



Case Description

A challenging case of concurrent multiple sclerosis and anaplastic astrocytoma

Georges Sinclair^{1,2,3}, Yahya Al-saffar¹, Philippa Johnstone³, Mustafa Aziz Hatiboglu², Alia Shamikh⁴

¹Department of Neurosurgery, ⁴Department of Neuropathology, Karolinska University Hospital, Stockholm, Sweden, ²Department of Neurosurgery, Bezmialem Vakif University Medical School, İstanbul, Turkey, ³Department of Oncology, Royal Berkshire NHS Foundation Trust, Reading, United Kingdom.

E-mail: *Georges Sinclair - georges.sinclair@gmail.com; Yahya Al-saffar - yehya.al-saffar@sll.se; Philippa Johnstone - philippa.johnstone1@nhs.net; Mustafa Aziz Hatiboglu - azizhatiboglu@yahoo.com; Alia Shamikh - alia.shamikh@sll.se



***Corresponding author:**

Georges Sinclair,
Department of Oncology,
Royal Berkshire NHS
Foundation Trust,
London Road, Craven Road,
Reading, RG1 5AN, UK.

georges.sinclair@gmail.com

Received : 29 October 18

Accepted : 08 March 19

Published : 23 August 19

DOI

10.25259/SNI_176_2019

Quick Response Code:



ABSTRACT

Background: Cases of gliomas coexisting with multiple sclerosis (MS) have been described over the past few decades. However, due to the complex clinical and radiological traits inherent to both entities, this concurrent phenomenon remains difficult to diagnose. Much has been debated about whether this coexistence is incidental or mirrors a poorly understood neoplastic phenomenon engaging glial cells in the regions of demyelination.

Case Description: We present the case of a 41-year-old patient diagnosed with a left-sided frontal contrast enhancing lesion initially assessed as a tumefactive MS. Despite systemic treatment, the patient gradually developed signs of mass effect, which led to decompressive surgery. The initial microscopic evaluation demonstrated the presence of MS and oligodendroglioma; the postoperative evolution proved complex due to a series of MS-relapses and tumor recurrence. An ulterior reevaluation of the samples for the purpose of this report showed an MS-concurrent anaplastic astrocytoma. We describe all relevant clinical aspects of this case and review the medical literature for possible causal mechanisms.

Conclusion: Although cases of concurrent glioma and MS remain rare, we present a case illustrating this phenomenon and explore a number of theories behind a potential causal relationship.

Keywords: Anaplastic astrocytoma, Gamma knife radiosurgery, Magnetic resonance imaging, Multiple sclerosis, Oligodendroglioma, Tumefactive multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is a demyelinating disease with complex clinical and radiological features. Although 85% of MS-cases develop a clinically isolated syndrome involving the optic nerves, brainstem, or spinal cord,^[10] MS lesions are also able to mimic a number of cerebral malignancies, particularly in the presence of gradual mass growth (tumefactive MS). Surgical intervention and microscopic evaluation are often necessary to ensure diagnosis;^[1] in this specific context, cases of concurrent MS and gliomas have been described.^[1,2,5,12,18,23,25,29,31] The origins of this type of coexistence (incidental or causal) remain a matter of debate; indeed, some of the reported theories include neoplastic changes taking place in areas of demyelination.^[29] As illustrated by this case, access to modern radiology and reliable microscopic assessment at the time of diagnosis and follow-up remain crucial in terms of treatment optimization and prolonged survival.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2019 Published by Scientific Scholar on behalf of Surgical Neurology International

