

# Duodenal adenocarcinoma following a neuroendocrine tumor in the duodenum

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Primary duodenal adenocarcinoma is a rare malignant neoplasm accounting for 0.3% of all gastrointestinal tract carcinomas. We herein present one case of duodenal adenocarcinoma after duodenal neuroendocrine carcinoma. Poorly differentiated duodenal neuroendocrine carcinoma with liver metastasis (TxNxM1) was confirmed, and eight cycles of palliative chemotherapy (5-fluorouracil/etoposide/cisplatin) were administered. The patient was then in a clinically complete response status. About 1 year later, newly developed adenocarcinoma was detected at the same site. It was completely surgically resected, and the patient was cured.

**Keywords:** Neuroendocrine tumors; Duodenal neoplasms; Drug therapy

## INTRODUCTION

The average annual age-adjusted incidence of malignant tumors of the small intestine is 9.9 per million people. The incidence is 3.7 per million people for adenocarcinomas, 3.8 for neuroendocrine tumors (NETs), 1.1 for lymphomas, and 1.3 for sarcomas [1]. Among these, adenocarcinoma is the most common malignancy affecting the duodenum, carcinoid is the most common tumor in the ileum, and sarcomas and lymphomas can develop throughout the entire small bowel [2]. In the duodenum, the proportions of adenocarcinoma, malignant endocrine tumor, lymphoma, and sarcoma were 73.8%, 13.7%, 6.3%, and 6.2%, respectively, despite the fact that the reported relative incidence varies considerably with the patient population under study [3].

The World Health Organization classification categorizes gastroenteropancreatic NETs into several groups: 1) well-differentiated NETs, 2) low-grade malignant carcinoma, 3) high-grade malignant carcinoma, and 4) mixed tumors (adenocarcinoma/neuroendocrine carcinoma) [4]. The prognosis of poorly differentiated NETs is poor [5]. Its survival time is known to be as short as 14.5 months.

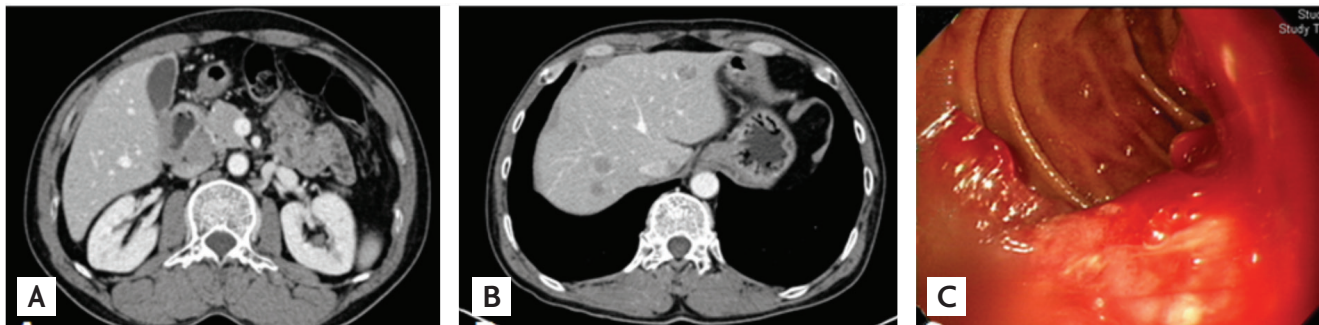
Despite this rareness, the patient in this case study had serial development of both a NET and adenocarcinoma in duodenum. Despite the poor prognosis of poorly differentiated metastatic NETs, the patient was cured by chemotherapy and remained tumor-free.

