

Oncology

Gastric neuroendocrine carcinoma with positive staining for prostate cancer markers including prostate-specific antigen and alpha-methylacyl-CoA racemase

Yuji Hakozaki^{a,*}, Taro Murata^a, Munehiro Yokoyama^b, Hisashi Matsushima^a, Maki Ogawa^b, Tomoko Masuda^a, Yoko Hirai^a, Haruki Kume^c

^a Department of Urology, Tokyo Metropolitan Police Hospital, Tokyo, Japan

^b Department of Pathology, Tokyo Metropolitan Police Hospital, Tokyo, Japan

^c Department of Urology, The University of Tokyo Graduate School of Medicine, Tokyo, Japan

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ABSTRACT

We report a case with prostate cancer and gastric neuroendocrine carcinoma. A 72-year old male presented with a gastric lesion 5 months after radical prostatectomy. The lesion was immunohistochemically positive for PSA, alpha-methylacyl-CoA racemase, synaptophysin, and chromogranin A, but negative for androgen receptor (AR). Differentiating gastric neuroendocrine carcinoma from gastric metastasis of prostate cancer is difficult, as both lesions exhibit similar acinar cell proliferation with prominent nucleoli.¹ We discuss the diagnostic process of this case and how AR was a useful specific marker for diagnosing primary gastric neuroendocrine carcinoma.

Introduction

The metastasis of prostate cancer to the gastrointestinal tract has previously been reported only in a few papers.^{1–3} We present a case in which a gastric lesion following radical prostatectomy showed positive immunohistochemical staining for prostate-specific antigen (PSA) and alpha-methylacyl-CoA racemase (AMACR). This suggested that the gastric lesion was a metastasis of prostate cancer. However, a solitary gastric metastasis arising from prostate cancer has not previously been reported. Additional immunohistochemical tests revealed positivity for synaptophysin and chromogranin A. Therefore, this patient was suspected of having either a gastric metastasis from prostate cancer or a primary gastric neuroendocrine carcinoma. We describe the differential diagnosis of these carcinomas.

Case presentation

A 72-year-old man underwent an examination for prostate cancer at our institution in May 2015. His serum PSA value was 7.61 ng/ml. Pelvic magnetic resonance imaging revealed a suspected prostate cancer lesion. A prostate biopsy in July 2015 revealed adenocarcinoma

with a Gleason score of 8 (4 + 4) from 2 cores. Whole body computed tomography (CT) and technetium bone scintigraphy showed no metastasis. We performed radical prostatectomy along with pelvic lymphadenectomy in October 2015. Histopathological examination revealed 3 foci of adenocarcinoma up to 6 mm in diameter and a Gleason pattern of 3 + 4 (Fig. 1a). Immunohistochemical staining was performed using HISTOFINE (Nichirei Biosciences, Tokyo, Japan). The immunohistochemical result showed positive staining for AMACR (Dako, Rabbit Anti-Human AMACR, EPMU1), PSA (Dako, Rabbit Anti-Human PSA, 35H9) and androgen receptor (AR) (Nichirei, Mouse Anti-Human AR, AR441) (Fig. 1b–d). There was no small cell component or lymphovascular invasion.

The patient received a medical checkup in March 2016, in which a barium swallow test showed a filling defect of the stomach. Gastroscopy showed a protruding area in the gastric body (Fig. 2a). The biopsied tissue was composed of acinar adenocarcinoma (Fig. 2b), and additional immunohistochemistry showed positive staining for AMACR and PSA (Fig. 2c and d) and negative staining for androgen receptor (AR).

The PSA value was 0.07 ng/ml at the time of gastroscopic detection of the lesion. There was no lymph node enlargement or any visceral metastasis on CT of the chest, abdomen and pelvis. After androgen

Abbreviations: PSA, prostate specific antigen; AMACR, alpha-methylacyl-CoA racemase; AR, androgen receptor; CT, computed tomography

* Corresponding author. Department of Urology, Tokyo Metropolitan Police Hospital, 4-22-1 Nakano, Nakano-ku, Tokyo, 164-0001, Japan.

E-mail addresses: yhakozaki11012@gmail.com (Y. Hakozaki), muratat-ky@umin.ac.jp (T. Murata), muneyoko@mrh.biglobe.ne.jp (M. Yokoyama), hmatsu53@me.com (H. Matsushima), heavens_door@alpha.ocn.ne.jp (M. Ogawa), t.masuda@keisatsubyoin.or.jp (T. Masuda), youko.11371423@gmail.com (Y. Hirai), kumeh-uro@h.u-tokyo.ac.jp (H. Kume).

