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Case Report

Multiple Extraneural Metastases of Anaplastic Oligodendroglioma

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Abstract

Oligodendrogliomas (ODGs) is a diffuse glial tumor that constitutes 4.2% of all brain tumors. Extraneural metastases, sometimes seen in glioblastoma multiforme, are extremely rare in ODG. In this report, we present a 63-year-old male patient who was diagnosed with Grade 3 ODG and had an intracranial mass resected in our clinic 4 years ago. The subject now presented with low back pain and was found to have widespread metastases. The prolongation of patient survival by current treatment regimens has revealed a growing number of ODG patients with metastases. We believe that back pain complaints in patients with ODG should be viewed as an indicator of metastasis.

Keywords: *Anaplastic oligodendroglioma, extraneural, metastases*

Introduction

Oligodendrogliomas (ODG) is a diffuse glial tumor that constitutes 4.2% of all brain tumors.[1,2] Although primary brain tumors can metastasize, this fact is usually ignored both by neurosurgeons and neuro-oncologists during patient follow-up. Liwnicz and Rubinstein[3] reported on a panel of 116 patients with extraneural metastatic brain tumors; the most common were glioblastoma multiforme (41.4%), medulloblastoma (26.7%), ependymoma (16.4%), and astrocytoma (10.3%). ODG rarely metastasized (5.25%). According to a review published by Li *et al*.,[4] to date a total of 61 metastatic ODG cases have been reported in the English literature. In this report, we present a patient with anaplastic ODG and multiple extraneural metastases.

Case Report

A 63-year-old man was admitted with complaints of low back pain. No significant deficits were found in a neurological examination. Four years ago, he had a gross total resection of a right frontal, highly contrast-enhancing 42 mm × 32 mm × 28 mm mass in our hospital [Figure 1]. Histopathological analysis of the tumor revealed atypical glial cells, focal necrosis, large areas of bleeding, frequent apoptosis, and 3–4 mitoses. S100 and focal glial fibrillary acidic protein (GFAP) staining was observed. The tumor was negative for epithelial membrane antigen, and Ki-67 expression was observed in 15–20% of the cells [Figure 2a]. In light of these findings, the mass was diagnosed as an anaplastic ODG and the subject was treated with postoperative radiotherapy (60 Gy in thirty fractions). Chemotherapy was not performed. Magnetic resonance imaging indicated no recurrence of the tumor after an interval of 6 months. The subject had no postoperative neurological deficits.

The man was presently scanned by magnetic resonance imaging. No intracranial lesion was detected, but there were multiple calvarial nodular lesions and an involvement of bone marrow in multiple vertebrae. In addition, epidural contrast-enhancing lesions at T5 and T9 and contrast-enhancing lesions in psoas muscle at L1 and L2 levels were found [Figure 3]. Positron emission tomography revealed lymph node invasion in the bilateral supraclavicular area, jugular notch, right parasternal area, right retrocrural area, and retrocaval areas. Multifocal lymph node invasion was detected in the cranium, left mandibular head, sternum, vertebrae, ribs, both upper extremities, pelvic bones, both femurs, and hypermetabolic lesions in the right psoas muscle at the L1–L2 level [Figure 4]. Surgery was not planned due to a lack of deficits. A CT guided Tru-cut needle biopsy was obtained from the lesion at the L1–L2 level. The biopsy contained small number of round, oval, and

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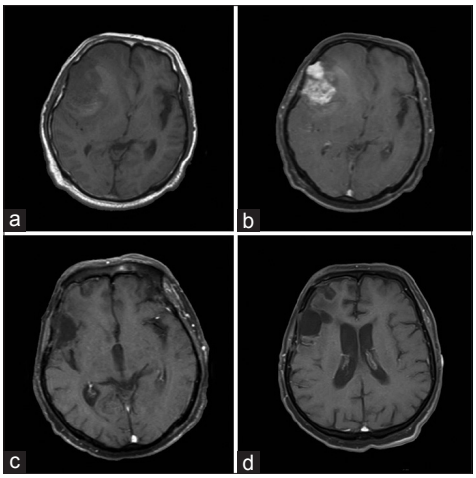

Figure 1: Intense contrast-enhancing mass in preoperative T1 (a) and contrast-enhanced T1-weighted (b) axial images. No residual or recurrent lesions in contrast-enhanced T1-weighted axial images were detected in the 1st (c) and 3rd (d) year after surgery

some spindle cells, but was negative for all immunological markers indicative of plasmacytoma, melanoma, lymphoma, and epithelial neoplasia. The tumor cells showed diffuse positive staining for GFAP and mild positive staining for S100. A second biopsy was obtained and after reviewing the patient's clinical information and re-examining the samples taken from his intracranial tumor, determined to be a glial tumor metastasis [Figure 2b]. The patient underwent radiotherapy, and then died from multiple organ failures 3 months later.