**CASE REPORT**

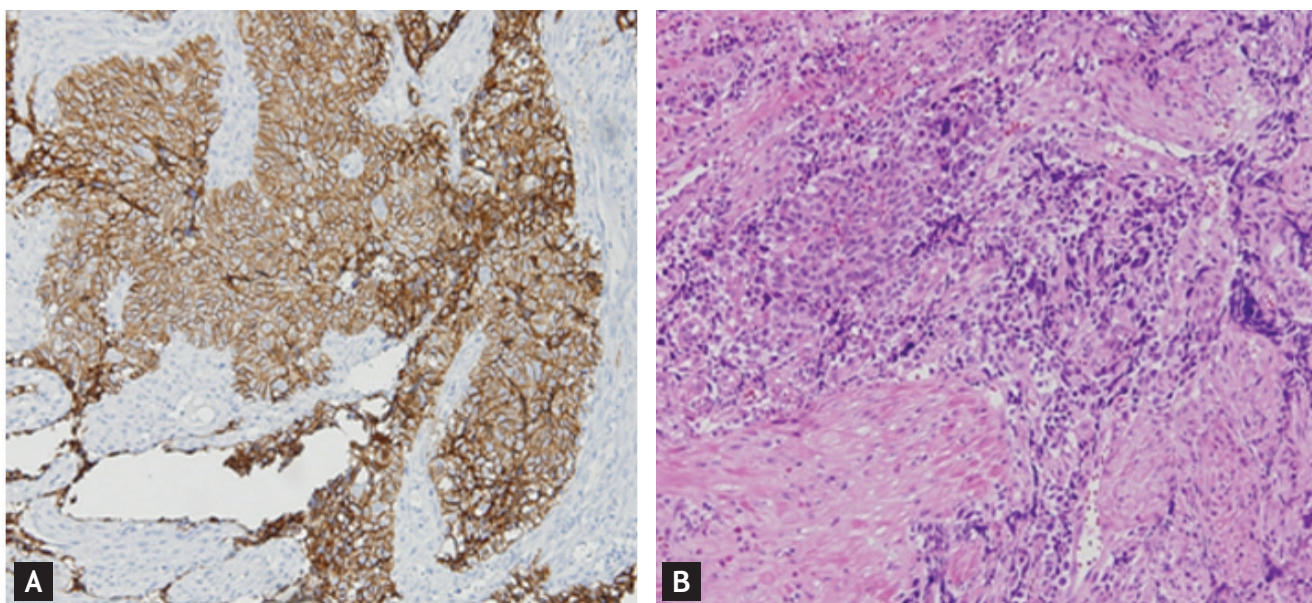
A 60-year-old male was admitted to the gastrointestinal medical clinic of Severance Hospital to undergo an operation for duodenal cancer.

The patient had developed renal tuberculosis 30 years previously, received medical treatment for several months, and was completely cured. In June 2009, he visited a local clinic after experiencing general weakness and melena over a period of 1 month, was diagnosed with duodenal cancer with multiple liver metastases (Fig. 1A and 1B), and was transferred to our hospital.

Esophagogastroduodenoscopy (EGD) (Fig. 1C) confirmed an ulcerofungating mass with poorly differentiated neuroendocrine carcinoma at the superior duodenal angle of the duodenum (Fig. 2A and 2B). Initial computed tomography (CT) showed multiple liver metastases. From November 2009 to January 2010, six cycles of palliative chemotherapy comprising 5-fluorouracil (5-FU) at 1,000 mg/m<sup>2</sup> (days 1 to 3), etoposide at 100 mg/m<sup>2</sup> (days 1 to 3), and cisplatin at 70 mg/m<sup>2</sup> (day 1) were performed. After these treatments, fludeoxyglucose uptake was no longer seen on positron emission tomography (PET)-CT. There was no remnant malignant lesion on EGD, and the patient had only patholog-



**Figure 1.** In June 2009, computed tomography (CT) and esophagogastroduodenoscopy revealed a duodenal tumor with liver metastasis. (A) CT findings: homogeneous, poorly enhanced wall thickening of the duodenum and a large, homogeneous, poorly enhanced node (2.6 cm) in the triangular area were found. (B) CT findings: innumerable homogeneously enhancing metastatic nodules in the liver were detected. (C) Endoscopic finding: ulcerofungating mass at the superior descending angle.



