CASE REPORT

A case of oligodendroglioma and multiple sclerosis: Occam's razor or Hickam's dictum?

Afsaneh Shirani,¹ Gregory F. Wu,¹ Caterina Giannini,² Anne H. Cross¹

¹Department of Neurology, Washington University in Saint Louis School of Medicine, St Louis, Missouri, USA

²Department of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, Rochester, USA

Correspondence to

Dr Afsaneh Shirani,
ashirani@wustl.edu

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SUMMARY

Tumefactive appearing lesions on brain imaging can cause a diagnostic dilemma. We report a middle-aged man who presented with right-sided optic neuritis. A brain MRI showed enhancement of the right optic nerve, and non-enhancing white matter lesions including a 3 cm right frontal lesion with adjacent gyral expansion. Cerebrospinal fluid analysis showed five oligoclonal bands not present in serum. Glatiramer acetate was started for suspected tumefactive multiple sclerosis (MS). A follow-up brain MRI 6 months later showed persistence of the frontal gyral expansion. A brain biopsy led to the diagnosis of an oligodendroglioma, isocitrate dehydrogenase-mutant and 1p/19q co-deleted (WHO grade II), managed with surgical resection and radiotherapy. Postoperative brain MRI showed a new enhancing periventricular lesion, making the choice of optimal disease-modifying therapy for MS challenging. This case highlights the possibility of coexistence of MS and oligodendroglioma, and emphasises the importance of a tissue diagnosis when atypical MS imaging features are present.

BACKGROUND

Tumefactive lesions on brain imaging can pose a diagnostic challenge in patients with or without known multiple sclerosis (MS).¹ Although tumefactive MS brain lesions are well described, differential diagnoses for such lesions include neoplasms. A brain biopsy may be required for tumefactive lesions with atypical imaging manifestations in the setting of MS. Here we report a case of a man in his 40s who was initially suspected to have tumefactive MS. However, atypical imaging features warranted a tissue diagnosis which revealed an oligodendroglioma coexisting with MS.

CASE PRESENTATION

A 44-year-old right-handed man presented with sudden-onset right-sided optic neuritis. He had no previous history of neurological dysfunction, and his medical history was notable only for obstructive sleep apnoea and a remote head trauma to the right frontal region during military service. His family history was negative for any demyelinating disease or intracranial neoplasms, however his father had died of lymphoma.

INVESTIGATIONS

Brain MRI showed enhancement of the right optic nerve near the orbital apex (figure 1D), and multiple

fluid-attenuated inversion recovery (FLAIR) lesions without any associated enhancement including a 3 cm focal lesion in the right frontal lobe with expansion of the adjacent gyri (figure 1A,B). Also present were several white matter lesions in periventricular, juxtacortical (adjacent to cortex) and subcortical areas (figure 1C). Cerebrospinal fluid (CSF) analysis revealed five CSF-restricted oligoclonal bands, and an elevated IgG index of 0.71 (reference range: <0.66), with normal cell count, protein and glucose.

TREATMENT

Following a 3-day course of intravenous methylprednisolone, he began glatiramer acetate (40 mg subcutaneously three times per week) for MS with a suspected right frontal tumefactive lesion. His visual acuity returned to normal over 3 months. A follow-up brain MRI 6 months later demonstrated resolution of the right optic nerve enhancement, but persistence of the right frontal lesion and its associated adjacent gyral expansion (figure 1E). In addition, an MRI of the cervical spinal cord showed a short segment dorsal lesion in upper cervical cord (figure 1F). Given continued cortical expansion, concerns were raised for a slow growing neoplasm in his right frontal lobe. The patient underwent right frontal craniotomy and biopsy, with a low grade glioma found on frozen section. The tumour was subsequently resected. Pathology showed an oligodendroglioma, isocitrate dehydrogenase-mutant and 1p/19q co-deleted (WHO grade II) (figure 2). Radiation therapy was initiated.

OUTCOME AND FOLLOW-UP

An early postoperative follow-up brain MRI showed a new small focus of enhancement in the right posterior periventricular white matter compatible with a new demyelinating lesion (figure 1G,H). The patient remained on glatiramer acetate at the time of this report pending a follow-up brain MRI 3 month after surgical resection of the tumour.

DISCUSSION

Oligodendrogliomas are glial tumours that comprise about 6% of primary central nervous system (CNS) tumours.² More commonly found in men than women, they have a peak incidence between 40 and 60 years of age.² Oligodendrogliomas most commonly occur in the frontal lobe, have a cortical-subcortical superficial location, show calcification and typically do not have robust

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Figure 1 Brain MRI of a 44 year-old man who presented with acute optic neuritis. The axial FLAIR image showing a relatively large focal right frontal lesion, and multiple small subcortical and periventricular white matter lesions (A). Postcontrast T1-weighted image demonstrating no enhancement of the right frontal lesion (B). Axial FLAIR image at a lower cut of the brain showing disseminated white matter lesions (C). Postcontrast T1-weighted image showing subtle enhancement of the right optic nerve (white arrow) more prominent in the orbital apex (D). Axial FLAIR image of a follow-up brain MRI 6 months later demonstrating no change in the size of the right frontal lesion but persistent expansion of the adjacent gyri (white arrow) (E). Sagittal STIR image at the same time showing a short segment dorsal lesion in upper cervical spinal cord (black arrow), a typical lesion location for MS (F). FLAIR image obtained following the resection of the right frontal lesion showing a new small right posterior periventricular lesion (G) associated with mild enhancement as shown in the postcontrast T1-weighted image in (H). FLAIR, fluid-attenuated inversion recovery; MS, multiple sclerosis; STIR, short tau inversion recovery.