CASE DESCRIPTION

A 41-year-old female patient developed epileptic seizures in 2008. Further investigation with magnetic resonance imaging (MRI) revealed a glioma-suspect tumor within the boundaries of the left frontal lobe as well as multiple supratentorial MS-like lesions scattered in both hemispheres. The routine cerebrospinal fluid (CSF)-analysis showed evidence of MS-activity, while the complementary MR spectroscopy (MRS) study suggested the presence of a concurrent oligodendroglioma. The ensuing needle biopsy on the left frontal lobe lesion showed solely inflammatory signs of demyelination, suggesting an evolving tumefactive MS-plaque [Figures 1 and 2]. Despite anti-MS therapy (Natalizumab), the patient gradually developed clinical signs of mass-effect during the course of 2010; the subsequent radiology further strengthened the suspicion of a concurrent low-grade glioma. The patient underwent microsurgery twice followed by prophylactic radiation therapy to the surgical cavity shortly after [Figures 3 and 4]; the corresponding histopathologic evaluation suggested the presence of an oligodendroglioma, WHO Grade 2–3. During the next 5 years, the patient underwent systemic treatment due to a series of tumor-/MS- [Table 1] relapses. A follow-up MRI in April 2017 showed a tumor regrowth next to the surgical site deemed not suitable for microsurgery. The contrast enhancing part of the recurrence was treated in October 2017 using gamma knife radiosurgery (GKRS), applying 18Gy at the 50% isodose line [Figure 5]. A histopathologic reevaluation of the previously collected samples pre-GKRS demonstrated the presence of an anaplastic astrocytoma (AA) [Figure 2, Tables 2 and 3]. MRI-examinations post-GKRS (up to the last follow-up) showed gradual regression of the treated lesion without evidence of adverse radiation effects. At the time of paper submission, the patient was suffering from right foot palsy from her second surgical resection as well as fatigue due to chemotherapy. Her general condition and neurological status remained otherwise stable up to this stage (Karnofsky Performance Status 70). Table 1 illustrates the post-biopsy timeline relevant to this case (2010–2018).

DISCUSSION

General aspects

MS is a chronic inflammatory demyelinating disease with contentious evolution. MS-plaques are not uncommonly misdiagnosed as malignant processes, a phenomenon known as tumefactive MS; in fact, some groups have reported that up to 6% of all MS-cases are confused with other diseases, including primary brain neoplasms.^[5] To make matters more complicated, brain malignancies may themselves mimic tumefactive MS-lesions. Although seldom reported,

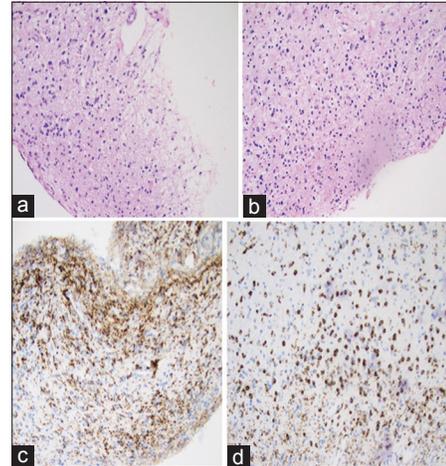


Figure 1: Re-evaluation (2017) of available samples from needle biopsy performed in 2008 (2 samples of <4 mm). (a) Hematoxylin and Eosin glial biopsy with a mild increase in astrocytes. (b) Inflammatory process dominated by foamy macrophages (confirmed by immunohistochemistry). (c+d) CD68 immunohistochemistry: presence of a large number of macrophages.

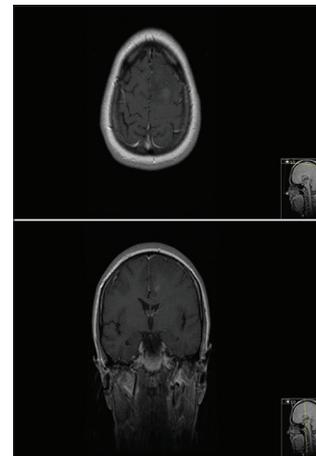


Figure 2: T1-weighted magnetic resonance imaging, axial (top), and coronal (bottom) cross sections before biopsy (2008).

gradual deterioration during the course of MS might be due not only to an incomplete recovery after a period of relapse and/or aggregation of neurological damage but also to an underlying neoplastic process.^[25] In this context, variables such as lesion size >20 mm, extensive perifocal edema, evolving mass effect, and “abnormal” contrast enhancement patterns are “alarming” signs indicating the presence of a glioma.^[6,18,23] Although gliomas (astrocytomas, oligodendrogliomas, and glioblastomas) and central nervous system (CNS)-lymphomas remain the predominant type of MS-concurrent malignancies, other tumors such as meningiomas, ependymomas, gangliogliomas, and metastatic lesions have also been reported.^[1,2,11,14,20,23,25] The

