□報告□

A rare case of facial nerve palsy due to bone metastases of intrahepatic cholangiocarcinoma: a new way to alleviate symptoms by radiotherapy

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Abstract

Bone is a frequent site for metastasis of many cancers, and temporal bone metastasis can cause facial nerve palsy although the most initial symptom of temporal bone metastasis is facial pain. Temporal bone metastasis of intrahepatic cholangiocarcinoma is rare. We report this case of a 70-year-old man with facial nerve palsy caused by metastasis of intrahepatic cholangiocarcinoma in the right temporal bone which was treated with radiotherapy resulting in relieving symptoms. Thus, radiotherapy to the temporal bone should be considered for facial nerve palsy by bone metastasis as a palliative treatment.

Keywords：facial nerve palsy, temporal bone metastasis, intrahepatic cholangiocarcinoma, radiotherapy

Ⅰ. Introduction

The presence of facial nerve palsy causes not only physical pain but also emotional distress such as depression and emotional stability[1)] and diminishes the quality of life[2)]. Although many cases are due to Bell's palsy of unknown cause, temporal bone metastasis of malignancy can induce facial nerve palsy by compression to the facial nerve[3, 4)]. Palliative treatment at any stage is desirable because alleviating its symptoms contributes to improving the patient's quality of life. However, palliative treatment options for facial nerve palsy by temporal bone metastasis are not established. Facial nerve palsy due to intrahepatic cholangiocarcinoma has not been reported. We present a case of facial nerve palsy due to temporal bone metastasis of intrahepatic cholangiocarcinoma that was successfully treated with radiotherapy. We also present a review of the literatures on temporal bone metastases from intrahepatic cholangiocarcinoma and show the similarities between the literatures and the present one.

Ⅱ. Case report

A 70-year-old man was referred to our hospital for early gastric cancer. Plain and contrast-enhanced abdominal computed tomography (CT) revealed a hypovascular liver lesion (Figure 1A) and he was admitted to our hospital for liver biopsy. Gastric cancer showed features of early cancer (Figure 1B) with poorly differentiated adenocarcinoma (por)/signet ring cell carcinoma (sig), and immunohistochemically was $CK7^{+}$, $CK20^{-}$, CEA^{+} (Figure 1C right panel), and $HER2^{-}$. On the other hand, the liver lesion was adenocarcinoma

受付日：2022年6月6日　受理日：2022年7月13日
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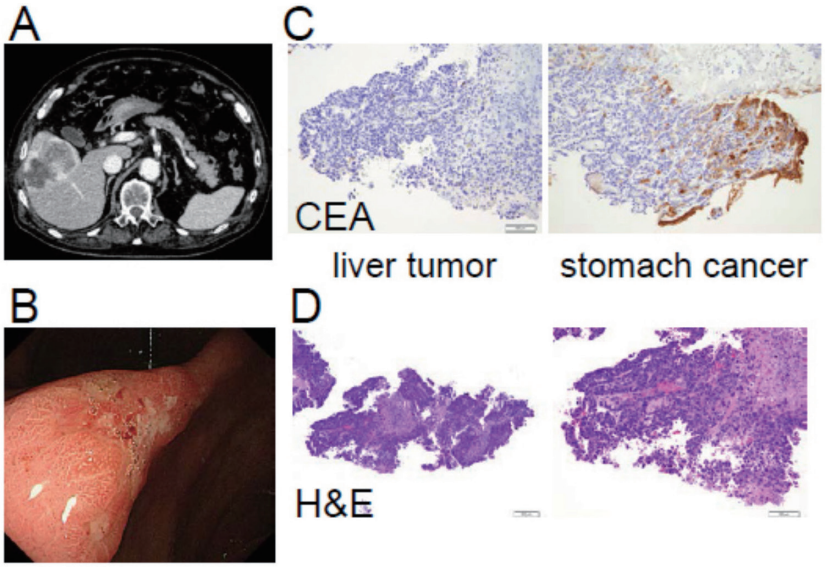

