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Case Report

High-grade spheno-orbital meningioma in patients with systemic lupus erythematosus: Two case reports and literature review

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ABSTRACT

Background: Spheno-orbital meningiomas (SOMs) are often benign. The association of meningioma and systemic lupus erythematosus (SLE) is rarely discussed in the literature. Here, we report two patients with high-grade, SOMs with a prolonged history of SLE and review the literature.

Case Description: The first case is a 52-year-old female patient with a 15-year history of SLE diagnosis who was referred to our center with a 1-year history of proptosis and excessive tearing of the left eye. This patient was operated for the left SOM with histopathological diagnosis of the World Health Organization (WHO) Grade III rhabdoid meningioma. The second case is a 36-year-old female patient with a 12-year history of SLE diagnosis who presented to our clinic with a 5-year-history of progressive right eye proptosis and occasional headaches. She was operated for the right SOM with histopathological diagnosis of the WHO Grade II chordoid meningioma.

Conclusion: Rhabdoid and chordoid SOMs are uncommon and no previous report discussed their occurrence in patients with SLE. The association of high-grade meningiomas and SLE deserves further exploration.

Keywords: Chordoid meningioma, Rhabdoid meningioma, Spheno-orbital meningioma, Systemic lupus erythematosus

INTRODUCTION

Spheno-orbital meningioma (SOM) is a complex and unique pathological condition that accounts for 9% of all intracranial meningiomas.[34,39] These tumors originate from the dural sheath of the sphenoid bone and are characterized by their invasion into the orbit, optic canal, superior orbital fissure, and cavernous sinus. Interosseous tumor growth in SOM results in hyperostosis and soft-tissue growth.[11,17,25,43,52] Patients with SOM classically present with proptosis, vision loss, limited ocular motility, and headache.[17,23,39,51] SOMs are often low grade. High-grade meningiomas, such as Grade II and Grade III, in the spheno-orbital region are rare.[35,56] Furthermore, among the different types of high-grade meningiomas, chordoid and rhabdoid SOMs in particular are rarely encountered.

Systemic lupus erythematosus (SLE) is an autoimmune, multiorgan, connective tissue disease with diverse pathogenesis and unexplored etiology that frequently affects women.[40] Increased

risk of malignancies was observed in patients with SLE;[54] however, no study has previously identified an increased risk of central nervous system (CNS) malignancies or high-grade meningiomas in patients with SLE.

In this paper, we describe two patients who were diagnosed with SLE and referred to us for the surgical treatment of SOM. These patients exhibited uncommon histopathological variants of SOM.

CASE REPORT

Case 1

A 52-year-old female patient with a 15-year history of SLE diagnosis was referred to our center with a 1-year history of proptosis and excessive tearing of the left eye. On examination, she was found to have a visual acuity of 20/20 in the right eye and 20/25 in the left eye, with intact extraocular movement and facial sensation. She had been on a regimen of azathioprine therapy to manage her SLE.

Radiological imaging showed left SOM with extension into the superior orbital fissure, left cavernous sinus, and left petrous apex. In addition, there was a small extension toward the left cerebellopontine angle (CPA) with significant hyperostosis of the sphenoid bone and lateral orbital wall [Figure 1]. Azathioprine therapy was discontinued preoperatively.

The patient was subsequently operated through the left pterional approach. The histopathological examination established a diagnosis of the World Health Organization (WHO) Grade III rhabdoid meningioma (RM) [Figure 2]. Postoperatively, the patient's recovery was uneventful. However, postoperative radiological imaging findings showed residual lesions at the left cavernous sinus and CPA that were not amenable to resection. The patient received external beam radiation therapy (EBRT; 60 Gy in 30 fractions) and showed gradual improvement of proptosis with no new neurological deficits.

Case 2

A 36-year-old female patient with a 12-year history of SLE diagnosis presented to our clinic with a 5-year history of progressive right eye proptosis and occasional headaches. On examination, she was found to have right eye exophthalmos with normal visual acuity, as well as intact extraocular motility and normal facial sensation bilaterally. She was on a regimen of hydroxychloroquine to manage her lupus. In addition, she used steroids, which was discontinued a year ago because of remission.