**Figure 2.** Pathology and immunohistochemistry findings. CD56 was positive (A, immunohistochemistry,  $\times 100$ ; B, H&E,  $\times 100$ ). The nuclei were vesicular and contained coarsely granular chromatin and prominent nucleoli. The tumor has infiltrated the submucosa: poorly differentiated neuroendocrine carcinoma.



ically confirmed chronic gastritis. Two more cycles of chemotherapy were performed. He was subsequently confirmed to have no evidence of disease in February 2010.

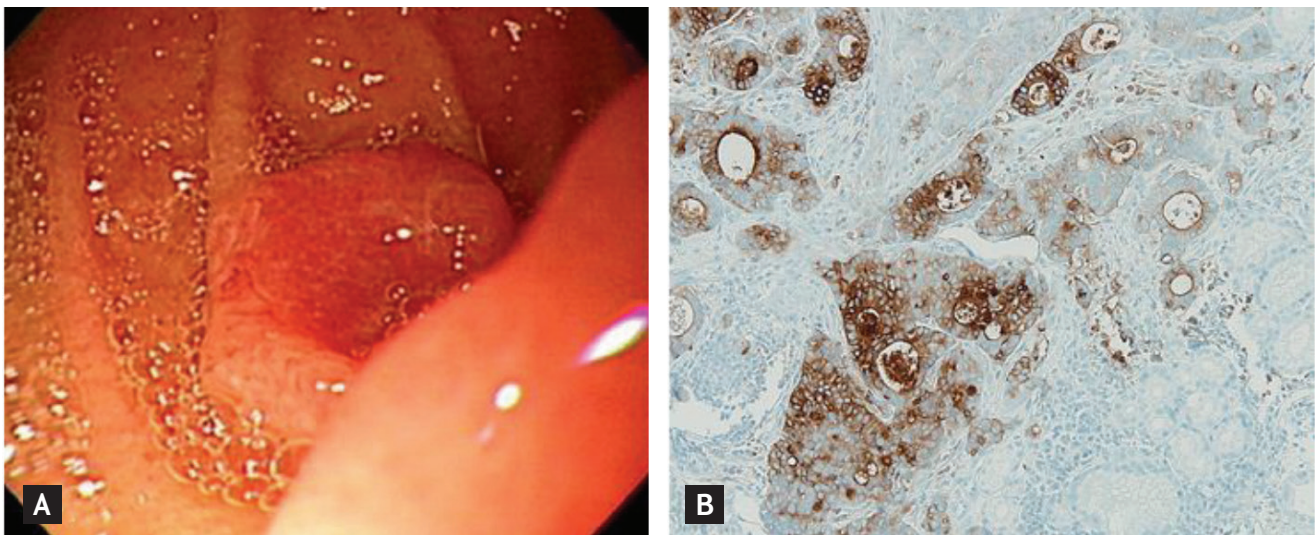
In June 2010, a polyp was detected in the former lesion site and was confirmed to be chronic inflammation by EGD biopsy. There were no abnormal findings on CT. In February 2011, a polyp was detected by EGD at the same site as that of the former polyp (Fig. 3A). This was pathologically confirmed to be adenocarcinoma by immunohistochemical staining. Chromogranin A and synaptophysin, which are neuroendocrine markers, were negative. Carcinoembryonic antigen (CEA), which is usually detected in cases of adenocarcinoma, was positive (Fig. 3B). The patient was admitted for an operation. Upon examination, his vital signs were normal. He reported no symptoms, and there was no palpable mass, organs, or tenderness in the abdomen. The results of a complete blood count were normal, as were the plasma levels of routine chemistry and tumor markers (CEA and CA 19-9). Magnetic resonance imaging (MRI) and PET-CT showed no abnormal findings at the site of the duodenal lesion, which was detected by EGD. However, there were suspicious metastatic lesions at segments 6/7 and segment 7 of the liver, so intraoperative radiofrequency ablation was planned and performed on 28 February 2011. The duodenal adenocarcinoma was not invading the mesentery. Pylorus-preserving pan-

creaticoduodenectomy was performed. A definite lesion was not found by intraoperative sonography, but a lesion was found attached to the right margin of the right hepatic vein on preoperative MRI. Thus, right posterior segmental curative resection of the liver was performed.

