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【 CASE REPORT 】

A Rare Case of Clival Metastasis in a Patient with Gastric Cancer

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Abstract:
We report a rare case of clival metastasis from gastric cancer. A 73-year-old man with advanced gastric cancer treated with nivolumab as a third-line chemotherapy experienced headache, tongue deviation, and difficulties in speaking clearly. We suspected stroke or brain metastasis, but brain contrast-enhanced magnetic resonance imaging demonstrated a clival mass, diagnosed as clival metastasis from gastric cancer. The tumor could not be identified by plain computed tomography and plain magnetic resonance imaging alone. He received palliative radiotherapy (30 Gy/10 fr); his symptoms improved gradually. Although metastasis from gastric cancer to other organs is common, bone metastases are rare.

Key words: clival metastasis, gastric cancer, radiotherapy, contrast-enhanced magnetic resonance imaging

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Introduction

Gastric cancer is the fifth most common cancer and the third most common cause of cancer related deaths annually (1). The main sites of gastric cancer metastases are the liver, lungs, and peritoneum; however, the incidence of bone metastasis due to gastric cancer is reported to be rare, at only 0.9-2.1%. The reported frequency of bone metastasis from gastric cancer is 13.4-15.9% in an autopsy series, which suggests that asymptomatic bone metastasis is likely underestimated. In previous reports, the most common sites of bone metastasis were the lumbar vertebra, thoracic vertebra, and pelvis (2). It is uncommon in the calvaria and in the clivus.

We herein present the case of a patient with clival metastasis arising from advanced gastric cancer.

Case Report

A 73-year-old Japanese man with advanced gastric cancer with peritoneal dissemination was treated using nivolumab monotherapy (3 mg/kg, every 2 weeks) as a third-line treatment for 1 year. HER2-negative gastric cancer located in the cardia invades the lower esophagus with small ascites in the pelvic floor. Before nivolumab treatment, he received chemotherapy with S-1 plus oxaliplatin as the first-line treatment. He exhibited a partial response (PR) followed by S-1 maintenance for half a year. Thereafter, he was administered ramucirumab plus paclitaxel as the second-line treatment for half a year. During the first-line and second-line treatment, the size of ascites and peritoneal dissemination did not increase. After six cycles of nivolumab, swelling of the left cervical lymph node, left pelvic bone metastasis, and small lung metastasis were apparent in the follow-up computed tomography (CT). He received radiotherapy to the pelvic bone metastasis because of severe pain. The lymphadenopathy immediately improved and the serum tumor markers also decreased; therefore, nivolumab treatment was continued. Over 12 cycles of nivolumab, primary tumor shrinkage was observed and the tumor markers significantly decreased. Overall, nivolumab was continued for approximately 1 year (28 cycles), but the primary tumor gradually again became enlarged (Fig. 1).

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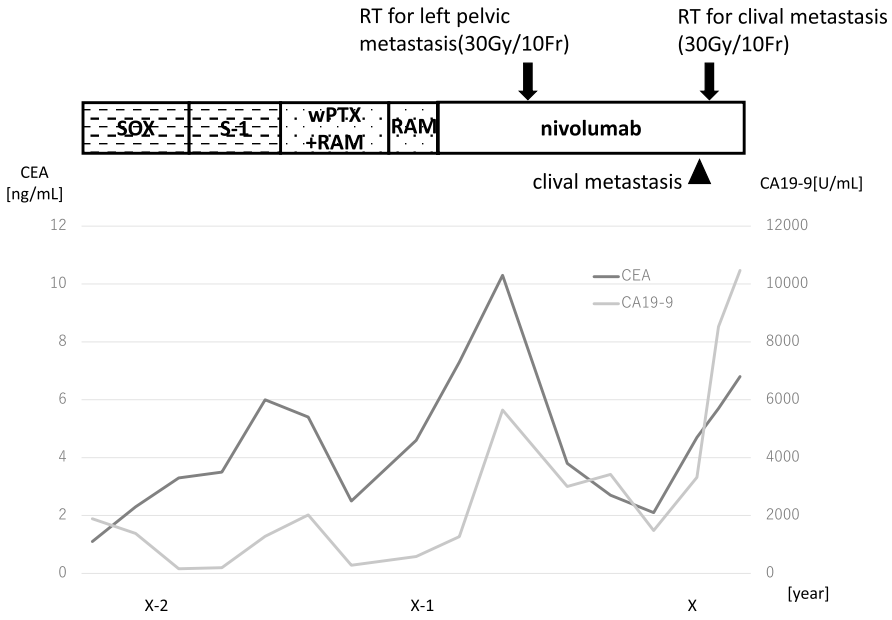

