Concurrent Diagnosis of Listeria Monocytogenes Meningo-Encephalitis and Glioblastoma: Case Report and Review of the Literature

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Abstract

Glioblastoma is the most common primary brain tumour in adults, with a poor prognosis in spite of maximal safe resection, and concomitant chemo irradiation. Confusion in the pre-operative setting of these patients is usually attributed to tumour progression or worsening mass effect, but other reversible causes also need to be excluded, especially when steroids have been commenced. We describe the case of a 66-year-old woman, found to have a ~3 cm peripherally enhancing right precentral gyrus lesion on CT and MRI, who developed acute fever and confusion as a neurosurgical inpatient almost two months after presenting symptoms of mild left face and upper limb weakness first began. Eventually requiring intubation and ventilator support follow up imaging demonstrated progressive hydrocephalus but little lesional change. As part of a comprehensive septic screen, cultures of cerebrospinal fluid, obtained via lumbar puncture and ventricular catheterization, revealed positive growth for Listeria monocytogenes, whilst a stereotactic needle biopsy of the lesion confirmed IDH-wild type glioblastoma and negative bacterial growth. Although the patient initially responded to intravenous antibiotic therapy and full supportive care including tracheostomy, palliative measures were institute after she was left fully dependent for her care needs, and she succumbed three months later without receiving adjuvant glioblastoma treatment. This case illustrates the need for vigilance in detecting treatable causes of confusion in this immune compromised patient group.

Keywords: Glioblastoma; Listeria monocytogenes; Meningitis; Encephalitis; Infection; Cerebral abscess

Introduction

A 66-year-old right hand dominant woman was referred to clinic with a six week history of weakness and altered sensation affecting the left side of the face and upper limb, associated with difficulty chewing food and drooling. Examination revealed a left pronator drift and mild left-sided pyramidal weakness, with a subtle upper motor neuron left facial droop. MRI brain showed a ~3 cm diameter heterogeneously enhancing lesion, involving the right motor cortex; incomplete peripheral restricted diffusion was also noted. Importantly, before coming to clinic the patient had already been started on dexamethasone week earlier, following neurosurgical consultation, after presenting to the Emergency Department with deteriorating left-sided hemiparesis.

Owing to increasing difficulties with activities of daily living, the patient was admitted directly from clinic for pre-operative workup, with a view to timely surgery for the lesion. However, four days post-admission, the patient suddenly developed high fever and confusion with progressive neurological decline, ultimately requiring intubation and ICU admission. Blood cultures were positive for gram-positive cocci, and CT brain showed progressive hydrocephalus, leading to insertion of a right frontal external ventricular drain. CSF cultures confirmed Listeria, and a repeat MRI was performed which showed progressive non-obstructive hydrocephalus, but no significant change to the pre-existing right motor cortex lesion (Figure 2a,2b). Intravenous ampicillin and meropenem were commenced, eventually transitioning to ampicillin and gentamicin. However, in the setting of severe Listeria meningoencephalitis, it was felt that intracranial abscess needed to be excluded in spite of the inconclusive MRI appearance of the lesion, and day six post-inpatient admission, the patient underwent a frameless stereotactic needle biopsy of the right frontal lesion, as well as insertion of a left-sided external ventricular drain. Biopsy confirmed the diagnosis of WHO meningitis and abscess.
Grade IV IDH-wild type glioblastoma; certainly, no pus was aspirated. Despite insertion of a tracheostomy, gastrostomy and further neuroendoscopic procedures to alleviate the low pressure non-obstructive hydrocephalus, the patient was left fully dependent for her care needs, and palliative measures were instituted. She eventually succumbed almost three months later, without undergoing adjuvant Stupp protocol chemo irradiation.

### Discussion

To our knowledge, this is the second reported case of concomitant diagnosis of *Listeria meningoencephalitis* and glioblastoma, although in this case, meningitis was diagnosed in the pre-operative setting, rather than post-operatively [1]. *Listeria monocytogenes* is a gram-positive, facultatively anaerobic, rod, acquired through the consumption of contaminated cheeses, unwashed fresh vegetables and uncooked meats. The diagnosis of *Listeria monocytogenes* meningitis is confirmed by the findings of leukocytosis, gram-positive rods on gram stain and *Listeria* culture on CSF analysis, usually acquired via lumbar puncture. Listerial CNS infection usually manifests as meningitis, although abscess [2], encephalitis [3] and brainstem encephalitis [4] are other well described clinical presentations. One of the hallmarks of *Listeria meningitis/encephalitis* is it typically affects the immune compromised, (i.e. organ transplant recipients, haemato logic and solid malignancies, AIDS, *diabetes mellitus*) as well as neonates, pregnant women and the elderly, although Listerial brainstem encephalitis, interestingly, tends to occur in the immune competent [5]. The advent of immune modulatory therapies for a range of chronic inflammatory disorders, vasculitides and connective tissue disorders may potentially increase the incidence of Listeria meningitis in the future [6].

Whilst listerial meningitis usually presents with the classic clinical features of features such as fever, headache and neck stiffness, listerial brainstem encephalitis may be heralded by a more atypical presentation, usually a biphasic clinical picture, initially with 3-4 days of fever, headache and vomiting, followed by cerebellar signs, together with asymmetrical cranial neuropathies, sensorimotor deficit and stupor [3]. Additionally, listerial meningitis may differ in presentation compared to meningitis from more common pathogens, in that seizures, secondary non-communicating hydrocephalus, focal neurological deficit, bacteremia, negative CSF culture and sub-acute presentations (24+ hours) are more likely [3,5]. This is interesting in light of this reported patient, who was admitted directly to the inpatient unit of our institution from clinic, and whose steroid administration may have somewhat masked and/or possibly precipitated her presentation. MR imaging can distinguish well between intracranial abscess and intracranial glioma through the utilization of DWI/ADC sequences and MR spectroscopy; sensitivity and specificity of ADC/DWI alone in this setting approaches 96%, and almost 100% when MRS is also employed [7].

The mainstay of antibiotic treatment is ampicillin and gentamicin, especially as increasing resistance of *Listeria monocytogenes* to penicillin mono therapy has been documented [5]. Vancomycin and trimethoprim-sulfamethoxazole are efficacious. Listerial meningitis has an overall reported mortality of ~15%, meaning that rapid diagnosis and institution of management are critical [3]; that mortality rate doubles in the setting of hydrocephalus, even when treated with surgical CSF diversion [8].

### Conclusion

This case illustrates the importance of thorough investigation and prompt management of acute or sub-acute confusion in a patient with a known intracranial space occupying lesion, especially in the elderly or otherwise immune compromised. MR imaging, through spectroscopy and DWI, is highly capable of distinguishing intracranial abscess from tumour, but in the setting of concomitant severe *bacterial meningoencephalitis*, frameless stereotactic biopsy may still be required in order to clinch the diagnosis.

### References

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**Figure 1a,1b:** MRI brain, performed prior to clinic presentation: Axial T1-weighted contrast enhanced images show ~3 cm peripherally enhancing lesion within the right precentral gyrus; Axial DWI shows patchy, peripheral restricted diffusion.

**Figure 2a,2b:** MRI brain, performed prior to frameless stereotactic needle biopsy of right motor cortex lesion: Coronal T1-weighted contrast enhanced images show an essentially unchanged lesion within the right precentral gyrus, with the presence of communicating hydrocephalus noted, as evidenced by the dilated temporal horns; DWI demonstrates more confluent restricted diffusion.
