Prostate Small Cell Carcinoma and Skin Metastases: A Rare Entity

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Key Words

Prostate carcinoma · Skin metastases · Small cell carcinoma

Abstract

Objectives: To report a rare case of small cell carcinoma of the prostate with unusual skin metastasis. **Clinical Presentation and Interventions:** A 60-year-old was evaluated for difficulty in urinating. Abdominal computed tomography scans revealed a prostatic mass invading the surrounding tissues and multiple perirectal, periprostatic, para-aortic and pericaval lymph nodes. Needle biopsy specimens showed both small cell carcinoma and adenocarcinoma. He was treated with combination chemotherapy: cisplatin and etoposide and bilateral orchiectomy. After six cycles of the chemotherapy, disease progressed and the patient did not respond to salvage therapy; hence, palliative care was instituted. During the follow-up, papillary lesions were observed in the scrotal skin; biopsy showed metastatic small cell carcinoma. **Conclusion:** Small cell carcinoma of the prostate is an aggressive disease with a highly metastatic potential; but skin metastases are very uncommon. It has poor prognosis despite therapy. Management resembles that of small cell carcinoma of the lung.

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Introduction

Prostate cancer is the second leading cause of cancer deaths in men; approximately 95% of prostate carcinoma is adenocarcinoma [1]. Small cell carcinoma of the prostate (SCCP) is rare and occurs only in about 0.5–2% of patients with prostate cancer. Adenocarcinoma usually accompanies SCCP [1]. The histogenesis of SCCP is not precisely known. According to one hypothesis, SCCP is derived from the malignant transformation of normal prostatic neuroendocrine cells [2]. Another hypothesis postulates that SCCP is derived from multipotential stem cells of the prostatic epithelium [2, 3]. Due to the nature of the totipotent basal cells of the prostate, SCCP may also develop from conventional adenocarcinoma of the prostate [3]. Based on a previous report [4], 47% of patients with SCCP present with recurrence of conventional adenocarcinoma, and 17.7% presented with combined adenocarcinoma. SCCP is aggressive and usually metastatic at diagnosis [4, 5]; however, metastases to skin are rare.

Case Report

A 60-year-old man was admitted with polyuria, constipation, fatigue and difficulty urinating for 1 month. On digital rectal examination, there was an enlarged and irregular prostate; there were no other abnormalities on the rest of the physical examination. Standard laboratory analyses including serum prostate-spe-

cific antigen were normal but serum creatinine was mildly elevated. Abdominal computed tomography (CT) scans revealed an enlarged prostate mass (7 × 6 × 8 cm) invading the rectum, seminal vesicle and bladder, and multiple perirectal, periprostatic, para-aortic and pericaval lymph nodes. Histopathological diagnosis of prostate adenocarcinoma (with Gleason score 5 + 4 = 9) and small cell carcinoma were made by needle biopsy. The adenocarcinoma component of the tumor was seen focally. Small cell component of the specimen stained positive for chromogranin and synaptophysin. Thoracic CT showed enlarged mediastinal lymph nodes. A positron emission tomography/computerized scan following administration of fluorine-18 fluoro-2-deoxy-glucose showed uptake in the prostate and surrounding tissues, and in the mediastinal lymph nodes; no pulmonary uptake was observed. Bronchoscopy was normal; however, histopathological examination of the pulmonary aspirate showed malignant cells, consistent with a neuroendocrine (small cell) carcinoma. Serum neuron-specific enolase (NSE) was 105 µg/l.

Combination chemotherapy with cisplatin and etoposide was started. After 1 cycle, a bilateral orchiectomy was performed for androgen blockade. After the third cycle, the level of NSE decreased to 25 µg/l; a partial response of the pelvic mass was observed on CT. The 6 cycles of chemotherapy were completed. However, final CT scans showed no further change in the pelvic mass. Oral etoposide was started. One month later, the serum NSE was 120 µg/l and an abdominal ultrasound revealed increase in the size of the pelvic mass. A right nephrostomy tube and J stent were placed for development of bilateral hydronephrosis. Due to progression of the disease, salvage chemotherapy containing of vincristine, adriamycin and cyclophosphamide was begun. After 2 cycles, a deep vein thrombosis developed and CT scan showed progression in the mediastinal lymph nodes. Chemotherapy and palliative treatment was instituted. After 1 month, the patient was admitted with bleeding papillary lesions on the scrotum. Biopsy of these lesions was consistent with metastatic small cell carcinoma (fig. 1). He died before treatment for skin metastasis. The death occurred 11 months after the initial diagnosis.

Discussion

SCCP is a rare entity. The natural history is similar to that of small cell carcinoma of the lung (SCCL), with aggressive course and early widespread metastases to the visceral organs. The most common sites of metastases are bones, regional and distant lymph nodes, the liver, lungs, bone marrow, soft tissues and brain [4]. However, skin metastases are uncommon and have been presented in only a few reports [5, 6].

The morphology of SCCP is also similar to that of SCCL in that a high mitotic index, vascular invasion and necroses are frequent findings. The prevalence of neuroendocrine cells in the prostate has been correlated with higher-grade malignancy and poor prognosis [3]. For this reason, the immunohistochemical diagnosis of SCCP is crucial when determining treatment. The histogenesis of

Fig. 1. Metastasis of SCCP into the skin (HE).

SCCP is not clear; the most accepted hypothesis is that it arises from totipotent stem cells of the prostate that differentiate into either epithelial or neuroendocrine carcinomas [6]. This is supported by the fact that in approximately half of patients with SCCP, the malignancy is diagnosed as a recurrence of adenocarcinoma of the prostate [7]. Given that in many patients recurrent adenocarcinoma of the prostate is never rebiopsied, the true prevalence of SCCP is not known [3]. Histological re-evaluation of resistant conventional prostate adenocarcinoma may be useful in diagnosing small cell differentiation and changing the treatment modality.

The most common immunohistochemical markers used to diagnose SCCP are NSE, chromogranin, synaptophysin, CD-56 and TTF-1 [4]. In our patient, the level of serum NSE was very helpful. Elevated serum PSA levels can be detected if tumor contains a large amount of adenocarcinoma component. In our case, because of the tiny amount of adenocarcinoma component of the tumor, serum PSA level was within normal limit. Various hormones also have been revealed immunohistochemically; these include ACTH (30%), serotonin (50%), gastrin (50%), vasoactive intestinal peptide (100%), bombesin (50%), antidiuretic hormone (50%) and somatostatin (33%) [4]. In the serum calcitonin and ACTH are detected most frequently [3, 8]. Therefore, paraneoplastic syndrome may be observed in some patients.

Because of the rarity of SCCP, there is no standard treatment modality; treatment is similar to that of SCCL. Recommended chemotherapy regimens consist of vincristine, doxorubicin and cyclophosphamide, or etopo-

side and cisplatin with or without doxorubicin [6, 9]. Gemcitabine, docetaxel and carboplatin also have been used in studies, and good benefits have been seen with tolerable adverse effects [9]. In the current case, orchiectomy was performed to treat the adenocarcinoma. No common opinion exists on androgen blockade. One patient with SCCP cured by prostatectomy has been reported [10]. However, SCCP usually presents with distant metastases and is therefore not appropriate for surgery [4]. There is no standard recommendation for radiotherapy. However, for local control, some centers advocate concurrent radiotherapy with chemotherapy [11].

Conclusion

Due to widespread metastatic pattern, oncologists should be vigilant about uncommon sites of metastases of SCCP. The histopathological evaluation of hormone-refractory prostate carcinoma should be made carefully so that the most appropriate treatment is chosen.

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