Figure 1. **History of gastric cancer treatment. The trend in tumor markers (CEA and CA19-9) was a good reflection of disease progression. Nivolumab was well tolerated with no serious adverse events for about 1 year. CA19-9: carbohydrate antigen 19-9, CEA: carcinoembryonic antigen**

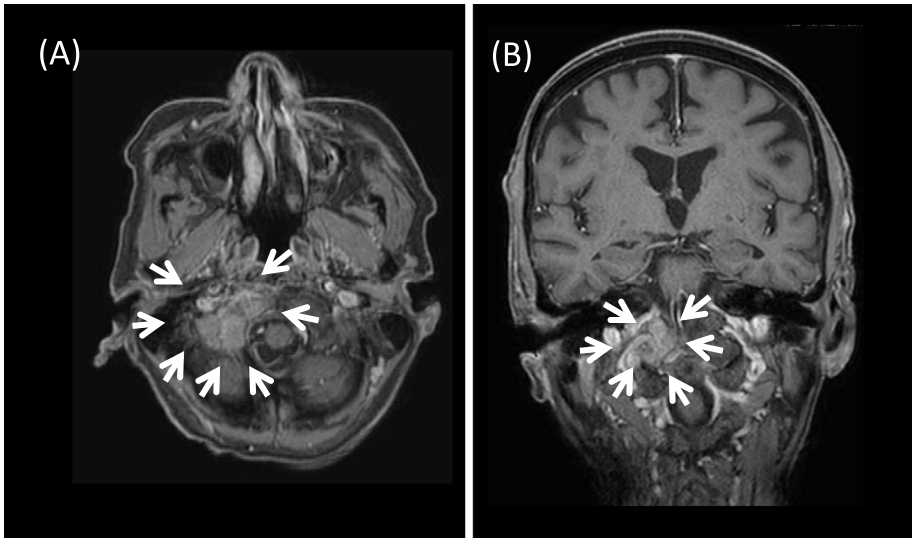

Figure 2. **T1-weighted axial (A) and sagittal (B) contrast-enhanced magnetic resonance image (MRI). A clival mass involving the right jugular process and the right hypoglossal canal was discovered on brain contrast-enhanced MRI (white arrow).**

One day, he experienced occipital headache, and took non-steroidal anti-inflammatory drugs (NSAIDs) at home. After 5 days, as his headache did not improve, he visited our hospital because he experienced tongue deviation and difficulty in speaking clearly. We suspected a cranial nerve disorder caused by stroke or brain metastasis. However, neither plain CT nor magnetic resonance imaging (MRI) of the brain showed stroke, cerebral hemorrhage, or brain metastasis, but a clival mass involving the right jugular process and the right hypoglossal canal was discovered in brain contrast-enhanced MRI. We found heterogeneity in a clival mass with diffuse enhancement after gadolinium administration (Fig. 2). Upon subsequent review, the irregular bone cortex near the right hypoglossal canal was found on the plain CT (Fig. 3). It was diagnosed as a clival metastasis from gastric cancer. We believed that it was responsible for his headache, glossopharyngeal nerve palsy, and hypoglossal nerve palsy. He received palliative radiotherapy (30 Gy/10 fr) (Fig. 4); subsequently, his headache and tongue deviation gradually improved, but he experienced transient dysgeusia. He is now

receiving treatment with trifluridine and tipiracil hydrochloride (FTD/TPI) as fourth-line treatment and his cranial nerve disorder has clearly improved.

