

Long-Term Survival by Resection and Adjuvant Chemotherapy With S-1 in Pancreatic Signet Ring Cell Carcinoma: a Case Report With Literature Review

Akihiko Takagi (✉ akihiko-takagi@i.shizuoka-pho.jp)

shizuoka General Hospital <https://orcid.org/0000-0002-1357-7437>

Satoshi Tokuda

Shizuoka Kenritsu Sogo Byoin

Takeo Toda

Shizuoka Kenritsu Sogo Byoin

Kazuya Higashizono

Shizuoka Kenritsu Sogo Byoin

Keisei Taku

Shizuoka Kenritsu Sogo Byoin

Makoto Suzuki

Shizuoka Kenritsu Sogo Byoin

Hideyuki Kanemoto

Shizuoka Kenritsu Sogo Byoin

Noriyuki Oba

Shizuoka Kenritsu Sogo Byoin

Case report

Keywords: adjuvant chemotherapy, pancreas, signet ring cell carcinoma.

DOI: <https://doi.org/10.21203/rs.3.rs-53988/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: Signet ring cell carcinoma (SRCC) of the pancreas is a very rare histologic variant of pancreatic carcinoma with very poor prognosis. We present a case of pancreatic SRCC with good prognosis achieved by resection and adjuvant chemotherapy with S-1 one year, which is the standard treatment for advanced resected gastric cancer in Japan. The stomach carried a higher incidence of SRCC than other sites.

Case presentation: A 70-year-old man presented with abdominal discomfort, and ultrasonography revealed a mass in the pancreas. Computed tomography showed a hypovascular tumor in the head of the pancreas, 51 mm in diameter, with invasion to the portal vein and duodenum. The patient underwent pancreaticoduodenectomy (PD) with portal vein resection and reconstruction. The pathological diagnosis was SRCC of the pancreas without invasion to the portal vein, pT3N1M0 Stage IIB (UICC classification). Subsequently, postoperative adjuvant chemotherapy with S-1 was initiated to prevent recurrence. The patient has remained recurrence-free for 2 years and 6 months after PD.

Conclusion: Adjuvant chemotherapy with S-1 may be an important factor for improving the prognosis of patients with resectable SRCC of the pancreas.

Background

Signet ring cell carcinoma (SRCC) of the pancreas is extremely rare, representing < 1% of pancreatic cancers [1]. The prognosis of this tumor has been reported to be very poor [2]. Among a few reported cases of pancreatic SRCC in the literature, there is no case with long-term survival. The efficacy of adjuvant chemotherapy improving the prognosis has been reported in pancreatic ductal adenocarcinoma. Herein, we present a case of pancreatic SRCC with over 2-years recurrence-free survival achieved by resection and 1 year adjuvant chemotherapy with S-1.

Case Presentation

A 70-year-old man visited at a local clinic with abdominal discomfort. Ultrasonography revealed a hypoechoic mass in the head of the pancreas; thus, he was referred to our department. The laboratory test results showed markedly elevated level of carcinoembryonic antigen (CEA) at 1,706.0 ng/ml (reference range < 5.0 ng/ml). The level of carbohydrate antigen 19 – 9 (CA 19 – 9) was 8 U/ml (reference range < 37 U/ml) within normal limit. Serum amylase, bilirubin, and hepatobiliary enzymes were also in normal range. Abdominal computed tomography (CT) revealed a hypovascular tumor lesion, 51 × 50 × 39 mm in diameter, with invasion to the portal vein and duodenum (Fig. 1). Positron emission tomography-CT showed high fluorodeoxyglucose accumulation in the tumor (SUV max 10.8) and no evidence of regional lymph node metastasis or distant metastasis in the liver or lungs. The tumor was considered resectable by portal vein resection. Based on the clinical diagnosis, we performed pancreaticoduodenectomy (PD) with portal vein resection and reconstruction. The macroscopic findings of the resected specimen revealed a nodular tumor in the pancreatic head sized 63 × 50 × 40 mm. Pathological examination revealed SRCC (Fig. 2) with direct invasion in the duodenum and no invasion in the portal vein. There were multiple lymph node metastases in lesion of #5, #8 and peritumor. The pathological diagnosis according to the UICC classification was T3N1M0 Stage IIB, R0 resection. We consulted a medical oncologist and initiated 1-year adjuvant chemotherapy with S-1 according to the Japanese guideline of gastric