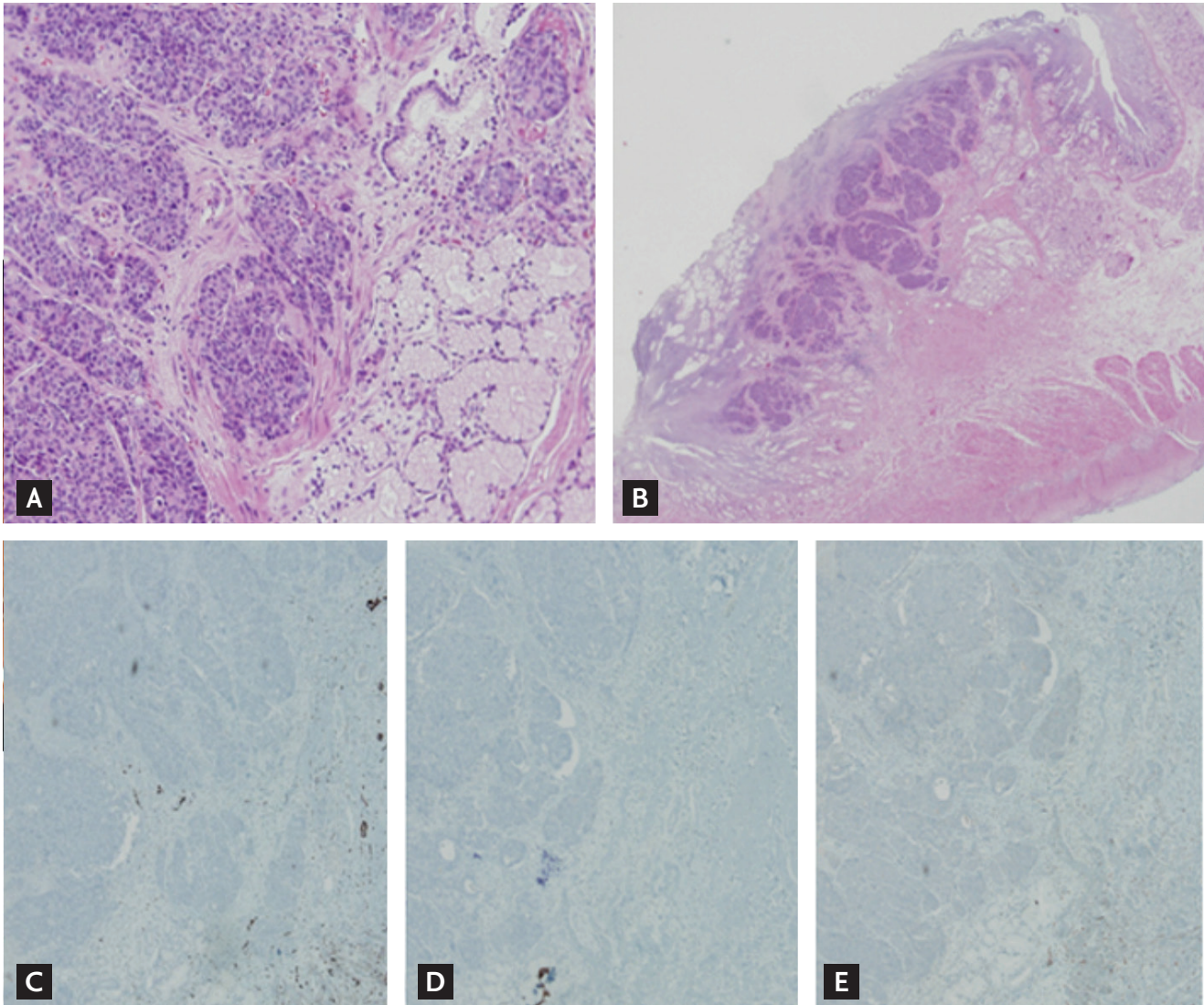
The surgical pathology results showed moderately differentiated duodenal adenocarcinoma at the site of the primary lesion, and mild nonspecific reactive hepatitis was confirmed in the liver via immunohistochemical staining (Fig. 4). At the site of the primary lesion, there were no neuroendocrine cells; only pure adenocarcinoma cells were present. Therefore, the final stage was T<sub>1</sub>N<sub>0</sub>M<sub>0</sub>, and the patient underwent no further adjuvant chemotherapy. The patient is undergoing follow-up in the outpatient department without recurrence.

