

## 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.

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## Keynote message

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

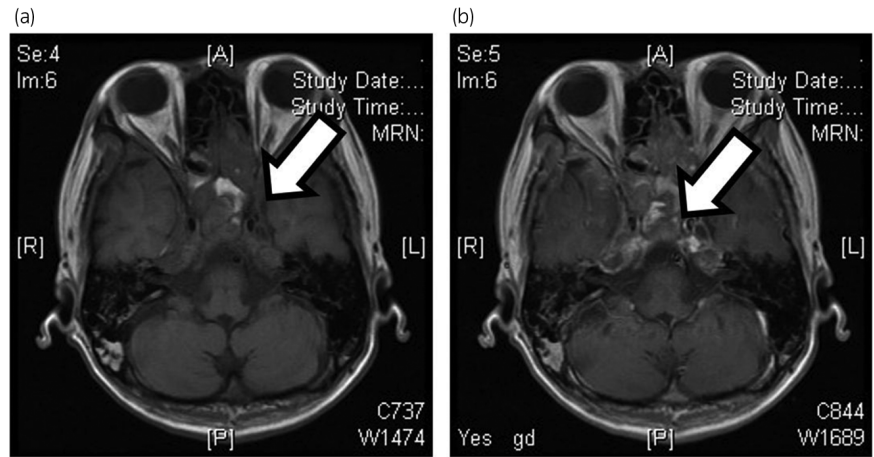
## Introduction

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 nery 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



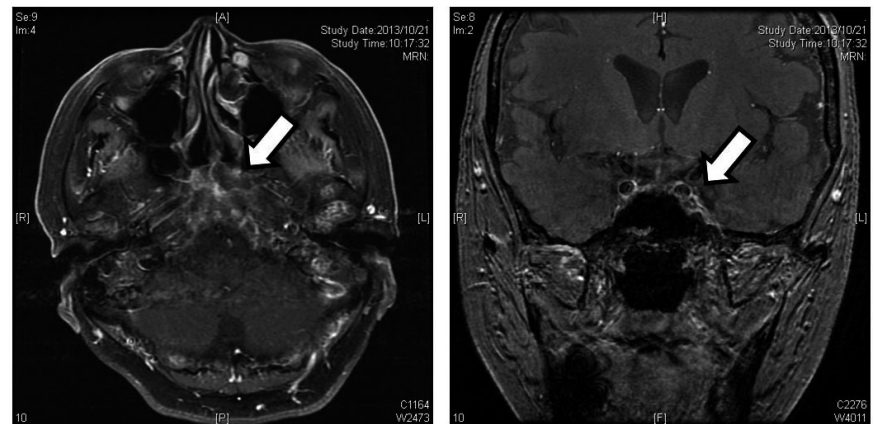
**Fig. 1** (a) MRI (T1WI) shows diffuse bone metastasis at the skull base. Dura mater is thickened nonuniformly. Dura mater invasion is suspected. (b) MRI (T1WI with gadolinium) shows irregular contrast effects at the skull base.

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.

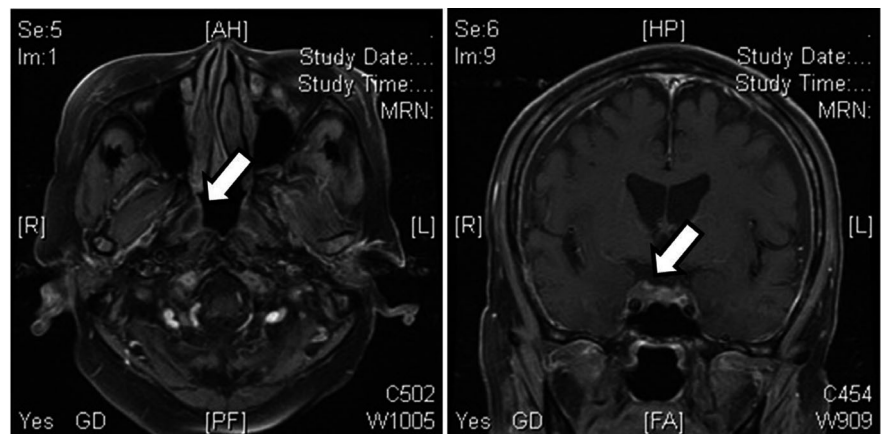
## Case 2

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



**Fig. 2** MRI (T1WI) shows multiple bone metastasis at skull base. Geniculate ganglion of facial nerve is enhanced by contrast agent.