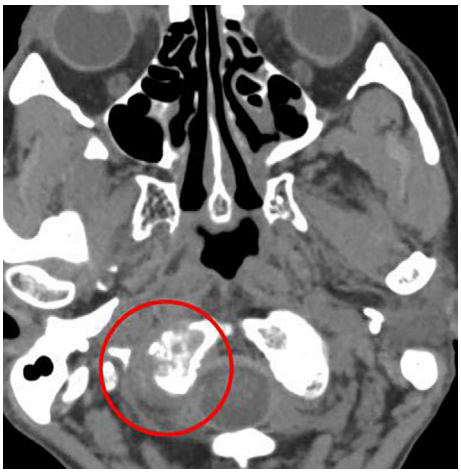

Figure 3. Plain computed tomography. Neither plain CT nor MRI showed stroke, cerebral hemorrhage, or brain metastasis. Upon subsequent review, the irregular bone cortex near the right hypoglossal canal was found on plain CT.

Discussion

Clival tumors represent 0.1-0.4% of all intracranial tumors, with chordomas and chondrosarcoma being the most frequent tumors in this region (3). The isolated metastatic lesions of the clivus are an extremely rare subset of clival lesions; there are only 56 such cases reported in the literature. In these cases, the most common primary tumors were prostatic and renal carcinomas (4). There were only three case reports of clival metastasis arising from gastric cancer (5-7). The histology of the three reported cases was as follows: one was signet-ring cell carcinoma and two were poorly differentiated adenocarcinoma. In the present case, the histology of the primary tumor was tubular adenocarcinoma. In each case, nivolumab was not administered as it had not been approved at the time (Table). There have been only a few cases of clival metastasis from other organs, with the most common neurologic disorder being diplopia caused by sixth cranial nerve palsy. The cranial nerve symptom at the sixth nerve is often recognized as a concomitant symptom (7).

There is no ideal imaging modality to distinguish skull base lesions, such as bone malignancies or bone metastasis.