Figure 1　Characteristics of the liver and gastric tumors.
(A) Abdominal contrast enhanced computer tomography. (B) Endoscopic photo of the gastric cancer. (C) Fixed tissues were sectioned into 4 μm thick slices. The sections of the liver tumor and stomach cancer were stained with anti-CEA antibody (713121, Nichirei Bioscience, Tokyo, Japan) (original magnification × 100). Diaminobenzidine tetrahydrochloride was used as peroxidase substrate, and sections were counterstained with hematoxylin. (D) The liver section was stained with hematoxylin and eosin (H&E) (lower magnification (original magnification × 40, left panel) and hyper magnification (original magnification × 100, right panel)).

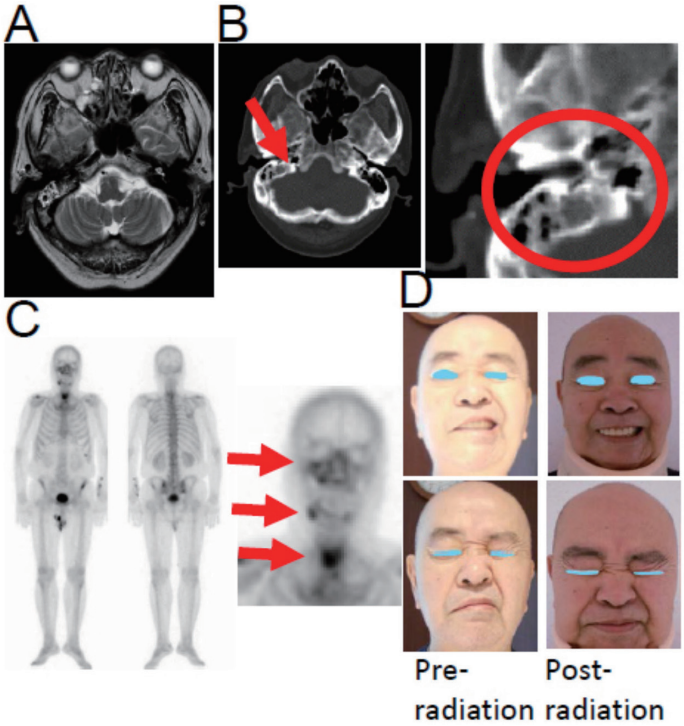

Figure 2　Images of temporal bone metastasis.
(A) T2 weighted axial image of MRI. (B) CT using the bone window setting. The red arrow shows an osteolytic change. (C) Bone scintigraphy using Tc-99m-HMDP. The red arrows show the accumulation of the radioisotope. (D) Pictures of his face at pre- and post-radiotherapy.

with papillary to tubular structures (Figure 1D), $CK7^{+}$, $CK20^{-}$, CEA^{-} (Figure 1C left panel), and $HER2^{-}$, and was diagnosed as moderately differentiated cholangiocarcinoma. There were no risk factors for either gastric or cholangiocarcinoma. The morning of the admission date, he found himself paralyzed on the right side of his face. On physical examination, he had facial nerve palsy on the right side of his face without pain and paresthesia. Other cranial nerve examinations were normal. Magnetic resonance image (MRI) showed right mastoiditis and no cerebral infarction, hemorrhage, or occupying lesions in the intracranial cavity (Figure 2A). CT showed osteolytic changes in the right temporal bone where the facial nerve exists (Figure 2B). Bone scintigraphy revealed accumulation of the radioisotope to the bones including the right temporal bone (Figure 2C) suggesting that the bone metastases of the intrahepatic cholangiocarcinoma cause his facial nerve palsy. In addition, the image examinations revealed bone metastasis in the mandible and the cervical vertebra (C7) and lung metastasis. His laboratory findings showed elevation of biliary enzymes and tumor makers (S-pancreas-1 antigen, duke pancreatic monoclonal antigen type 2, carbohydrate antigen 19-9) (Table 1). Because the stomach lesion was diagnosed as early-stage cancer, we considered that these metastases were from intrahepatic cholangiocarcinoma rather than stomach cancer. Because the initial diagnosis for the facial nerve palsy was Bell's palsy, he was treated with prednisolone (50 mg/day) and acyclovir (1,000 mg/day) for 7 days. However, the treatment resulted in no improvement in his symptoms. After accurate diagnosis by image examinations, radiotherapy was performed for the tumors in the temporal bone and vertebra before systemic chemotherapy because of the possibility of spinal cord injury by bone fracture of C7. After radiation therapy (39 Gy/13 fr for the temporal bone and 35.1 Gy/13 fr for C7 from hospital day 8) was completed, his facial nerve palsy was relieved (Figure 2D). Soon after the radiation therapy, gemcitabine (1,700 mg) and cisplatin (44 mg) were infused on day 1 and day 8 (21 days for 1 course). However, during the second course, CT revealed massive growth of the intrahepatic cholangiocarcinoma that occupied almost all of the right lobe of the liver. Shortly after that, the patient had an onset of disseminated intravascular coagulation syndrome and died permanently 57 days after the admission date. During all periods after the radiotherapy, the symptoms of facial paralysis did not recur. The patient and his family have provided permission to publish these features of his case including his face

