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Single Case

Advanced Adenosquamous Carcinoma of the Ampulla of Vater Treated with Adjuvant Chemotherapy after Pancreaticoduodenectomy

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Keywords

Adenosquamous cell carcinoma · Ampullary cancer · Biliary cancer · Pancreatic cancer · Hepatobiliary pancreatic surgery

Abstract

Introduction: Adenosquamous carcinoma (ASC) of the ampulla of Vater (AmV) is rare. The prognosis is generally worse in patients undergoing resection of ASC of the AmV than in those undergoing resection of adenocarcinoma of the AmV because the former shows early recurrence after surgery. A treatment strategy for ASC of the AmV has not been established, and the efficacy of adjuvant chemotherapy after curative resection is unclear. Given the paucity of data, we report a case of ASC of the AmV that was curatively resected and treated with adjuvant chemotherapy. ***Case Presentation:*** A 66-year-old man presented with pruritus and anorexia. Contrast-enhanced computed tomography revealed a tumor measuring 1.6 cm in diameter located at the AmV and distal bile duct. Biopsy revealed adenocarcinoma of the AmV. The patient underwent subtotal stomach-preserving pancreaticoduodenectomy. Histopathological examination contradictorily revealed ASC of the AmV and lymph node metastases. The postoperative course of the patient was uneventful, and he was discharged on day 25. The patient underwent S-1 adjuvant chemotherapy for 6 months and did not exhibit any postoperative recurrence for a follow-up duration of 28 months. ***Conclusion:*** Although treatment strategy for ASC of the AmV has not been established, our case shows that surgery followed by S-1 adjuvant chemotherapy could improve prognosis of patients with such tumors. However, further research is required to determine the efficacy of adjuvant chemotherapy and treatment strategies for resectable ASC of the AmV.

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Introduction

Cancer of the ampulla of Vater (AmV) [1] accounts for 0.2% of all gastrointestinal cancers [2]. Most cancers of the AmV are adenocarcinomas. Adenosquamous carcinoma (ASC) is a rare type of AmV malignancy [3, 4] that includes two components: adenocarcinoma and squamous carcinoma [4–6]. Studies on the treatment of ASC of the AmV are lacking because of its low prevalence. Consequently, treatment strategy after its curative resection, such as adjuvant chemotherapy and radiation therapy, has not been established [7]. Moreover, the prognosis is worse in patients with ASC of the AmV than in those with adenocarcinoma of the AmV [8]. Hence, given the paucity of data, we report a case of ASC of the AmV that was curatively resected and treated with adjuvant chemotherapy.

Case Report

A 66-year-old Asian man presented to Asahi General Hospital with symptoms of pruritus and anorexia. The patient had no significant medical history. He did not smoke tobacco but habitually consumed alcohol. Laboratory examinations showed elevated levels of serum total bilirubin (7.2 mg/dL), aspartate aminotransferase (353 IU/L), and alanine aminotransferase (625 IU/L) because of obstructive jaundice. The serum levels of carcinoembryonic antigen and carbohydrate antigen 19–9 were 2.1 ng/mL and 2,880 U/mL, respectively, while those of squamous cell carcinoma antigen were not examined. Contrast-enhanced computed tomography revealed a tumor measuring 1.6 cm in diameter located at the AmV and distal bile duct (Fig. 1a). Dilatation of the intrahepatic and common bile ducts was also visualized (Fig. 1b). Endoscopic retrograde cholangiopancreatography revealed a tumor in the AmV (Fig. 1c). Histopathological examination of the biopsy specimen revealed an adenocarcinoma. Therefore, the patient underwent subtotal stomach-preserving pancreaticoduodenectomy (PD) with radical lymphadenectomy. No intraoperative complication occurred. The operative time was 498 min, and the estimated blood loss was 314 mL. The tumor was white in color, measured 25 × 22 × 22 mm, and infiltrated through the duodenal mucosa to the muscularis propria, pancreas, and common bile duct (Fig. 2a, b). Macroscopic vascular invasions of the tumor were found. Histopathological examination of the resected specimen revealed a combination of moderately differentiated tubular adenocarcinoma and squamous carcinoma with pavement-like arrangements (Fig. 3a–d). Infrequent invasion of lymphatic vessels was also observed. Two of the 29 dissected lymph nodes showed metastases and only had the adenocarcinoma component. Therefore, the patient was diagnosed with advanced ASC of the AmV, pT3bpN1pM0 pStage IIIA, according to the eighth classification of the Union for International Cancer Control Staging. The patient developed no postoperative complication and was discharged on postoperative day 25. We administered S-1 (TS-1; Taiho Pharmaceutical, Tokyo, Japan), containing tegafur (a prodrug of fluorouracil), gimeracil, and oteracil potassium at a 1:0.4:1 M ratio [9] as adjuvant chemotherapy for 6 months according to the Japan Pancreas Society clinical practice guidelines for pancreatic cancer published in 2019. The patient did not exhibit any recurrence during the outpatient postoperative follow-up of 28 months.