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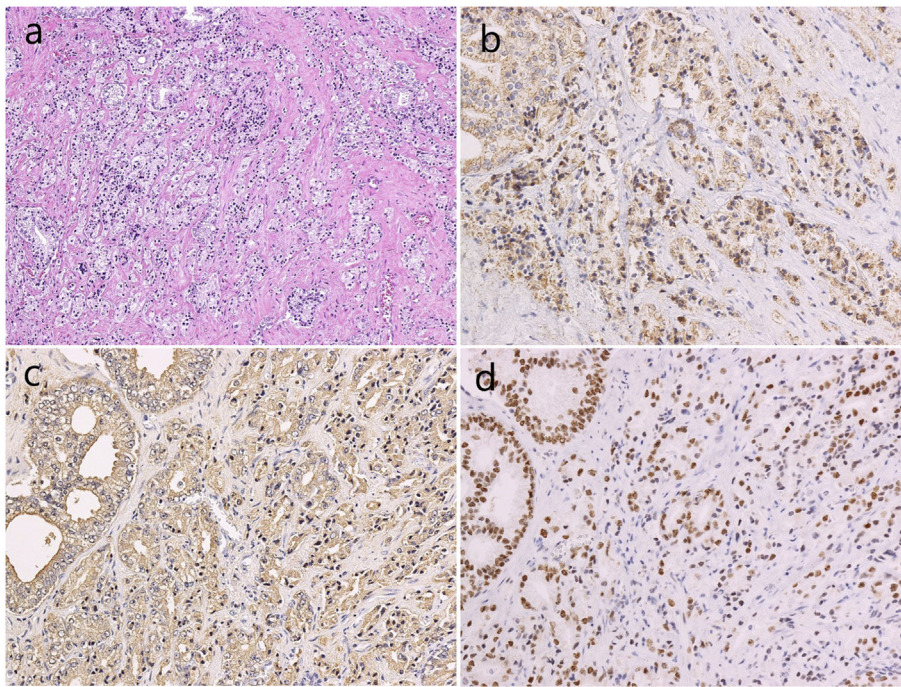


Fig. 1. (a) The histology of radical prostatectomy was Gleason's grade 3 + 4 (hematoxylin-eosin stain). (b) all neoplastic cells were diffusely positive for alpha-methylacyl-CoA racemase (AMACR) (immunohistochemical stain for AMACR). (c) all neoplastic cells were positive for prostate specific antigen (PSA) (immunohistochemical stain for PSA). (d) all neoplastic cells were positive for androgen receptor (AR) (immunohistochemical stain for AR).

deprivation therapy, the PSA level declined to 0.01 ng/ml in June 2016.

The patient received distal gastrectomy in July 2016. A tumor 5 cm in diameter was found in the gastric body. Pathological examination confirmed an adenocarcinoma with a number of vessels invading the submucosa. Microscopic examination showed vascular invasion that had spread through the muscularis propria. Immunohistopathology revealed positivity for AMACR, PSA, synaptophysin (Nichirei Biosciences, Mouse Anti-Human synaptophysin, 27G12), and chromogranin A (Nichirei Biosciences, Rabbit Anti-Human chromogranin A, Code No.412751) but negativity for AR (Fig. 2e and f). Comparison of immunostaining markers is shown in Table 1 between a gastric lesion and resected prostate cancer. A follow-up CT after surgery revealed multiple metastatic lesions in the liver in April 2017. The patient was given oral daily doses of 30 mg sandostatin. CT showed growing liver tumors in June 2017. The patient continued to receive androgen deprivation therapy until August 2017 when he exhibited a consistently low PSA level of 0.01 ng/ml.

Discussion

In this case, negative staining for AR, a specific marker for prostate cancer, was a useful marker, and considering the clinical course, it was necessary for our diagnosis.

AR has been reported to be 95% sensitive for prostate carcinomas.¹ PSA and AMACR are also known as specific markers for prostate tumors, and Dennis et al. advised that PSA staining should be performed first to rule out prostate cancer when diagnosing metastatic adenocarcinoma of unknown origin because of its high specificity.² However, positive staining for PSA and AMACR alone cannot lead to a conclusive diagnosis because the specificities of these markers are limited. Anenkov et al. reported that AMACR staining was positive in 46 of the 51 neuroendocrine carcinomas of the stomach that they investigated,³ and 3% of gastric cancers in their study were positive for PSA staining.⁴ Considering these reports, gastric neuroendocrine carcinomas may show positive staining for PSA and AMACR.

The clinical course of this case was inconsistent with gastric metastasis for two primary reasons. First, there was no finding of high-risk cancer in our histopathological examination of the radical prostatectomy. Gastric metastasis often arises from high-risk prostate

cancer.^{4,5} The initial PSA level was 7.61 ng/ml and the Gleason score of the prostatectomy was 3 + 4. Bilici et al. reported a gastric metastasis arising from a prostate tumor with a Gleason score of 3 + 4,⁵ but the PSA level was 244.8 ng/ml before treatment. Other reports showed gastric metastasis arising from a prostate tumor that had a Gleason score of 5 or ductal adenocarcinomas,⁴ and PSA levels were above 1000 ng/ml. Second, no metastatic lesion was detected in our patient at the time of gastroscopic detection of the lesion. In general, prostate cancers metastasize to the bones or lymph nodes; visceral metastases such as those to the liver, brain, and lungs occur in advanced cases. Gastric metastasis is followed by other metastatic lesions.^{4,5} However, in this case we only found a gastric lesion, and CT and bone scintigraphy did not reveal any metastatic lesions. To the best of our knowledge, a solitary gastric metastasis arising from a prostate tumor has not been reported to date.

