An Extracranial Metastasis of Glioblastoma Mimicking Mucoepidermoid Carcinoma

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Key words
- Extracranial metastasis
- Glioblastoma (GBM)
- Mucoepidermoid carcinoma (MEC)
- Parotid

Abbreviations and Acronyms
GBM: Glioblastoma
GFAP: Glial fibrillary acid protein
IDH: Isocitrate dehydrogenase
MEC: Mucoepidermoid carcinoma

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BACKGROUND: **Glioblastoma (GBM) is the most common and aggressive primary malignant tumor of the brain and central nervous system. Extracranial metastases of GBM are rare, with few case reports published to date. The tumor cells of GBM show strong immunopositivity for glial fibrillary acid protein.**

CASE DESCRIPTION: **A 47-year-old man without comorbidities presented with a 1-year history of an augmenting right parotid lump. A right total parotidectomy with selective neck dissection was performed. The hematoxylin–eosin-stained slice of a parotid lymph node collected intraoperatively revealed destruction of normal lymph node structure by medium-sized pleomorphic cells scattered in groups; their cytoplasm was lightly stained and pale. There were abundant myxoid stroma in the interstitial tissue. This characteristic mimicked mucoepidermoid carcinoma. An immunohistochemistry test demonstrated that the tumor cells were positive for glial fibrillary acid protein. A diagnosis of extracranial metastasis of GBM was made after confirmation with postoperative pathologic examination and the review of the intracranial resection specimen.**

CONCLUSIONS: **We believe that this is the first reported case of extracranial metastasis of GBM resembling mucoepidermoid carcinoma in the microscope features. Pathologists and clinicians should be alert to this rare lesion and consider this differential diagnosis after excluding other common parotid lesions.**

INTRODUCTION

Glioblastoma (GBM) is the most common and aggressive primary malignant tumor in the brain and central nervous system. Its median survival time is 15 months.[1] Although the treatment modalities have improved, it remains largely incurable.[2] Based on the isocitrate dehydrogenase (IDH) mutation status, GBM is now classified into 2 types of GBM, IDH-wildtype and GBM, IDH-mutant. The histologic grade of GBM is IV.[3,4] The tumor cells of GBM are strongly positive for glial fibrillary acid protein (GFAP).

Extracranial metastases of GBM are rare, with few case reports published to date. Here we report an extracranial GBM that resembled mucoepidermoid carcinoma (MEC) metastasized to the parotid gland and parotid lymph nodes. The patient underwent a right total parotidectomy with selective neck dissection.

CASE REPORT

A 47-year-old man without comorbidities presented with a 1-year history of a right

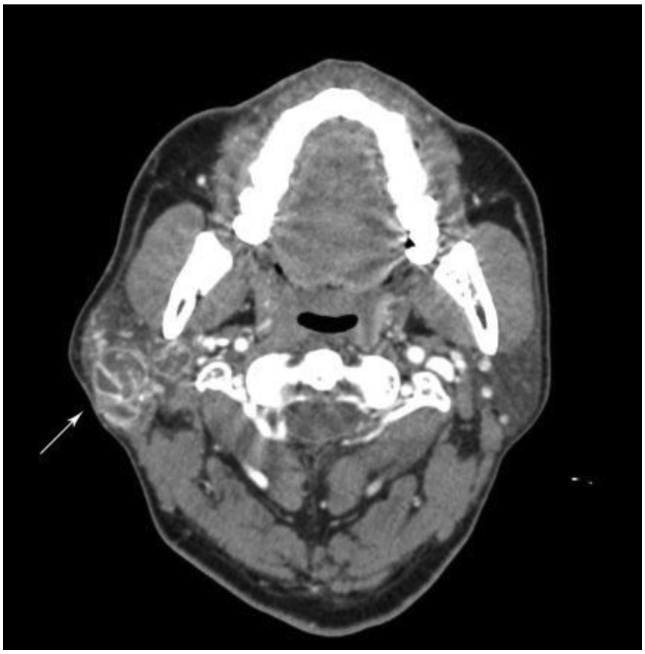

Figure 1. Computed tomography of a right parotid mass (the area *arrow* pointed) and neck liquefied lymph nodes.

parotid lump that was increasing in size. Examination revealed a well-demarcated parotid mass with a diameter of 4 cm and pain on touch. This man had a history of brain GBM resection 2 years ago, and received postsurgical radiotherapy.

