

## 췌장 두부에 발생한 선방세포암 증례 및 문헌 고찰

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### Rapidly Growing Acinar Cell Carcinoma of the Pancreatic Head: A Case Report and Literature Review

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Pancreatic acinar cell carcinoma (ACC) is a rare neoplasm accounting less than 1% of malignant pancreatic tumors. A 47-year-old male patient visited the emergency room with epigastric pain. Computed tomography or magnetic resonance imaging revealed a 4.7-cm heterogeneously enhanced solid and cystic mass with internal necrosis located in the head of the pancreas. Radiological diagnosis was borderline malignancy such as neuroendocrine tumor or solid pseudopapillary neoplasm. Two months later, the necrotic mass in the pancreas head had grown up to 11 cm, compressing the duodenum, superior mesenteric vein, and proximal transverse colon. Pylorus preserving pancreatoduodenectomy with segmental resection of transverse colon was performed. Histopathological examination revealed that the tumor was pancreatic ACC. The patient recovered without any complication and was doing well without recurrence for 12 months after surgery.

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## INTRODUCTION

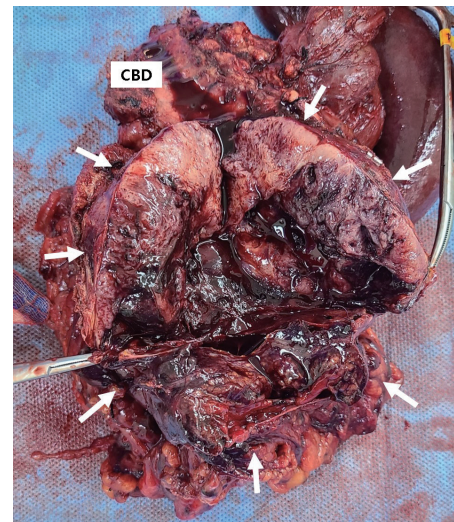
Pancreatic acinar cell carcinoma (ACC) is a very rare malignant neoplasm accounting for less than 1% of primary pancreatic neoplasms.<sup>1</sup> Because of the rarity of ACC, many issues such as diagnosis, surgical treatment, adjuvant therapy or therapeutic outcomes remain unclear. In general, although typical ductal adenocarcinoma is uncommonly confused for ACC, the preoperative diagnosis of ACC is difficult, imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI) only infrequently providing diagnostic clues and tissue

diagnosis often requiring additional immunohistochemical assays.<sup>2,3</sup> ACC is often mistaken for pancreatic neuroendocrine tumor (PNET), solid pseudopapillary tumor (SPT) or pancreatoblastoma.<sup>2</sup> For treatment strategy, curative-intent surgery should be proposed when the disease is localized, not differing from that of pancreatic ductal adenocarcinoma (PDAC).<sup>4</sup> However, the role of adjuvant chemotherapy has not been proven and the prognostic factors are rarely investigated. Here, we report a case of rapidly growing pancreatic ACC and review the literature to better understand this rare form of pancreatic malignancy.