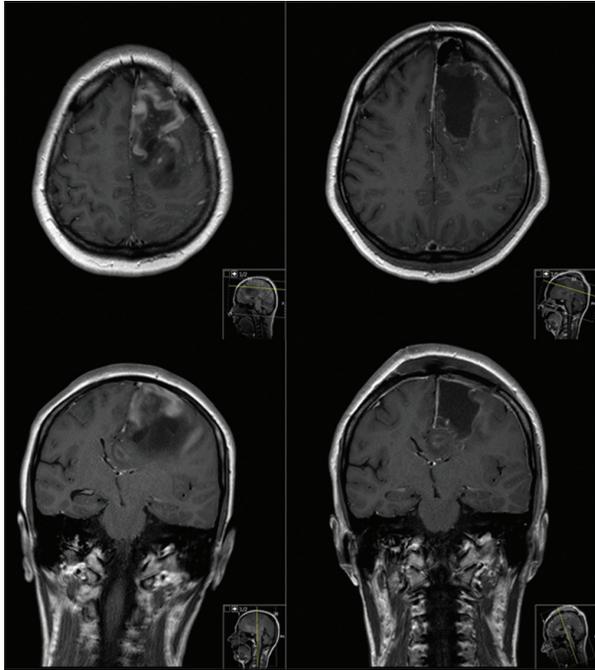


Figure 3: First microsurgery (August 2010): T1-weighted magnetic resonance imaging, axial (top), and coronal (bottom) cross sections. Left column: preoperative images. Right column: postoperative images.

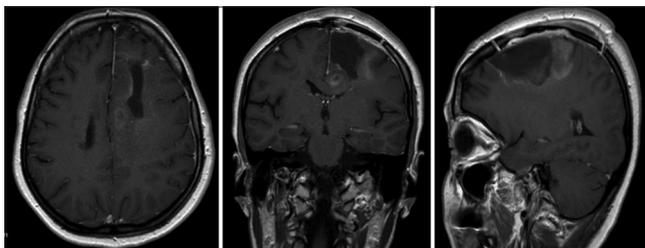


Figure 4: T1-weighted magnetic resonance imaging (October 2010) before second resection (November 2010). Axial (left), coronal (center), sagittal (right) cross sections: tumor regrowth.

concurrent presence of more “indolent” tumors (such as low-grade gliomas) may further complicate matters in terms of diagnostics, treatment, and evolution. Clinical experience, access to modern radiology, and reliable microscopic analysis are often deemed necessary (if not mandatory) to distinguish between these tumor groups.

Radiology

- Glioma: In the context of glial tumors (including astrocytomas), preoperative MRI-examinations may provide key data as to the plausible grade of malignancy.^[32] Distinct variables such as (i) the degree of heterogeneity of contrast enhancement (T1-weighted series), (ii) extension of underlying edema (T2-weighted studies), (iii) development of mass effect, and

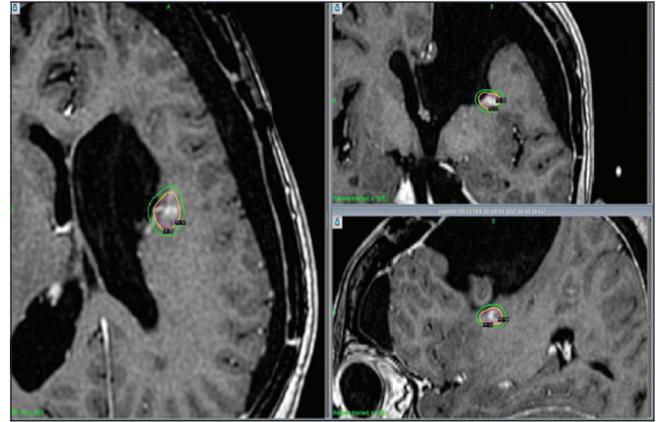


Figure 5: Gamma knife treatment plan on stereotactic T1-weighted magnetic resonance imaging: Axial (left), coronal (Top, right), and sagittal cross sections (Bottom, right). Yellow line: prescription isodose at the margin (18Gy-50%). Green line: 10Gy-isodose.

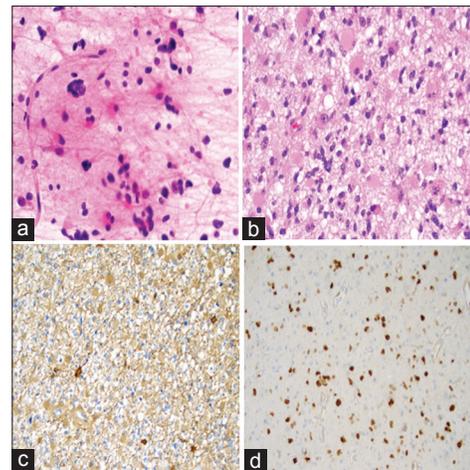


Figure 6: Re-evaluation (2017) of 25 mm sample collected from the second resection (November 2010). (a) Hematoxylin and Eosin glial biopsy with moderately increased atypical astrocytes with gemistocytic features and with few mitoses. (b) Smear from the same biopsy: moderate increase in astrocytes with variation in size and shape. (c) Glial fibrillary acidic protein immunohistochemistry: positive in glial cells with astrocytic features. (d) KI-67 proliferation index about 25%. Samples from the first resection were not made available.