Radiological imaging findings showed right SOM with extension into the orbit and cavernous sinus [Figure 3].

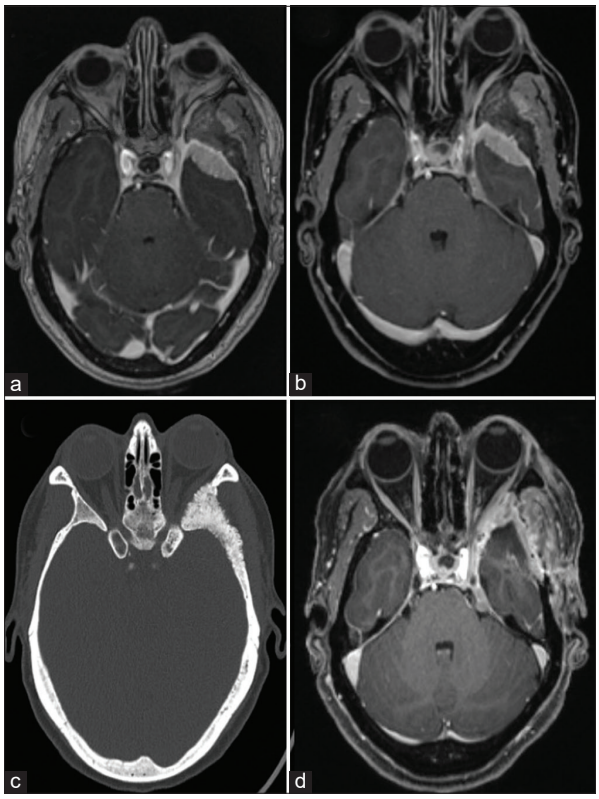

Figure 1: Case 1. (a and b) Preoperative T1-weighted postgadolinium administration MR images demonstrating left SOM with extension into the superior orbital fissure, left cavernous sinus, left petrous apex, and left cerebellopontine angle (CPA). (c) Preoperative CT head bone window demonstrating hyperostosis. (d) Postoperative T1-weighted postgadolinium administration MR images demonstrating postoperative changes as well as residual lesion at the left cavernous sinus and CPA.

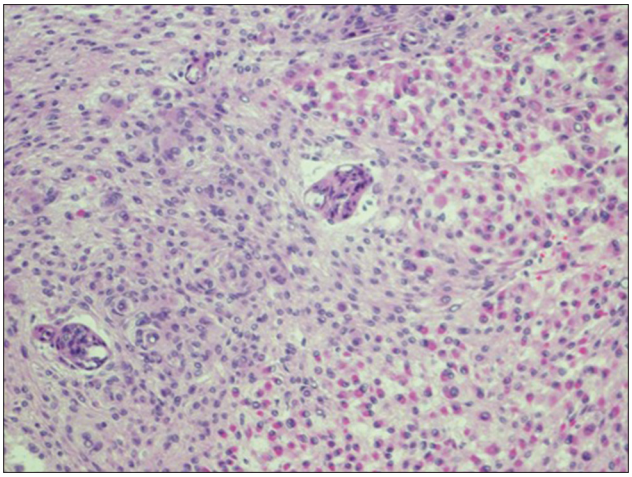

Figure 2: Case 1. Hematoxylin and eosin staining showing rhabdoid meningioma, ×20.