Discussion

The rarity of extraneural metastasis of primary brain tumors has been attributed to the absence of lymphatic drainage from the brain, the inability of neural tissue to grow outside the central nervous system (CNS), the blood-brain barrier, and the short survival times of the patients.[1,5] In addition, due to the absence of many types of connective tissue within the brain parenchyma, metastases of primary CNS tumors do not contain the specialized subpopulation of cells capable of invading most connective tissue, thus limiting tumor spread within the peripheral organ.[6]

Including our case, a total of 62 ODG cases with single or multiple extraneural metastases have been reported. Bone and bone marrow metastases were described in 48 of the cases, whereas lymph node metastasis was found in 23 cases. Liver, scalp, lung, pleura, chest wall, iliopsoas muscle, adrenal gland, parathyroid gland, spleen, pancreas, breast, and thymus are other organs of metastasis.[4] Zustovich *et al*.[7] reported that high rates of metastasis to bone and bone marrow at gliomas will be related to neural cell adhesion molecule (NCAM). NCAM is largely expressed by gliomas and also by osteoblast. The reason for the high predilection for the bone and bone marrow showed by metastatic ODG might be explained on the basis of the NCAM can perform hemophilic NCAM-NCAM

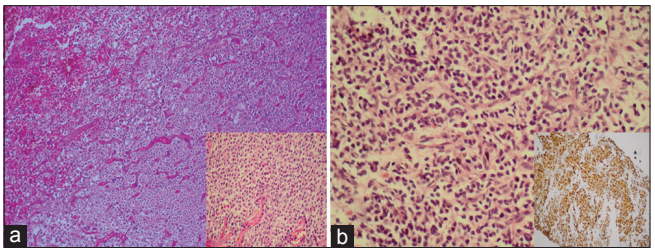

Figure 2: (a) Glial cells with round nuclei associated with Grade 3 oligodendroglioma in a sample of the original intracranial mass; H and E, ×100 (inset: ×400). (b) Dense, atypical cellular proliferation with the presence of oval nuclei in the spinal metastasis; H and E, ×400 (inset: Positive staining for glial fibrillary acidic protein, ×200)

bindings which may be the molecular basis of the implants of ODG cells in the bone and bone marrow.

Primary brain tumors usually metastasize through local invasion, cerebrospinal fluid (CSF), lymphatics, and the bloodstream.[8] There is no lymphatic drainage in the brain and spinal cord, but infiltration of tumor cells into the dura mater makes lymphatic spread possible.[4] Shunt surgery increases the risk of initiating metastasis via the CSF, which accounts for 1–2% of ODG metastatic events.[9] Hoffman and Duffner[10] reported that only 24 of 282 patients with extraneural metastatic glioma did not undergo surgical intervention, suggesting that surgical intervention may increase the chances of metastasis. Metastasis via the bloodstream is thought to occur during surgery or through the meninges.[11,12]

The median survival time of the published metastatic ODG cases was 38 months (range: 3–288 months). Increased survival time is thought to correlate with an increased likelihood of metastasis.[4] Molecular studies on ODG have revealed that 1p/19q co-deletions increase the tumor's sensitivity to chemotherapy and radiotherapy, extending survival time.[13,14] Overall survival time was found to be 6–7 years in patients with 1p/19q co-deletions but only 2–3 years in patients without the co-deletions.[15,16] The authors suggest that ODG tumors with 1p/19q co-deletions may be more prone to metastasis over time. Li *et al*.[4] did not report 1p/19q co-deletion data in their review.