(iv) presence of necrosis, and cyst formation (T1/T2-weighted studies) are strongly associated to WHO III-IV tumors. As in the case of our patient, complementary MRS and positron emitting tomography may also provide valuable data to identify the presence of glial tumors; further details on their application can be found elsewhere.^[4,8]

- MS: Lesions are commonly found within the confinements of the posterior fossa, periventricular areas, spinal cord, and optic nerves. Dual-echo and fluid-attenuated inversion recovery (FLAIR) imaging

Table 1: Evolution post-biopsy relevant to this case (2010–2018).

Timeline	Imaging results	Treatment	Microscopy analysis
August 2010	MRI, MRS, and Methionine-PET suggest the presence of a low-grade glioma	Subtotal decompressive mass resection due to mass effect	Anaplastic oligodendroglioma according to reviewed notes (Tissue samples not available)
November 2010	Follow-up postop MRI: Signs of focal recurrence	Gross total tumor resection+postop radiation treatment to the cavity (60 Gy in 2 Gy fractions)	WHO Grade 2 oligodendroglioma; deletion in 1 p not 19q
April 2012–August 2013	Follow-up MRI studies: Gradual appearance of scattered MS-suspected lesions (including the surgical site)	Assessed as MS-relapse despite inconclusive CSF-analysis; Rituximab started in August 2013	None: surgery deemed not indicated due to MS-origin
August 2013–June 2014	Follow-up MRI: stable conditions	Ongoing Rituximab	None due to stable imaging
September 2014	Progressive right-sided hemiparesis: MRI shows tumor recurrence next to the surgical site. MRS and PET examinations inconclusive	Temodal added to Rituximab	None: surgery deemed as high risk intervention
September 2014 – March 2015	Follow-up MRI studies: Substantial tumor regression	Temodal halted in March 2015; Rituximab undisrupted	None due to treatment response
March 2015–Jan 2017	Follow-up MRI studies: stable conditions	Ongoing rituximab	None due to stable follow-up
April 2017–October 2017	Follow-up MRI studies: focal tumor relapse (next to the surgical cavity)	Gamma Knife treatment (18Gy/50% isodose) to the lesion. “Adjunct” Temodal due to diffuse FLAIR-signaling in the infra- and supratentorial space at the time of stereotactic MRI	Reanalysis of collected material (second resection): Anaplastic astrocytoma
October 2017–October 2018	Follow-up MRI studies: stable conditions post-GKRS	Rituximab discontinued post-GKRS	None due to stable follow-up

GKRS: Gamma knife radiosurgery, MRI: Magnetic resonance imaging, FLAIR: Fluid-attenuated inversion recovery, PET: Positron emitting tomography, MRS: MR-spectroscopy, MS: Multiple Sclerosis

reveal focal areas of hyperintensity while T1-weighted MRI (with Gd) help discerns between active and inactive MS-lesions, as enhancement results from an increase in blood-brain barrier permeability in areas of “active” inflammation.^[10] Furthermore, the presence of persistent “black-hole” areas in pre- and post-Gd T1-weighted series mirrors the severity of MS-evolution in terms of axonal loss and demyelination.^[10] However, as in the case of gliomas, MR-signal specificity remains an issue, particularly in the face of edema, inflammatory processes, de- and remyelinating activity, gliosis, and axonal loss, as all of these features share complex patterns of hyperintensity on FLAIR and dual-echo studies.^[10] Further details on the use of MRI in the field of MS can be found elsewhere (www.magnims.eu).^[28,34,35]

Microscopic assessment

CSF-analysis and MS

From a general perspective, the presence of demyelinating activity can be confirmed through CSF-analyses; common traits of MS-disease in CSF-analysis can be found in Table 4. In this case, our review of medical notes suggests that the evaluation of CSF-samples at initial diagnosis and follow-up proved difficult. Unfortunately, more accurate data concerning these samples have not been made available.

