Case Report

Cranial nerve palsy caused by metastasis to the skull base in patients with castration-resistant prostate cancer: Three case reports

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ABBREVIATIONS & ACRONYMS
ADT = androgen deprivation therapy
CAB = combined androgen blockade
CR = complete response
CT = computed tomography
DTX = docetaxel
EBRT = external beam radiation therapy
EOD = extent of disease
MRI = magnetic resonance imaging
NR = no response
NSE = neuron-specific enolase
PCa = prostate cancer
PR = partial response
PSA = prostate-specific antigen

Introduction: Skull base metastasis of prostate cancer associated with cranial nerve palsy is rare. We observed three patients with aggressive prostate cancer who experienced cranial nerve palsy.

Case presentation: Case 1 was a 53-year-old patient who was treated with carboplatin and etoposide. He noticed sensory abnormalities on his left mouth edge. Head magnetic resonance imaging revealed skull base metastasis. Case 2 was a 50-year-old patient who received docetaxel. This patient exhibited ptosis of the left eye. Skull base metastasis was detected by magnetic resonance imaging. External beam radiation therapy was performed. Case 3 was a 64-year-old patient who was treated with docetaxel. He experienced ptosis of the right eye and diplopia. He was also treated with external beam radiation therapy.

Conclusion: External beam radiation therapy exhibited some efficacy against the symptoms, but skull base metastasis of treatment-resistant prostate cancer has poor prognosis. Three patients died within 3 months after symptoms occurred with or without external beam radiation therapy.

Key words: case report, cranial nerve palsy, external beam radiotherapy, prostate cancer, skull base metastasis.

Keynote message

We experienced three cases of skull base metastasis of DTX-resistant castration-resistant PCa that resulted in nervy palsy. Three patients died within 3 months after symptoms occurred with or without EBRT.

Introduction

The skull base metastasis of PCa with cranial nerve palsy is rare. We experienced three cases of skull base metastasis of DTX-resistant castration-resistant PCa that resulted in nervy palsy. In all cases, the cancer progressed rapidly, and the patients died within 3 months after symptoms occurred.

Case presentation

Case 1

A 53-year-old male patient was diagnosed with PCa. His initial PSA level was 42.7 ng/mL and Gleason score was 4 + 5. The pathology was adenocarcinoma. Neuroendocrine component was not included. CT revealed multiple lymph node metastases. Bone scintigraphy showed multiple bone metastases (EOD 3). Metastases were found in the skull, but skull base metastases were not clear. We started ADT, but the patient’s PSA level started to increase after 4 months. We subsequently administered DTX with prednisone. After three cycles of DTX, the patient’s PSA level increased to 89.6 ng/mL, and liver metastasis emerged. In addition, his NSE level increased to 42.5 ng/mL. We targeted the neuroendocrine component and started carboplatin (CBDCA) and etoposide (VP-16). After one cycle of CBDCA and VP-16 therapy, sensory abnormalities on the patient’s left mouth edge were observed. Skull base...
metastasis at the middle cranial fossa and paralysis of the left trigeminal nerve (cranial nerve V3) were suspected. Head MRI revealed multiple skull base metastases at the middle cranial fossa (Fig. 1). We promptly planned to administer EBRT, but the patient lost conscious prior to the start of treatment and died.

Case 2

A 50-year-old male patient was diagnosed with PCa. His initial PSA level and Gleason score were 51.3 ng/mL and 4 + 3. CT revealed multiple lymph node metastases. Bone scintigraphy showed no bone metastasis. ADT was performed for 20 months. Following treatment, the patient’s PSA level had increased to 114.6 ng/mL. We started DTX plus prednisone. After three cycles of DTX, his PSA level had increased to 209.9 ng/mL. Although bone scintigraphy revealed multiple bone metastases (EOD 3), skull base metastases were not detected. This patient experienced ptosis of the left eye, drooping mouth, and difficulty closing the left eye. Clinical examination confirmed palsy of the left facial nerve (cranial nerve VII). Head MRI detected skull base metastasis.
at the geniculate ganglion of the facial nerve (Fig. 2). EBRT (39 Gy) was planned to treat the skull base metastasis. Progression of PCa occurred during EBRT, and the patient’s general condition worsened. Before EBRT was completed, the patient died of cachexia.

