CASE REPORT

REVISED Case Report: Concurrent primary CNS lymphoma and meningothelial meningioma - nuances of diagnosis and management [version 2; peer review: 1 approved, 1 approved with reservations]

Samir Kashyap ^{1,2}, Jacob Bernstein^{1,2}, Ira Bowen^{1,2}, Rosalinda Menoni^{1,2}, Dan Miulli^{1,2}

¹Department of Neurosurgery, Riverside University Health System, Riverside, CA, 92555, USA

²Department of Neurosurgery, Arrowhead Regional Medical Center, Colton, CA, 92324, USA

v2 First published: 25 Jan 2019, 8:103
<https://doi.org/10.12688/f1000research.17770.1>
 Latest published: 28 Aug 2019, 8:103
<https://doi.org/10.12688/f1000research.17770.2>

Abstract

Background: The incidence of two distinct primary intracranial pathologies is an exceedingly rare phenomenon. Although meningiomas are well known to coexist with other primary intracranial malignancies there are only nine reported cases of a meningioma occurring simultaneously with primary CNS lymphoma in the literature. We report a case of a woman who sustained multiple injuries due to two distinct intracranial pathologies, however, lateralizing signs were unrecognized for two weeks prior to her final diagnosis.

Case Description: A 64-year-old female with history of diabetes mellitus type 2 initially presented to the Emergency Department, two weeks prior, following a mechanical fall at home resulting in a left bimalleolar fracture. CT imaging revealed a right occipital mass with significant vasogenic edema causing 12mm of midline shift. MRI revealed two distinct homogeneously contrast-enhancing lesions: a right occipital mass with dural-based attachment, as well as a homogeneously contrast-enhancing lesion adjacent to the right posterolateral ventricle. FLAIR signal changes were also appreciated and were noted to extend across the corpus callosum, raising concerns for a high-grade glial process. She underwent a right occipital craniotomy with gross total resection of the right occipital mass as well as subtotal resection and biopsy of the second lesion. Final pathology of the extra-axial lesion was found to be meningothelial meningioma and the deep lesion was found to be diffuse large B-cell lymphoma.

Discussion: We describe a rare instance of simultaneous meningioma and primary CNS lymphoma that was found to be the underlying

Open Peer Review

Approval Status ? ✓

	1	2
version 2 (revision) 28 Aug 2019		✓ view
version 1 25 Jan 2019	? view	? view

1. **Eric Bessell** , Nottingham City Hospital, Nottingham, UK

2. **Kuntal Kanti Das** , Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

Any reports and responses or comments on the article can be found at the end of the article.

cause of a traumatic injury several weeks after the incident. We review the current diagnosis and management nuances in the setting of multiple intracranial oncologic processes.

Keywords

CNS lymphoma, Meningioma, Collision tumor

Corresponding author: Samir Kashyap (skashyap41@gmail.com)

Author roles: **Kashyap S:** Conceptualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Bernstein J:** Writing – Original Draft Preparation, Writing – Review & Editing; **Bowen I:** Writing – Review & Editing; **Menoni R:** Writing – Review & Editing; **Miulli D:** Conceptualization, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2019 Kashyap S *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Kashyap S, Bernstein J, Bowen I *et al.* **Case Report: Concurrent primary CNS lymphoma and meningothelial meningioma - nuances of diagnosis and management [version 2; peer review: 1 approved, 1 approved with reservations]** F1000Research 2019, 8:103 <https://doi.org/10.12688/f1000research.17770.2>

First published: 25 Jan 2019, 8:103 <https://doi.org/10.12688/f1000research.17770.1>

REVISED Amendments from Version 1

Additional details regarding the workup, intra- and post-operative management of the patient were included as well as further details on discussing the association between primary CNS lymphoma and meningioma.

Any further responses from the reviewers can be found at the end of the article

Introduction

The incidence of two distinct primary intracranial pathologies is an exceedingly rare phenomenon. The reported incidence of such an occurrence is approximately 1 in a million annually (Lee *et al.*, 2002). Although meningiomas, given their benign and slow-growing nature, are well known to coexist with other primary intracranial malignancies such as glioblastoma, metastases, adenomas, there are only nine reported cases of a meningioma occurring simultaneously with primary CNS lymphoma (PCNSL) in the literature (Gordon *et al.*, 2011; Slowik & Jellinger, 1990). Here, we report a case of a woman who sustained multiple injuries due to two distinct intracranial pathologies, however, lateralizing signs were unrecognized for two weeks prior to her final diagnosis.