Written informed consent was obtained from the patient for publication of this case report and its accompanying images. The copies of the written consent forms are available for review on request.

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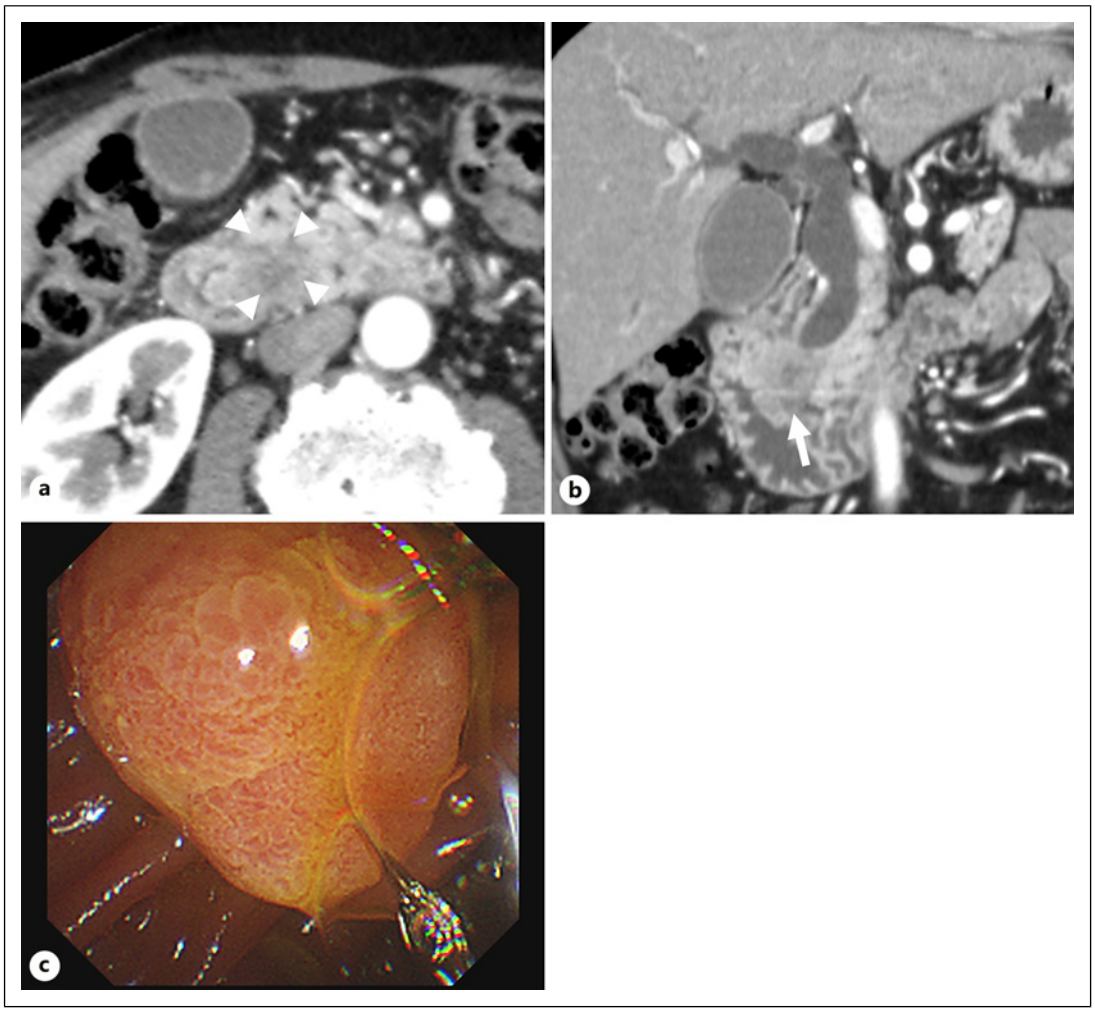