Right frontotemporal craniotomy was performed for tumor resection. The histopathological examination established a

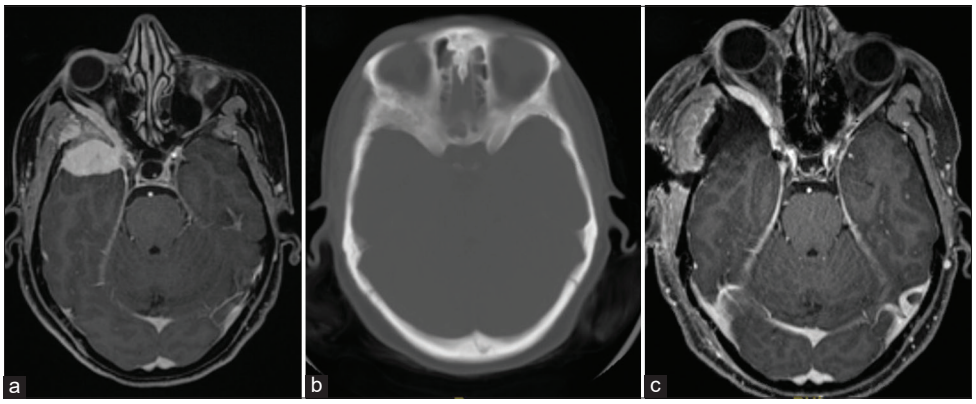

Figure 3: Case 2. (a) Preoperative T1-weighted postgadolinium administration MR images demonstrating right SOM extending into the right orbit and cavernous sinus. (b) Preoperative CT head demonstrating hyperostosis. (c) Postoperative T1-weighted postgadolinium administration MR images demonstrating intraorbital residual lesion approaching the superior orbital fissure.

diagnosis of the WHO Grade II chordoid meningioma (CM) [Figure 4]. Subsequent, postoperative follow-up imaging findings showed intraorbital residual lesion approaching the superior orbital fissure that was difficult to resect. The patient underwent EBRT (60 Gy in 30 fractions and 54 Gy in 30 fractions) using simultaneous integrated boost due to intraorbital component. The patient reported improvement of symptoms with no new neurological deficits.

Literature review methods

To investigate for previous reports of cases of meningioma occurring in patients with SLE, we searched the PubMed database using the following terms; meningioma AND "systemic lupus erythematosus," meningioma AND "autoimmune disease," and meningioma AND "connective tissue disease." Data on age, sex, time of meningioma diagnosis, location of meningioma, histopathological grade of meningioma, and medications used for the treatment of SLE were collected for each case.

Literature review results

Seven cases were identified and were available for review in addition to one case that was retrieved through cited references. Ten cases were analyzed [including our two cases; Table 1]; all were female with a mean age at presentation of 47 years. The clinical presentation constitutes headaches in 75% and psychiatric symptoms in 37%. The mean time from SLE diagnosis to the development of meningioma was 18 years. Four of the cases identified were operated; the histopathological data were available for two patients which determined benign (WHO Grade I) meningiomas. With regard to the medications used for the treatment of SLE, seven patients were receiving steroids, three were receiving azathioprine, five were receiving antimalarial medications, one was receiving mycophenolate mofetil, and one was receiving cyclosporine.

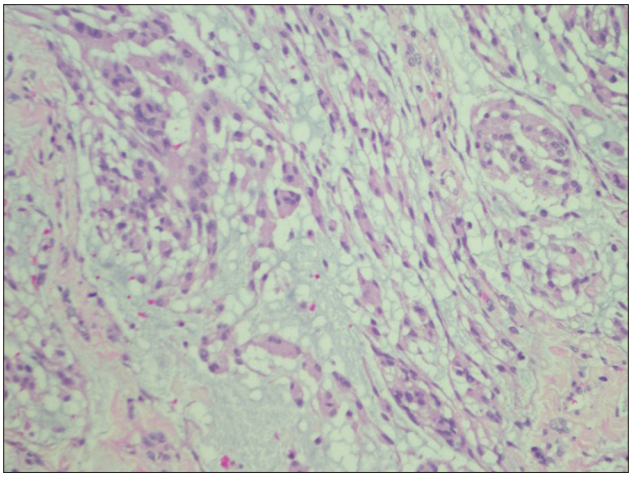

Figure 4: Case 2. Hematoxylin and eosin staining showing chordoid meningioma, ×20.

DISCUSSION

This report describes two rare histopathological variants of SOM that occurred in patients with a prolonged history of SLE. The association of meningioma and SLE has been discussed earlier;[10,13,42,49,59] however, no previous report discussed an association of high-grade meningioma and SLE.