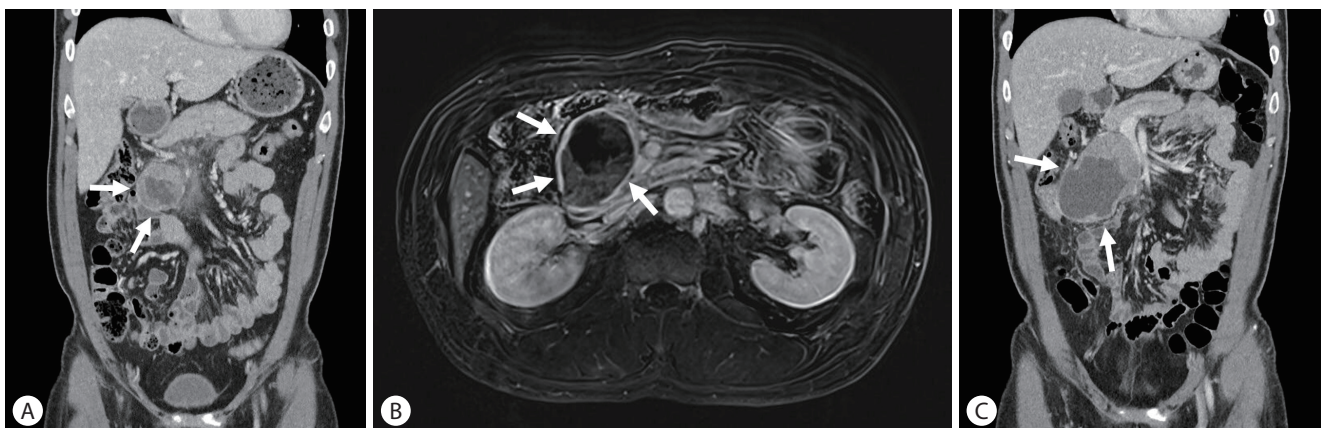
## CASE

A 47-year-old male visited Emergency Department of Chung-Ang University Hospital due to severe pain in the epigastric area lasting 1 week. On physical examination, there was mild tenderness in the right upper quadrant of the abdomen, but the examination results were otherwise negative. His past medical history was unremarkable. CT of the abdomen and pelvis revealed a 4.7 cm heterogeneously enhanced solid and cystic mass located in the head of the pancreas without obstruction of the biliary or pancreatic duct (Fig. 1A). MRI showed a well-defined hypo-enhancing mass with peripheral diffusion restriction, internal necrosis and peripancreatic infiltration with minimal fluid collection (Fig. 1B). The patient's serum lipase level was elevated at 2,138 IU/L (reference 67-21), while serum amylase level was 40 IU/L (reference 20-84) within normal range. All other laboratory parameters showed results within normal limits including carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9). CEA was 1.19 ng/mL (reference 0-3.8) and CA19-9 was 12.4 U/mL (reference 0-32). Owing to the patient's private business schedule, he refused to undergo operation at the initial visit and returned 2 months later. Over those 2 months, the necrotic mass in the pancreas head had grown up to 11 cm, compressing the duodenum, superior mesenteric vein, and proximal transverse colon (Fig. 1C). However, because the tumor was thought to be resectable, without further work-up such as

preoperative histologic diagnosis, surgery was performed. Exploration for the mass demonstrated involvement of the entire head of pancreas, transverse colon and its mesentery. Pylorus preserving pancreatoduodenectomy with segmental resection of transverse colon was performed (Fig. 2). Histopathological examination of the resected specimen revealed that the lesion consisted of highly cellular malignant epithelial tumor cells with scarce stroma and hemorrhage (Fig. 3A). Tumor cells were characterized by round nuclei with prominent nucleoli and acinar patterns (Fig. 3B). Immunohistochemistry demonstrated that the



**Fig. 2.** Gross appearance of resected specimen. The bulky and lobulated solid tumor with central hemorrhage was located in the pancreas head. Arrows mark the boundaries of the tumor. CBD, common bile duct.