Histopathologic assessment

- MS: Histological characteristics of chronic MS lesions are well known to neuropathologists; however, diagnosing MS at early stages may prove complex, particularly in

Table 2: Immunohistochemical reassessment (2017) from the second resection (November 2010): Anaplastic astrocytoma (WHO Grade 3). Samples from the first resection were not made available.

Markers	Status
GFAP	+
Vimentin	+
ATRX lost sign for mutation	+
Oligo2	+
Map 2	+
P53 sign for mutation	+
H3 K27	-
LICAM	-
Neu N	-

WHO: World Health Organization

Table 3: Molecular markers and FISH analysis (2017) from second resection (November 2010): Anaplastic astrocytoma (WHO grade 3). Samples from the first resection are currently not available.

Analysis	Status
IDH1 mutation	Confirmed
MGMT methylation	Confirmed
P53 mutation	Confirmed
(FISH analyses): No 1p/19q codeletion	No codeletion

WHO: World Health Organization, FISH: Fluorescent *in situ* hybridization

the context of needle biopsy where meager samples frequently represent small areas of a larger lesion. Although larger samples collected from “wider” surgical margins increase diagnostic accuracy, a complete microscopic interpretation of this type of lesion may prove difficult. In this aspect, key microscopic features of early MS lesions are described in Table 5.

- Glial tumors: The reevaluation made for the purpose of this article exposed the presence of a diffuse, infiltrating isocitrate dehydrogenase (IDH) 1-mutant AA [Figures 1 and 6, Tables 2 and 3]. AAs are more commonly diagnosed without the presence of a less-malignant precursor neoplasm. The presence of morphological components resembling an oligodendroglioma is compatible with AA, particularly in the absence of the 1p/19q codeletion. IDH-mutant AA is not rare and corresponds histologically to the WHO Grade III; these tumors have an intrinsic tendency for malignant progression to IDH-mutant glioblastoma. The principal histopathological features of AA are those of a diffusely infiltrating tumor with increased mitotic activity, distinct nuclear atypia, and

Table 4: Common traits of MS-disease in CSF-analysis.^[26,30]

- IgG bands on electrophoresis: most reliable marker accounting for 90% of all MS patients
- IgG fraction often increased >11% of the overall CSF-fraction
- Increased IgG/albumin index in CSF but not in serum generally reported (Indicating IgG-production within the boundaries of the CNS)
- Moderate increase in overall CSF protein levels and white cell count (mainly T-lymphocytes) can be seen. Total CSF protein exceeding 110 mg/dl and cell counts >50/cubic rule out MS
- Antibodies to different viral agents can also be found, particularly to measles (70% of all MS-patients)
- Myelin protein leaking from plaques can also be identified using radioimmunoassay

MS: Multiple Sclerosis, CSF: Cerebrospinal fluid, IgG: Immunoglobulin G, CNS: Central nervous system

Table 5: Key microscopic features of early MS disease.^[17]

- Neighboring areas of ongoing remyelination and active demyelination
- Extensive macrophage invasion
- Perivascular and parenchymal T cell infiltrates
- Relative axonal preservation
- Reactive astrocytosis with the formation of so-called gemistocytes
- Possible presence of Creutzfeldt-Peters cells (single dividing astrocytes)

MS: Multiple Sclerosis

high cellularity. Further signs may include multinucleated tumor cells and abnormal mitoses.^[36] With progressive anaplasia, nuclear morphology becomes more atypical with increasing variation in nuclear size, shape, and coarseness; in this context, dispersion of chromatin and increasing nucleolar prominence and quantity are also features of evolving anaplasia. Necrosis and microvascular proliferation (multi-layered vessels) are not expected by normal standard.^[36]

Causal relation?

Reports of concurrent MS and glial cell tumors can be traced back as early as 1912; however, despite significant advances in the field of neuro-diagnostics, the number of reported cases of coexistent MS and gliomas remains limited (<100 cases). This is probably due to the condition's rareness and entangled histopathological characteristics, the repertoire of diagnostic tools used during disease evolution, and the degree of

