Case Report

Small-Cell Carcinoma of Prostate: A Case Report and Literature Review

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ABSTRACT

One case of small-cell carcinoma (SCC) of prostate was identified at Shangyu people's hospital. This 70-year-old male had a prior diagnosis of prostatic adenocarcinoma when he was first admitted to the hospital and received anti-androgen treatment. 9 months later, he was readmitted to the hospital and was diagnosed as SCC through biopsy. The article was written to evaluate the clinical and pathological characteristics and treatment of SCC of prostate.

Key words: Small-cell carcinoma; Prostatic neoplasms

INTRODUCTION

Small-cell carcinoma (SCC) is most often discovered in lung and it also can be found in other organs. The primary SCC of the prostate is a rare and aggressive clinical entity. Because of lacking of typical clinical symptoms and reliable tumor markers, early diagnosis is difficult to make. The patients often presents with advanced metastasis at the time of diagnosis. In some patients who were given androgen deprivation therapy (ADT), the disease changed form adenocarcinoma to SCC.

By now, in the world no more than 200 cases of primary SCC of prostate were reported. Because of the rarity of the condition, no standard therapeutic regime has been developed. Reported cases have generally been managed by chemotherapeutic regimens similar to those recommended for small cell lung cancer.

A case, diagnosed as adenocarcinoma of prostate for the first time and SCC for the second time, was retrieved from the files of department of pathology, Shangyu people's hospital. The purpose of the article is to review the clinical and pathological characteristics of the SCC of prostate.

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CASE REPORT

Clinical Data

The patient was a 70-year-old male when he was first admitted to hospital with the presenting symptom of urinary retention for 2 years. Rectal touch revealed that the enlarged prostate had no induration. The serum prostate-specific antigen (PSA) level during this admission was >100 ng/ml and fPSA level was 25.92 ng/ml. Urinalysis revealed 3+ occult blood and 1+ leukocyte. An abnormal strengthening district of 25×28 mm in the left side of the enlarged prostate was shown on computerized tomography (CT) scan which implied a tumor in the prostate. There was no evidence of involvement of bladder and rectum on CT. There was also no evidence of a metastatic disease. Initial treatment included transurethral resection of prostate and orchiectomy. The adjuvant chemotherapy with flutamide was given after the operation for 3 months before renal dysfunction.

Nine months later he was readmitted for hematuria that started 10 days prior to admission. A CT showed soft tissue mass arising from the bladder urethral opening area. He was operated on for the second time.

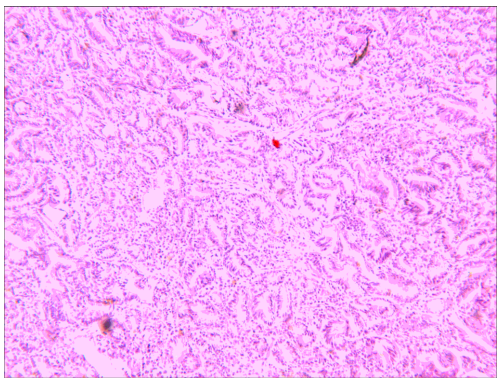

Figure 1. A HE staining when he was initially diagnosed as adenocarcinoma (×100).

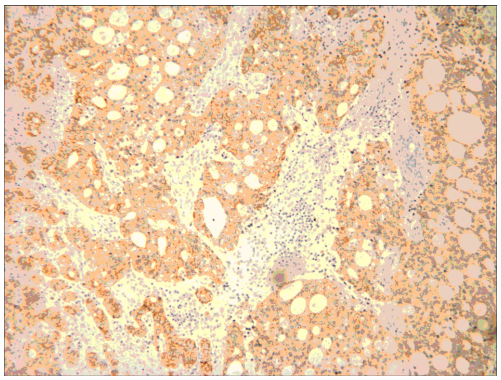

Figure 2. The IHC staining of PSA for the firstoperated specimen (×100).

