Case Reports in Gastroenterology

Case Rep Gastroenterol 2022;16:308–312
DOI: 10.1159/000524727
Received: February 21, 2022
Accepted: April 15, 2022
Published online: May 17, 2022

Single Case

Primary Duodenal Adenocarcinoma Expressing Carbonic Anhydrase IX

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Keywords
Duodenal adenocarcinoma · Texture and color enhancement imaging · Carbonic anhydrase IX

Abstract
Primary duodenal adenocarcinoma is a rare malignancy whose carbonic anhydrase IX (CA9) expression remains poorly understood. A 73-year-old man visited our hospital for a medical checkup. Transnasal endoscopy revealed a submucosal, tumor-like lesion with a central depression located in the descending part of the duodenum on white light imaging. On texture and color enhancement imaging mode 1, the lesion was highlighted as a reddish, elevated lesion with an irregular mucosa in its central depressed area. Pancreaticoduodenectomy was performed on the suspicion of duodenal adenocarcinoma for biopsy and endoscopic diagnosis, which led to the lesion being diagnosed as tubular adenocarcinoma, pT1b (SM). Immunohistological staining revealed an adenocarcinomatous component positive for CA9, as well as a normal duodenal mucosa. To our knowledge, this report is among the first to describe CA9-expressing primary duodenal adenocarcinoma.

Introduction

Primary duodenal adenocarcinoma is a rare malignancy that accounts for about 20–25% of small intestine cancers, which, in turn, accounts for 5% of all alimentary tract tumors [1]. Carbonic anhydrase IX (CA9) is a stable transmembrane zinc metalloenzyme and plays an important role in the growth and survival of tumor cells under hypoxia [2, 3]. CA9 has been

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reported to be expressed in the normal epithelium of the stomach, duodenum, and jejunum [4], as well as in various cancers such as head and neck, gastric, rectum, breast, and ovarian cancers [5]. Therefore, CA9 appears to represent a promising target that interferes with tumor pH regulation and energy metabolism [6], while CA9 expression in duodenal adenocarcinomas remains poorly elucidated. We herein report a case of primary duodenal adenocarcinoma expressing CA9.

Case Report/Case Presentation

A 73-year-old man visited our hospital for a medical checkup. Transnasal endoscopy (GIF-1,200 N with the EVIS X1 video system; Olympus Medical Systems, Tokyo, Japan) revealed a submucosal, tumor-like lesion with a central depression located in the descending part of the duodenum on white light imaging (Fig. 1a). On texture and color enhancement imaging (TXI) mode 1, the lesion was highlighted as a reddish, elevated lesion with an irregular mucosa in its central depressed area (Fig. 1b).

Pancreaticoduodenectomy was performed on the suspicion of duodenal adenocarcinoma for biopsy and endoscopic diagnosis. Histological examination showed the lesion to be tubular adenocarcinoma, 12 × 11 mm, pT1b (SM, 2,000 μm), INFb, ly0, v0, pN0, pPM0, pDM0, pRM0 (Fig. 2). Immunohistological staining revealed an adenocarcinomatous component positive for MUC6 (Fig. 3a) and CA9 (Fig. 3b, c) and negative for MUC2, MUC5AC, and CD10. The level of CA9 expression in the lesion was comparable to that in the normal duodenal mucosa (Fig. 3b).

Discussion/Conclusion

Our case has two important clinical implications. First, CA9 may hold promise as a potential marker for duodenal cancer. Primary duodenal adenocarcinoma is rare, and its CA9 expression remains poorly elucidated in the literature.

To date, two studies of CA9-expressing duodenal adenocarcinomas have been reported [5, 7]. In one study, CA9 was shown to be not only expressed in 36% (63/175) of all small

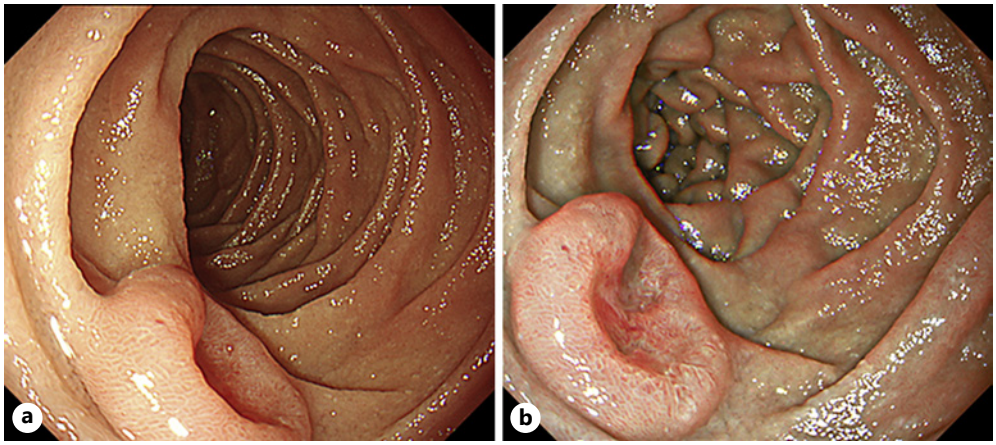

Fig. 1. Transnasal endoscopy. Transnasal endoscopy revealed a submucosal, tumor-like lesion with a central depression located in the descending part of the duodenum on WLI (**a**). On TXI mode 1, the lesion was highlighted as a reddish, elevated lesion with an irregular mucosa in its central depressed area (**b**). WLI, white light imaging.

