

Skip Metastase on the Left Neck Lymph Nodes of the Prostatic Adenocarcinoma with Neuroendocrine Differentiation and Accompanying Thyroid Micropapillary Carcinoma

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Received: 2 March 2008 / Accepted: 5 March 2008 / Published online: 2 April 2008
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Abstract We discuss here the thyroid micropapillary carcinoma that was detected incidentally when investigating the primary focus of the left neck multiple lymph node metastases occurring 8 months later in a patient of ours, whose pathological examination of radical prostatectomy and bilateral inguinal lymph node dissection was reported to be pT3N0 and whole body scanning for metastases, was negative.

Keywords Prostate neuroendocrine adenocarcinoma · Skip metastase · Thyroid papillary carcinoma

Introduction

Prostate cancer takes the second place among causes of cancer related deaths in males after lung cancer in US [1]. Prostate cancer makes metastases on the regional lymph nodes most frequently, and bones, lungs, bladder, liver and adrenal glands follow with the same order [2].

Case Report

The patient presenting with symptoms of pollacuria, nocturia, and decrease in erection performance is 52 years of age, married with two children, and there is nothing notable in the family history. Tumoral structures were found consisting of more than 50% of the six specimens of the TRUS+Bx that was performed upon finding the prostate (++) in DRE, PSA 16.8 and 16.4. Pathology was came as gleason 3+2 adeno Ca. Right nerve-sparing radical prostatectomy and bilateral inguinal lymph node dissection was performed on the patient that whole body scanning studies were negative. He was discharged on the postoperative day 20 with no symptoms.

Prostatectomy material was 66 g in weight and $7.5 \times 5 \times 4.5$ cm in size, and a solid nodule of yellow color with a diameter of 2.5 cm localized in the left basal region was observed in the macroscopic examination. Following the routine paraffin follow-up, tumor was observed in the microscopic examination in an adenoid and cribriform pattern formed by cells with marked hyperchromatic nucleoli and with many mitotic figures (Fig. 1a; Gleason score: 3+4=7/10). Widespread perineural invasion and involvement of the capsule was noted. Total 16 reactive non-neoplastic lymph nodes were picked from the bilateral inguinal lymph node dissection material. The case was considered to be PT3 pN0.

Nearly 8 months later he applied to another center with multiple swellings in the left side of the neck, and when the result of the thyroidal fine needle aspiration biopsy was reported to be papillary thyroid cancer, and the result of the lymph node fine needle aspiration biopsy was reported to be thyroid papillary carcinoma metastasis, total thyroidec-

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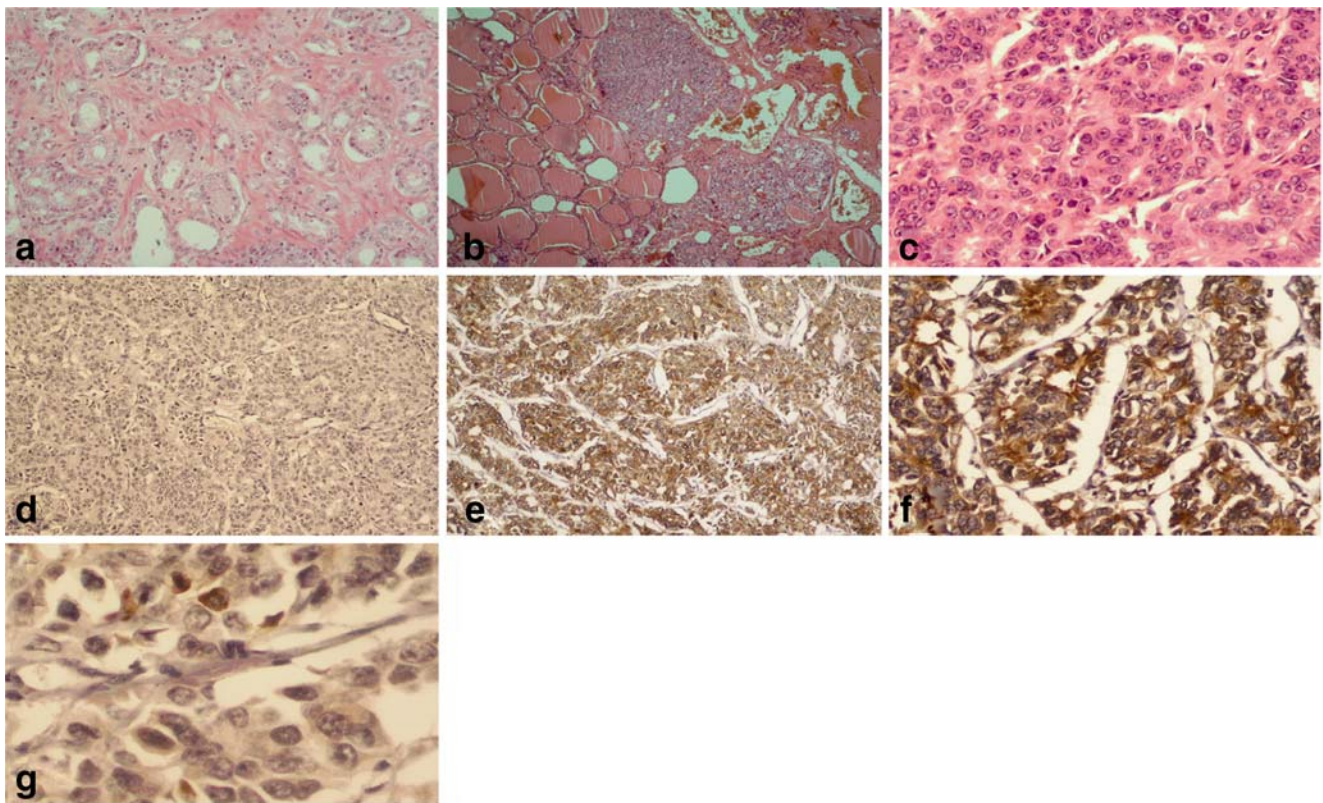