In our patient, the initial surgery may have led to metastasis through vascular and/or lymphatic routes. In addition, the proximity of the tumor to the dura mater may have led to its invasion. The fact that our patient survived for 51 months, 13 months over the average, may have also contributed to the occurrence of metastasis. One limitation of our study is that we did not perform a genetic analysis of our patient's primary tumor or metastases. However, it is interesting that the metastases accumulated after 4 years without a residual or recurrent lesion in the brain, unlike most metastatic ODG cases in the literature.

Conclusion

Although extraneural metastasis of primary brain tumors is a rare phenomenon, the prolongation of survival times

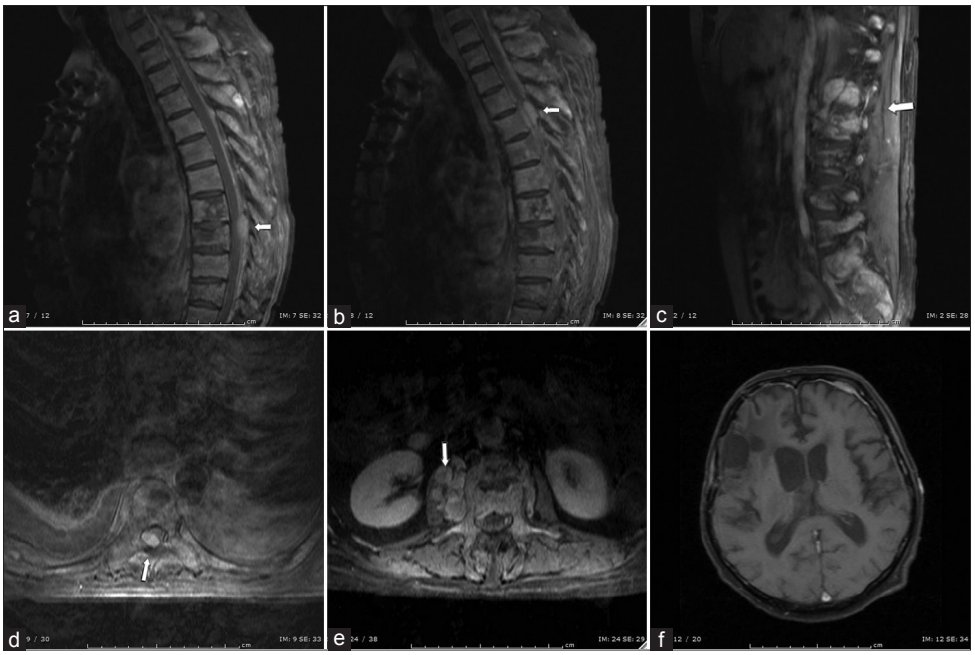

Figure 3: Metastatic lesions (shown by arrows) in T1-weighted sagittal (a-c) and axial (d and e) images at T9 and L2 levels. No recurrent lesions were detected in the brain in contrast-enhanced T1-weighted axial images (f)

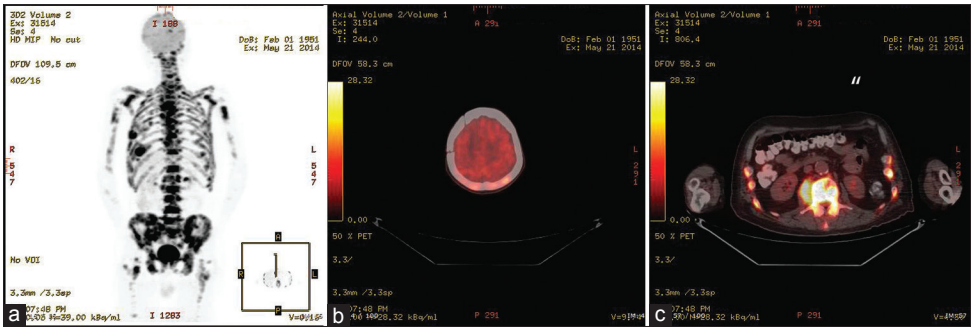

Figure 4: Positron emission tomography images showing (a) multifocal bone involvement and (b and c) hypermetabolic lesions (shown by arrows) in the cranium (b) and right L2 level (c)

by current treatment strategies has revealed a growing number of patients with extraneural metastases. As our patient presented only with back pain, we believe that back pain complaints in patients with ODG should be taken as a possible indicator of metastasis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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