cancer. Thirty months after the surgery, the patient is well and without recurrence. There were no grade 3/4 adverse events according to the CTCAE classification. At 21 months after surgery, hepatoma that was enhanced in the early phase and washed out in the late phase was detected, with elevated PIVKA-II, a tumor marker of hepatocellular carcinoma (HCC). Diagnosis of HCC was made, and hepatectomy was performed. Intraoperatively, there were no findings of recurrence of the pancreatic cancer. In addition to the regular examination, the pathologist performed an immunohistochemical study; the pathological diagnosis was HCC. After PD for pancreatic SRCC, the levels of the tumor makers of pancreatic cancer, CEA and CA19-9, have remained within normal limits (Fig. 3).

Discussion And Conclusions

SRCC is composed almost exclusively of poorly cohesive neoplastic epithelial cells containing intracytoplasmic mucin that displaces the nuclei towards the periphery. SRCC of the pancreas is extremely rare and has a very poor prognosis [3]. According to the study using the Surveillance, Epidemiology, and End Results database from 2000 to 2014, the incidence of pancreatic SRCC is 0.4–0.5% among all cases of pancreatic carcinoma [1]. Among the eight cases reported thus far (Table 1) [4–11], surgical treatment with radical resection, pancreatoduodenectomy, and/or total pancreatectomy could be performed in four cases, and there was only one case of borderline-resectable tumor treated with neoadjuvant chemotherapy with gemcitabine.

Two studies have reported on the prognosis of patients with pancreatic SRCC. In the first, where the prognosis was investigated according to the tumor location (esophagus, stomach, small intestine, appendix, colon, and rectum), the group with pancreatic SRCC had the worst median overall survival (3.4 months) [1]. The second study evaluated the predictive effects of epidemiological factors and treatment interventions on the overall survival. The 1-, 2-, and 5-year overall survival rates were 17%, 9%, and 4%, respectively, and surgical interventions (pancreatectomy and pancreatectomy with radiation therapy, no case with adjuvant therapy) were associated with improved overall survival [2].

To the best of our knowledge, the present is the first report of adjuvant chemotherapy and long-term postoperative survival in pancreatic SRCC. We performed adjuvant chemotherapy with S-1, which is an oral fluoropyrimidine that contains tegafur, a prodrug of 5-fluorouracil, gimeracil, and oteracil potassium. The efficacy of S-1 for improving the postoperative survival has been reported in gastric cancer [12], which has the highest incidence of SRCC among gastroenterological tumors [1], and pancreatic cancer [13]. According to the Japanese guidelines, adjuvant chemotherapy with S-1 is recommended for gastric and pancreatic cancer [14–15]. The difference in the therapeutic regimens for the two types of cancer is the length of drug administration; 1 year for gastric and 6 months for pancreatic cancer. However, SRCC of the pancreas has a higher risk of recurrence and poorer survival rates than those of typical ductal adenocarcinoma [2]; therefore, we scheduled and performed 1-year adjuvant therapy.

In summary, we report a rare case of pancreatic SRCC with long-term survival. This case indicates that radical resection and adjuvant chemotherapy with S-1 may be an important treatment strategy for resectable pancreatic SRCC.

