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Short Commentary

Treatment for Neuroendocrine Prostate Cancer

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ABSTRACT

Neuro-Endocrine Prostate Cancer (NEPC) accounts for approximately 1% of all initial prostate cancer diagnoses [1]. NEPC is a rare disease and is known to have a very poor prognosis. The standard treatment for NEPC is the same as for Small Cell Carcinoma of the Lung (SCLC), but no effective treatment has been established at this time. Novel therapies have been reported, including new chemotherapies, immune checkpoint inhibitors and gene therapy. We hope that effective treatment methods will be established as soon as possible in the future.

Keywords: Neuroendocrine Prostate Cancer (NEPC); Small Cell Lung Cancer (SCLC); Neuron-Specific Enolase (NSE); ProGastrin-Releasing Peptide (proGRP); Etoposide and Cisplatin (EP)

NEPC: Neuroendocrine prostate cancer

The frequency of neuroendocrine carcinomas of the prostate is low, accounting for approximately 1%-5% of all prostate cancers [2]. Small cell carcinoma is the common neuroendocrine cancer in the prostate, large cell carcinoma is very rare [3].

The frequency of differentiation from adenocarcinoma to neuroendocrine carcinoma during the course of treatment is reportedly 10%-100% [1]. However, the frequency of neuroendocrine carcinoma at the time of initial diagnosis, as in the present case, is approximately 1% [1].

NEPC is one of the neuroendocrine cancers that can occur in the lungs, gastrointestinal tract, bladder, skin and is pathologically classified as either large cell or small cell carcinoma. In other organs, most are diagnosed with small cell carcinoma and large cell carcinoma is very rare [4].

Small cell carcinoma is pathologically characterized by an enlarged nucleus and lack of cytoplasm. Positive results for neuroendocrine markers such as synaptophysin and chromogranin are also characteristic, and the diagnosis is confirmed by immunostaining pathology. And, blood markers such as Neuron-Specific Enolase (NSE) and Progastrin-Releasing Peptide (proGRP) are also often elevated. The prognosis for most NEPC remains poor. The average survival time is 9.8 months (7.3 months for patients with metastases at the time of initial diagnosis) [5].

Treatment for localized cancer

Some studies have reported successful multidisciplinary treatments, including radiotherapy, for localized cancer [6]. However, there is no established treatment for localized NEPC. Because NEPC has many similarities to SCLC, the NCCN prostate cancer guidelines state that it should be treated according to SCLC [7]. Surgical resection for stage T2 cases and chemotherapy plus radiation therapy for stage T3 cases are considered options, but there is no clear evidence for this, so treatment should be considered on a case-by-case basis. SCLC is characterized by prophylactic whole-brain irradiation because brain metastases appear within 2 years in about half of the cases. The occurrence of brain metastases should also be noted, since the risk of brain metastases is reported to be 8.0%-15.7% in NEPC, whereas the risk is about 0.8% in prostate cancer in general [8,9].

Treatment for metastatic cancer

NEPC is rarely detected as a localized cancer; more than 70%-75% of NEPC have distant metastases at the time of detection [5,10]. Therefore, systemic chemotherapy is the mainstay of treatment, although no effective treatment has been established. Chemotherapy similar to that used for SCLC, such as the EP therapy or irinotecan and cisplatin therapy, is often used [11].

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The authors have experienced a case in which EP therapy was successful and the patient maintained complete resolution [12]. The patient had multiple metastases and a large pelvic mass occupying pelvis. In addition to EP, olaparib in patients with BRCA-positive and pembrolizumab in patients with microsatellite instability-high have been reported to be successful in a small number of cases [12]. Other clinical trials have reported the efficacy of treatment with cabazitaxel in combination with carboplatin [13].

On the other hand, clinical trials using atezolizumab and durvalumab, which are considered effective in SCLC, were also conducted, but reportedly did not show sufficient efficacy [14,15]. In addition, newer treatments such as Aurora-A inhibitors, DLL3-targeted therapy, and CEACAM5-targeted therapy have also been reported to be effective, and results from further clinical trials are expected [16].

CONCLUSION

Prostate neuroendocrine carcinomas are rare and have poor prognoses. Therefore, information regarding treatments that can improve prognosis is needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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