**Case 3**
A 64-year-old male patient was diagnosed with PCa. The patient’s initial PSA and Gleason score were 146 ng/mL and 4+5. MRI revealed PCa with bladder invasion. No

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**Table 1** Previous reports about skull base metastasis of PCa with cranial nerve palsy

| Author            | Year | Number of cases | Cranial nerve palsy | Treatment before skull base metastasis | Treatment for skull base metastases | Improvement in cranial nerve palsy | Improvement in headache | Survival after treatment for skull base metastases |
|-------------------|------|-----------------|---------------------|----------------------------------------|------------------------------------|-----------------------------------|------------------------|-----------------------------------------------|
| McDermott RS      | 2004 | Case 1          | VII                 | ADT                                    | EBRT [skull base] 30 Gy/10-Fr       | CR                                | Unknown               | 9 months                        |
|                   |      | Case 2          | XII                 | Chemotherapy                           | EBRT [whole brain] 20 Gy/5-Fr       | CR                                | Improved              | 3 months                        |
|                   | 2004 | Case 3          | VII                 | Chemotherapy                           | EBRT [whole brain] 30 Gy/10-Fr       | CR                                | Unknown               | 29 months                       |
|                   | 2004 | Case 4          | V                   | Chemotherapy                           | EBRT [skull base] 20 Gy/5-Fr         | CR                                | Unknown               | 11 months                       |
|                   | 2004 | Case 5          | III, V, VI          | Chemotherapy                           | EBRT [whole brain] 30 Gy/10-Fr       | PR                                | Unknown               | 1 month                         |
|                   | 2004 | Case 6          | VI                  | Chemotherapy                           | EBRT [whole brain] 20 Gy/5-Fr        | PR                                | Unknown               | 2 months                        |
|                   | 2004 | Case 7          | VI                  | Chemotherapy                           | EBRT [whole brain] 27 Gy/9-Fr        | CR                                | Unknown               | 2 months                        |
|                   | 2004 | Case 8          | VI                  | Chemotherapy                           | EBRT [skull base] 20 Gy/5-Fr         | CR                                | Unknown               | 31 months                       |
|                   | 2004 | Case 9          | III                 | Chemotherapy                           | EBRT [skull base] 20 Gy/5-Fr         | CR                                | Unknown               | 7 days                          |
|                   | 2004 | Case 10         | VI                  | Chemotherapy                           | EBRT [whole brain] 9 Gy/3-Fr         | PR                                | Unknown               | 17 days                         |
|                   |      | Case 11         | III, IV, V, VI, XII  | ADT                                    | EBRT [skull base] 30 Gy/10-Fr       | CR                                | Unknown               | 1 month                         |
|                   |      | Case 12         | XII                 | ADT                                    | EBRT [whole brain] 30 Gy/10-Fr       | CR                                | Unknown               | 1 month                         |
|                   |      | Case 13         | II, III, V          | Chemotherapy                           | EBRT [skull base] 30 Gy/10-Fr       | PR                                | Unknown               | 27 months                       |
|                   |      | Case 14         | II                  | Chemotherapy                           | EBRT [whole brain] 30 Gy/10-Fr       | Not assessed                      | Not assessed           | 2 days                          |
|                   |      | Case 15         | V                   | Chemotherapy                           | EBRT [whole brain] 30 Gy/10-Fr       | CR                                | Unknown               | 3 months                        |
| O’Sullivan JM      | 2004 | 32              | II: 1, III: 2, V: 6, VI: 7, VII: 4, VIII: 2, IX: 1, XII: 6, III + XII: 1, V + VI + XII: 1, VIII + XII: 1 | Unknown | EBRT 27 cases: 20 Gy/5-Fr, 3 cases: 30 Gy/10-Fr | CR: 25%, PR: 25%, NR: 50% | Unknown | 14 cases are less than 2 months |
| Chacon G           | 2006 | 1               | IX-XII (Collet Sicard syndrome) | None (initial symptom) | Unknown | Unknown | Unknown | Unknown |
| Salamanca JI       | 2006 | 1               | XII (Occipital condyle syndrome) | None (initial symptom) | ADT | CR | Improved | More than 8 months |
| Malloy KA          | 2007 | 1               | VI                  | None (initial symptom) | EBRT | PR | Unknown | More than 2.5 years |
| Mitchell DM        | 2008 | 1               | VII, XII            | None (initial symptom) | EBRT 20 Gy/5-Fr | NR | Unknown | Unknown |
| Kollas AG          | 2010 | 1               | III, IV, V1 and V2, VI, VII, IX, X, XII | None (initial symptom) | EBRT | PR | Unknown | 13 months (this patient died of pneumonia) |
| Izumi K            | 2010 | Case 1          | III                 | CAB                                    | EBRT 40 Gy/20-Fr | CR | Unknown | Unknown |
|                   |      | Case 2          | VII                 | CAB                                    | EBRT 50 Gy/25-Fr | CR | Unknown | More than 1 year |
|                   |      | Case 3          | VI                  | CAB                                    | EBRT 44 Gy/22-Fr | CR | Unknown | More than 13 months |
| Villatoro R        | 2011 | 1               | IX-XII (Collet Sicard syndrome) | None (initial symptom) | ADT | PR | Unknown | More than 3 months |
| Abdullah Z         | 2011 | 1               | XII                 | None (initial symptom) | ADT | NR | Unknown | 32 months |
| Abhilash K         | 2014 | 1               | XII                 | None (initial symptom) | Unknown | Unknown | Unknown | Unknown |
| Bourlon MT         | 2014 | 1               | VII                 | ADT                                    | EBRT | NR | Unknown | More than 3 cycles of DTX |
| Castello MM        | 2017 | 1               | III, IV, VI        | None (initial symptom) | EBRT | NR | Improved | More than 1 year |
| Reshko L           | 2018 | 1               | V                   | Castration-resistant PCa drug | Gamma Knife 44 Gy | PR | Unknown | 3 months |