Case presentation

A 64-year-old Hispanic female with a past medical history of type 2 diabetes mellitus and hypertension presented with a chief complaint of left hemiparesis and paresthesias and was activated as a code stroke. The history appeared to be limited due to the patient being Spanish-speaking only. (Although the use of translators is routine, in the emergency department, they are not always readily available in time-sensitive situations.) She did not receive tPA because she stated her left-sided symptoms were not new and she had progressively worsening clumsiness of her left side and that she had been falling to her left. Computed tomography (CT) of head revealed a right occipital mass with significant vasogenic edema causing 12mm of midline shift (Figure 1). Of note, she presented to urgent care two weeks prior to presentation after sustaining a mechanical fall at home. She

was diagnosed with a left bimalleolar fracture, placed in a cast, and scheduled for outpatient follow up with orthopedics for surgical evaluation. No further workup was considered at that time by the initial provider.

Clinical exam

The patient was alert and oriented to person, place and time in Spanish. Cranial nerve exam revealed no deficits and no evidence of visual field cut. Motor examination revealed left hemiparesis (4+/5 in the upper and lower extremities), but was limited by the previous casting of her distal left malleolar fracture. Sensory examination revealed slight diminished sensation in the left upper and lower extremities with similar limitations as motor examination.

Clinical course

The patient was started on dexamethasone 6mg every 6 hours and admitted to the ICU. No obvious abnormalities were noted on her CBC with differential. A CT chest, abdomen and pelvis was performed which did not demonstrate any evidence of metastatic lesion. An MRI brain with and without contrast revealed two homogeneously contrast-enhancing lesions: a 4.8×6.1×3cm right parieto-occipital extra-axial mass with dural-based attachment, as well as a 3.4×1.8×2.2cm homogeneously contrast-enhancing lesion adjacent to the right posterolateral ventricle. FLAIR signal changes were also appreciated and were noted to extend across the splenium of the corpus callosum, raising concerns for a high-grade glial process (Figure 2).

Given the degree of mass effect, presence of neurological deficit and no evidence of metastasis, no further workup was pursued due to the necessity of surgical intervention. After preoperative clearance, a right occipital craniotomy was performed with anticipation for gross total resection of the right parieto-occipital lesion and biopsy with likely subtotal resection and biopsy of the second lesion. Preliminary pathology from intraoperative frozen specimen were consistent with meningioma (extra-axial lesion) and high-grade glioma (periventricular lesion). With the use of intraoperative neuronavigation, gross total resection was performed for the extra-axial lesion and maximal, safe resection of the periventricular lesion was performed. This lesion

Figure 1. CT head (axial view) demonstrating a calcific right parietal lesion with vasogenic edema as well as a periventricular lesion with associated edema causing 12mm of midline shift.

was accessed via the meningioma cavity after it was removed. She tolerated the procedure well and had an improved neurological exam postoperatively. Her left hemiparesis improved compared with pre-operative exam, however, she did have very minor left visual field deficits. Post-operative MRI demonstrated

gross total resection of meningioma and subtotal resection of what was later confirmed to be diffuse large B-cell lymphoma (Figure 3). During this same admission, she also underwent open reduction, internal fixation (ORIF) of her left bimalleolar fracture without complication. She was discharged home in stable condition.

Figure 2. Pre-operative MRI demonstrating diffuse FLAIR changes with evidence of FLAIR signal crossing midline via the splenium of the corpus callosum (top). T1-post contrast reveals 2 distinct lesions – a homogeneously enhancing extra-axial lesion in the right parietal lobe as well as a homogeneously enhancing periventricular lesion (bottom).