Fig. 1. Preoperative contrast-enhanced computed tomography and endoscopic findings. **a** Axial section of computed tomography. The tumor is seen as a lower density lesion during the portal phase (surrounded by arrowheads). **b** Coronal section of computed tomography. Both intrahepatic and extrahepatic ducts are dilated because of obstruction caused by the tumor of the AmV (arrow). **c** Endoscopic image. The AmV shows inflammation.

Discussion

Our case report describes a patient who underwent PD for advanced ASC of the AmV with lymph node metastases followed by S-1 adjuvant chemotherapy and displayed extended survival results after curative multimodal treatments. Carcinoma of the AmV is an uncommon malignancy [6, 10]. Most carcinomas of the AmV are adenocarcinomas, and other histopathological types of AmV malignancies are extremely rare [10]. ASCs are defined as tumors that contain both granular and squamous elements [3, 10]. The histogenesis of ASCs is unknown [3, 7, 10]. They are frequently observed in organs such as the intestine, stomach, esophagus, and vagina, which predominantly exhibit adenocarcinomas and squamous carcinomas [10]. The following four hypotheses regarding the histogenesis of ASC of the AmV have been reported: (i) pluripotent epithelial stem cells capable of inducing the malignant transformation of both cell types, (ii) squamous metaplasia, (iii) adenocarcinoma transforming into squamous cell carcinoma, and (iv) collision of both malignant tumors [3, 6, 10].

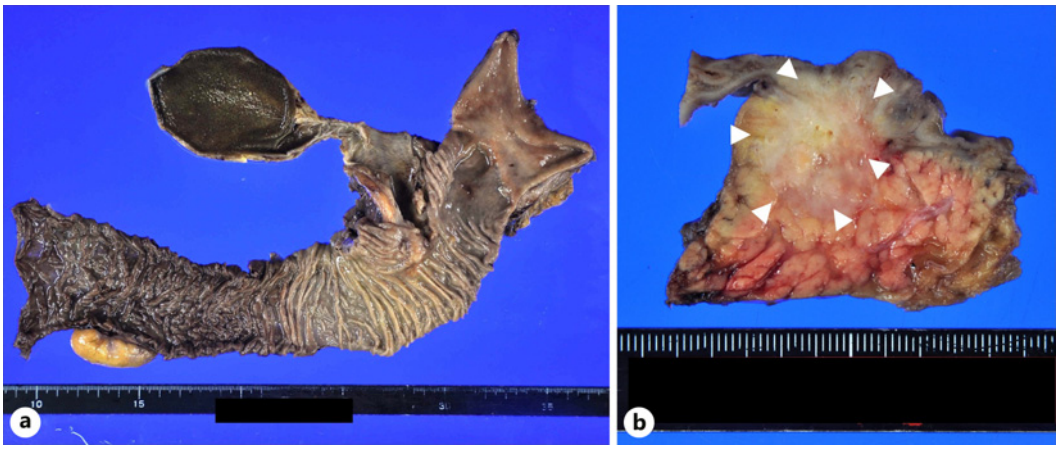

Fig. 2. Surgically resected specimen. **a** The specimen of PD. **b** The cross-section of the pancreatic head. The tumor at the ampullar of Vater is seen as a white nodule (surrounded by arrowheads).