multidisciplinary experience. Despite the latter, our case has a striking resemblance to a number of reports.^[2,5,29] In this context, a few questions arise: Is there a causal relation between MS and malignant processes? If so, are there any explanatory onco-immunological mechanisms behind it? Has neoplastic activity a more “indolent” repercussion on MS-evolution, and if so, why? Despite the restricted number of studies on the latter subjects, some data might cautiously suggest that all latter questions seem to share a set of interactive explanatory mechanisms. New foundations for a causal relation between MS and CNS-tumors were laid by Acqui *et al.* when the group reported the transformation of a MS-plaque into an ependymoma;^[3,23] since then, different groups have worked to lay further foundations on a causal-effect issue.^[2,12,15,23,29] A retrospective analysis involving 11 patients with concurrent MS and oligodendroglioma by Green *et al.* reported a more benign course of MS, possibly due to mitotically active oligodendrocyte precursors able to promote focal neoplastic changes while enhancing remyelination;^[12] in a theoretical context, the proliferation and overrepresentation of these oligodendrocytes might promote a number of immunosuppressive regulatory factors such as nerve growth factor and cytokines (interleukin-10) that are able to suppress further MS-mediated injury while increasing the risk of tumor transformation.^[12,21] In contrast, Podbielska *et al.* suggested that the combined cytotoxic effects of the pro-inflammatory cytokines tumor necrosis factor- α and interferon- γ (common in MS-brain and oncogenic mechanisms) can instead “enhance” MS-injury by increasing ceramide-enriched exosome activity and cell death signaling in oligodendrocyte cells;^[24] whether these mechanisms enhance or “delay” MS-evolution, the above data seem to point to possible causal pathways.^[12,21,24] Furthermore, knowing that most MS risk genes belong to the immune system and that particular region in the genetic repertoire related to the innate immune system seem to be associated with an increased risk of gliomas, the theoretical idea of a causal “immuno-genetic” mechanism appears possible.^[23] In the context of our case, the potential role of DNA methylation in this concurrent condition is also worth considering due to the fact that MS-brain tissue is able to harbor regions of increased or decreased methylation, while the promotion of DNA hypermethylation in gliomas is a proven predictive factor of drug response and clinical impact.^[23] However, despite the latter epigenetic traits, further studies are warranted to elucidate a plausible cause-effect scenario in this particular context. Therapeutic MS-immunomodulators such as Fingolimod have also been suggested to have the potential to develop glioblastomas through the activation of P21-activated kinase-1;^[31] despite its proven clinical safety, one case of glioma was reported using azathioprine in a renal transplant recipient.^[21] Cases of gliomas evolving from pharmacologic immunomodulators

remain rare but suggest a possible environmental relationship between immunosuppression and malignant transformation.

John Cunningham (JC)-virus

As previously described in this paper, different groups seem to share common thoughts concerning plausible environmental-modulated mechanisms and malignant transformation of glial cells during the process of remyelination; the role of the human polyoma JCV remains interesting in this context.^[9,23,27] JCV was initially isolated from a patient attained with progressive multifocal leukoencephalopathy (PML) in 1971. Since then, studies have suggested a possible association between the agent and the development of PML and malignancies in the CNS. JCV is present in the majority of the human population; infection occurs by childhood and adolescence. Yet, seroconversion is bound to occur in 50–80% of those reaching adulthood.^[3] The initial stages of the infection remain largely subclinical in immunocompetent patients; kidney (and possibly the bone marrow) remain the selective site(s) of long-life, persistent infection.^[3] However, cases of JCV-modulated cytolytic activity in the CNS have been widely reported, primarily in immunosuppressed patients. Oligodendrocyte and astrocyte cell lines are mainly affected; PML-evolution through oligodendrocyte nuclei disruption is bound to happen at this stage.^[3] HIV- and MS-patients undergoing immunomodulatory treatment (such as natalizumab and rituximab) are at particularly high risk for PML.^[9] Furthermore, studies in animals have suggested a strong carcinogenic association to JCV-tumor (T) antigen expression, including glial tumors, primitive neuroectodermal tumors, neuroblastomas, and malignant peripheral nerve sheath tumors.^[9] Although Rencic *et al.* reported a case of oligoastrocytoma with nuclear staining of tumor cells with antibodies against the JCV T-antigen,^[27] more studies in human tissues are warranted to provide further evidence of a possible relationship between JC-virus and the evolution of glial tumors in human tissue, particularly in immunosuppressive conditions. Unfortunately, this type of staining is currently not available at our institution; hence, not included in our re-evaluation.