List Of Abbreviations

CA19-9, carbohydrate antigen 19 – 9

CEA, carcinoembryonic antigen

CT, computed tomography

HCC, hepatocellular carcinoma

PD, pancreaticoduodenectomy

PIVKA-II, protein induced by vitamin K absence or antagonist-II

S-1, tegafur, gimeracil, oteracil potassium

SRCC, signet ring cell carcinoma

Declarations

Not applicable

Declarations

Not applicable

Ethics approval and consent to participate

Ethics approval was obtained from our hospital's review board.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Availability of data and material

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Acknowledgements

Not applicable.

Authors' contributions

All authors participated in the patient's care and support. HK and NO provided the final approval for publication. All authors read and approved the final manuscript.

References

1. Li H, Zong Z, Zhou T, Sun L, Wang A, Zhang K, et al. Trends of incidence and survival in patients with gastroenteropancreatic signet ring cell carcinoma: an analysis from the Surveillance, Epidemiology, and End Results program. *J Gastrointest Oncol*. 2019;10:979-88.
2. Patel M, Hans HS, Pan K, et al. The impact of epidemiological factors and treatment interventions on survival in patients with signet ring cell carcinoma of the pancreas. *Am J Clin Oncol*. 2018;41:1176-84.
3. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. 4th ed. Lyon: International Agency for Research on Cancer; 2010.
4. Chow LT, Chow WH. Signet-ring mucinous adenocarcinoma of the pancreas. *Chin Med Sci J*. 1994;9:176-8.
5. Terada T. Primary signet-ring cell carcinoma of the pancreas diagnosed by endoscopic retrograde pancreatic duct biopsy: a case report with an immunohistochemical study. *Endoscopy*. 2012;44:E141-2.
6. Nauta S, Knoester I, van Zanten M, van Geenen E. A patient with signet ring cell carcinoma of the pancreas with a prolonged course: a case report. *JOP*. 2016;17:313-5.
7. Kaji K, Seishima J, Yamato M, Miyazawa M, Komura T, Marukawa Y, et al. Clinical utility of endoscopic ultrasound-guided fine-needle aspiration in mixed adenoneuroendocrine carcinoma with signet-ring cells of the pancreas: a case report and review of the literature. *Clin J Gastroenterol*. 2016;9:43-8.
8. Radojkovic M, Ilic D, Ilic I. Primary signet ring cell carcinoma of the pancreas with a good response to chemotherapy: case report and literature review. *Tumori*. 2017;103:e50-2.
9. Sakai T, Koshita S, Ito K, Kanno Y, Ogawa T, Kusunose H, et al. Signet-ring cell carcinoma derived from a main duct-type intraductal papillary mucinous neoplasm of the pancreas: a case report with long-term follow-up. *Intern Med*. 2018;57:1093-9.
10. Yepuri N, Naous R, Richards C, Dhir M, Jain A. Poorly differentiated signet ring cell carcinoma of pancreas masquerading as chronic pancreatitis. *J Surg Case Rep*. 2018;8:1-3.
11. Alexander D, Rashid L, Hollis M, Kavuturu S. Primary signet ring cell carcinoma of the pancreatic head: a case report. *Clin Case Rep*. 2019;7:2235-8.
12. Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, et al. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. *N Engl J Med*. 2007;357:1810-20.
13. Uesaka K, Boku N, Fukutomi A, Okamura Y, Konishi M, Matsumoto I, et al. Adjuvant chemotherapy of S-1 versus gemcitabine for resected pancreatic cancer: a phase 3, open-label, randomised, non-inferiority trial (JASPAC 01). *Lancet*. 2016;388:248-57.
14. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). *Gastric Cancer*. 2017;20:1-19.
15. Japan Pancreas Society. Clinical practice guidelines for pancreatic cancer 2016. Tokyo, Japan: Kanahara & Co, Ltd; 2016. [In Japanese]

Tables

Table 1. Reported cases of signet-ring cell carcinoma of the pancreas.