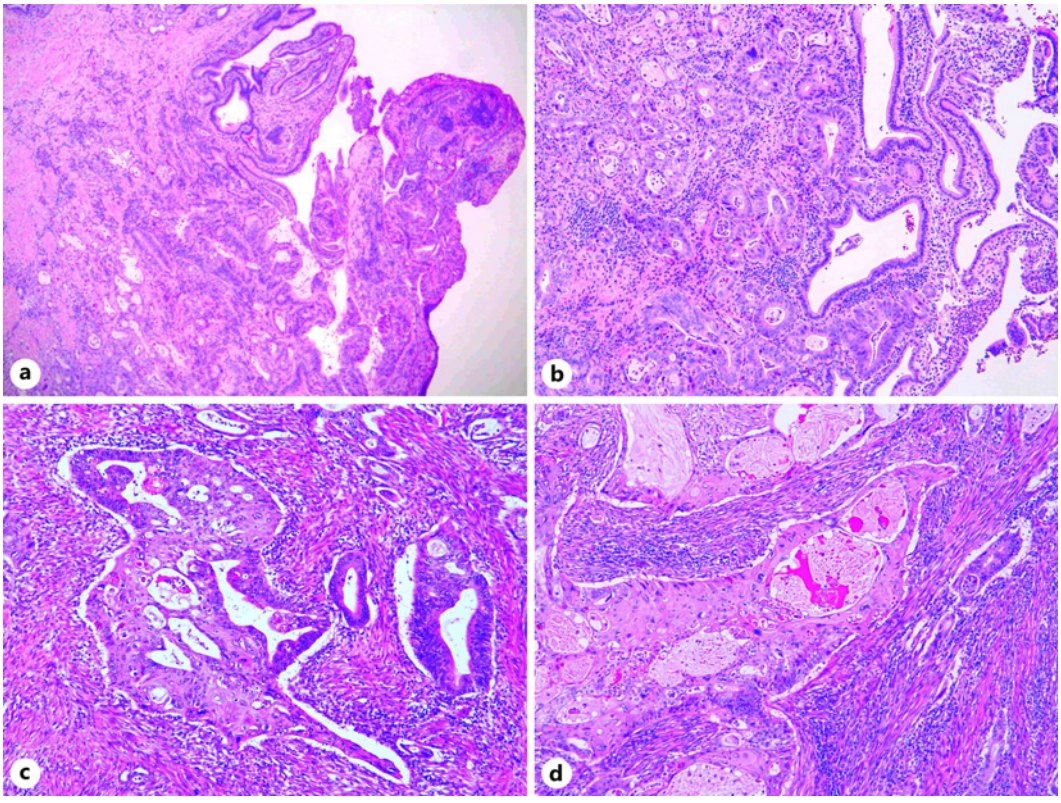

Fig. 3. Histopathological examination findings using hematoxylin and eosin staining. **a** The low magnification rate image of the AmV. The adenocarcinoma is dominant proximal to the AmV. A combination of adenocarcinoma and squamous cell carcinoma be observed in some regions. **b** A combination of adenocarcinoma and squamous cell carcinoma (magnification: ×40). **c** A combination of adenocarcinoma and squamous cell carcinoma (magnification: ×400). The adenocarcinoma is a moderately differentiated tubular adenocarcinoma. **d** Dominant region of squamous cell carcinoma components (magnification: ×400).

