 ± 2.6 cm, retroperitoneal fibrosis: 8.7 ± 0.5 cm).

DISCUSSION

We presented perivascular cuffing as the sole imaging finding of pancreatic adenocarcinoma.

There are numerous studies describing the appearance of pancreatic adenocarcinoma on imaging modalities, with the most common features being a hypovascular mass, dilatation of biliary and pancreatic ducts, invasion to adjacent structures, and metastases [19]. However, PDAC diagnosis could be quite challenging. Yang et al. [19] described atypical PDAC manifesting as a cystic mass, a mass without dilatation of upstream ducts, multiple masses, or a lesion diffusely infiltrating a majority of the pancreas without distorting its configuration. Yoon et al. [20] showed that approximately one-fourth of small (≤ 20 mm) PDAC and three-fifths of the well-differentiated pancreatic cancers manifested as iso-attenuating mass. In our study, we described another atypical presentation of PDAC

manifested as isolated circumferential soft tissue perivascular cuffing of either or both SMA and celiac arteries, without concomitant mass [21].

The typical imaging appearance of retroperitoneal fibrosis consists of a soft tissue periaortic infiltration, which most commonly extends from the level of the renal arteries to the iliac vessels and can often encase the ureters [9]. Less commonly, infiltration may be located more cranially, involving the SMA or celiac [22-24]. Our study findings support these typical imaging features described in literature.

In our cohort, the perivascular appearance of PDAC was like vasculitis but was different from retroperitoneal fibrosis. Circumferential soft tissue perivascular cuffing was thicker in retroperitoneal fibrosis compared to either vasculitis or PDAC. Also, unlike in retroperitoneal fibrosis, PDAC did not involve the aorta, and there was no associated hydronephrosis.

Tumor markers were neither sensitive nor specific as none of the patients demonstrated elevation of tumor markers. Furthermore, as the clinical presentation of PDAC is often insidious, 2/3 of our PDAC patients were suspected to have vasculitis at some point of their clinical investigation, one received a course of steroid therapy.

LIMITATIONS

Our study included a small, retrospective cohort. Although all PDAC were biopsy proven, the diagnosis of most of the retroperitoneal fibrosis and vasculitis patients were established on the integration of clinical, laboratory, and imaging

findings. Yet, all patients had at least one-year follow-up, sufficient to rule out diagnosis of PDAC. In addition, all patients in the PDAC group had a pathological diagnosis of adenocarcinoma.

CONCLUSION

Celiac and SMA perivascular cuffing can be the sole finding in PDAC and may be indistinguishable from vasculitis. This entity may differ from retroperitoneal fibrosis as it does not involve the aorta, or iliac and renal arteries, and demonstrates thinner walls and no hydronephrosis. Physicians should look for this rare, atypical PDAC appearance.

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There are two kinds of fools: One says, "This is old, therefore it is good";
the other says, "This is new, therefore it is better."
William R. Inge (1860–1954), English author, Anglican priest, professor of divinity at Cambridge, and dean of St Paul's Cathedral

Words ought to be a little wild,
for they are the assault of thoughts on the unthinking.
John Maynard Keynes (1883–1946), English economist and philosopher