Brain metastasis masquerading as glioblastoma multiforme and lymphoma

Diagnostic challenges in neurosurgery

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INTRODUCTION

Brain tumors include a number of different pathologic entities that can present clinically in a number of ways. Dull holocephalic headaches are common. They sometimes correspond to the laterality of the tumor, and may have a morning predilection.¹ Additional common presenting symptoms include focal neurological deficits and seizures. The localization of deficits is important in predicting tumor location and type. Cognitive dysfunction is more common with frontal lobe lesions, and symptoms include anhedonia, mood and personality changes, and fatigue.² Focal muscle weakness can be localized to a variety of locations along the corticospinal tract, including the frontal lobe and precentral gyrus, internal capsule and brainstem. Parietal lobe dysfunction can lead to cortical sensory deficits, lack of spatial orientation, paresthesias and loss of coordination.

Brain tumors can be classified into lesions originating from the central nervous system (CNS), or metastases from a systemic origin. Metastases are the most common brain tumors, whereas glioblastoma multiforme (GBM) is the most common primary brain tumor.^{3,4} In adults with systemic malignancies, 10-30% will develop brain metastases.⁵ Metastases usually spread hematogenously, and localize to the white-grey matter junctions.^{6,7} Despite the majority of brain tumors being metastases, many patients present without a known primary.³ As such, a thorough diagnostic work-up is imperative, although imaging is sometimes not definitive. In this report, we examine the case of an adult male who presented with worsening balance and was identified to have a brain tumor. The diagnostic characteristics and challenges are discussed.

CASE REPORT

PATIENT PRESENTATION

A right-handed 67 year-old man presented to a peripheral hospital with acutely worsening balance before being transferred to University Hospital. He first slipped and fell in summer 2015, sustaining a mild head injury with no loss of consciousness. His balance and coordination continued to deteriorate, and he eventually required a cane to ambulate. In December 2015 he was observed to be using inappropriate cutlery and was having general dexterity issues. He also developed right arm and hand numbness, followed by difficulty seeing objects on his right and bumping into objects on this side. These symptoms were accompanied by a dull and progressive headache at the right posterosuperior aspect of his head. The headache was intermittent, did not depend on the time of day, and was not associated with nausea or vomiting. He had also lost 20-30 pounds over the previous year.

The patient's past medical history was significant for a 50 pack-year smoking history, episodes of bronchitis and pneumonia, alcohol abuse, and Vitamin B12 deficiency. His only regular medication was Advil as needed for headaches; he had not received B12 supplementation for approximately 7 months. His grandson was born with a brain tumor of unknown etiology. He worked in packaging in Toronto before moving to Walkerton 7 months prior to symptom onset.

On exam, the patient was alert and oriented, although he had some difficulty following instructions. He demonstrated a right homonymous hemianopsia. There was a right pronator drift, and increased tone on the right. He had a marked bilateral upper limb intention tremor. There was full power bilaterally. He had difficulty performing right-sided fine finger movement, and right upper limb dysmetria and dysidiadochokinesis. There was a right-sided upgoing Babinski reflex. The patient had diffusely decreased light touch and pinprick sensation on his right arm (40-70% less than his left side). Finally, he had a wide-based gait while using a cane for support.

INVESTIGATIONS & MANAGEMENT

Prior to admission to University Hospital, the patient underwent a computed tomography (CT) scan of his head. This revealed a 39 x 39 x 46 mm ring-enhancing mass in the left occipital lobe with extensive edema, compression of the left lateral ventricle, and midline shift to the right. A suspicious lesion was also noted in his upper right lung lobe, along with enlarged mediastinal lymph nodes. The preliminary diagnosis was a metastasis from the lung. A subsequent magnetic resonance imaging (MRI) scan of the head with gadolinium contrast showed a lobulated, irregularly ring-enhancing tumor with central necrosis (Fig. 1 A-D). Diffusion within the lesion walls was restricted. The appearance was suspicious for a high grade primary malignancy or lymphoma, although a metastasis could not be excluded given the history.

The patient was immediately started on dexamethasone, which mildly improved his symptoms. After a discussion with the patient and his family, it was decided to perform a craniotomy and surgical resection. There were no intra-operative complications and a gross total resection was achieved. Post-operative CT imaging demonstrated complete tumor resection (Fig. 1 E,F). Intraoperative frozen section pathology demonstrated a high grade poorly differentiated neoplasm that was suspicious for lymphoma. Final pathology was consistent with metastatic undifferentiated large (non-small) cell lung carcinoma. No other metastases were identified.

Figure 1. Pre- and post-operative imaging of left occipital ring-enhancing lesion. Coronal (A,B) and axial (C) T1-weighted MRI demonstrates a lobulated, heterogeneous, irregular lesion with central necrosis that enhances following gadolinium administration (B,C). There is extensive surrounding vasogenic edema evident on T2-weighted MRI (D). Post-operative axial CT imaging (E,F) demonstrates complete lesion resection with blood within the resection cavity. No residual tumor is evident following contrast administration (F).