A computed tomography scan revealed multiple focuses in the inferior right parotid, the right parotid ear area, and the right deep parotid lobe, of which the diameters measured from 0.5 to 2 cm. The computed tomography features were edge and center liquefied enhancement, with unclear sticky border. The right deep cervical area showed multiple focuses, the diameters were about 0.5 cm, and were suspected to be liquefied round lymph nodes. The right temporal bone presented a defective postoperative change. In addition, there was a 1.2 × 0.8 × 0.8 cm oval low-density lesion in the defective edge of the right temporal bone (Figure 1).

The immediate pathologic examination of a parotid lymph node collected intraoperatively revealed destruction of normal lymph node structure by medium-sized pleomorphic cells scattered in groups; their cytoplasm was lightly stained and pale. There were abundant myxoid stroma in the interstitial tissue. This feature was similar to MEC (Figure 2). These tumor cells were positive for GFAP (Figure 3). The postoperative pathologic examination, performed by 2 professional pathologists, showed medium-sized pleomorphic cells infiltrated into the parotid gland, lightly acidophilic cytoplasm, pleomorphic nucleus and pathological mitosis. Microvascular proliferation was encountered (Figure 4). These cells were positive for GFAP (Figure 5).

We reviewed the previous intracranial resection specimen for comparison. The slices displayed a tumor consisted of medium-sized cells with hyperchromatic nuclei and vacuolated, clear cytoplasm (Figure 6). The tumor cells in the intracranial sample were positive for GFAP (Figure 7). A cytologic diagnosis of metastatic GBM was determined.

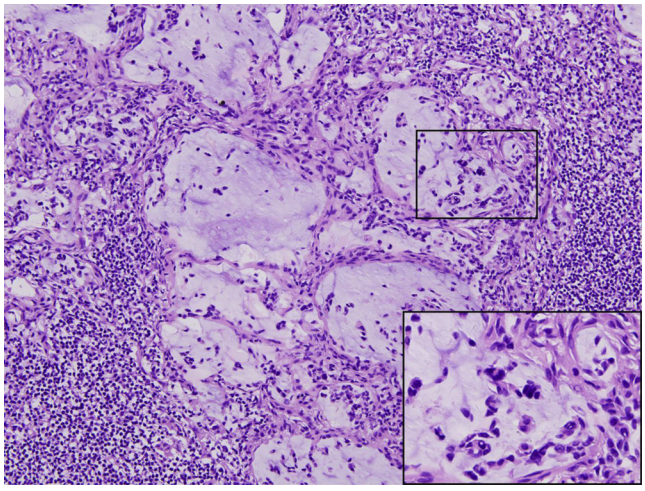

Figure 2. Microscopic appearance of tumor cells in the parotid lymph node showing mucoepidermoid carcinoma–like features. (Hematoxylin–eosin staining, original magnification was ×20.)

DISCUSSION

GBM is the most common and aggressive primary brain and central nervous system malignant tumor. Reported cases of GBM metastases in the literature are rare. They have been reported to occur in 0.4%–0.5% of all cases.[5] The documented cases of GBM extracranial metastases included cases that spread to oral cavity,[5] osseous, spine, vertebral, ribs, sternum, skull, acetabulum, lung, liver, lymph nodes, abdominal, spleen, adrenal gland, subcutaneous tissue, scalp, and parotid gland.[6-11] Currently, the prognosis of patients with extracranial metastases of GBM is poor, and most die within 6 months of diagnosis.[12]