Figure 3. Post-operative MRI demonstrating similar FLAIR changes as pre-operative MRI (top). T1-post contrast reveals gross-total resection of the previously seen extra-axial lesion in the right parieto-occipital region as well as subtotal resection of right periventricular lesion (bottom). The midline shift is significantly improved from pre-operative MRI (Figure 2).

Final pathology

Extra-axial lesion: Meningothelial Meningioma

Periventricular lesion: Diffuse Large B-Cell Lymphoma (+CD20, +BCL-6, +BCL-2, +MUM-1, +KI67)

Follow-up

At one month clinic follow-up, she was noted to have an intact motor exam with stable visual field deficits on gross examination. She went into complete remission after a course of methotrexate, cytarabine, and Rituxan and 4 cycles of radiation therapy. She tolerated the treatment relatively well with minor symptoms. At one and two year follow-ups, she continues to be in remission with no signs of recurrence on imaging. Her family reported no evidence of cognitive decline, however, no specific cognitive testing was performed.

Discussion

We report a rare case of a concurrent meningioma and primary CNS lymphoma (PCNSL), a rare occurrence entity that has only nine reported cases in the literature. The most common concurrent intracranial tumors reported in the literature are meningioma and glioblastoma (Zhang *et al.*, 2018). It is rare to find two or more primary intracranial tumors simultaneously in patients without previous radiation therapy or underlying phacomatosis such as Neurofibromatosis-2 (NF2). The annual incidence of this phenomenon is estimated to be less than one per million (Gordon *et al.*, 2011; Lee *et al.*, 2002).

Accurate diagnosis is essential as the surgical management of these conditions are opposite of one another. One area in which the management in our patient could be improved is a more accurate history and neurological examination. This was likely affected by the fact that she was a non-English speaker and highlights the importance of accurate history taking with a translator to ensure optimal care. Surgical management of PCNSL is typically limited to biopsy if CSF analysis is inconclusive. This is because PCNSL is particularly chemo- and radiosensitive. Conversely, gross total resection is the gold standard in the management of meningiomas and gliomas (Baraniskin & Schroers, 2014; Gordon *et al.*, 2011; Hoang-Xuan *et al.*, 2015; Korfel & Schlegel, 2013; Muñiz *et al.*, 2014). The same principle applies for steroid administration. The administration of glucocorticoids is not recommended in lymphoma as it could affect the diagnostic yield while it is a mainstay in the treatment of vasogenic edema (Hoang-Xuan *et al.*, 2015). Interestingly in our case, the initiation of high-dose dexamethasone did not affect our diagnosis. The typical diagnostic workup for CNS lymphoma consists of CSF analysis for markers such as *IL-10*, *CXCL13*, *CD19*, *CD20* or flow cytometry (Baraniskin *et al.*, 2011; Baraniskin & Schroers, 2014; Muñiz *et al.*, 2014; Rubenstein *et al.*, 2013). Due to the mass effect that

is exerted by meningiomas, CSF analysis is difficult without a craniotomy as a lumbar puncture would not be recommended in such a setting. MRI is the gold standard diagnostic modality for meningiomas, however, this is complicated by the fact that CNS lymphoma can mimic any and every intracranial pathology, making it difficult to discern whether lymphoma should be considered as a possibility (Bühning *et al.*, 2001; George *et al.*, 2007; Kulkarni *et al.*, 2012).

The most common association of two primary intracranial tumors is that of meningioma and glioma (>40 reported cases), however given that these tumors are two of the most common primary intracranial tumors this is thought by many to be coincidental, however associations between the two pathologies have been proposed (Ruiz *et al.*, 2015; Slowik & Jellinger, 1990; Suzuki *et al.*, 2010; Zhang *et al.*, 2018). In a report of two patients with concurrent meningioma and high grade gliomas, Ruiz *et al.* reported a mutation in *K409Q* of the *KLF4* gene within the meningiomas (Ruiz *et al.*, 2015). Suzuki *et al.* reported an oncogenic effect due to overexpression of platelet-derived growth factor (PDGF) receptors (Suzuki *et al.*, 2010). It is also postulated that meningiomas may serve as an oncogenic factor in the development of meningiomas by either inducing a genetic mutation or inciting an inflammatory response in glial cells and B-cell proliferation (Gordon *et al.*, 2011; Slowik & Jellinger, 1990).