CONCLUSION

Although cases of concurrent glioma and MS remain rare, their entangled evolution might pose a challenge in terms of diagnosis and treatment. Modern MRI-protocols are crucial in the diagnosis of MS and gliomas; however, further studies are warranted to overcome issues concerning MR-signal specificity, particularly in the face of a concurrent condition. In this context, microscopic evaluation remains largely dependent on reliable diagnostic markers and multidisciplinary expertise. At least, in theory, MS and CNS malignancies might synergistically concur through a set of shared micro-

environmental and immune-modulated mechanisms. From that perspective, a casual origin cannot be fully ruled out. More studies on the subject are warranted and encouraged.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

None of the authors has any conflicts of interest to disclose.

REFERENCES

- Aarli JA, Mørk SJ, Myrseth E, Larsen JL. Glioblastoma associated with multiple sclerosis: Coincidence or induction? *Eur Neurol* 1989;29:312-6.
- Abrishamchi F, Khorvash F. Coexistence of multiple sclerosis and brain tumor: An uncommon diagnostic challenge. *Adv Biomed Res* 2017;6:101.
- Acqui M, Caroli E, Di Stefano D, Ferrante L. Cerebral ependymoma in a patient with multiple sclerosis case report and critical review of the literature. *Surg Neurol* 2008;70:414-20.
- Brendle C, Hempel JM, Schittenhelm J, Skardelly M, Reischl G, Bender B, *et al.* Glioma grading by dynamic susceptibility contrast perfusion and ¹¹C-methionine positron emission tomography using different regions of interest. *Neuroradiology* 2018;60:381-9.
- Butteriss DJ, Ismail A, Ellison DW, Birchall D. Use of serial proton magnetic resonance spectroscopy to differentiate low grade glioma from tumefactive plaque in a patient with multiple sclerosis. *Br J Radiol* 2003;76:662-5.
- Carvalho AT, Linhares P, Castro L, Sá MJ. Multiple sclerosis and oligodendroglioma: An exceptional association. *Case Rep Neurol Med* 2014;2014:546817.
- de la Lama A, Gómez PA, Boto GR, Lagares A, Ricoy JR, Alén JF, *et al.* Oligodendroglioma and multiple sclerosis. A case report. *Neurocirugia (Astur)* 2004;15:378-83.
- Diamandis E, Gabriel CPS, Würtemberger U, Guggenberger K, Urbach H, Staszewski O, *et al.* MR-spectroscopic imaging of glial tumors in the spotlight of the 2016 WHO classification. *J Neurooncol* 2018;139:431-40.
- Ferenczy MW, Marshall LJ, Nelson CD, Atwood WJ, Nath A, Khalili K, *et al.* Molecular biology, epidemiology, and pathogenesis of progressive multifocal leukoencephalopathy, the JC virus-induced demyelinating disease of the human brain. *Clin Microbiol Rev* 2012;25:471-506.
- Filippi M, Rocca MA. MR imaging of multiple sclerosis. *Radiology* 2011;259:659-81.
- Golombiewski EE, McCoyd MA, Lee JM, Schneck MJ. Biopsy proven tumefactive multiple sclerosis with concomitant glioma: Case report and review of the literature. *Front Neurol* 2015;6:150.
- Green AJ, Bollen AW, Berger MS, Oksenberg JR, Hauser SL. Multiple sclerosis and oligodendroglioma. *Mult Scler* 2001;7:269-73.
- Ho KL, Wolfe DE. Concurrence of multiple sclerosis and primary intracranial neoplasms. *Cancer* 1981;47:2913-9.
- Imitola J, Wagoner J, Khurana JS. Rapid dissemination of granular cell astrocytoma arising from periventricular stem cell regions in chronic multiple sclerosis. *J Neurooncol* 2015;124:147-9.
- Khalil A, Serracino H, Damek DM, Ney D, Lillehei KO, Kleinschmidt-DeMasters BK, *et al.* Genetic characterization of gliomas arising in patients with multiple sclerosis. *J Neurooncol* 2012;109:261-72.
- Khan OA, Bauserman SC, Rothman MI, Aldrich EF, Panitch HS. Concurrence of multiple sclerosis and brain tumor: Clinical considerations. *Neurology* 1997;48:1330-3.
- Kuhlmann T, Lassmann H, Brück W. Diagnosis of inflammatory demyelination in biopsy specimens: A practical approach. *Acta Neuropathol* 2008;115:275-87.
- Lin M, Reid P, Bakhsheshian J. Tumefactive multiple sclerosis masquerading as high grade glioma. *World Neurosurg* 2018;112:37-8.
- Malmgren RM, Detels R, Verity MA. Co-occurrence of multiple sclerosis and glioma case report and neuropathologic and epidemiologic review. *Clin Neuropathol* 1984;3:1-9.
- Mandel JJ, Goethe EA, Patel AJ, Heck K, Hutton GJ. Newly diagnosed ganglioglioma in an adult patient with multiple sclerosis. *J Neurol Sci* 2016;369:51-2.
- Mantero V, Balgera R, Bianchi G, Rossi G, Rigamonti A, Fiumani A, *et al.* Brainstem glioblastoma in a patient with secondary progressive multiple sclerosis. *Neurol Sci* 2015;36:1733-5.
- Mathews T, Moosy J. Mixed glioma, multiple sclerosis, and charcot-marie-tooth disease. *Arch Neurol* 1972;27:263-8.
- Plantone D, Renna R, Sbardella E, Koudriavtseva T. Concurrence of multiple sclerosis and brain tumors. *Front Neurol* 2015;6:40.
- Podbielska M, Szulc ZM, Kurowska E, Hogan EL, Bielawski J, Bielawska A, *et al.* Cytokine-induced release of ceramide-enriched exosomes as a mediator of cell death signaling in an oligodendroglioma cell line. *J Lipid Res* 2016;57:2028-39.
- Preziosa P, Sangalli F, Esposito F, Moiola L, Martinelli V, Falini A, *et al.* Clinical deterioration due to co-occurrence of multiple sclerosis and glioblastoma: Report of two cases. *Neurol Sci* 2017;38:361-4.
- Rathbone E, Durant L, Kinsella J, Parker AR, Hassan-Smith G, Douglas MR, *et al.* Cerebrospinal fluid immunoglobulin light chain ratios predict disease progression in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2018;89:1044-9.
- Rencic A, Gordon J, Otte J, Curtis M, Kovatich A, Zoltick P, *et al.* Detection of JC virus DNA sequence and expression of the viral oncoprotein, tumor antigen, in brain of