## DISCUSSION

Therapeutically, patients with poorly differentiated metastatic neuroendocrine cancer are usually advised to undergo cytoreductive chemotherapy corresponding to the medical treatment of small cell carcinoma of the lungs [5,6]. Thus, the patient in this case study underwent eight cycles of palliative chemotherapy (5-FU/etoposide/cisplatin) to treat duodenal neuroendocrine carcinoma with poorly differentiated T<sub>x</sub>N<sub>x</sub>M<sub>1</sub>. Al-



**Figure 3.** (A) Endoscopic finding: duodenal polypoid mass at the superior descending angle. (B) Immunohistochemistry finding: carcinoembryonic antigen was positive (immunohistochemistry,  $\times 100$ ).



**Figure 4.** The tumor cells are arranged in a glandular pattern: adenocarcinoma, moderately differentiated (A, H&E,  $\times 100$ ; B, H&E,  $\times 12.5$ ). Immunohistochemistry findings: (C) CD56 was negative; (D) chromogranin A was negative; (E) synaptophysin was negative (C, D, E, immunohistochemistry,  $\times 40$ ).

though the cure rate is extremely poor, as mentioned above, the patient continued to show no evidence of disease for 1 year.

After 1 year without evidence of disease, moderately differentiated duodenal adenocarcinoma was identified and resected completely. An analysis of 491 cases claimed that the optimal treatment of small bowel adenocarcinoma continues to be complete resection, and periampullary and most proximal duodenal carcinomas require pancreaticoduodenectomy for curative resection [7]. Therefore, the patient in this case underwent pylorus-preserving pancreaticoduodenectomy.

Only inflammation was present in the liver pathology results, and a sufficient resection margin was confirmed during pathological examination of the duodenal adenocarcinoma with a low TNM stage (pT1NoMo). In stage I duodenal adenocarcinoma, which is completely resected, the median overall survival and 5-year overall survival rate are reportedly 136.5 months and 68.6%, respectively. There are currently no obvious benefits of adjuvant chemotherapy in terms of survival in early stage duodenal adenocarcinoma [8]. Hence, routine check-ups several months apart to monitor for recurrence have been adequate in this patient [9].



In conclusion, in the present case duodenal poorly differentiated neuroendocrine carcinoma was successfully cured with chemotherapy. Moreover, adenocarcinoma, the pathology of which is totally different, was found at the same site and was also cured surgically. This is a very rare case of successful management.

In other respects, it is possible that the duodenal neoplasm of this patient had both neuroendocrine and adenocarcinoma components initially. The presence of an exocrine component in gastrointestinal neuroendocrine neoplasms, especially in high-grade neuroendocrine carcinomas, has been widely documented. Therefore, if we assume that the duodenal neoplasm had a small adenocarcinoma component, the duodenal adenocarcinoma discovered later can be explained by the idea that the neuroendocrine component had disappeared secondary to chemotherapy and that only the adenocarcinoma component remained. However, the initial pathology assessment utilized only several small tissues obtained by EGD forceps. As a result, the presence and the proportion of the adenocarcinoma component in the initial duodenal neoplasm cannot be confirmed. Nevertheless, poorly differentiated multiple metastatic neuroendocrine cancers were treated, a pathologically complete response was obtained, and the remnant adenocarcinoma was resected completely. This case is very rare in this respect.

#### Conflict of interest

No potential conflict of interest relevant to this article is reported.

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