Fig. 1 **a** Undifferentiated prostatic adenocarcinoma (H&E $\times 200$), **b** thyroid papillary carcinoma (H&E $\times 200$), **c** metastatic adenocarcinoma in supraclavicular lymph nodes (H&E $\times 400$), **d** thyroglobulin negativity in

metastatic tumor (IHC $\times 200$), **e** PSA positivity in metastatic tumor (IHC $\times 200$), **f** chromogranin positivity in metastatic tumor (IHC $\times 400$), **g** isolated synaptophysin positivity in metastatic tumor (IHC $\times 400$)

tomy+left neck lymph node dissection was performed. The pathology result was micropapillary carcinoma 1 mm in diameter in the left lobe of the thyroid (Fig. 1b), and metastatic adenocarcinoma in total nine lymph nodes (Fig. 1c). Metastases in the lymph nodes did not have the appearance of papillary carcinoma, and immunohistochemical staining with thyroglobulin (Neomarker, MS-1380-P, Westinghouse-USA) was negative (Fig. 1d). Therefore, considering the primary tumor of the patient, PSA staining (Neomarker, Ab-6, Westinghouse-USA; Fig. 1e) and chromogranin (Neomarker, SP12, Westinghouse-USA; Fig. 1g), and synaptophysin (Dako, A0010, Glostrup-Denmark; Fig. 1f) staining for solid foci were performed. The tumor was commonly PSA(+), and it was stained more markedly with chromogranin, and in a more isolated fashion with synaptophysin to display individual positive cells. The neuroendocrine panel was worked also on the prostate tumor blocks later. Neuroendocrine differentiation was observed in the solid foci with less frequency as compared to that of the metastases.

When the control PSA of the patient in the control visit 1.5 months later was 41.6 ng/ml, bilateral orchiectomy was performed. In the post-orchiectomy third month control we found the total PSA value as 34.0 ng/ml, and free PSA

1.46 ng/ml. It was attempted to find the possible metastatic foci using whole body bone scintigraphy and PET SCAN. However, upon failing to find any metastatic foci in any of the procedures, bicalutamide 100 mg/day was started. PSA value in the control visit of the first 3 months was 8.31 ng/ml, and it was 7.1 ng/ml in the sixth month. He did not accept any extra treatment modalities, and his general health condition is now well.

Discussion

Prostate cancers frequently make metastases to regional lymph nodes. In a series consisting of 753 post mortem examinations, regional lymph node metastases in 63% of the cases were shown, and while a portion of these involved pelvic and paraaortic lymph nodes another portion involved only paraaortic region [3]. Distant metastases to supra diaphragmatic lymph nodes are rare, and occur most frequently in the left supraclavicular region in a limited number of cases; however, this is seen only in patients with widespread metastases [4–7].

There is a significant population of neuroendocrine cells located in the secretory epithelium in the normal prostate

gland. There are three types of the neuroendocrin cells of the prostate gland: major type contain both serotonin and thyroid stimulating hormone. The two minor types contain calcitonin and somatostatin. Neuroendocrine cells are also called APUD (amine precursor uptake decarboxylase) cells. These cells are found in the human body in pituitary, hypothalamus, and pineal glands centrally, and in the lungs, GIS, thyroid and prostate peripherally [8]. Chromogranin A appears to be the best marker indicating the neuroendocrine differentiation in blood and in tissues; the serum values are used to demonstrate the occurrence of the hormone resistance or progression in prostate cancers [9]. Synaptophysin is a calcium-binding protein, and found in pre-synaptic neuronal sacs and neurosecretory granules of the neuroendocrine cells. PSA is the antigen of the normal prostate epithelium and carcinomas, and is a reliable marker of the prostate cancer [10].

Ninety-five percent of the prostate cancers are adenocarcinomas [11]. Although neuroendocrine differentiation in adenocarcinomas differ according to the sensitivity of the technique used, it is found to be between 10% and 100% [9]. It has been advocated that neuroendocrin differentiation is the indicator of a poor prognosis, and the presence of active cellular products like growth factor as well as the lack of androgen receptors that will in turn cause lack of response to the hormonal therapy has been suggested as the cause [12].

Prostatic neuroendocrine tumors are included in the neuroendocrine neoplasm (MEN) syndromes. Thyroid medullary carcinomas accompany these syndromes [13, 14]. In addition, prostate carcinomas have been reported to make metastases in thyroid follicular adenomas in a very limited number of cases that had applied to relevant clinics with nodular goiter diagnoses and fine needle aspiration cytology (FNAC) is diagnostic [15]. In our case, the erroneous assessment of the FNAC on the lymph node was corrected thanks to the result of the pathological examination after the total thyroidectomy+lymph node dissection surgery.

We believe that thyroid papillary Ca accompanying the adenocarcinoma of the prostate, and skip left supraclavicular lymph node adenocarcinoma metastasis occurring in the early period is the first case in the literature. Early PSA recurrence in the patient must be considered as a warning in

such cases. Possible accompanying tumors in various organs and metastases must be kept in mind if the pathologies of the prostate adenocarcinoma of the patients display neuroendocrine differentiation, and patients must be evaluated accordingly.

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