**Fig. 3** MRI (T1WI with gadolinium) shows increasing contrast effects at the base of the skull.

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

**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 <sup>10</sup>	2004	Case 1	VII	ADT	EBRT (skull base) 30 Gy/10-Fr	CR	Unknown	9 months
	2004	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
	2004	Case 11	III, IV, V, VI, XII	ADT	EBRT (skull base) 30 Gy/10-Fr	CR	Unknown	1 month
	2004	Case 12	XII	ADT	EBRT (whole brain) 30 Gy/10-Fr	CR	Unknown	1 month
	2004	Case 13	II, III, V	Chemotherapy	EBRT (skull base) 30 Gy/10-Fr	PR	Unknown	27 months
	2004	Case 14	II	Chemotherapy	EBRT (whole brain) 30 Gy/10-Fr	Not assessed	Not assessed	2 days
	2004	Case 15	V	Chemotherapy	EBRT (whole brain) 30 Gy/10-Fr	CR	Unknown	3 months
O'Sullivan JM <sup>8</sup>	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 <sup>3</sup>	2006	1	IX-XII (Collet Sicard syndrome)	None (initial symptom)	Unknown	Unknown	Unknown	Unknown
Salamanca JI <sup>11</sup>	2006	1	XII (Occipital condyle syndrome)	None (initial symptom)	ADT	CR	Improved	More than 8 months
Malloy KA <sup>12</sup>	2007	1	VI	None (initial symptom)	EBRT	PR	Unknown	More than 2.5 years
Mitchell DM <sup>13</sup>	2008	1	VII, XII	None (initial symptom)	EBRT 20 Gy/5-Fr	NR	Unknown	Unknown
Kolias AG <sup>14</sup>	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 <sup>15</sup>	2010	Case 1	III	CAB	EBRT 40 Gy/20-Fr	CR	Unknown	Unknown
	2010	Case 2	VII	CAB	EBRT 50 Gy/25-Fr	CR	Unknown	More than 1 year
	2010	Case 3	VI	CAB	EBRT 44 Gy/22-Fr	CR	Unknown	More than 13 months
Villatoro R <sup>4</sup>	2011	1	IX-XII (Collet Sicard syndrome)	None (initial symptom)	ADT	PR	Unknown	More than 3 months
Abdullah Z <sup>16</sup>	2011	1	XII	None (initial symptom)	ADT	NR	Unknown	32 months
Abhilash K <sup>17</sup>	2014	1	XII	None (initial symptom)	Unknown	Unknown	Unknown	Unknown
Bourlon MT <sup>18</sup>	2014	1	VII	ADT	EBRT	NR	Unknown	More than 3 cycles of DTX
Castello MM <sup>19</sup>	2017	1	III, IV, VI	None (initial symptom)	EBRT	NR	Improved	More than 1 year
Reshko L <sup>20</sup>	2018	1	V	Castration-resistant PCa drug	Gamma Knife 44 Gy	PR	Unknown	3 months

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.<sup>1,2</sup> 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.<sup>3,4</sup> 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.<sup>2</sup> 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.<sup>5</sup> However, bone scintigraphy has two limitations. One being purely osteolytic metastases and the other being bone superscans which corresponds to diffuse bone metastasis.<sup>6,7</sup>

In a review of 32 cases of skull base metastasis of PCa with cranial nerve palsy, all patients were treated with palliative EBRT.<sup>8</sup> 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.<sup>8</sup> Other treatment for skull base metastasis is Gamma Knife. Gamma Knife is reported to show a local control rate of 88.9% with low rate of side effects.<sup>9</sup> We reviewed reports of PCa with skull base metastasis (Table 1). In most cases, EBRT exhibited some efficacy against cranial nerve palsy and/or head pain, but the prognosis of skull base metastasis after chemotherapy was poor. Contrarily, the prognosis of skull base metastasis after radiation was good when found before ADT or DTX therapy.

Review of skull base metastases reported symptomatic skull base metastases to have worse prognosis than

asymptomatic skull base metastases.<sup>2</sup> Cranial nerve palsy in DTX-resistant castration-resistant PCa, including our case, has poor prognosis.<sup>8</sup> Head screening may be needed at the DTX-resistant stage.

In the present report, we described three cases of skull base metastasis of PCa that resulted in cranial nerve palsy. Symptoms after DTX treatment indicate poor prognosis. We may need early detection of skull base metastasis to improve poor prognosis.

## Conflict of interest

The authors declare no conflict of interest.

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