Meningioma is the most common primary intracranial tumor in adults, accounting for one-third of all primary intracranial tumors, with a female-to-male ratio of 2:1; and most patients have low-grade meningioma.[36] High-grade, atypical (Grade II), and anaplastic (Grade III) meningiomas are rarely encountered in clinical settings, and they represent <10% of all meningiomas.[2,16]

RM is an uncommon variant of meningioma, which represents 0.28% of all meningioma;[60] it was first described two decades ago by Kepes *et al*.[28] and Perry *et al*.[37] Subsequently, in the 2000 WHO classification of CNS tumors, RM was added

Table 1: Reported cases of meningioma in patients with systemic lupus erythematosus.

Author	Age/ sex	Time from SLE diagnosis to meningioma diagnosis	Clinical presentation	Meningioma location	Histopathology	SLE treatment
Bilaniuk *et al*., 1977[10]	48/F	Not reported	Seizures and psychosis	Tentorial	Not reported	Not reported
Richardson *et al*., 2000[42]	68/F	44 years	Headaches	Occipital	Not operated	Steroids and hydroxychloroquine
Castellino *et al*., 2009[13]	60/F	17 years	Exophthalmos	Retro-orbital	Not operated	Cyclophosphamide, steroids
	39/F	14 years	Headache, anxiety, severe depression, and panic attack	Parietal	Meningothelial, WHO Grade I	Steroids and azathioprine
	54/F	7 years	Headache, depression, and cognitive dysfunctions	Falcine	Not operated	Steroids and cyclosporine
Sankaran *et al*, 2015[49]	30/F	1 year	Headaches	Falcine	Not reported	Steroids, hydroxychloroquine, and mycophenolate mofetil
	41/F	2 years	Headaches and vomiting	Convexity, frontal	Not reported	Steroids, hydroxychloroquine, and azathioprine
Yoo*et al*., 2016[59]	49/F	1 week	Headaches	Convexity, parietal	Meningothelial, WHO Grade I	Steroids and hydroxychloroquine
The present report	52/F	15 years	Proptosis	Spheno-orbital	Rhabdoid, WHO Grade III	Azathioprine
	36/F	12 years	Proptosis, decrease vision, and headaches	Spheno-orbital	Chordoid, WHO Grade II	Steroids and hydroxychloroquine

F: Female, WHO: World Health Organization

as a distinct Grade III malignant meningioma due to its aggressive course and malignant histological features.[30] RMs are associated with poor prognosis, a relatively high risk of recurrence (87%), extracranial metastasis (13%), and death (53%).[37,60] In addition, these tumors have bone involvement, with 56% of the tumors manifesting definite hyperostosis.[29]

CM was additionally introduced by Kepes *et al*.[27] in their 1988 report. In their original report, they described seven cases of CM that occurred exclusively in children with Castleman's syndrome. Subsequently, in 1993, CM was added to the WHO classifications of CNS tumors as a Grade II atypical meningioma.[18] These tumors have histological features resembling those of chordoma and account for 0.5–1% of all intracranial meningiomas.[18] Unlike RMs, CMs are less aggressive with a recurrence rate of 11–22%.[57]

Meningiomas of the cranial base show an indolent growth pattern and are often classified as low-grade meningiomas as compared with its noncranial base counterparts. The low-grade nature of these meningiomas has been theoretically attributed to the fact that most cranial base meningiomas present earlier; thus, cases of aggressive or malignant transformation are less likely to occur due to early intervention.[46] In addition, cases of SOM represent a considerable surgical challenge because of its invasion into the cavernous sinus and superior orbital fissure; therefore, some authors argued that the primary goal of surgical treatment is to improve symptoms rather than complete resection.[23]