It is difficult to differentiate a gastric neuroendocrine carcinoma from a gastric metastasis of prostate cancer, as both such lesions have similar acinar cell proliferations and prominent nucleoli.³ However, treatment options for these two cancers are entirely different and it is important to diagnose these cancers at an early stage. A comprehensive approach that incorporates immunohistochemical findings and aspects of the clinical course is necessary to diagnose these cancers.

Conclusion

To differentiate neuroendocrine carcinomas from gastric metastases of prostate cancers, it is necessary to evaluate immunohistochemical findings and aspects of the clinical course. Additionally, the specificities of markers should be considered carefully.

Consent

The patient provided informed consent. This study was approved by the institutional review board.

Conflicts of interest

None.

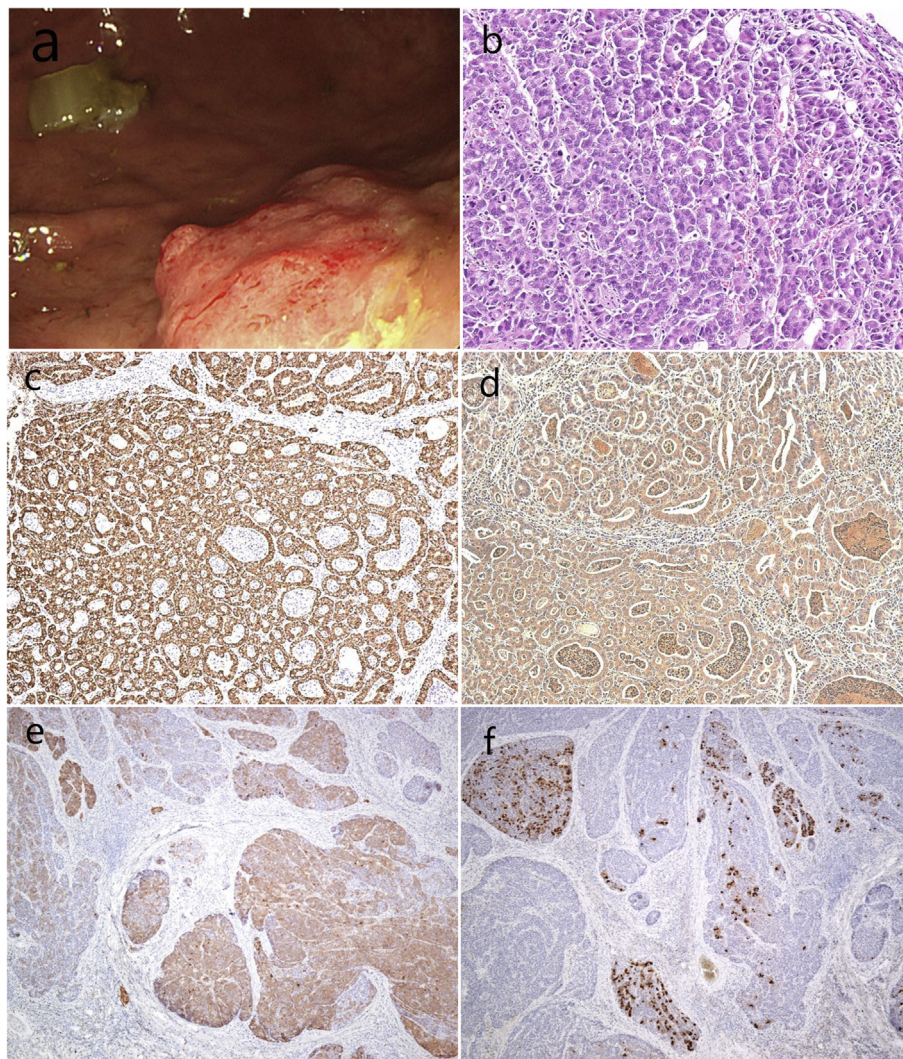


Fig. 2. (a) The protruding lesion in the gastric body observed on endoscopy. (b) Acinar cell proliferation was seen (hematoxylin-eosin stain) (c) Nearly all neoplastic cells were diffusely positive for alpha-methylacyl-CoA racemase (AMACR) (immunohistochemical stain for AMACR). (d) Most of the neoplastic cells were positive for prostate specific antigen (PSA) (immunohistochemical stain for PSA). (e) Almost all neoplastic cells were diffusely positive for synaptophysin (immunohistochemical stain for synaptophysin). (f) Areas of the neoplastic cells were positive for chromogranin A (immunohistochemical stain for chromogranin A).

Table 1
Comparison of immunostaining markers between a gastric lesion and resected prostate cancer.

	Gastric lesion	Resected prostate cancer
AR	Negative	Positive
PSA	Positive	Positive
AMACR	Positive	Positive
Synaptophysin	Positive	Negative
Chromogranin A	Positive	Negative

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