According to the criteria proposed by Weiss, a diagnosis of extracranial metastases of primary central nervous system tumors must include the following conditions: 1) a clinical history strongly suggestive of a primary central nervous system tumor; 2) pathologic findings of metastatic lesions in accordance with characteristics of the intracranial primary tumor, despite the acceptance of some degree of anaplastic degeneration compared with

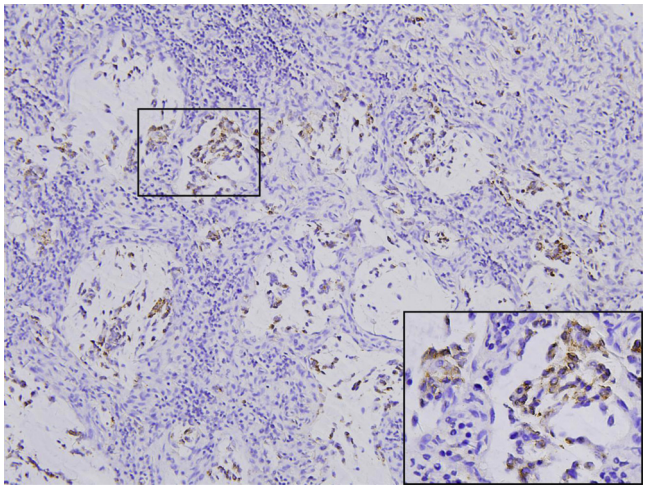

Figure 3. Positive immunohistochemical staining of the tumor cells in the parotid lymph node for glial fibrillary acid protein. (Immunohistochemistry test, original magnification was ×20.)

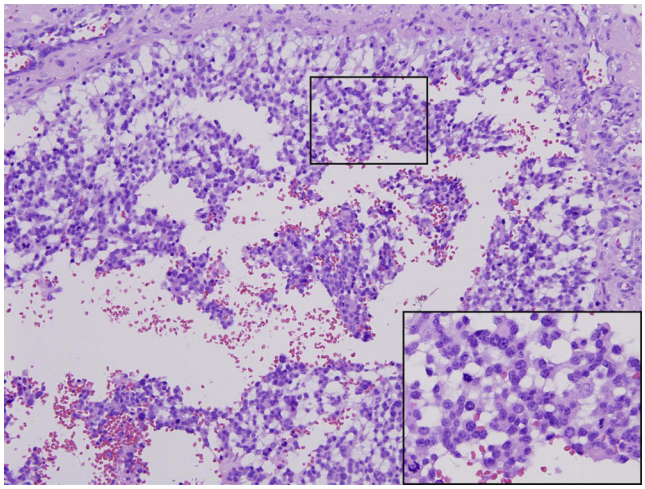

Figure 4. Microscopic appearance in the parotid gland showing medium-sized tumor cells infiltrated into the parotid gland, pleomorphic nucleus, pathologic mitosis, and microvascular proliferation. (Hematoxylin–eosin staining, original magnification was ×20.)

the primary tumor; and 3) a comprehensive autopsy or whole-body examination to eliminate other primary neoplasms.[12] In our case, the diagnosis of extracranial metastases of GBM met all of the criteria.

The GBM extracranial metastasis to parotid is very rare among all the metastatic sites. In our case, the immediate pathologic examination specimen was a parotid lymph node. Its abundant myxoid interstitial structure and unusual site almost led to a mistaken diagnosis of MEC. MEC is the most common salivary gland malignancy.[13] It consists of 3 main types of cells in microscope: epidermoid, mucous, and intermediate cells. MEC also contains other types of cells, including aquamous, maternal, clear, columnar, and other less-common cell types.[14,15] Based on the extent of cyst formation, differentiation of the 3 main cell types, and cytomorphologic changes, current grading systems of MEC are established.[15-17] Among MEC, mucous cells are swollen or balloon-shaped with clear cell boundaries. The nuclei are compressed by myxoid cytoplasm and located near the periphery of the cell. Their cytoplasm is slightly basophilic and pale. All these features were similar with the microscope features of our immediate pathological examination specimen.