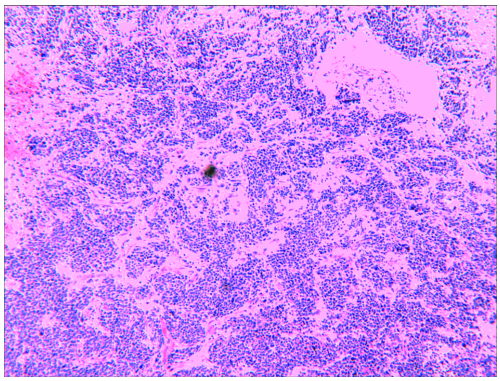

Figure 3. A HE staining when he was diagnosed as SCC (×100).

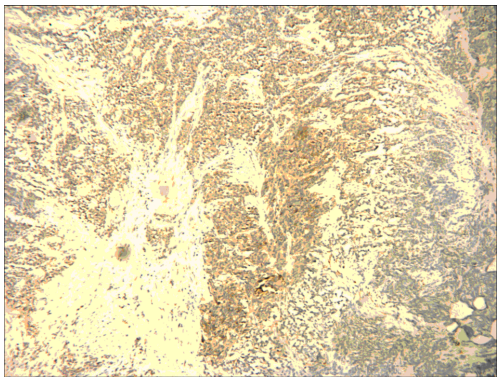

Figure 4. The IHC staining of Syn for the second time operated specimen (×100).

Pathological Examination

Pathological examination of the first resection specimen revealed prostatic adenocarcinoma with the Gleason score of 3+4 (Figure 1). Microscopically, the prostatic biopsy revealed that the tumor cells with enlarged nuclei and nucleoli were arranged in irregular tubular architecture for the first time. And the scattered neoplastic glands infiltrated widely between benign glands. The immunohistochemistry (IHC) staining results of the first time prostatic biopsy were negative for 34 E12, P63, CgA, NSE, S-100 and 5-HT, but positive for PSA and P504S, weakly positive for Syn (Figure 3).

But the second operation excision sample was diagnosed as SCC (Figure 2). Because the biopsy showed that the tumor cells were arranged in solid-sheet and nest structures, showing the histologic type of diffuse infiltrative carcinoma. Coagulative necrosis could be found. Small round or oval cells resembling lymphocytes or oat cells were the main constituents of the tumor. The IHC staining results were negative for PSA, P504S, CK, CD3, CD79α, CD20, LCA, 5-HT and CgA, but positive for Syn (+++) and NSE(+) (Figure 4). This time the slices including HE and IHC staining were interviewed by doctors of Fudan University Shanhai Cancer Center and the same result was given. He has been followed up till now.

DISCUSSION

Overview

In United States, prostate cancer (PC) is the second most commonly diagnosed malignancy in elderly men and the main leading cause of cancer-related deaths in the male population, second only to lung cancer[1, 2]. The PC is common seen in the old man after the age of 50 and the highest incidence rate was in the group of 70-year-old. With the extension of human life and the improvement of technique, the detection rate of PC was gradually increased.

About 95% of the malignant prostatic neoplasms are adenocarcinomas[3] and traces of neuroendocrine differentiation can be found in the adenocarcinomas in 10% to 100% of the cases. The first time the patient was diagnosed as adenocarcinomas and the IHC staining confirmed the presence of local neuro-endocrine differentiation.

Clinical Features

Approximately 68% of PC arise in the peripheral zone (PZ)[1]. With rectal touch, the enlarged prostate with or without nodes could be found. The clinical features of PC are similar to benign prostatic hyperplasia (BPH), and urinary obstruction with or without hematuria is the main symptom. Like adenocarcinomas, SCC arises in the periphery of the prostate gland and hence can occur without urinary symptoms. PSA is secreted primarily by epithelial cells that line the prostatic acini and ducts[4]. PSA expression shows cell specificity and is tightly regulated by androgens through the androgen receptor (AR)[5]. So the serum PSA level can be used for monitoring treatment responses, prognosis and progression in patients with PC. For the lack of AR, the serum PSA level is low in SCC. So the serum PSA level couldn't be used as diagnostic standard of SCC. The clinical features of SCC differ from those of adenocarcinoma of the prostate in that SCC is typically aggressive and often existing distant visceral or nodal metastases. The most common sites of metastases were bone, retroperitoneal lymph nodes, liver, and lungs. Early diagnosis is difficult because of a tendency for early spread to visceral organs and lack of concordant elevation of PSA. Torotz[6] once reported an old man complaining of right upper abdominal pain associated with weight loss. The patient denied any obstructive or irritative urinary symptoms, and his serum PSA level was normal. After examination he was diagnosed as SCC of prostate with extensive hepatic metastases.

