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Case Report

A Case of Advanced Submandibular Gland Cancer in Which Increased Prostate-Specific Antigen and Multiple Bone Metastases Wrongly Suggested Concurrent Prostate Cancer

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Keywords
Advanced submandibular gland cancer · Increased prostate-specific antigen · Multiple bone metastases · Misleading signs · Concurrent prostate cancer

Abstract
A 73-year-old man, followed for prostatic hyperplasia, developed submandibular gland cancer. Initially, because of the concurrent presence of elevated serum prostate-specific antigen (PSA) and multiple bone metastases, he was clinically determined as having stage IV prostate cancer in addition to stage II submandibular gland cancer, and radical surgery for his submandibular gland cancer was performed first. However, subsequent detailed examinations of the prostate gland showed no prostate cancer, and a diagnosis of advanced submandibular gland cancer with increased PSA and multiple bone metastases was established. Serum PSA is highly specific for prostate diseases and is widely used as a tumor marker of prostate can-

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cer. However, clinicians should be aware that, in patients with non-prostate cancer, the detection of increased PSA and multiple bone metastases does not necessarily indicate the concurrent presence of prostate cancer.

Introduction

Serum prostate-specific antigen (PSA), a single-chain glycoprotein with a molecular weight of 30 kDa, is a serine protease highly specific for prostate diseases, and widely used as a tumor marker of prostate cancer [1]. PSA is also known to rarely increase in patients with cancers other than prostate cancer, although several case reports have been published [2–5]. This report describes our recent experience with a case of advanced submandibular gland cancer in which increased PSA and multiple bone metastases were misleading and impaired accurate staging and prompt initiation of chemotherapy.

Case Report

Our patient was a 73-year-old man with an Eastern Cooperative Oncology Group (ECOG) performance status of 2, being followed for prostatic hyperplasia at another hospital as an outpatient since 2009. Around January 2017, he began having a progressive swelling from the right side of the jaw to the neck and, therefore, visited the other hospital. Right cervical lymph node fine-needle aspiration cytology revealed class V, while CT demonstrated right submaxillary gland swelling and right cervical lymph node swelling, leading to a diagnosis of right submandibular gland cancer with right cervical lymph node metastases. Around this time, the patient's serum PSA had also increased from 7 to 30 ng/mL, based on which concurrent prostate cancer was suspected. Bone scintigraphy showed multiple vertebral body metastases and bilateral iliac bone metastases, for which multiple bone metastases from prostate cancer were considered at the other hospital. His right submandibular gland cancer was clinically assessed as stage II, and radical surgery was performed.

Subsequently in May 2017, the patient was referred to our hospital for a definite diagnosis and treatment of prostate cancer, in the context of complication by submandibular gland cancer. On CT performed at our hospital, the multiple bone metastases showed osteolytic changes. An MRI of the prostate gland detected no apparent abnormalities. Prostate biopsy showed no findings of malignancy. On the basis of these findings, prostate cancer and multiple bone metastases from prostate cancer could be ruled out. On the other hand, tissue specimens from the submaxillary gland showed findings of submaxillary duct carcinoma (salivary duct carcinoma; SDC), and immunostaining revealed CK7(+), CK20(–), androgen receptor(+), GCDFP-15(+), and PSA(+) (Fig. 1). On the basis of these findings, although postoperatively, the patient's SDC was re-staged as pT2N3M1 stage IV, with the presence of multiple cervical lymph node metastases and multiple bone metastases.

Thereafter, chemotherapy for advanced submandibular gland cancer was initiated. After 2 cycles of chemotherapy consisting of carboplatin + fluorouracil + cetuximab, his serum PSA level showed an obvious decreasing trend (from 30.5 to 6.0 ng/mL), supporting that the serum PSA levels in this case derived from SDC.

Discussion

In the present case, the increased PSA with multiple bone metastases were misleading, and impaired accurate staging of SDC and prompt initiation of chemotherapy for SDC. In fact, possible metastasis of prostate cancer to the submaxillary gland was also considered in the present case, on the basis of the increased serum PSA and the positive immunostaining of submaxillary gland tissue for PSA.