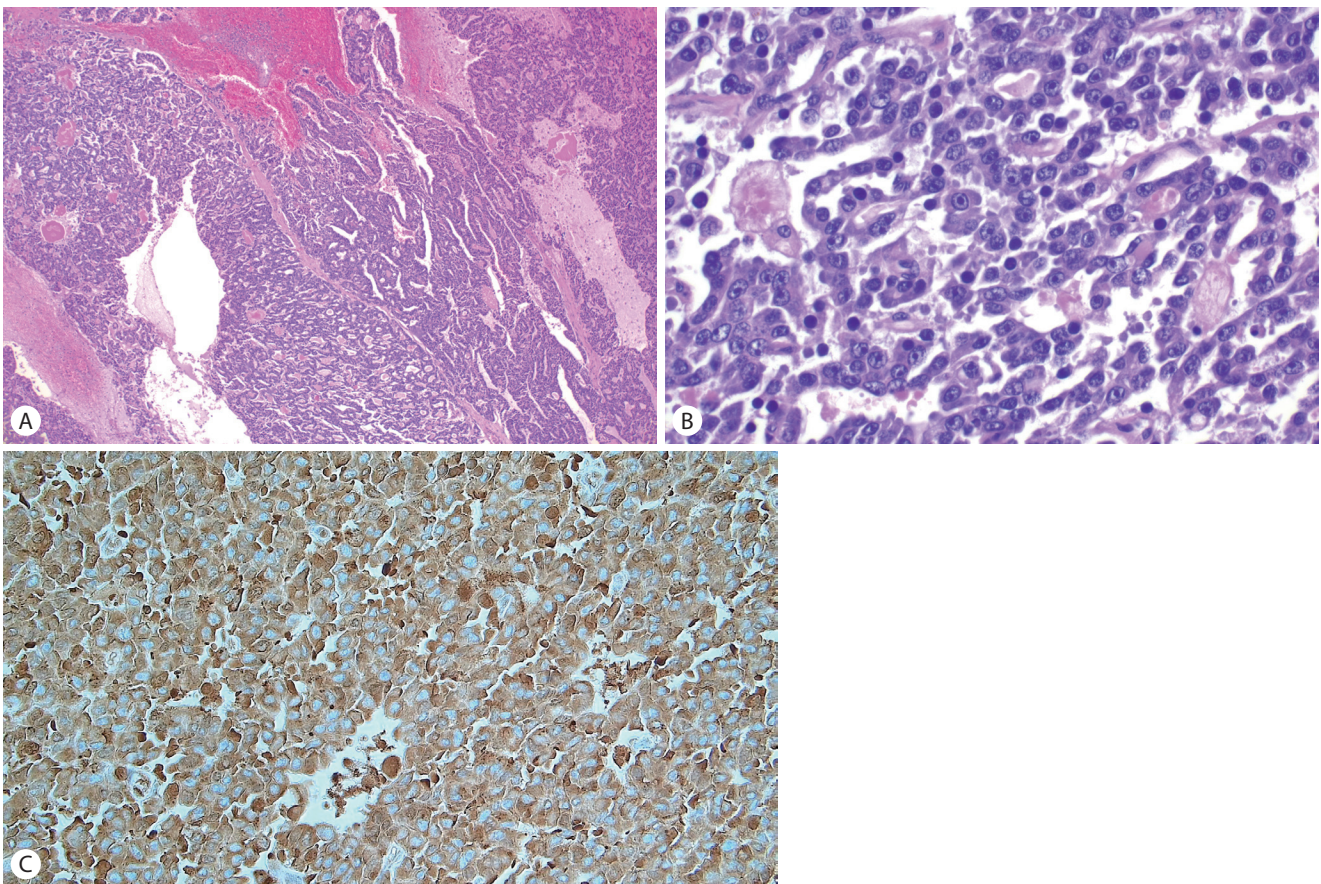
**Fig. 1.** (A) Abdominal computed tomography (CT) scan demonstrated 4.7-cm heterogeneously enhanced solid and cystic mass located in the head of the pancreas (arrows). (B) Magnetic resonance imaging showed a same sized well-defined hypo-enhancing mass with peripheral diffusion restriction, internal necrosis (arrows). (C) Two months later, abdominal CT scan demonstrated rapidly growing 11-cm sized necrotic mass (arrows).

tumor cells were positive for trypsin (Fig. 3C), cytokeratin (CK), CK7, and E-cadherin. They were negative for CK19, chromogranin, synaptophysin and beta-catenin. These findings were consistent with those of pancreatic ACC. Tumor cells were observed to extend to the peripancreatic soft tissue without the presence of perineural invasion or regional lymph node metastasis. All surgical margins were tumor-free. The patient's postoperative course was uneventful. He rejected adjuvant chemotherapy and was doing well without recurrence for 12 months.

## DISCUSSION

Pancreatic ACC is a rare neoplasm, although acinar cells are predominant in the normal pancreas.<sup>1</sup> ACC have an expansile growth pattern with relatively good demarcation, so the invasion of the common bile duct is less than that of PDAC.<sup>2</sup> Therefore,

there are more cases of non-specific symptoms such as abdominal pain than jaundice. Pancreatic ACC is often misdiagnosed as PDAC, PNET, or SPT. Approximately 50% of patients experience hyperlipasemia, and 10-15% of patients develop lipase hypersecretion syndrome, a type of paraneoplastic syndrome characterized by subcutaneous fat necrosis, polyarthralgia, and hypereosinophilia.<sup>3</sup> Pancreatic ACC is usually an exophytic, well-marginated, and hypovascular mass on CT and MRI. And it may contain cystic areas due to necrosis in case of large size.<sup>4</sup> Unlike ACC, PDAC is not well marginated and functioning PNET is more vascular. But, similar to ACC, non-functioning PNET may present as large well-marginated masses with internal hemorrhagic-cyst areas.<sup>4</sup> And typical CT appearance of SPT is a large well-encapsulated mass with solid and cystic components caused by hemorrhagic degeneration.<sup>5</sup> In terms of pathological diagnosis, ACC presents with different histological patterns, the