Case	Author	Year	Age	Sex	Tumor size (mm)	Type of therapy	Resectability at diagnosis	Overall survival time (dead/alive)
1	Alexander D, et al.	2019	79	Female	40	PD	R	6M (alive)
2	Yepuri N, et al.	2018	62	Female	NA	None	UR (SMA)	8M (dead)
3	Sakai T, et al.	2018	74	Male	16	TP	R	12M (alive)
4	Radojkovic M, et al.	2018	67	Female	45→15	NAC→PD*	BR	6M (alive)
5	Kaji K, et al.	2016	late 60s	Male	30	Chemotherapy**	UR (M1 HEP)	18M (alive)
6	Nauta S, et al.	2016	71	Male	NA	Palliative surgery***	UR	18M (dead)
7	Terada T.	2012	61	Male	NA	PD	R	6M (alive)
8	Chow LT & Chow WH.	1994	88	Male	50	None****		
9	Our case	2020	70	Male	63	PD	R	30 (alive)
<p>PD: pancreaticoduodenectomy</p> <p>TP: total pancreatectomy</p> <p>NAC: neoadjuvant chemotherapy</p> <p>R/BR/UR: resectable/borderline resectable/unresectable</p> <p>M: month</p> <p>* NAC was performed with gemcitabine</p> <p>** cisplatin+etoposide→S-1→gemcitabine+nab-paclitaxel</p> <p>*** palliative surgery</p> <p>**** post-mortem examination case</p>								

Figures

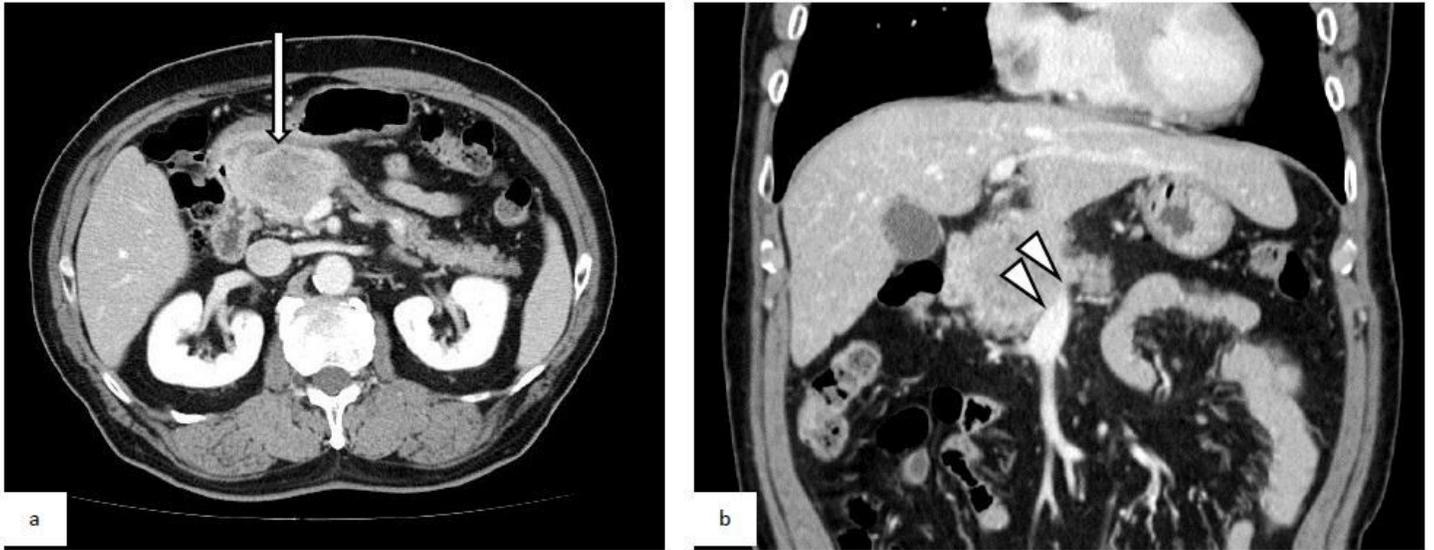


Figure 1

Abdominal computed tomography images. a) Axial image showing a tumor of the pancreatic head (arrow), 50 mm in diameter. b) Coronal image showing that the tumor was close to the portal vein (arrowheads).