High-grade SOMs, specifically RMs and CMs, are rare. Various case series have discussed the natural history and outcomes of SOMs and demonstrated that Grade I meningiomas occur in 78%,[5] 83%,[35] 84%,[23,33] 87%,[25] 90%,[24] 94%,[22] and 100%[48,52,56] of the patients examined in these reports. In addition, in the previously discussed cases series, Grade II SOM constituted 5.6%,[22] 9%,[24] 10%,[5,26] and 16% of the cases.[23] Interestingly, Grade III meningiomas are the least reported among the three SOM grades, representing 3%[26] and 10.5% of all SOMs.[5] These case series, however, did not report on the specific subtypes of Grade II and Grade III SOMs. Sporadic cases of rhabdoid and chordoid sphenoidal meningiomas have been reported.[9,29]

An association between SOM and other medical conditions, specifically, hypothyroidism has been identified;[47] however, this association was not studied further. SLE is an inflammatory autoimmune disease with multiple organs involvement. The production of autoantibodies and

serum cytokine dysregulation is pathognomonic of this disease.[58] The risk of malignancies among patients with SLE has received more attention recently. A higher risk of hematological malignancies,[7,54,55] lung cancer,[8,54] bladder cancer,[54] hepatobiliary,[54] and gynecological malignancies[3] has been observed among patients with SLE.

Prevailing theories have proposed an association between malignancies and SLE, including relatively high expression of interleukin 6 (IL-6) and IL-10 in patients with non-Hodgkin lymphoma and in patients with SLE.[31] Moreover, cyclophosphamide exposure has been reported as a risk factor for bladder cancer,[38,54] as was a higher susceptibility to specific viral infections such as Epstein–Barr virus and human papilloma virus in patients with SLE, both of which play a role in the pathogenesis of hepatobiliary and gynecological malignancies.[14,31,54]

IL-6 expression was suggested to be an important factor in the pathogenesis of CM;[1,19] therefore, patients with SLE may have an increased risk of developing CM. Moreover, SLE is treated with a variety of medical therapies, including glucocorticoids, antimalarials (hydroxychloroquine, chloroquine, and mepacrine), methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, calcineurin inhibitors (cyclosporine A and tacrolimus), thalidomide, rituximab, and belimumab.[21] Only few studies have identified an increased risk of malignancies with the use of specific medications; they include an increased risk of hematological malignancies and lung cancer among patients on azathioprine therapy for rheumatoid arthritis but not for SLE,[32,53] increased risk of bladder, skin, and hematological malignancies among patients on cyclophosphamide therapy for rheumatoid arthritis,[4,41] as well as increased risk of bladder cancer among patients on cyclophosphamide therapy for SLE.[38] Nonetheless, the use of antimalarial drugs (e.g., hydroxychloroquine) was not associated with an increased risk of malignancies in patients with SLE.[45] One of our patients was receiving azathioprine and the other one was receiving hydroxychloroquine.

The role of estrogen and progesterone receptors in the development of meningioma is well established. This was evident by accelerated growth of meningiomas during pregnancy and in postmenopausal women receiving exogenous hormone therapy.[6,15,44] Moreover, Grade I meningiomas primarily affect females whereas males are more likely to be affected by high-grade meningiomas.[36] SLE largely affects women with a female-to-male ratio of 9:1.[58] This female predominance remains undetermined; however, the role of estrogen in the development of SLE was proposed.[20]

From the current literature, we identified eight cases of meningiomas that were reported in patients with SLE.[13,49,59] Histopathological date was available for two patients which determined benign (WHO Grade I) meningiomas. These reports suggested a possible role of estrogen and progesterone exposure in the pathogenesis of meningioma in those patients. Nonetheless, two previous studies failed to identify an increased risk of meningioma in patients with autoimmune diseases.[12,50] These studies, however, did not stratify meningiomas based on their histopathological grading.

CONCLUSION

This report provides an insight into the possible attribution of SLE to the development of high-grade meningiomas. We report an unusual association between rare histopathological entities of SOM and SLE. The use of specific medications to manage SLE as well as the overexpression of IL-6 observed in both CM and SLE might play a role in the pathogenesis of high-grade (rhabdoid and chordoid) SOM. However, further epidemiological and genetic studies are needed to validate this association. Moreover, a coincidental association cannot be ruled out given that both meningioma and SLE are common disease conditions.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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