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Case Report

Rapid growth of metastatic brain tumor from gastric undifferentiated pleomorphic sarcoma: A case report

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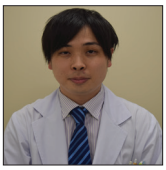

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ABSTRACT

Background: Brain metastasis from undifferentiated pleomorphic sarcoma (UPS) is a rare occurrence, and its clinical course is little known. In this report, we investigate a case of a rapidly growing brain metastasis from gastric UPS.

Case Description: An 82-year-old man with a known gastric tumor, pathologically compatible with UPS, underwent partial gastrectomy at an outside facility. 3 months later, a 4-cm brain tumor was detected, which was completely resected. The patient was diagnosed with metastatic tumor from previously treated gastric UPS. Within 2 months of the initial resection, a large recurrent mass was detected in the same location, which was again removed. Although the patient underwent radiotherapy and chemotherapy for other metastatic tumors, he died 5 months after the second craniotomy.

Conclusions: Brain metastasis from gastric UPS is rare and difficult to treat. Although aggressive treatment, such as surgical intervention, may improve patient survival in some cases, the timing of treatment is challenging because cerebral metastasis rapidly grows and and patients frequently suffer from synchronous systematic metastasis. Therefore, early detection and close follow-up of rapidly progressing brain metastasis are important to improve treatment outcomes.

Keywords: Brain metastasis, metastatic tumor, undifferentiated pleomorphic sarcoma

INTRODUCTION

Undifferentiated pleomorphic sarcoma (UPS) mostly occurs in the extremities and deep-seated soft tissuesbut has been reported to be found on the limbs (68%) and in the abdominal cavity/retroperitoneum (16%).[8,19] It commonly occurs in men older than 40 years, with a prevalence of 1–2 cases/10,000 people.[8,19] UPS has a poor prognosis, with a reported 2-year survival rate of 60%.[8,19] Gastric UPS are rare occurrences, and reports on clinical presentation are scarce.[8] Kabashima *et al.* analyzed the data on 16 patients with gastric UPS. The average age in these patients was 61 years, and the main chief complaint was pain. The average diameter of tumor was reported at 6.7 cm, and the 2-year survival rate was 25%.[8] In particular, brain

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metastasis from gastric UPS has not been reported in the available literature.[1,8,15,16,18,20] The central nervous system (CNS) appears not to be a common site for metastatic gastric UPS, probably due to its highly aggressive nature, with UPS often metastasizing primarily to the lung and liver.[8] Besides, the short overall survival (OS) for this primary disease[8] means that we rarely ever see patients at the later stages of the disease. In this case report, we review a case of rapidly growing brain metastasis from gastric UPS and discuss the management of such metastatic brain tumors.

CASE REPORT

This case report is a sequel to that by Kabashima *et al.*[8] An 82-year-old man underwent laparoscopy-assisted partial gastrectomy for gastric tumor at an outside hospital. The gastric tumor was pathologically diagnosed as UPS, which is a rare high-grade sarcoma. The patients' clinical course after his partial gastrectomy and the case-specific histopathological findings are reported in detail by Kabashima *et al.*[8] 3 months after the patient's first surgery, he was referred to our hospital due to new-onset dizziness and headaches. Magnetic resonance imaging (MRI) revealed a large cerebellar tumor with marked peritumoral edema. The tumor had not been present on staging scans (whole-body computed tomography [CT]) conducted immediately after the gastrectomy. On admission, brain CT revealed a 43 mm × 38 mm × 32 mm tumor in the left hemisphere of the cerebellum. MRI revealed that the tumor was iso-to-hyperintense on T1-weighted image (T1WI) and hyperintense on T2WI and demonstrated strong contrast enhancement after gadolinium injection [Figure 1]. Fluorodeoxyglucose positron emission-CT (^{18}FDG-PET-CT) revealed FDG uptake of SUV max 7.17. No other region with^{18}FDG uptake was detected.

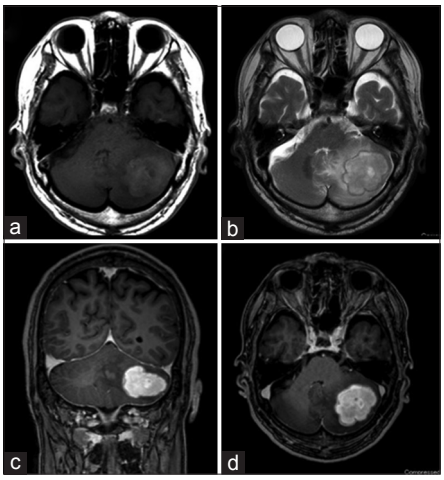

Figure 1: T1-weighted image (WI) (a) shows the 4-cm tumor in the left cerebellum with hypointense signal. T2WI (b) shows the tumor with hyperintense signal. Axial (c) and coronal (d) images showed the tumor after application of contrast enhancement.