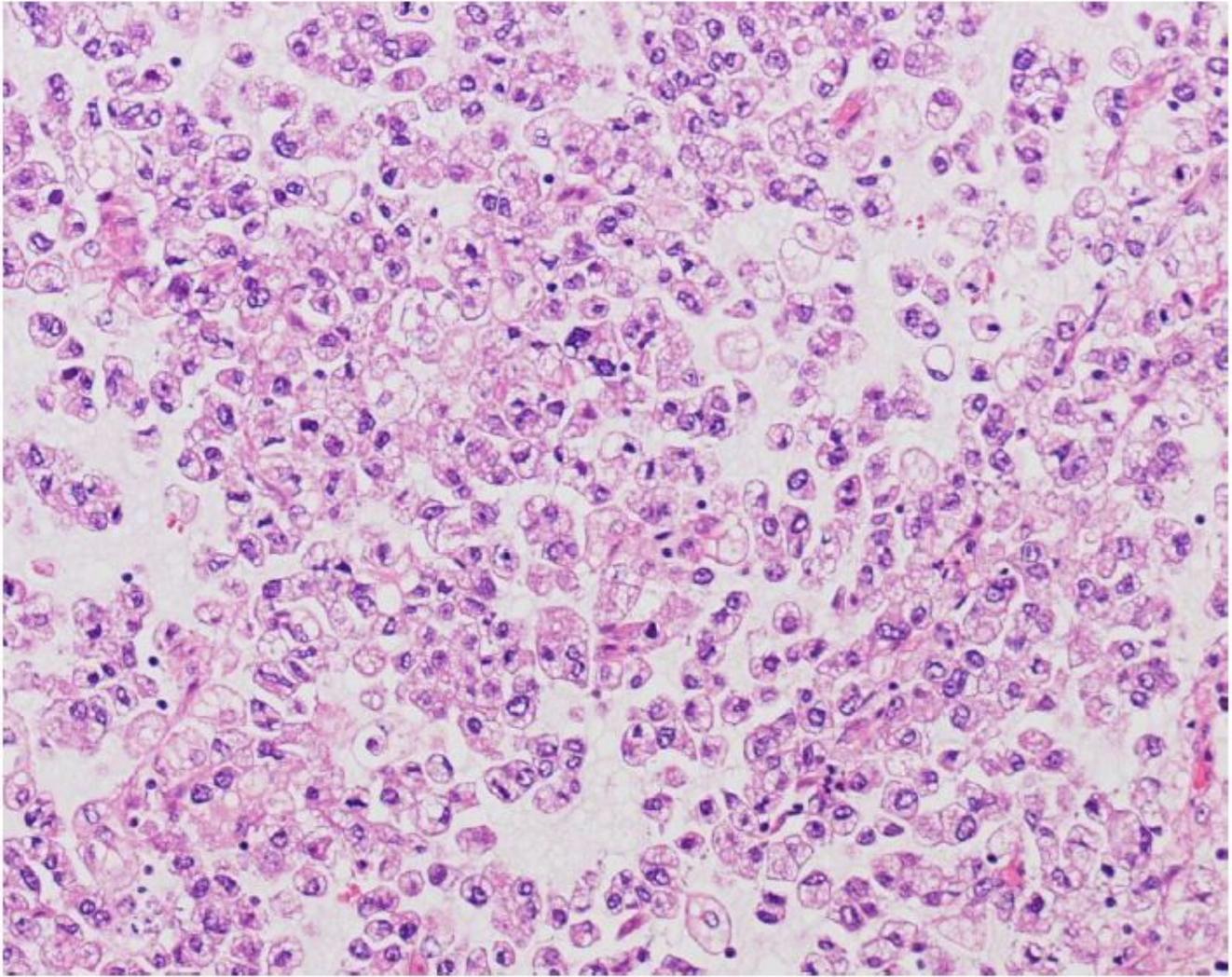


Figure 2

Pathological findings of the resected specimen (main pancreatic tumor). Signet ring cell carcinoma, hematoxylin & eosin staining ($\times 200$).