Simultaneous presentations tend to affect adults and have a female predominance due to the nature of meningiomas and their apparent relationship with progesterone and estrogen receptors (Pravdenkova *et al.*, 2006). Since meningiomas typically have an indolent course, this is likely why they are often found concurrently with another primary intracranial pathology. In the setting of simultaneous extra-axial and intra-axial lesions, primary CNS lymphoma must remain a consideration to ensure accurate diagnosis and treatment. Prompt treatment in our case contributed to a good outcome. The outcome in our case fares well in comparison to previously reported cases as their average survival was 6 months in those patients whose outcomes were reported.

Consent

The patient and her family gave written informed consent for presenting all pertinent clinical information in this case report.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References

Baraniskin A, Kuhnhen J, Schlegel U, *et al.*: Identification of microRNAs in the cerebrospinal fluid as marker for primary diffuse large B-cell lymphoma of the central nervous system. *Blood*. 2011; 117(11): 3140–3146.
[PubMed Abstract](#) | [Publisher Full Text](#)

Baraniskin A, Schroers R: Modern cerebrospinal fluid analyses for the diagnosis of diffuse large B-cell lymphoma of the CNS. *CNS Oncol*. 2014; 3(1): 77–85.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

Bühning U, Herrlinger U, Krings T, *et al.*: **MRI features of primary central nervous system lymphomas at presentation.** *Neurology*. 2001; 57(3): 393–396.

[PubMed Abstract](#) | [Publisher Full Text](#)

George B, Kumar R, Johns P, *et al.*: **Contiguous synchronous occurrence of primary cerebral lymphoma and meningioma.** *Br J Neurosurg*. 2007; 21(1): 35–38.

[PubMed Abstract](#) | [Publisher Full Text](#)

Gordon AS, Fallon KE, Riley KO: **Meningioma interdigitated with primary central nervous system B-cell lymphoma: A case report and literature review.** *Surg Neurol Int*. 2011; 2: 181.

[PubMed Abstract](#) | [Free Full Text](#)

Hoang-Xuan K, Bessell E, Bromberg J, *et al.*: **Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology.** *Lancet Oncol*. 2015; 16(7): e322–32.

[PubMed Abstract](#) | [Publisher Full Text](#)

Korfel A, Schlegel U: **Diagnosis and treatment of primary CNS lymphoma.** *Nat Rev Neurol*. 2013; 9(6): 317–327.

[PubMed Abstract](#) | [Publisher Full Text](#)

Kulkarni KM, Sternau L, Dubovy SR, *et al.*: **Primary dural lymphoma masquerading as a meningioma.** *J Neuroophthalmol*. 2012; 32(3): 240–242.

[PubMed Abstract](#) | [Publisher Full Text](#)

Lee EJ, Chang CH, Wang LC, *et al.*: **Two primary brain tumors, meningioma and glioblastoma multiforme, in opposite hemispheres of the same patient.** *J Clin Neurosci*. 2002; 9(5): 589–591.

[PubMed Abstract](#) | [Publisher Full Text](#)

Muñiz C, Martín-Martín L, López A, *et al.*: **Contribution of cerebrospinal fluid sCD19 levels to the detection of CNS lymphoma and its impact on disease outcome.** *Blood*. 2014; 123(12): 1864–1869.

[PubMed Abstract](#) | [Publisher Full Text](#)

Pravdenkova S, Al-Mefty O, Sawyer J, *et al.*: **Progesterone and estrogen receptors: opposing prognostic indicators in meningiomas.** *J Neurosurg*. 2006; 105(2): 163–173.

[PubMed Abstract](#) | [Publisher Full Text](#)

Rubenstein JL, Wong VS, Kadoch C, *et al.*: **CXCL13 plus interleukin 10 is highly specific for the diagnosis of CNS lymphoma.** *Blood*. 2013; 121(23): 4740–4748.

[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

Ruiz J, Capilla E, Díaz JF, *et al.*: **Secretory meningioma with KLF4 K409Q mutation in collision with glioma.** *Clin Neuropathol*. 2015; 34(6): 322–329.