Pathological Featured and the Etiology

SCC is a rare malignancy of neuroendocrine cell lineage arising in the human prostate, accounting 0.5%–2% of all primary prostatic tumors[7]. By now, no more than 200 cases of SCC of prostate were reported[8]. SCC is a special type of PC, so it couldn't be estimated using Gleason grading system. Microscopically, the tumor cells were arranged in solid-sheet and nest structures，showing the histologic type of diffuse infiltrative carcinoma. Small round or oval cells resembling lymphocytes or oat cells were the main constituents of the tumor[9]. SCC which is more aggressive than adenocarcinoma has a predilection to produce visceral metastases, lytic bony lesions. Li[10] believed that the appearance of SCC represented the increasing degree of malignancy. Two cases reported by him occurred distant metastases and one patient died for extensive lung metastasis. Xiao[11] once reported that one patient with SCC of prostate died for multiple organ failure caused by metastasis.

The pathogenesis of prostatic SCC remains controversial, 3 theories have been proposed to date. The first theory postulates that SCC of the prostate originates from neuroendocrine cells. The second theory proposes that SCC of the prostate results from dedifferentiation of prostatic adenocarcinoma; the presence of PSA staining in some neuroendocrine cells appears to support this hypothesis. The third theory suggests that stem cells which have the ability to differentiate into either epithelial or neuro-endocrine type carcinomas are the direct precursors of SCC of the prostate. And now the most widely accepted view is the third one[12]. Our finding in the present case supported the third hypothesis.

Treatment and Prognosis

PC retains androgen receptor (AR) signaling pathways[13] and thus is nearly universally responsive initially to ADT. ADT exploits the androgen dependency of PC cells by either reducing endogenous androgen levels that circulate within the body or by directly blocking AR activity with chemical inhibitors[14]. Unfortunately, however, essentially all ablated patients eventually relapse[15]. At present, some scholars think that SCC of the prostate is an aggressive malignancy, and may develop in patients with previously diagnosed adenocarcinoma who have received ADT. Wright et al.[14] pointed out that androgen withdrawal caused androgen-dependent PC cells to adopt a pronounced neuroendocrine (NE) phenotype, which suggested that AR repressed an intrinsic NE transdifferentiation process in PC cells and induced the transcription of prostate-specific genes associated with cellular growth and maintenance of the differentiated prostate-epithelial phenotype. Philipple et al.[16] found that in their study, approximately two-third of the patients developed SCC after a prior history of prostatic adenocarcinoma, and nearly all of these patients had received prior ADT for a period of several years. Brownback[7] believed that the transition of the adenocarcinoma to SCC represented proliferation of the native neuroendocrine cells in response to androgen-ablation therapy and he also pointed out that SCC often presented with advanced metastasis at the time of diagnosis. After treatment

with ADT, our patient developed SCC with locally invasive disease after a prior diagnosis of adenocarcinoma. The result also supported the assumption that in some patients the ADT may cause the transition of the adenocarcinoma to SCC.

To our knowledge, the optimal treatment strategy for SCC of the prostate has yet to be determined and the median survival duration from the time of diagnosis of SCC was 17.1 months. Patients usually died in one year after the diagnosis. At present, the best therapeutic regimen is the excision of the tumor in the earlier period. Some studies also have proposed that multimodality therapy using a combination of chemotherapy and radiotherapy may offer an improved therapeutic benefit. But many studies also showed that the chemotherapy had no obvious effects on SCC. Papandreou[17] observed 36 patients with SCC of prostate treated by a combination of doxorubicin, etoposide and cisplatin, and he found that the survival remain disappointedly brief while 61% of the patients had objective response. We believe that further improvement in therapy will come from understanding the biology of this disease, predicting its occurrence, and integrating new therapies into the treatment of it.

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