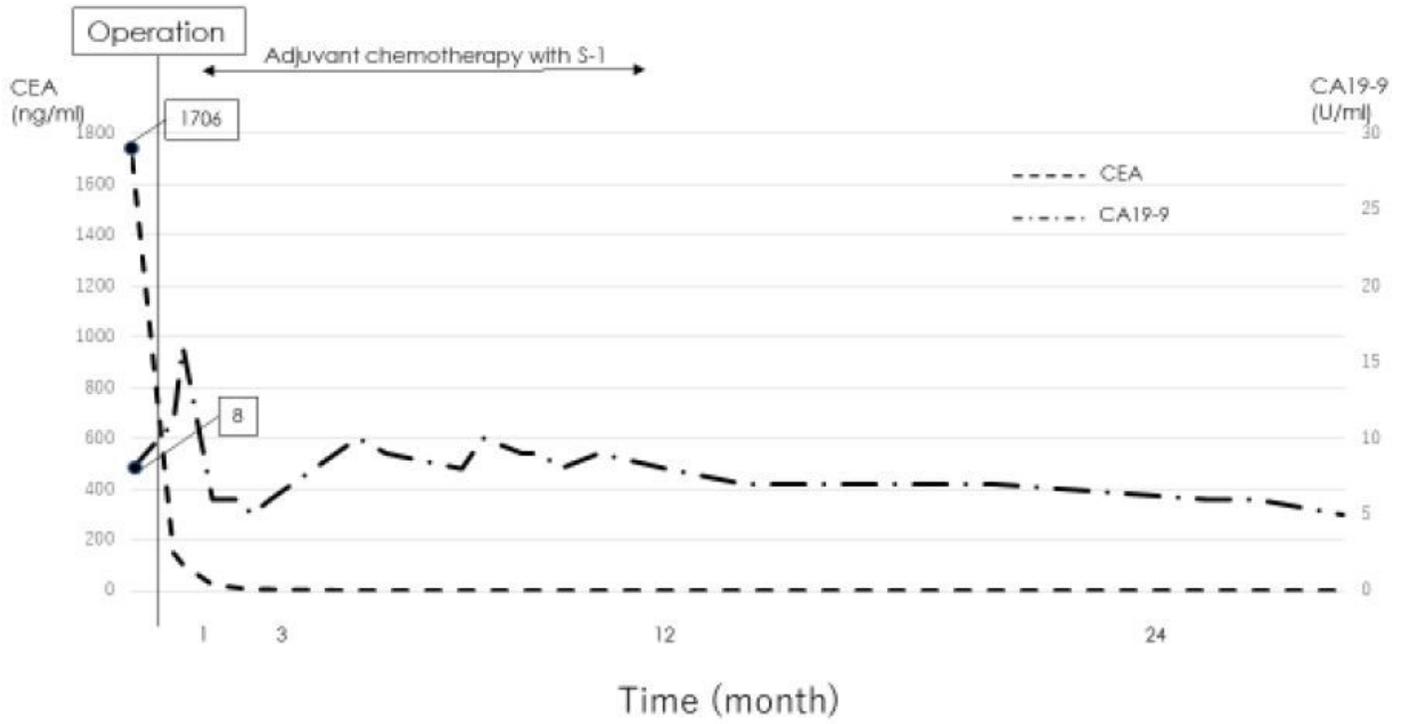


Figure 3

Change in tumor marker levels.