To date, pathological similarity has been described between SDC and prostate cancer or breast cancer [6]. Specific similarities are that (1) hematoxylin and eosin (HE) staining of the ductal lumens shows the characteristic findings of both comedo necrosis and cribriform pattern; (2) tumor cells do not show a keratinizing tendency or intercellular bridge; and (3) mucus staining (with mucicarmine alcian blue) shows no evidence of mucus production in the cytoplasm. However, Fan et al. [7] reported that immunostaining of SDC was positive for PSA in 2 of 13 cases. In addition, rare cases of increased serum PSA in association with extrapulmonary small cell carcinoma, renal cell carcinoma, lung adenocarcinoma, or periurethral gland carcinoma have been reported [2–5]. Also, SDC can be HER2-positive, though negative in the present case; and in the treatment of patients with HER2-positive SDC, add-on trastuzumab to a taxane anticancer agent has been reported to prolong survival, compared with taxane monotherapy [8, 9]. Given that stage IV submandibular gland cancer is a highly aggressive malignancy, with a 3-year survival rate of only 23% [10], a definite diagnosis should be made accurately to promptly initiate appropriate systemic chemotherapy.

In conclusion, clinicians should be aware that, in patients with non-prostate cancer, the detection of increased PSA and multiple bone metastases does not necessarily indicate the concurrent presence of prostate cancer.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that they have no relevant financial interests.

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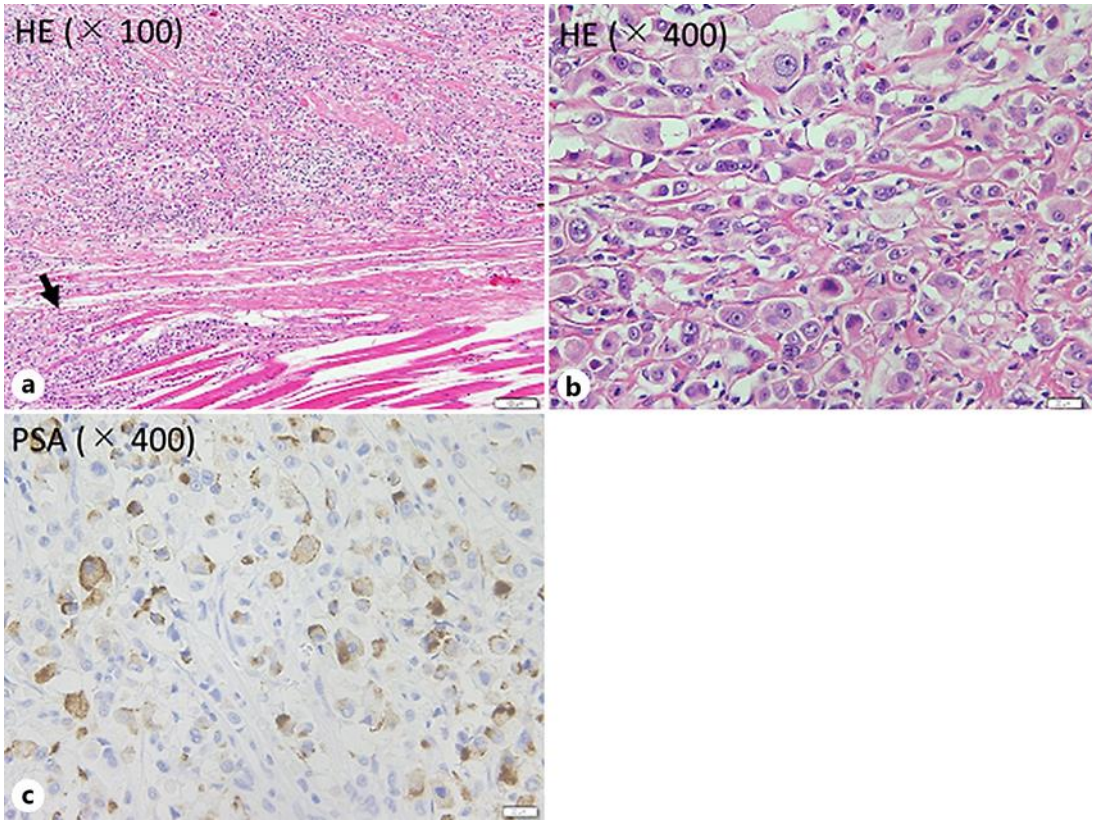

Fig. 1. Histological findings of salivary duct carcinoma. **a** H&E staining of submaxillary gland duct carcinoma (×100). Cancer cells grow to solidity and invade striated muscles (arrow). **b** Circular or irregular nucleus with clear nucleoli, and cells with abundant basic cell grow to solidity. These are rich in color, such as large nuclei and polyhedral cells, and oncocyte-like cells also mix (×400). **c** Immunostaining for PSA shows the focal presence of PSA-positive cells (×400).