enhancement.³ Oligodendroglial tumours overall have a better prognosis compared with astrocytic neoplasms.⁴ The molecular genetic signature of oligodendrogliomas includes IDH mutation and 1p/19q co-deletion.² Patients with this genetic signature have been shown to be more sensitive to treatment.⁴

Our patient was initially thought to have a tumefactive MS lesion rather than a tumour. Tumefactive demyelinating lesions are typically well-circumscribed supratentorial lesions >2 cm with a predilection for frontal and parietal lobes.⁵ Initial presentations are often polysymptomatic, with motor, cognitive and sensory symptoms predominating, but aphasia, agnosia, seizures and visual field defects are also reported.⁶ Tumefactive demyelinating lesions often enhance postcontrast and may display an incomplete or open ring pattern of enhancement.⁵ In our patient, careful interpretation of the repeat brain MRI with recognition of the persistent gyral expansion led to further investigation to rule out a neoplastic process.

Concurrence of MS and oligodendroglioma has been reported rarely.^{7–12} Whether the association between MS and oligodendroglial tumours is by chance or related to a shared genetic or pathogenic factor between the two disorders remains debatable. Studies of cancer comorbidity in patients with MS compared with the general population have shown

differing results.¹³ It can be speculated that exposure to long-term immunosuppressive-immunomodulatory treatment may be associated with an increased risk of cancer.^{14 15} However, our patient was not exposed to any disease-modifying drugs (DMDs) for MS prior to identification of his tumefactive lesion.

In most previously reported cases of oligodendroglioma and MS, manifestations of MS began long before tumour identification (on average 15 years).⁷ Our case stands apart from prior cases in that the tumour-like lesion was present at the time of first symptoms of MS. One might speculate that the presence of an oligodendroglioma could lead to autoimmune demyelination by stimulating an immune response to oligodendrocytes.⁷ Alternatively, one may hypothesise that reactive glial cells in MS plaques may have increased susceptibility to neoplastic transformation.^{14 16} Another speculation centres around the possible role of oncogenic viruses such as John Cunningham virus (JCV) capable of remaining latent in myelin-producing oligodendrocytes.¹⁷ Latent JCV-DNA antigens expressed in the CNS (at low levels) have been suggested as possible targets of the host immune response underlying focal demyelination.^{17 18} However, all these hypothetical associations remain unproven, and the exact nature of the

Figure 2 The figure illustrates a classic oligodendroglioma of moderate cellularity with scant proliferative activity consistent with a WHO grade II tumour (H&E) (A). Tumour cells express mutant IDH-1 protein (R132H) (B). Tumour cells also retain expression of *ATRX* gene (C), and show low expression of p53 protein (D). This pattern of staining is typical of oligodendroglioma, but different from IDH-mutant astrocytoma which frequently shows loss of *ATRX* expression and p53 overexpression as a consequence of *ATRX* and *TP53* gene mutations. By FISH analysis, tumour cells show loss of 1p (E) and 19q (F) probes consistent with 1p/19q co-deletion. All histological photos were originally taken at $\times 400$. *ATRX*, α -thalassaemia/mental-retardation-syndrome-X-linked; FISH, fluorescence in situ hybridisation; IDH-1, isocitrate dehydrogenase-1.

relationship between oligodendroglioma and MS (if any) is still a matter of speculation.

Choice of DMDs in these patients remains challenging. Most of the described cases of oligodendroglioma and MS have been reported to have a mild MS disease course.⁷ Given the importance of immune system in antitumour activities and cancer immunosurveillance, if a DMD is needed for MS disease activity in these patients, it may be prudent to use a non-immunosuppressive DMD with a good safety profile. However, due to the rarity of concurrence of MS and oligodendroglioma, evidence-based data to guide DMD selection are lacking.

This case highlights the possibility of coexistence of MS and oligodendroglioma. It is a reminder that patients do not always adhere to Occam's razor, the principle that the simplest answer to a problem (or a unifying diagnosis) is often the correct one. This case rather highlights the possibility of

Hickam's dictum—a counterargument which states that a man can have as many diseases as he damn well pleases. This case also emphasises the importance of obtaining tissue diagnosis in the presence of imaging features atypical for MS. While the nature of the relationship between MS and oligodendroglioma remains debatable, further studies of patients affected by both conditions, and their specific therapeutic responses, may provide insights into the pathogenesis of these conditions.

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Learning points

- Multiple sclerosis (MS) and oligodendroglioma may coexist though the concurrence is rare.
- Although tumefactive MS brain lesions are well described, differential diagnoses for such lesions include neoplasms.
- It is important to obtain a tissue diagnosis in the presence of atypical imaging features for MS.

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