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metastasis was detected. EBRT (60 Gy) was administered to treat PCa. In addition, ADT was performed for 1 year. After antiandrogen switching, we started treatment with DTX plus prednisone. The patient’s PSA decreased to 0.14 ng/mL after 10 cycles of DTX but gradually increased thereafter. After 24 cycles of DTX, a few bone metastasis (EOD 1) emerged on CT. After 29 cycles of DTX, PSA level was elevated to 423.9 ng/mL and ptosis of the right eye and diplopia appeared. CT revealed no obvious findings, but MRI uncovered bone marrow brightness of the skull base and an irregular contrast effect (Fig. 3). Skull base metastasis of the cavernous sinus and paralysis of the right oculomotor nerve (cranial nerve III) were suspected. Palliative EBRT (30 Gy) was administered, which resulted in symptom improvement. One month after EBRT, his pancytopenia gradually worsened because of bone marrow metastasis. Subdural hematoma emerged 2 months after radiation therapy. Despite emergency drainage, he died the same month.

**Discussion**

PCa is associated with frequent bone metastasis, and in some cases there are skull base metastases. PCa is reported to account for 12–38.5% of cases of skull base metastasis, whereas breast and lung cancers are responsible for 29–40% and 14–15% of cases, respectively.1,2 Conversely, skull base metastasis of PCa with cranial nerve palsy is rare. Skull base metastasis of PCa leading to complex forms of cranial nerve palsy such as Collet-Sicard syndrome (9th, 10th, 11th, and 12th cranial nerves) and Vernet syndrome (9th, 10th, and 11th cranial nerves) has been reported.3,4 The pattern of palsy is multiple. In the present report, we observed cranial nerve palsy of 3rd, 5th, and 7th cranial nerves in three patients, respectively.

Contrast-enhanced head MRI is the best modality for detecting skull base metastasis.2 It is difficult to identify some small skull base metastases on CT. In Cases 2 and 3, MRI was used to detect skull base metastases, which CT failed to detect. Some bone skull metastasis of PCa is detected by bone scintigraphy.5 However, bone scintigraphy has two limitations. One being purely osteolytic metastases and the other being bone superscans which corresponds to diffuse bone metastasis.6,7

In a review of 32 cases of skull base metastasis of PCa with cranial nerve palsy, all patients were treated with palliative EBRT.8 EBRT improved 16 cases (50%) of cranial nerve dysfunction and eight cases (25%) had complete response. The median survival after EBRT was 3 months, and 14 patients died within 2 months.9 Other treatment for skull base metastasis is Gamma Knife. Gamma Knife is reported to be very effective in treating cranial nerve palsy.9 Kotecha R, Angelov L, Barnett GH et al. Calvarial and skull base metastases: expanding the clinical utility of Gamma Knife surgery. J. Neurosurg. 2014; 121(Suppl): 91–101.

**Conflict of interest**

The authors declare no conflict of interest.

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