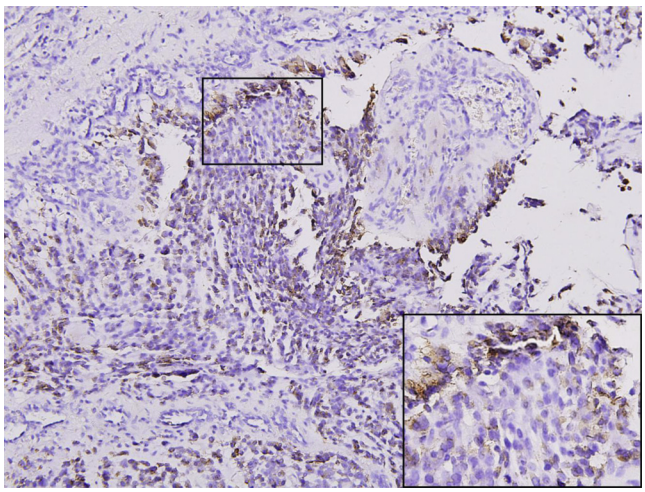

Figure 5. Positive immunohistochemical staining of the tumor cells in the parotid gland for glial fibrillary acid protein. (Immunohistochemistry test, original magnification was ×20.)

However, the mucous cells in MEC show positive for mucicarmine and periodic acid–Schiff stains.[14] This characteristic was different from our case, whose cells were positive for GFAP. Pathologists should pay attention to this resemblance and divergence to avoid mistaken diagnoses. The history is also pivotal data that could not be neglected.

Although the complex extracranial metastatic mechanism still remains unclear, iatrogenic spread because of surgery intervention may be the prime reason.[12] During the surgery, tumor cells obtain access to the bloodstream through defects in the meningeal and parenchymal blood vessels that are created from surgery manipulations.[18] However, there are case reports about extracranial metastases in the absence of surgical operations.[19] For the present case, in which metastases occurred in parotid and its lymph nodes, we speculate that lymphatic spread may be the underlying mechanism.

Our speculation is in contrast to an earlier hypothesis in another case report about GBM extracranial metastasis to parotid gland, where early hematogenous spread may be the underlying mechanism for extracranial metastases.[10] Louveau et al.[20] discovered the central nervous system lymphatic system. In their study, the lymphatic vessels lining the dural sinuses expressed all of the molecular hallmarks of lymphatic endothelial cells, carried both fluid and immune cells from the cerebrospinal fluid, and were connected to the deep cervical lymph nodes. This finding opposed the traditional opinion that the brain and

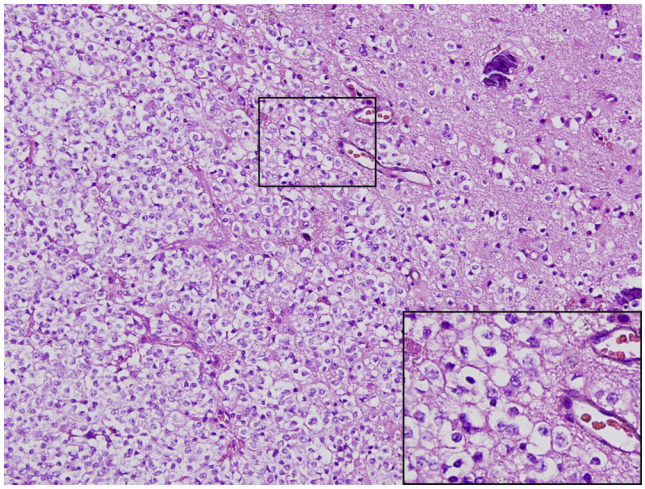

Figure 6. Microscopic appearance of intracranial tumor cells showing hyperchromatic nuclei and vacuolated, clear cytoplasm with microvascular proliferation. (Hematoxylin–eosin staining, original magnification was ×20.)

spinal cord lacked a lymphatic system that would allow systemic dissemination.[12] This assumption supports our hypothesis and could provide a new clue for the detection of extracranial metastatic mechanisms. In addition, recent studies reported that circulating GBM cells can be isolated from the bloodstream,[21] perhaps leading to metastasis.