Table 1　Laboratory data.

		Normal range
WBC	10,090/mm^3	3,500~9,700
Hb	14.4 g/dL	13.6~18.3
Plt	155,000/mm^3	14.0~37.9
TP	6.7 g/dL	6.7~8.3
Alb	3.3 g/dL	3.9~4.9
t-Bil	0.8 mg/dL	0.2~1.2
ALP	191 IU/L	104~338
AST	17 IU/L	8~38
ALT	14 IU/L	4~44
γ-GTP	93 IU/L	16~73
BUN	13.5 mg/dL	8.0~20.0
Cre	0.46 mg/dL	0.61~1.04
Na	138 mEq/L	135~145
K	3.5 mEq/L	3.5~5.0
Cl	102 mEq/L	98~108
CRP	3.27 mg/dL	0.61~1.04
SPAN-1	45 U/mL	0.0~30.0
DUPAN-2	260 U/mL	0~150
CA19-9	250.1 U/mL	0~37.0
CEA	3.2 ng/mL	0~5.0
DCP	16 mAU/mL	0~40
AFP	2.44 mg/mL	0~8.78
PSA	0.158 ng/mL	0~4.000
HBsAg	0.00 mIU/mL	0.00~0.049
HBsAb	0.70 mIU/mL	0.0~9.999
HCVAb	0.09 S/CO	0.0~0.999

WBC, white blood cell; Hb, hemoglobin; Plt, platelet; TP, Total protein; Alb, albumin; t-Bil, total bilirubin; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma glutamyltransferase; BUN, blood urea nitrogen; Cre, creatinine; Na, sodium; K, potassium; Cl, chloride; CRP, C-reactive protein; SPAN-1, S-pancreas-1 antigen; DUPAN-2, duke pancreatic monoclonal antigen type 2; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; DCP, des-gamma-carboxy prothrombin; AFP, alpha-fetoprotein; PSA, prostate-specific antigen; HBsAg, hepatitis B surface antigen; HBsAb, anti-hepatitis B surface antibody; HCVAb, anti-hepatitis C antibody.

Table 2　Clinical characteristics of patients with skull metastases from intrahepatic cholangiocarcinoma.

No.	Author name (year of publication)	Age/sex	Symptoms	Location of skull metastasis	Metastasis to other organs	Treatment to the skull
1	Current case	70 y/M	Paralysis of right VII	Right temporal bone, mandible	C7, lung	Focal radiotherapy
2	Hanna et al. (2020)	61 y/M	Palpation of the mass	Right occipital bone	Th9-Th11, L2, L5	Total resection of the tumor, focal radiation and chemotherapy
3	Wang et al. (2019)	50 y/F	Pain and dizziness	Occipital bone	Liver, adrenal gland, and verebrae	Total resection of the tumor and chemotherapy
4	Fujimoto et al. (2013)	58 y/F	Pain and swelling around the left eyelid	Left orbit, Right parietal bone	none	Stereotactic radiosurgery
5	Fujimoto et al. (2014)	56 y/F	Pain	Left orbit, left parietal bone, left temporal bone	Lung	Chemotherapy and stereotactic radiosurgery
6	Fujimoto et al. (2015)	65 y/M	Pain and paralysis of Right IX X XI XII	Right petrous bone, Right occipital bone	Upper cervical vertebra	Chemotherapy and radiotherapy
7	Miyamoto et al. (2007)	67 y/F	Pain	Left occipital bone	Th12	Stereotactic radiosurgery and focal radiation