**Fig. 3.** Microscopic architectural pattern of acinar cell carcinoma. (A) Histological examination with hematoxylin and eosin staining (H&E) ( $\times 100$ ) revealed high cellular tumor with scarce stroma and hemorrhage and (B) tumor cells characterized by round nucleus with prominent nucleoli and acinar pattern (H&E,  $\times 400$ ). (C) Tumor cells showed immunohistochemically positive for trypsin ( $\times 400$ ).

**Table 1.** Characteristics of patients with acinar cell carcinoma of the pancreas

Study	Country	No. of patients	Mean age (years)	Sex, male (%)	Stage I/II (%)	Pancreatic head (%)	Size (cm)	R0/R1	Median OS (mo)	5YSR (%)	Adjuvant treatment	Recurrence (%)	Median relapse time (mo)
Webb <sup>9</sup> (1977)	USA	11	51	50	18	55	6.4	18	5	N/A	N/A	N/A	N/A
Klimstra et al. <sup>2</sup> (1992)	Italy	28	62	85	N/A	56	10.8	N/A	18	26	N/A	N/A	N/A
Ordóñez and Mackay <sup>10</sup> (2000)	USA	4	38	50	25	50	15	25	21.5	0	Chemotx, RT	N/A	N/A
Holen et al. <sup>1</sup> (2002)	USA	39	60	79	51	53	5.3	72	19	N/A	Chemotx, RT	72	N/A
Chiou et al. <sup>11</sup> (2004)	Taiwan	10	64	70	50	60	7.2	N/A	18.8	N/A	None	N/A	N/A
Basturk et al. <sup>12</sup> (2007)	USA	7	59	57	100		4.9		25		None	N/A	N/A
Kitagami et al. <sup>13</sup> (2007)	Japan	115	60	67	76	51		76.5	41	43.9* (0)		N/A	N/A
Schmidt et al. <sup>15</sup> (2008)	USA	865	67	64	35	42	5.9	75.7	27	36.2	Chemotx, RT	N/A	N/A
Wisniski et al. <sup>14</sup> (2008)	USA	672	56	54	40	28		N/A	47 (123*)	42.8	N/A	N/A	N/A
Seth et al. <sup>16</sup> (2008)	USA	14	57	33	86	64	3.9	N/A	33	N/A	Gemcitabine	57	N/A
Seki et al. <sup>17</sup> (2009)	Japan	4	63	75	25	62		100		N/A	Gemcitabine, S-1	100	7
Matos et al. <sup>18</sup> (2009)	USA	17	60	N/A	59	76	N/A	76.5	39	N/A	Chemotx, RT	43 (liver)	N/A
Butturini et al. <sup>3</sup> (2011)	Italy	9	53	67	57	67	N/A	100	31	22	Gemcitabine	100 (liver)	18
Lowery et al. <sup>19</sup> (2011)	USA	40	65	73	55	55	4	89.5	56.9*	N/A	Chemotx, RT	42	7.8
Glazer et al. <sup>20</sup> (2016)	USA	21	64	76	33	66	N/A	78.6	N/A	5	Gemcitabine	N/A	N/A
Egal et al. <sup>21</sup> (2019)	France	44	66	82	63	63	4.5	95.9	55.5 (107*)	N/A	FOLFIRINOX	N/A	12

OS, overall survival; N/A, not available.  
\* Resected patients.