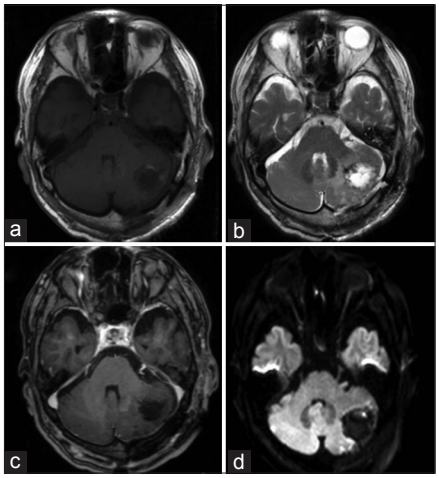

Figure 2: Postsurgical contrast T1-weighted magnetic resonance-images show complete resection of the tumor. (non-contrast T1-weighted image [WI] (a), T2WI (b), contrast T1WI (c), and diffusion- WI (d)).

The patient underwent standard suboccipital craniotomy without navigation or monitoring, performed in the prone position, and the cerebellar tumor was completely resected. The consistency of the white–yellow tumor tissue was dense, and the tissue plane between tumor and normal brain was clearly identified and microscopic gross total resection was achieved, and his postoperative course was uneventful. Postoperative MRI (within 24 h) and contrast MRI (within 72 h) revealed complete resection of the tumor [Figure 2]. Symptoms improved after surgery, and he had no deficit and was discharged to go home after 20 days from his operation.

Histopathological analysis showed a proliferation of spindle-to-polygonal-shaped tumor cells with enlarged irregular nuclei and eosinophilic cytoplasm arranged in sheet-like patterns, accompanied by chronic inflammatory infiltration and hemangiopericytomas Staghorn-type branching vessels [Figure 3a and b]. Employing Ki-67 stains, mitotic figures were frequently observed. Immunohistochemical panel demonstrated that tumor cells were positive for p53 [Figure 3c] and p16, focally positive for cytokeratin AE1/AE3 CAM5.3, alpha-smooth muscle actin, desmin, and muscle-specific actin (HHF35), but negative for multiple other markers such as cytokeratin CK5/6, CK903, CK14, p40, EMA, GFAP, Oligo-2, IDH-1, ERG, STAT6, and GRIA2. The automated count of MIB-1-labeling index was high and estimated at 37%. We compared brain specimen from the specimen of the stomach after microscopic analysis, and both specimens showed the same histological characteristic. Pathological findings were compatible with that of metastatic tumors from gastric UPS.

The patient underwent repeat brain imaging after 1 and ½ months at follow-up, and no apparent brain tumor residual or recurrence was observed. Only 2 weeks after that last visit, the patient started complaining of headache and nausea. A repeat MRI was ordered, which revealed a 4-cm recurrent cerebellar tumor in the same region, indicating that the 4-cm mass must have grown almost entirely within 2 weeks' window. Since 2 weeks prior, he had

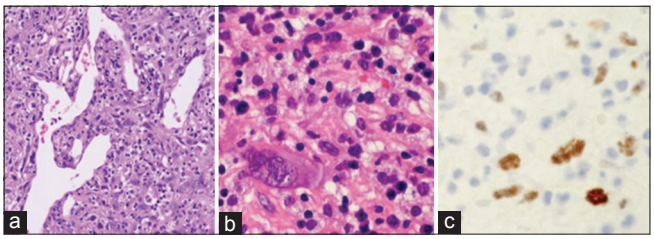

Figure 3: Hematoxylin and eosin (H and E) staining (a) low-power field, (b) high-power field) showed a proliferation of spindle-to-polygonal-shaped cells with irregular nuclei and eosinophilic cytoplasm arranged in a sheet-like pattern, accompanied by chronic inflammatory infiltration and hemangiopericytomas Staghorn-like branching vessels. Immunochemical staining for p53 marker was positive (c).

undergone a non-contrast CT with 5-mm slice thickness. Systemic restaging was not performed because the pathological diagnosis was not clear. Again, the patient was taken to surgery and the recurrent tumor mass was completely resected. Histopathological findings were indistinguishable from the previous metastatic tumor again with a MIB-1 labeling index of 37%. After the second operation, the patient received focused brain radiation therapy with added local irradiation (40Gy/20Fr) and three dimensional intensity-modulated radiation therapy (30 Gy/3 Fr) to the tumor cavity. However, a second 9-mm metastatic brain tumor appeared in the temporal lobe. In addition, at the time of radiation therapy to the two lesions of the CNS, further metastatic tumors were detected in the patient's tonsils. Although systemic chemotherapy was initiated adriamycin (30 mg/m^2) plus ifosfamide (2 g/m^2) (AI) at an age-adjusted dose of 75% and administered together with dexamethasone coverage;[11] the metastatic tonsilar tumor grew rapidly, indicating that chemotherapy was not effective. Further local radiotherapy in this region also had no effect. The patient was thus transferred to a palliative hospital where he expired 10 days later.