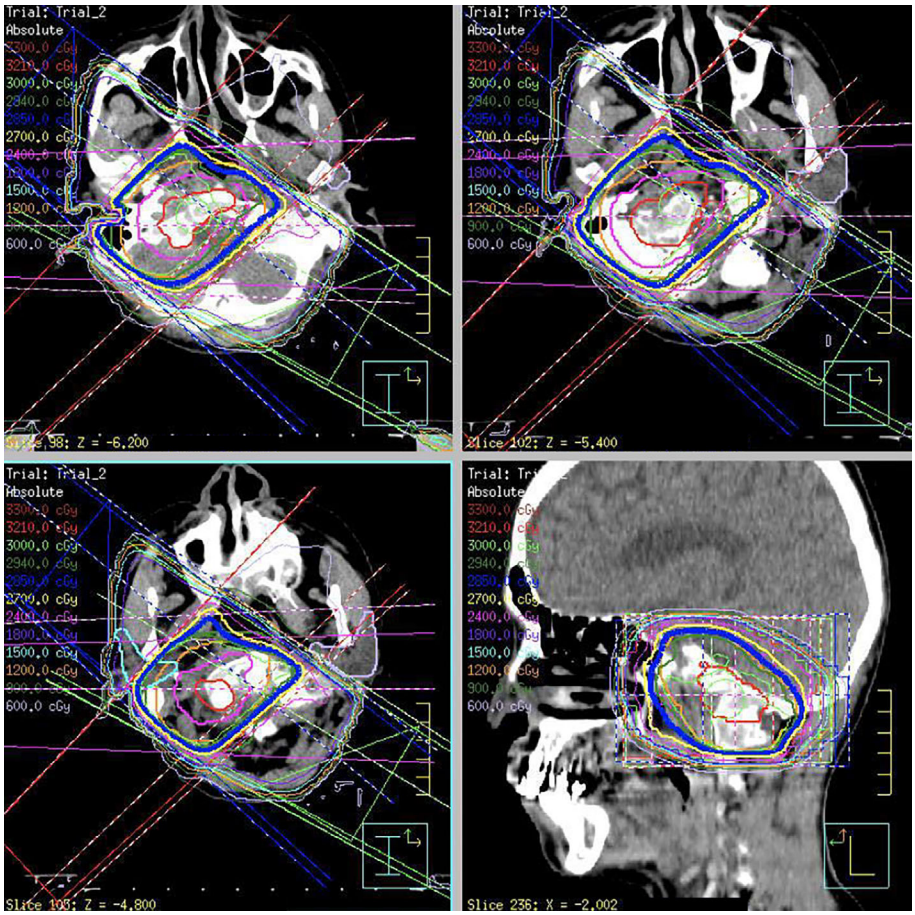

Figure 4. Radiation therapy. We performed palliative radiotherapy (30 Gy/10 fr). His headache and tongue deviation gradually improved. The adverse event of transient dysgeusia occurred. At the time of writing, his neurologic disorder had clearly improved and his symptoms had not recurred.

Table. **Cases of Clival Metastasis from Gastric Cancer.**

Reference	Sex / age	Symptoms	CN involved	Histopathology of primary tumor	Treatment
(6)	42 / male	CN VI palsy	VI	por	Surgery + Chemotherapy (FP)
(5)	64 / male	Headache, diplopia, bilateral VI CN palsy	VI	sig	Surgery + Gamma Knife + Chemotherapy (PTX)
(7)	42 / female	Headache, CN VI and III palsy	III, VI	por	Radiotherapy + Chemotherapy (FOLFOX)
Present case	73 / male	Headache, CN IX and XII palsy	IX, XII	tub2	Radiotherapy + Chemotherapy (NIVO)

CN: cranial nerve, por: poorly differentiated carcinoma, sig: signet ring cell carcinoma, tub2: moderately differentiated tubular adenocarcinoma, FP: fluorouracil plus cisplatin, FOLFOX: fluorouracil plus oxaliplatin, NIVO: nivolumab, PTX: paclitaxel

It is said that a clivus with a uniformly low signal intensity that is hypointense relative to the pons on T1 should be considered abnormal in an adult patient. T2-weighted images may help distinguish metastasis from chordoma-like tumors because metastasis show a higher cellular density and lower cytoplasm to nucleus ratio (3, 4, 7). In our case, a clival mass was not detected in T1/T2-weighted images, however, we found heterogeneity in a clival mass with diffuse enhancement after gadolinium administration. An endoscopic endonasal approach for the biopsy of clival lesions for diagnosis is reported to be relatively safe, but it may lead to cerebrospinal fluid (CSF) leakage, meningitis, and encephalocele (8). We diagnosed this clival mass as metastasis from gastric cancer rather than a clival carcinoma due to the clinical course.

There are no data on the treatment of clival metastasis from gastrointestinal tumors owing to the rarity of this lesion. Symptomatic skull base metastases often require external beam radiation therapy as palliative treatment (4). Small tumors (<30 mm), or previously irradiated skull base lesions, may benefit from gamma knife radiosurgery (9). In this case, we performed palliative radiotherapy and continued treatment with nivolumab because the tumor markers and metastasis of other organs were not exacerbated. After palliative radiotherapy, his neurologic symptoms gradually improved, and the tumor markers gradually increased. Unfortunately, the primary tumor continued to grow; therefore, he was advanced to the next-line chemotherapy. At the time of this submission, this patient was alive and had no disease progression for 6 months after this event; and his neurologic symptoms did not recur despite the poor overall prognosis of skull base metastasis, which has been described in previous reports (2-4, 7).

We have reported the rare case of clival metastasis from gastric cancer. When a patient treated with chemotherapy develops cranial nerve symptoms, we often suspect stroke or brain metastasis. If there is no evidence for this on brain CT or MRI, the differential diagnosis of intracranial bone metastasis should be considered and brain contrast-enhanced MRI should be performed.

The patient has given consent for his story to be published.

The authors state that they have no Conflict of Interest (COI).

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