neoplastic cells are uniform and arranged in architectural patterns, most typically acinar or solid.<sup>2</sup> The most common pancreatic neoplasm that are confused for ACC are PNET and SPT because of similar architectural pattern. Therefore, immunohistochemical staining for pancreatic enzymes including trypsin, chymotrypsin are used for diagnosis.<sup>3</sup> Trypsin is found to be the most commonly expressed enzyme followed by lipase, chymotrypsin and amylase. Compared to other markers, synaptophysin, chromogranin A, E-cadherin were markers for PNET and vimentin, nuclear labeling of  $\beta$ -catenin were markers for SPT.<sup>6</sup> Unlike that in PDAC, mutations of the K-ras oncogene, and the tumor suppressor gene p53 are not frequent in pancreatic ACC, however, chromosomal imbalances are common.<sup>7,8</sup>

We searched the medical literature for studies describing therapeutic management and clinical outcomes for ACC. Case series and case reports with more than four patients were included. Among a total 142 manuscripts, 16 studies were included and Table 1 shows the summary of the included studies.<sup>1-3,9-21</sup> A total 1,901 patients were identified from the included studies had a mean age of 62 years, and 61% were men. In the present review, 40% of patients with ACC were located at pancreatic head and 41% of patients had resectable disease (stage I/II). There were three nation-wide study using national database, Japan pancreatic cancer registry, Surveillance, Epidemiology, and End Results (SEER) and National Cancer Database (NCDB).<sup>13-15</sup> Among them, two studies from USA compared the clinical features and outcomes between ACC and PDAC.<sup>14,15</sup> Patients with ACC were more likely to be male (63.5% vs. 49.9%, 53.6% vs. 48.4%) and white (83.4% vs. 81.3%, 84.7% vs. 80.3%). ACC was more frequently located in the body/tail of the pancreas compared to PDAC (27.4% vs. 18.2%, 32.8% vs. 16.4%). More patients with ACC were presented with localized disease (34.6% vs. 22.4%, 14.7% vs. 8.4%) and curative resection rate was higher in the patients with ACC than in those with PDAC (64.35 vs. 55.9%, 69.1% vs. 27.3%). Overall 5-year survival rate for patients with ACC was significantly better than that of patients with PDAC (42.8% vs. 3.8%).<sup>13</sup> In all three national wide studies, surgical resection significantly improved overall 5-year survival rate of the patients with ACC (43.9% vs. 0.0%, 72% vs. 22%, 36.2% vs. 10.4%). Surgery with any form of adjuvant therapy was associated with a better survival compared to patients

who received surgery alone (41.2% vs. 32.7%).<sup>15</sup> Since no standard chemotherapeutic regimens have yet been established for ACC, similar chemotherapeutic regimens to those for PDAC have often been used. Recently, it has been reported that the administration of platinum- or irinotecan- containing chemotherapy regimens such as FOLFIRINOX, are effective for advanced ACC and further more prospective clinical trials are needed.<sup>22,23</sup> Multivariate cox proportional hazard regression model suggested that survival of the patients with ACC was significantly better than that of the patients with PDAC (hazard ratio 0.24, 95% confidence interval 0.22-0.27).<sup>14</sup>

Pancreatic ACC is a rare malignant disease that cannot be easily differentiated from other common pancreatic tumors preoperatively. However, compared with PDAC, ACC seems to have a better prognosis, especially after resection. Therefore, for the relatively younger male patients with large pancreatic tumor with cystic component like the present case, surgeons should keep ACC in mind and should perform resection and adjuvant chemotherapy actively.

## 요약

췌장 선방세포암은 췌장암 중 1% 미만을 차지하는 매우 드문 암으로, 수술 전 영상 검사상 췌장관세포암, 췌장 고형성가유두상 종양, 신경내분비 종양 등과 감별이 어려운 경우가 많다. 현재까지 명확하게 정립된 치료법은 없으며, 조기 진단 및 종양의 완전 절제만이 생존율 향상을 가져온다고 보고되고 있다. 그러나 췌장 관세포암에 비하여 종양 절제 후 비교적 좋은 예후를 보여준다. 본 증례와 같이 비교적 젊은 남자 환자가 낭성 부분을 포함한 크기가 큰 고형성 췌장 종양을 주소로 내원하였을 경우 췌장 선방세포암을 염두에 두고 적극적인 수술 치료를 고려해야 할 것이다.

국문 색인: 암; 선방세포; 췌장

## Conflicts of Interest

The authors have no conflicts to disclose.

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