- immunocompetent patient with oligoastrocytoma. *Proc Natl Acad Sci U S A* 1996;93:7352-7.
28. Rovira À, Wattjes MP, Tintoré M, Tur C, Yousry TA, Sormani MP, *et al.* Evidence-based guidelines: MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis-clinical implementation in the diagnostic process. *Nat Rev Neurol* 2015;11:471-82.
 29. Sega S, Horvat A, Popovic M. Anaplastic oligodendroglioma and gliomatosis Type 2 in interferon-beta treated multiple sclerosis patients. Report of two cases. *Clin Neurol Neurosurg* 2006;108:259-65.
 30. Shankar SK, Rao TV, Srivastav VK, Narula S, Asha T, Das S, *et al.* Balo's concentric sclerosis: A variant of multiple sclerosis associated with oligodendroglioma. *Neurosurgery* 1989;25:982-6.
 31. Sharim J, Tashjian R, Golzy N, Pouratian N. Glioblastoma following treatment with fingolimod for relapsing-remitting multiple sclerosis. *J Clin Neurosci* 2016;30:166-8.
 32. Upadhyay N, Waldman AD. Conventional MRI evaluation of gliomas. *Br J Radiol* 2011;84 Spec No 2:S107-11.
 33. Vrenken H, Jenkinson M, Horsfield MA, Battaglini M, van Schijndel RA, Rostrup E, *et al.* Recommendations to improve imaging and analysis of brain lesion load and atrophy in longitudinal studies of multiple sclerosis. *J Neurol* 2013;260:2458-71.
 34. Wattjes MP, Rovira À, Miller D, Yousry TA, Sormani MP, de Stefano MP, *et al.* Evidence-based guidelines: MAGNIMS consensus guidelines on the use of MRI in multiple sclerosis establishing disease prognosis and monitoring patients. *Nat Rev Neurol* 2015;11:597-606.
 35. Vieregge P, Nahser HC, Gerhard L, Reinhardt V, Nau HE. Multiple sclerosis and cerebral tumor. *Clin Neuropathol* 1984;3:10-21.
 36. Von Deimling A, Louis DN, Aldape K, Brat D, Collins VP, Eberhart C. WHO classification of tumours of the Central nervous system. Lyon: IARC; 2016. p. 24-7.

How to cite this article: Sinclair G, Al-saffar Y, Johnstone P, Hatiboglu MA, Shamikh A. A challenging case of concurrent multiple sclerosis and anaplastic astrocytoma. *Surg Neurol Int* 2019;10:166.