Published in final edited form as:

Clin Imaging. 2014 ; 38(4): 505–507. doi:10.1016/j.clinimag.2014.02.015.

Intramedullary Spinal Cord and Leptomeningeal Metastases from Intracranial Low-grade Oligodendroglioma

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Abstract

We present an unusual case of a patient with an intracranial low-grade oligodendroglioma who developed recurrence with an intramedullary spinal cord metastasis and multiple spinal leptomeningeal metastases. The intramedullary spinal cord metastasis showed mild enhancement similar to the original intracranial primary, while the multiple spinal leptomeningeal metastases revealed no enhancement. This is the seventh reported case of symptomatic intramedullary spinal cord metastasis from a low-grade oligodendroglioma.

Keywords

Intramedullary spinal cord metastasis; leptomeningeal metastasis; MRI; oligodendroglioma

Case Report

A 37-year old woman initially presented with mixed complex partial and generalized tonic-clonic seizures. MRI brain revealed an expansile T2-hyperintense tumor in the left frontal lobe, temporal lobe, insula/subinsula and basal ganglia with punctate nodular enhancement. Considered unresectable due to its deep location, a stereotactic biopsy revealed a low-grade glioma without anaplasia. With the punctate enhancing components suspicious for high-grade glioma components possibly missed by sampling error, and corresponding foci of increased relative cerebral blood volume (rCBV) at dynamic susceptibility contrast (DSC) perfusion imaging, she received partial brain radiation therapy (RT) with 5940 cGy administered in 33 fractions over 6 weeks without concomitant chemotherapy. A partial response was achieved with the tumor decreasing by >50% on the initial post-RT scan. The patient remained stable without adjuvant chemotherapy, and she was observed on only levetiracetam for seizure control.

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Four years later, the patient returned with complaints of migraine headaches, expressive aphasia and memory loss. An MRI brain showed an increased expansile T2-hyperintense tumor with new mildly enhancing components, and increased plasma volume and increased Ktrans at dynamic contrast enhanced (DCE) T1 perfusion. Fig 1. The patient was impaired on the Boston Naming Test (46/60) with word finding difficulties, hesitancy and paraphasias. A functional MRI suggested that the probable recurrent tumor could be safely albeit incompletely resected. Subtotal resection revealed a low-grade oligodendroglioma with 1p36 and 19q co-deletions by fluorescence in-situ hybridization, R132H mutant isocitrate dehydrogenase-1 by liquid chromatography-mass spectrometry and MIB-1 <3%. Given the favorable molecular and histological profile, she was again followed without adjuvant chemotherapy.

Fourteen months after the repeat craniotomy, and 5.8 years since initial diagnosis, the patient complained of worsening pain, numbness and weakness in her left leg as well as new thoracic back pain. MRI spine showed a partially exophytic intramedullary T2-hyperintense mildly enhancing tumor in the upper thoracic spine. Multiple nonenhancing slightly T2 hyperintense (although less than cerebrospinal fluid) leptomeningeal nodules in thoracolumbar spine were also present. Fig 2. The patient refused surgery and cerebrospinal fluid sampling was negative. Given the imaging similarity of these spinal lesions with the low-grade oligodendroglioma in the brain, however, these were presumed to represent intramedullary spinal cord and leptomeningeal metastases and not a disseminated second primary malignancy. The spinal cord metastasis was treated with RT to 4500 cGy administered in 25 fractions over 6 weeks. Six months after completion of thoracic RT, the intramedullary metastasis had resolved and the leg weakness had improved. Fig 3. The nonenhancing thoracolumbar leptomeningeal metastases continued to grow, however, and the patient complained of worsening thigh pain. RT was then prescribed to the leptomeningeal metastases with 4500 cGy administered in 25 fractions over 6 weeks. The pain improved after RT and the patient is now doing well now 1.5 years after diagnosis of the spinal metastases and 7 years after initial brain diagnosis.

Discussion

Leptomeningeal metastases are diagnosed in about 5% of all cancers.¹ Intramedullary metastases are less commonly diagnosed in about 2% of systemic cancers at autopsy.² Most leptomeningeal metastases from primary brain tumors are from malignant high grade tumors such as glioblastoma, anaplastic glioma and medulloblastoma. For malignant astrocytic gliomas, dissemination through the cerebrospinal fluid has been described at 10–21% at autopsy.^{3, 4} Even with a high grade tumor like glioblastoma, intramedullary metastases are uncommon with only 35 cases summarized in a recent review.⁵ The prevalence of leptomeningeal and intramedullary metastases, however, is likely increasing due to improvements in imaging technology and treatment regimens affording improved diagnosis and prolonged time to develop these complications.