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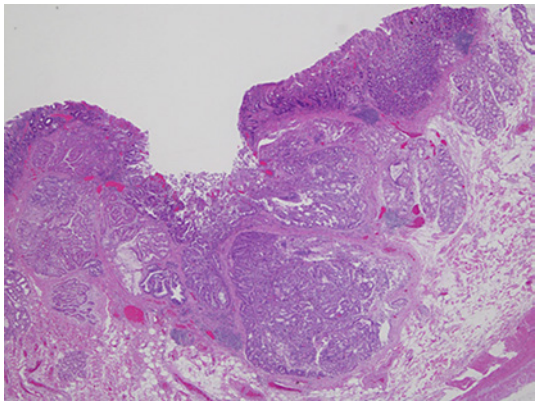

Fig. 2. A histopathologic examination of the resected specimen. Histological examination showed the lesion to be tubular adenocarcinoma, 12 × 11 mm, pT1b (SM, 2,000 μm) (magnification, ×20).

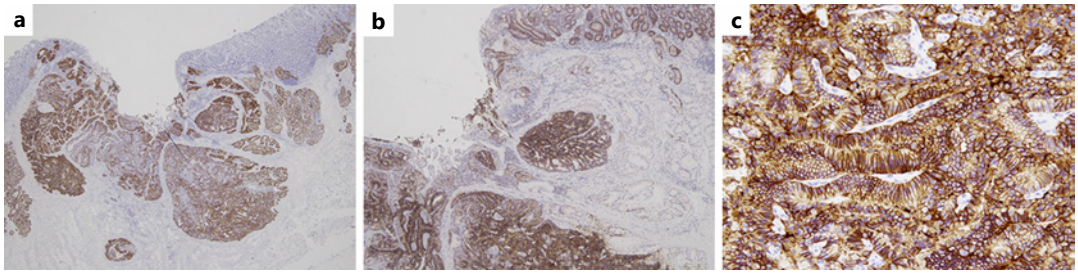

Fig. 3. Immunohistological staining of the resected specimen. Immunohistological staining revealed an adenocarcinomatous component positive for MUC6 (magnification, ×20) (**a**) and CA9 (magnification, ×40) (**b**) and (magnification, ×200) (**c**). The level of CA9 expression in the lesion was comparable to that in the normal duodenal mucosa (**b**).

intestine cancers evaluated (n = 175) including duodenal cancers (n = 95) but significantly more highly expressed in well- and moderately differentiated tumors than in poorly differentiated tumors, tumors with no lymph node metastasis, and low-stage carcinomas. In addition, tumors with CA9 overexpression were shown to be associated with better overall survival than those with no or weak CA9 expression [7]. In the other, CA9 was shown to be expressed in 70% of all duodenal adenocarcinomas evaluated, with the level of its expression shown to be comparable to that in normal duodenal crypts. Furthermore, CA9 overexpression tended to be associated with the absence of regional lymph node metastasis [5]. In the present case, the duodenal adenocarcinoma was shown to be well differentiated and localized with no lymph node metastasis, with the level of CA9 expression being comparable to that in the normal duodenal mucosa. These findings are consistent with the previous reports, suggesting that CA9 may be a good prognostic marker for primary duodenal carcinoma.

Given that studies have recently been conducted to evaluate CA9 expression in blood samples as a potential diagnostic marker for renal cell carcinoma [8] and breast cancer [9] with promising results, CA9 expression in blood samples may have potential as a diagnostic marker for primary duodenal carcinoma as well.

The second important issue that emerged in our case was that TXI proved useful for visualizing the irregular mucosa in the central depressed area of the lesion. TXI is an image-enhanced endoscopy that enhances brightness, surface irregularities, and subtle color changes [10]. The endoscopic feature of this case was a submucosal, tumor-like appearance with a central depression. Takinami et al. [11] reported that a submucosal, tumor-like appearance should be considered to represent submucosal invasion. In addition, it is speculated that the etiology

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of the central depression may be accounted for by the invasion of tumors resulting from de novo cancer into the submucosa [12], given that the depth of tumor infiltration was SM 2,000 μm in this case, consistent with the reports referred to above. TXI facilitated the endoscopic diagnosis of submucosal invasive primary duodenal adenocarcinoma even with transnasal endoscopy, highlighting the irregular mucosa in the central depressed area of the lesion. In conclusion, the pathological features and endoscopic imaging findings offered here should provide a clear presentation of the case and serve as a benchmark for future studies.

Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of National Hospital Organization Hakodate National Hospital (approval number: AP0000659784). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose in association with this study.

Funding Sources

The authors received no funding for this research.

Author Contributions

Kimitoshi Kubo reported the case and wrote the manuscript. Kimitoshi Kubo, Ryosuke Watanabe, Masayuki Higashino, and Mototsugu Kato were involved in this study as physicians treating the patient, and Noriko Mimura was responsible for the histopathological analysis of the surgical specimens. All authors declare that they contributed to the preparation of the manuscript at all stages and that they have read and approved the final version of the manuscript for publication.

Data Availability Statement

All data generated and/or analyzed during the course of this study are included in the article. Any further query may be addressed to the corresponding author.

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