CONCLUSIONS

To the best of our knowledge, this is the first reported case of extracranial metastasis to the parotid gland and parotid lymph nodes of GBM, whose microscopic features resemble those of MEC. Pathologists and clinicians should be alert to this rare lesion and consider this differential diagnosis after excluding other common parotid lesions.

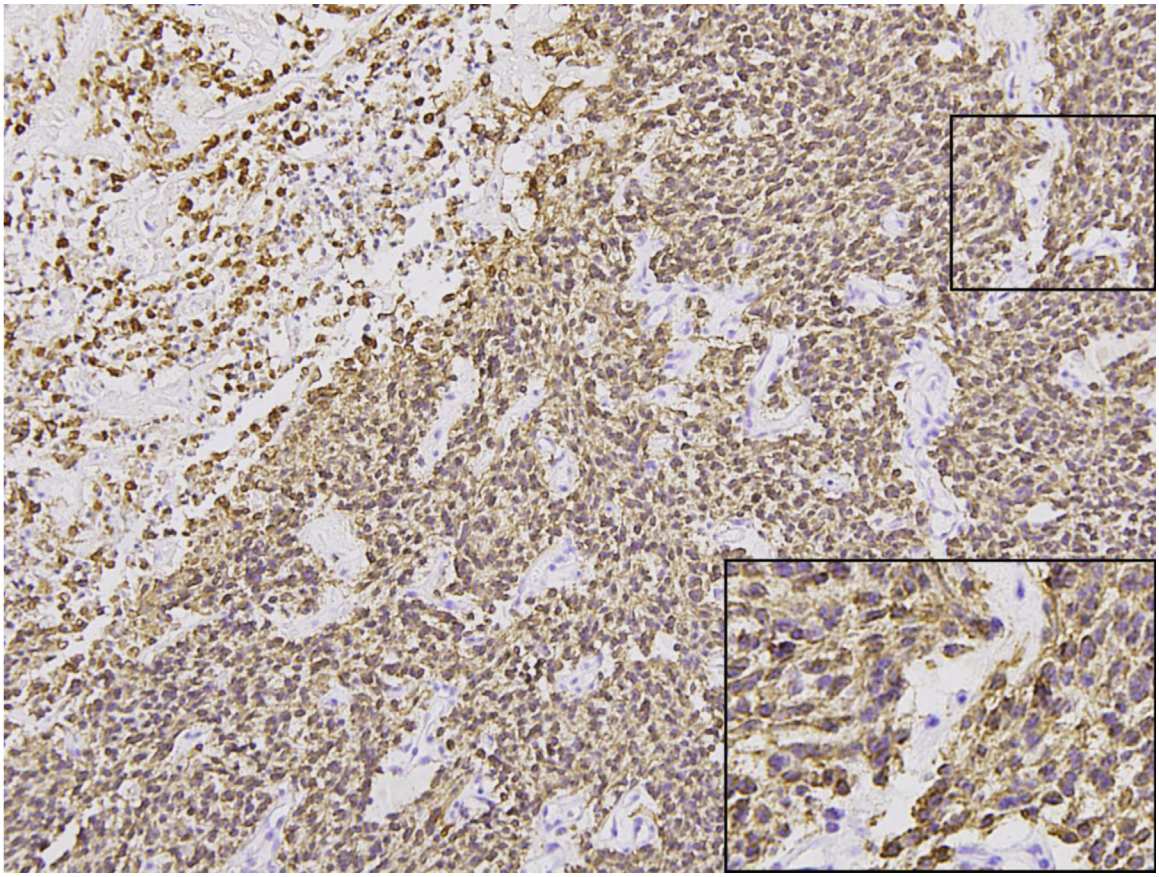

Figure 7. Positive immunohistochemical staining of the intracranial tumor cells for glial fibrillary acid protein. (Immunohistochemistry test, original magnification was ×20.)

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