[PubMed Abstract](#) | [Publisher Full Text](#)

Slowik F, Jellinger K: **Association of primary cerebral lymphoma with meningioma: report of two cases.** *Clin Neuropathol*. 1990; 9(2): 69–73.

[PubMed Abstract](#)

Suzuki K, Momota H, Tonooka A, *et al.*: **Glioblastoma simultaneously present with adjacent meningioma: case report and review of the literature.** *J Neurooncol*. 2010; 99(1): 147–153.

[PubMed Abstract](#) | [Publisher Full Text](#)

Zhang Z, Yang Y, Zhang K, *et al.*: **Collision Tumor of Glioblastoma and Meningioma: Case Report and Literature Review.** *World Neurosurg*. 2018; 117: 137–141.

[PubMed Abstract](#) | [Publisher Full Text](#)

Open Peer Review

Current Peer Review Status: ? ✓

Version 2

Reviewer Report 11 September 2019

<https://doi.org/10.5256/f1000research.22421.r53077>

© 2019 Das K. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Kuntal Kanti Das

Department of Neurosurgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

The paper is acceptable to me.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 20 August 2019

<https://doi.org/10.5256/f1000research.19429.r51975>

© 2019 Das K. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Kuntal Kanti Das

Department of Neurosurgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

The authors report an interesting case of co-occurrence of primary CNS lymphoma and meningioma in a 64-year-old lady and discuss the importance of preoperative suspicion in their management. The case is indeed interesting and clearly, the authors managed the case well.

My observations which the authors may like to clarify include:

1. Was the presence of hemiparesis not suspected when the patient presented with a fall 2 weeks earlier? Clearly, the tendency to fall on the left side must have been given due importance.
2. Details of the surgical approach are necessary. How was the periventricular lesion approached? Through a separate corticectomy or through the bed of the meningioma cavity? Was any intraoperative image guidance utilized?
3. Did you try to rule out systemic lymphoma? If so, how?
4. Apart from being a function of increased age, is there any connecting link between lymphoma and meningioma? Some more literature needs to be incorporated in this regard.

Apart from reporting a rare association, a case like this can be more educative if newer insights can be provided as to how do they co-occur and how should they be managed. I would be happy if the authors address these minor points.

Is the background of the case's history and progression described in sufficient detail?

Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Neurooncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 17 June 2019

<https://doi.org/10.5256/f1000research.19429.r49515>

© 2019 Bessell E. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Eric Bessell

Department of Clinical Oncology, Nottingham City Hospital, Nottingham, UK

The authors are correct in stating that a concurrent presentation of meningioma and primary CNS lymphoma (PCNSL) is very rare and worth publishing. The authors imply that the use of translators for the hispanic population in California is not routine. They should clarify this for an international audience. PCNSL can be rapidly progressive and urgent investigation is essential.

Most cases of PCNSL are diagnosed by stereotactic biopsy +/- CSF cytology and a surgical approach is uncommon. In this case the radiological appearance was of a meningioma as well as a lesion adjacent to the right postero-lateral ventricle. The frozen section of the latter lesion suggested a high-grade glioma and for this reason surgical removal of both tumours was indicated.

No detailed information is given on the staging investigations carried out which should include CT or PET/CT scanning, CSF cytology, bone marrow aspirate and trephine, slit-lamp examination of the eye and blood tests including LDH. Also baseline neuro-cognitive tests are indicated at the age of 64 years.

No detailed information is given on the chemotherapy given, the regimen with methotrexate, cytarabine and rituximab is not referenced and no doses are given and the number of cycles not stated. In addition the radiotherapy dose is in Gy with the number of fractions stated not in cycles. This information is essential in a patient of this age.

The authors state that at 2 years there is no recurrence but again give no indication of whether there has been any cognitive deterioration.

In the discussion the authors discuss the other brain tumours that occur concurrently with meningioma but don't discuss the outcome achieved in the other 9 cases reported and how they compare with the case they are reporting.

In summary this is an interesting case report which would be greatly enhanced if the additional information I have alluded to was included.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.**Reviewer Expertise:** International expert in primary CNS lymphoma and co-author of European Guidelines in 2015.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research