The most common pattern of dissemination for oligodendrogliomas is via the subarachnoid spaces, with oligodendroglioma tumor cells reported in the cerebrospinal fluid of up to 14% of patients⁶. Intramedullary metastasis from an intracranial oligodendroglioma is much less

common, with a review by Elefante et al. ⁷ reporting only 4 intramedullary cases, one of whom also had concurrent leptomeningeal metastases. Two of the 4 cases were high-grade oligodendrogliomas, as were another 2 cases reported by Godard et al. ⁸. The lack of high-grade disease in our case and half of Elefante et al.'s cases (or 42.9% of all 7 cases) suggests that high-grade disease is not a requirement for intramedullary dissemination of tumor.

The mechanism of intramedullary dissemination rather than the more common leptomeningeal dissemination remains unclear, even in these tumors with known propensity for cerebrospinal fluid dissemination. Postulated pathways into the spinal cord parenchyma include dissemination through the perivascular spaces or central canal, and direct invasion of leptomeningeal metastases across the pia ^{2, 7}. The latter is probably the most common as intramedullary and leptomeningeal metastases are found together in up to 27% of cases ⁹. Isolated intramedullary metastases may also occur from hematogenous dissemination ². The rarity of isolated intramedullary metastases in oligodendroglioma may reflect the rarity of extraneural metastases, with only 33 cases reported in the literature ¹⁰.

The low-grade oligodendroglioma had multiple positive prognostic factors including 1p19q codeletions and mutant IDH1 ¹¹. The intramedullary spinal cord metastasis and multiple spinal leptomeningeal metastases in our patient were diagnosed 5.8 years after the initial diagnosis of intracranial low-grade oligodendroglioma. The 5.8 years is longer than the 6 patients with intramedullary metastases reported by Elefante et al. ⁷ and Godard et al. ⁸, who had a mean interval of 0.92 years (range, 0–1.75). This may reflect the natural progression of this low-grade oligodendroglioma, as the patient had never received systemic chemotherapy.

In conclusion, intramedullary metastases may occur from intracranial oligodendrogliomas without high-grade tumor or malignant transformation, and present in a delayed manner after the intracranial tumor. With both synchronous as well as delayed intramedullary metastases possible, even vague signs and/or symptoms should prompt consideration of imaging of the entire neuraxis at diagnosis and after treatment. The nonenhancing leptomeningeal metastases also caution against overreliance on only contrast T1-weighted images for evaluation for disseminated disease.

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Fig 1.

Axial FLAIR (A) and contrast T1-weighted (B) images at diagnosis reveal a FLAIR hyperintense tumor in the left insula, subinsula and basal ganglia with punctuate nodular enhancement. Dynamic susceptibility contrast (DSC) T2* perfusion (C) map reveals increased rCBV in the basal ganglia (arrow). Corresponding images four years later (C, D) demonstrate recurrent T2 hyperintense tumor with ill-defined enhancement. Dynamic contrast enhanced (DCE) T1 perfusion maps show increased focally increased Ktrans (arrow, F) and plasma volume (arrow, G).

Fig 2.

A little more than 1 year later, sagittal T2-weighted (C) and contrast T1-weighted (D) images reveal the expansile T2 hyperintense intramedullary metastasis in the upper thoracic cord and mild enhancement at the T1–T2 level. Axial T2-weighted images demonstrate the intramedullary component at the T1 level (E) and extramedullary component with mild compression at the T4 level (F). Sagittal T2-weighted (G) and contrast T1-weighted (H) images through the lower spine demonstrate additional T2 hyperintense nonenhancing leptomeningeal metastases along the cauda equina nerve roots.

Fig 3.

Six months after completion of spinal RT to the thoracic spine, sagittal T2-weighted images (A, B) reveal complete resolution of the thoracic intramedullary/extramedullary spinal cord metastasis, although there is continued growth of the nonenhancing lumbosacral leptomeningeal metastases (compare 3B with 2D).