Pancreatic metastasis from locally recurrent neuroendocrine differentiated prostate cancer after radical prostatectomy

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ARTICLE INFO

Keywords:
Androgen deprivation therapy
Chemoradiotherapy
Neuroendocrine differentiated prostate cancer
Pancreatic metastasis

ABSTRACT

Pancreatic metastasis from prostate cancer (PC) is quite rare. Herein, we report the case of a 67-year-old man with pancreatic metastasis from a neuroendocrine differentiated PC (NEDPC), a local recurrence after radical prostatectomy and androgen deprivation therapy for 6 years. Chemoradiotherapy was initiated for the locally recurrent NEDPC, and it had almost disappeared after the therapy. However, rapidly enlarged pancreatic metastasis from the NEDPC was detected 6 months after therapy. There is no standard treatment available for pancreatic metastasis from NEDPC owing to its rarity; hence, further knowledge and clinical experience regarding it are crucial.

Introduction

Metastatic tumors in the pancreas account for only a small percentage of all pancreatic tumors. Prostate cancer (PC) frequently metastasizes to the bone, lung, or lymph nodes; however, pancreatic metastasis from PC rarely occurs. 1,2 Although pancreatic metastasis from hormone-naive PC can be treated by androgen deprivation therapy (ADT), there is no standard treatment for it from castration-resistant PC, including neuroendocrine differentiated PC (NEDPC). Herein, we report a case of pancreatic metastasis from NEDPC, which was a local recurrence after radical prostatectomy (RP) that developed from an adenocarcinoma following 6 years of treatment with ADT.

Case presentation

A 67-year-old man was referred to our department because of a retroperitoneal mass that had developed between his bladder and rectum and was detected by computed tomography (CT) (Fig. 1 A). PC [adenocarcinoma, pT3aN0M0, Gleason score 4 + 5, initial prostate-specific antigen (PSA) 14.5 ng/mL] had been previously diagnosed and he had undergone RP 8 years before the visit. ADT treatment was started 2 years after the RP because his serum PSA level had increased to 0.4 ng/mL. Periodic CT was annually performed, and the tumor was detected without subjective symptoms. During the visit, his serum PSA and neuron-specific enolase (NSE) levels were <0.01 ng/mL and 15.5 ng/mL (normal limit, <16.3 ng/mL), respectively. Transrectal needle biopsy was performed, and histopathological findings revealed neuroendocrine carcinoma (Fig. 1B–E). Because endoscopy did not reveal any gastrointestinal malignancies, the tumor was diagnosed as a locally recurrent NEDPC without metastasis. The patient received chemoradiotherapy [chemotherapy, three cycles of cisplatin + etoposide; intensity-modulated radiation therapy (IMRT), 54 Gy]. His tumor almost disappeared, and his serum NSE level decreased after the therapy (Fig. 1F). However, 6 months after treatment, he presented with upper abdominal pain; a rapidly enlarged tumor that obstructed the main pancreatic duct and common bile duct was revealed by CT exam (Fig. 2A and B). Endoscopic ultrasound-guided fine needle aspiration (EUS-guided FNA) was performed, and the pancreatic tumor was diagnosed as NEDPC metastasis (Fig. 2C–F). He received EUS-guided biliary drainage tube placement and radiotherapy [IMRT, 46.8 Gy] for the pancreatic metastasis, and the radiation was effective. However, multiple liver metastases were revealed at the end of the radiation therapy, and the patient died 3 months later (Fig. 3). His serum NSE level was 219.0 ng/mL at his death, but his serum PSA level remained <0.01 ng/mL under

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Abbreviations: ADT, androgen deprivation therapy; CT, computed tomography; EUS-guided FNA, Endoscopic ultrasound-guided fine needle aspiration; IMRT, intensity-modulated radiation therapy; NEDPC, neuroendocrine differentiated prostate cancer; NSE, neuron-specific enolase; RP, radical prostatectomy; PC, prostate cancer; PSA, prostate-specific antigen.

https://doi.org/10.1016/j.eucr.2020.101155
Received 22 February 2020; Accepted 16 March 2020
Available online 2 April 2020
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ADT throughout the clinical course.

Discussion

The pancreas is a rare site for metastasis from PC. Two previously performed autopsy studies suggested that <2% of patients with PC have pancreatic metastasis. Clinical reports on pancreatic metastasis from PC are quite rare, and <10 case reports are available in the literature. According to those reports, PC is likely to metastasize to the pancreas in the late stage of progression and the metastasis to the pancreatic head was thought as retroperitoneal lymphatic dissemination. Compared with several decades ago, the prognosis of patients with PC has now improved owing to several new drug treatments. Therefore, the frequency of pancreatic metastasis from PC may increase in the clinical setting because of the increasing long-term survival of patients with PC. To the best of our knowledge, this is the first report that clearly demonstrates pancreatic metastasis of NEDPC by histopathology.

NEDPC can be induced by long-term ADT and is considered a mechanism of castration resistance in PC. NEDPC is strongly resistant to conventional drug treatments, and metastatic NEDPC is life-threatening even today. Radiation therapy could improve the prognosis of patients with NEDPC if the NEDPC is detected as a localized disease. Actually, in
In the present study, radiation therapy was effective in the treatment of both NEDPC masses; unfortunately, the chemotherapy could not prevent the metastasis. Therefore, detecting NEDPC in the early stage is essential, but it remains a difficult task. The measurement of serum NSE level, a general neuroendocrine marker, can help detect NEDPC and can reflect the progression of the disease. However, in our study, the sensitivity and specificity of the serum NSE level were insufficient for the early detection of NEDPC. Positron emission tomography–CT is considered as an effective method for detecting NEDPC with or without metastasis; however, its frequent use may be impractical. It should be noted that the serum PSA level did not indicate the presence of the NEDPC or its progression in the current case.

To identify whether a pancreatic tumor is malignant and to select the subsequent treatment, primary tumors should be differentiated from secondary tumors. For typical differentiation, imaging examinations should be performed; however, differentiations based only on such examinations are often difficult. EUS-guided FNA is an invasive yet effective method, but this procedure cannot be performed in every hospital. The prognosis of patients with pancreatic metastasis from a malignancy in other organs depends on the type of the original cancer and the surgical resection characteristics of the metastasis. Till date, the prognosis of malignant pancreatic tumors, including metastatic ones, remains poor.

**Conclusion**

Pancreatic metastasis rarely occurs from PC and can be life-threatening if associated with NEDPC. There is no standard treatment for the disease owing to its rarity. Because its incidence might increase in the clinical setting, further knowledge and clinical experience regarding pancreatic metastasis from NEDPC are crucial.

**Consent**

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

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Declaration of competing interest**

None.

**Acknowledgments**

The authors would like to thank Enago (www.enago.jp) for the English language review. I would like to show my greatest appreciation to Dr. Kazuya Takahashi and Dr. Yukio Aruga, gastroenterologists, for their clinical supports.

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