Th, thoracic vertebra; C, cervical vertebra; L, lumbar vertebra.

photos. The research ethics committee of the international university of health and welfare hospital approved this report for publication.

Ⅲ．Discussion

In this patient, intrahepatic cholangiocarcinoma caused facial nerve paralysis due to temporal bone metastasis. Malignant tumors are a serious cause of facial nerve palsy[5-7]. Temporal bone metastases of malignancy are common in breast and lung cancer, but rarely in intrahepatic cholangiocarcinoma[6]. Only 6 cases have been reported in PubMed and the initial symptoms are pain and palpation of the mass (Table 2)[8-11]. In previous reports, the scalp and dura were pressed by cranial metastases resulting in those symptoms. In the present case, the symptom is only palsy probably due to a lack of scalp and dura compression because no visible mass formation was shown by image examinations. Fujimoto et al. reported that cranial metastases in intrahepatic cholangiocarcinoma were from the osseous pathway via the craniospinal venous system, intracranial veins, and ophthalmic veins[10]. Our case was also associated with spinal metastasis, further confirming the association. Therefore, it is necessary to search for vertebral metastases when cranial metastases are suspected.

Since facial nerve palsy decreases the quality of life[2], symptom relief will increase the quality. Several cases have reported improvement in facial nerve palsy due to bone metastases by treatments. The most effective treatment for palliation is chemotherapy[12] or operation[13]. However, these treatments are invasive and it is often difficult to undergo. In our case, only radiotherapy was used as a palliative treatment due to the large number of metastatic lesions that would be difficult to resect surgically. The treatment provided symptomatic relief of facial nerve paralysis although the long-term effects of the radiotherapy were unknown. Since radiotherapy is an effective palliative treatment for pain by skull-base metastases[14] and for nerve palsy[15], this case was treated with radiotherapy to the

temporal bone for facial nerve palsy in addition to C7. Since single radiation therapy is less invasive compared with chemotherapy or operation therapy, it should be considered aggressively for palliative treatment for facial paralysis due to bone metastasis with considering adverse effects of radiation therapy such as chronic external otitis and exudative otitis media.

In conclusion, the possibility of cranial metastasis should be considered when facial paralysis occurs in patients with bone metastases of cancer. In such cases, radiotherapy should be considered for palliation of symptoms.

Disclosure of conflict of interest

The authors have no conflict of interest.

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肝内胆管がんの側頭骨転移により顔面神経麻痺を発症し，放射線治療にて軽快した1例

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岡田　真也　　土橋　洋　　一石　英一郎　　佐藤　貴一　　髙後　裕　　大竹　孝明

抄　録

側頭骨転移は顔面の痛みの原因となるが，顔面神経麻痺も呈しうる．症例は，70歳男性．右季肋部痛を主訴に当院紹介され，CTおよび肝生検にて肝内胆管がんと診断された．肝生検前日に右顔面神経麻痺を発症し，画像検査にて側頭骨転移による乳突蜂巣炎が原因と診断された．側頭骨に対して放射線治療を行ったところ，顔面神経麻痺は改善した．側頭骨転移は肺癌や乳癌の報告が多く，肝内胆管癌はまれである．肝内胆管癌側頭骨転移による顔面神経麻痺に対し放射線治療を行った報告はなく，本症例はそれが症状緩和に有用であることを示した．

キーワード：肝内胆管がん，顔面神経麻痺，放射線治療，側頭骨転移