FOLLOW-UP

Following surgery, the patient's tremor resolved and his visual fields improved. He also reported improvement in his coordination and balance. He demonstrated no obvious remaining sensory deficits. His gait had normalized and he no longer required a cane for ambulation. He has since undergone whole brain and lung radiation therapy (RT) 9 weeks following his operation, with further consideration for systemic chemotherapy.

DISCUSSION

Patients with lung cancer tend to have the highest rates of brain metastases (16-20%).^{8,9} Prognosis for patients with metastases due to a lung primary depends upon age, Karnofsky performance score, presence of extracranial metastases, and number of brain

metastases.¹⁰ Depending on these parameters, patients' median survival ranges from 3-15 months. Treatment generally consists of dexamethasone and whole brain radiation therapy or stereotactic radiotherapy. Surgery and systemic chemotherapy are considered depending on tumor type and patient characteristics.¹¹

A major challenge in this case was the imaging diagnosis. GBM, primary central nervous system lymphoma, and brain metastasis were all considered. When a brain tumor is identified, gadolinium-enhanced MRI is the preferred investigation to better delineate the lesion.¹²⁻¹⁵ The differential for cerebral ring-enhancing lesions is broad and includes abscess, tuberculoma, neurocysticercosis, metastasis, GBM, subacute vascular insult (infarct, hemorrhage or contusion), demyelination, tumefactive demyelinating lesion, radiation necrosis, postoperative changes, and lymphoma.¹⁶ A helpful mnemonic for causes of ring-enhancing cerebral lesions is DR MAGIC L (Table 1).

Table 1. Cerebral Ring-Enhancing Lesions Mnemonic

D	Demyelinating disease
R	Radiation necrosis / Resolving hematoma
M	Metastasis
A	Abscess
G	Glioblastoma
I	Infarct (subacute phase)
C	Contusion
L	Lymphoma

Clinical presentation and demographics are always taken into consideration when formulating an imaging differential. Based on the patient's history, a subacute vascular lesion was unlikely. Tuberculoma and neurocysticercosis were also unlikely considering that the patient was born and has lived in Canada without a history of tuberculosis infection. He was not immunocompromised, making lymphoma unlikely. Furthermore, his age and sex made demyelinating conditions less likely. Abscess was also unlikely given his lack of obvious predisposing conditions or systemic signs of infection. Therefore, GBM and metastasis were at the top of the differential. Given the lung lesion and smoking history, metastasis was the primary consideration before even considering other imaging characteristics.

Thick and nodular lesion walls increase suspicion for neoplasm over abscess. GBM in particular often displays multilobar ring patterns.^{17,18} Furthermore, restricted diffusion in the lesion wall on diffusion weighted imaging (DWI) suggests GBM or demyelination. However, demyelination generally presents with an incomplete ring. In addition, abscesses demonstrate varying ring thickness (depending on the stage of formation). Regarding the tumor core, unrestricted diffusion on DWI favors a neoplastic necrotic core, as seen in the current case, whereas restricted diffusion favors an abscess. GBM generally presents as a large, irregular mass with several oth-

er smaller masses embedded within the edema. Metastases generally present as several smaller rounded lesions with disproportionate surrounding vasogenic edema at the white-grey matter border.

Overall, this patient's imaging displayed predominantly GBM-like characteristics, while his clinical history suggested metastasis. Even the preliminary intraoperative pathology report, suggestive of lymphoma, was non-confirmatory. This was significant intra-operatively as surgical de-bulking does not improve survival for patients with CNS lymphoma and surgery could have been aborted based on the frozen section result. A further consideration was that dexamethasone, which was administered prior to surgery, can render lymphomas undetectable on pathology. However, the gross appearance of the tumor at surgery, including the presence of a clear surgical plane, suggested metastasis. Maximal safe surgical resection would be optimal for both glioma and metastasis, so it was decided to move forward with gross total resection. Permanent tissue sections stained with hematoxylin and eosin and other special stains made the final diagnosis of a metastatic deposit.

CONCLUSION

MRI with contrast is one of the most important components of brain tumor workup, but it is not definitive. This case illustrates occasions when imaging and intraoperative pathology are inconsistent with the final pathology report. In this case, imaging characteristics of the tumor suggested a high-grade glioma, but a long smoking history and the presence of a spiculated lesion in the lung suggested metastasis. When there is suspicion of primary cancer and imaging suggests a non-metastatic lesion, 89% still turn out to be metastasis on biopsy.¹⁹ Important treatment decisions, including abandoning a surgical approach entirely, rely on a diagnosis derived from both clinical and imaging information.

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