DISCUSSION

Sarcoma is a malignant mesenchymal tumor that originates from connective tissue of visceral organs, the digestive tract, and other soft tissues.[5] UPS is a soft tissue tumor classified as a tumor of uncertain differentiation in the WHO classification published in 2002.[4] It was previously called malignant fibrous histiocytoma. According to the updated 2013 WHO classification, these tumors are typically high grade, show a wide range of morphological features, and often have a poor prognosis. Genetic subsets of these tumors seem to be emerging in younger patients, including round-cell sarcoma with EWSR1 translocations and non-ETS fusion partners, CIC-DUX4 translocation, and BCOR-CCNB3 fusion.[7] UPS usually occurs in the extremities and deep soft tissues, and any account for an UPS of the gastrointestinal lesion is extremely rare. To the best of our knowledge, only 17 gastric UPS cases have been reported thus far.[1,8,15,16,18,20]

Brain metastasis from sarcoma is uncommon event, and the frequency of brain metastasis in cases of metastatic systemic soft tissue sarcoma (STS) is 1–4%.[3,14,17] STS originates from the extraosseous connective tissue and represents about 1% of all adult cancers.[6] UPS, which is one specific diagnostic entity of STS, accounts for no more than 5% of adult STS.[12]

There are a few reports of brain metastasis from sarcoma of the gastrointestinal tract and its poor prognosis.[1] A previous investigation of 17 cases of gastric UPS revealed that 63% of the cases had metastasized, although no brain metastases were described.[1,8,15,16,18,20] To the best of our knowledge, this is the first case report of brain metastasis from gastric UPS.

The prognosis of brain metastasis from UPS is not fully understood. Based on data from a case series of brain metastasis from STSs, the median survival of patients was 11.8 months.[17] Chua *et al.* reported the prognosis of brain metastasis from sarcomas and revealed that the median OS was low at 3.5 months (95% confidence interval 1.1–6.3 months).[2]

The National Comprehensive Cancer Network guidelines for soft tissue tumors state that surgery is the most effective treatment, combined with either chemotherapy or radiotherapy depending on the patient's performance status.[13] Chemotherapy involves administration of alkylating drugs such as cisplatin, ifosfamide, and adriamycin.[13] Chua *et al.*[2] reported that, for patients with brain metastasis from sarcomas, aggressive therapy including surgical resection or multimodality treatment, especially chemotherapy, can improve OS (3.7 months vs. 1.2 months). Kasper *et al.* have also suggested that, in noneloquent areas, aggressive local surgical resection should be followed by postoperative radiosurgery, while for eloquent areas, primary stereotactic radiosurgery (SRS) can be administered as an alternative therapy.[10]

In our case, both the initial and the recurrent metastatic brain tumors were rapidly growing. The first brain metastasis was detected only 2 months after gastrectomy, despite a localized primary tumor (T2N0M0). Moreover, the recurrent brain metastasis was detected again within only 2 months after craniotomy. Despite successful gross total resection and adjuvant treatment, our patient died 6 months after developing his first symptom.

Compared to other gastric cancers, this growth rate of the tumor was considered high, as the mean interval from gastrectomy to the diagnosis of brain metastasis has been reported to be 9.6 months.[9] Considering that brain metastasis of non-small cell lung cancer takes about 58 days to double in size, the volumetric tumor doubling time in our case was significantly shorter.[21] When comparing our case to other STS cases in whom median survival of patients was 11.8 months,[17] the length of our patient's OS was, hence, short. In our case, the patient underwent aggressive treatment, but chemotherapy and radiotherapy were ineffective and the clinical course was poor although we decided on resecting the tumor twice. Aggressive treatment for sarcoma can improve OS and should be pursued when possible.[2,10] However, early and adequate detection of the tumor is important to make an accurate diagnosis and pursue the appropriate therapy.

Based on our experience with this infrequent UPS brain metastasis, we want to alert neurosurgical oncologists to consider the possibility of brain metastasis from these rare gastric UPSs in their differential. We recommend that the brain should be frequently screened by MRI after resection of such a gastric tumor because UPS brain metastasis has shown rapid growth and it may be difficult to detect them clinically on early routine checkups if there are no symptoms. Further studies are needed to identify the best treatment algorithm which may include surgery, SRS, and adjuvant chemotherapy.

CONCLUSIONS

Brain metastasis from gastric UPS is rare. Although the tumor growth is rapid and aggressive treatment is important, accurate pathological diagnosis is difficult due to the tumor's rarity and its rapid progression. To detect metastatic CNS tumors from UPS early, routine MRI screening should be considered.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. We got patient's consent for his images and other clinical information to be reported in the journal. On his passing, we obtained informed consent from his wife, as the next of kin. The consent was obtained with the understanding that names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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