Table 1. Reported cases of ASC of the AmV that underwent surgery

Year	Authors	Patients, *n*	Age, years	Sex	UICC TNM classification				Size, mm	Surgical procedure	Chemotherapy	Adjuvant chemotherapy	Prognosis, month	Outcome
					T	N	M	Stage						
2002	Ueno et al. [5] (2022)	1	47	M	3b	+	1	IV	22	PD	–	–	10	Dead
2013	Yang et al. [6] (2013)	5	64	M	2	1	0	IIA*	34	PD	–	Gemcitabine	>6	Alive
			82	M	2	0	0	IB*	–	Ampullectomy	–	–	14	Dead
			68	M	4	1	0	III*	–	PD	–	–	7	Dead
			34	F	4	0	0	III*	–	PD	–	–	10	Dead
			77	M	3	1	0	IB*	–	PD	–	–	6	Dead
2014	Kshirsagar et al. [3] (2014)	1	58	M	N/A	N/A	N/A	N/A	40	PD	–	–	N/A	N/A
2015	Hashimoto et al. [7] (2015)	1	81	F	1a	0	0	IA	11	PPPD	–	–	>20	Alive
2018	Carvalho et al. [8] (2018)	1	68	M	2	1	0	IIIA	–	PD	–	–	10	Alive
2018	Minlanetto et al. [14] (2018)	1	81	F	3b	1	0	IIIA	40	PD	–	–	16	Dead
2021	Li et al. [10] (2021)	1	67	F	2	0	0	IB	36	PD + gastrectomy	–	–	>6	Alive
2022	Kanagasabapathy et al. [4] (2022)	1	67	M	2	1	0	IIIA	16	PD	–	–	1.5**	Dead
Present case	Hakoda et al.	1	66	M	3b	1	0	IIIA	25	SSPPD	–	S-1	>28	Alive

PD, pancreaticoduodenectomy; PPPD, pylorus-preserving pancreaticoduodenectomy; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy; UICC, Union for International Cancer Control; N/A, not available.

*Classification of the seventh edition of the American Joint Committee on Cancer.

**Death due to a brainstem hemorrhage.

The standard therapy for carcinoma of the AmV is surgical resection [1], mainly PD. Ampullectomy can be performed if radical resection is not feasible [1, 3]. However, ASCs have a worse prognosis than adenocarcinomas because ASCs are likely to recur locally and can metastasize over long distances within a short postoperative duration [6]. The median prognosis after surgery for ASC of the AmV was only 8.5 months in a previous case [4]. Table 1 summarizes cases of ASC of AmV that were surgically treated reported in English literature. In previous cases of ASC of the AmV and lymph node metastases [5, 6, 10], the prognosis after surgery was <16 months, except in our case, which had a prognosis of 23 months without recurrence. This is because the biology of squamous carcinoma is worse than that of adenocarcinoma [11–13]. This characteristic of ASC of the AmV can contribute to the poor prognosis of patients undergoing surgery.

Nonsurgical treatment strategies have not been established because of the rarity of ASC in the AmV [7]. A previous report recommended chemoradiation instead of surgery in patients with ASC of the AmV based on preoperative examinations [6]. However, it is difficult to accurately diagnose ASC of the AmV preoperatively because ASC does not display specific characteristics during radiographic imaging and biopsy of the tumor does not always obtain the components of both adenocarcinoma and squamous carcinoma [3, 10]. In our case, preoperative biopsy failed to reveal the squamous carcinoma component. Furthermore, it is difficult to accurately diagnose ASC using radiographic imaging modalities [3]. Most patients are diagnosed with ASC after surgical resection, which is recommended as its first treatment option if the tumor is completely resectable.

Adjuvant chemotherapy should be considered after complete resection of tumors. However, reports on adjuvant chemotherapy for ASC of the AmV are limited. Platinum-based and gemcitabine-based chemotherapy regimens have been used for treatment [6]. In a previous study, gemcitabine (1,000 mg/m^2) was administered as adjuvant chemotherapy, but it did not show a favorable prognosis because of the early recurrence of multiple liver metastases [6].

Our case had poor prognostic factors, such as advanced ASC and lymph node metastases. However, the patient has been alive for >23 months after surgery without recurrence. Although treatment strategy for ASC of the AmV has not been established, our report showed that surgery followed by adjuvant chemotherapy with S-1 regimen was effective for the current patient. Nonetheless, further research is required to determine the efficacy of adjuvant chemotherapy and treatment strategies for resectable ASC of the AmV. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000537900).

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethics approval was not required for this case in accordance with the national guidelines.

Conflict of Interest Statement

All the authors declare that there is no conflict of interest.

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Author Contributions

H.H. prepared and wrote the initial version of the manuscript and organized the case report. Y.K. revised and edited the final version of the manuscript. H.H., Y.M., J.T., and M.N. managed the patient's care. Y.S. made the pathological diagnosis and is responsible for it. All authors have reviewed the final version of the manuscript and approved it for publication.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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