



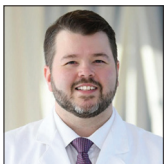
Case Report

Co-existence of multiple sclerosis and germinoma in an adult male: Case report

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ABSTRACT

Background: Concurrent diagnosis of multiple sclerosis (MS) and the central nervous system (CNS) germinoma is rare. The diagnostic criteria for MS rely primarily on clinical presentation, and CNS germinoma can present as an MS mimic. These factors contribute to the rarity of dual diagnosis.

Case Description: A 28-year-old man presented initially with bilateral optic neuritis, manifesting as persistently worsening vision for 2 years, and demyelinating plaques identified within the corpus callosum on magnetic resonance imaging. Initial work-up, in addition to clinical presentation, led to diagnosis of MS. Three months following the diagnosis of MS, the patient then presented with obstructive hydrocephalus due to a newly diagnosed intraventricular mass. The patient underwent an endoscopic third ventriculostomy and biopsy which confirmed diagnosis of CNS germinoma.

Conclusion: To the best of our knowledge, dual presentation of both MS and CNS germinoma has never been reported in the literature. The clinical presentation of bilateral optic neuritis (persisting for roughly 2 years before initial MS diagnosis), demyelinating plaques, and intrathecal oligoclonal bands before the development of an intraventricular mass indicates that both MS and CNS germinoma presented simultaneously in this patient. The treatment plan for this patient included carboplatin + etoposide, followed by adjuvant radiation and subsequent IVIG therapy.

Keywords: Dawson's fingers, Endoscopic third ventriculostomy, Germinoma, Multiple sclerosis

INTRODUCTION

Primary intracranial germinomas are derived from germinal stem cells and are most often located in the suprasellar or infundibular, and pineal regions of the brain.^[6] Patients frequently present with headaches, vision changes (often diplopia), and signs of generalized endocrine deficiencies such as fatigue and difficulty sleeping.^[6] Diagnosis of germinoma is largely based on clinical presentation and neuroimaging and is typically confirmed by biopsy.^[9] Multiple sclerosis (MS) is an autoimmune disease of the central nervous system (CNS) characterized by inflammation and demyelination.^[5] According to the updated McDonald criteria, diagnosis of MS depends on a constellation of clinical presentation, magnetic resonance imaging (MRI) findings and CNS specific cerebrospinal fluid (CSF) findings, with no better explanation for alternative etiology.^[10]

A few cases have been described in the literature, in which CNS germinomas were originally diagnosed as MS. This misdiagnosis occurs because detection of these diseases relies mostly on clinical symptoms coupled with neuroimaging, and both can present with abnormal brain

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MRI.^[2,7,8] While there are a small number of reports detailing initial misdiagnosis of MS in CNS germinoma patients, to the best of our knowledge, no study has yet to identify both in the same patient. In this case report, we present a patient, in which both MS and CNS germinoma was concurrently diagnosed close in time and discuss the complexities of treating both diseases simultaneously.

CASE PRESENTATION

Clinical presentation

The patient described is a 28-year-old man with a history of hypertension who initially presented to the ophthalmology department with a 2-year history of progressive, bilateral vision loss. Findings on exam included poor visual acuity, bilateral optic atrophy, reduced foveal threshold, and nonspecific inferior defects. Fundoscopic exam at this time revealed optic disc pallor and a cup-to-disc ratio of 0.3 bilaterally. Given these findings, the patient was subsequently referred to the department of neurology for evaluation of possible MS. Brain MRI revealed T2 FLAIR hyperintense lesions involving the body of the corpus callosum and the periventricular white matter without contrast enhancement, suggestive of demyelinating plaques [Figure 1]. CSF testing showed normal protein and cells (0 WBC/mm³, 17 RBC/mm³, 33 mg/dL protein, and 66 mg/dL glucose) along with elevated IgG index and 4 CNS specific oligoclonal bands, strongly increasing the suspicion for MS. MRI of the spine showed no additional lesions. Serological testing for MS mimics was largely unrevealing except for serum copper which was marginally low at 66 ug/dl (normal range 72–166 ug/dl).

Three months after the diagnosis of MS, the patient presented to an outside hospital with a severe right-sided headache and he was referred to our hospital for further evaluation secondary to imaging demonstrating hydrocephalus and intracranial mass. Of note, the patient had not begun treatment for MS at the time of his hospital admission. At time of presentation, the patient was alert and in no apparent distress. The patient characterized the headache as constant for the past month, and worsened in the week before presentation. He denied any vomiting or nausea and his neurological examination was unremarkable. No upper motor neuron findings or visual field deficits were present at the time of examination. Fundoscopic exam showed no relative afferent pupillary defect. MRI of his brain demonstrated an intraventricular mass located in the posterior third ventricle, obstructive hydrocephalus and worsening of corpus callosum and periventricular T2 hyperintense lesions [Figure 2]. An endoscopic third ventriculostomy was successfully performed to treat hydrocephalus and a biopsy was taken of the mass for pathological evaluation.

Pathology

Two small biopsy specimens were submitted for examination. The tumor contained solid sheets of polygonal cells of moderate size and centrally located nuclei. The cytoplasm was pale in some areas [Figures 3a and b] but was more eosinophilic in other areas. The nuclei were moderately sized and showed a limited variation in size. Prominent nucleoli were noted in many of the tumor cells [Arrow in Figures 3b and c] and were best appreciated in the cytologic preparation obtained during intraoperative consultation.

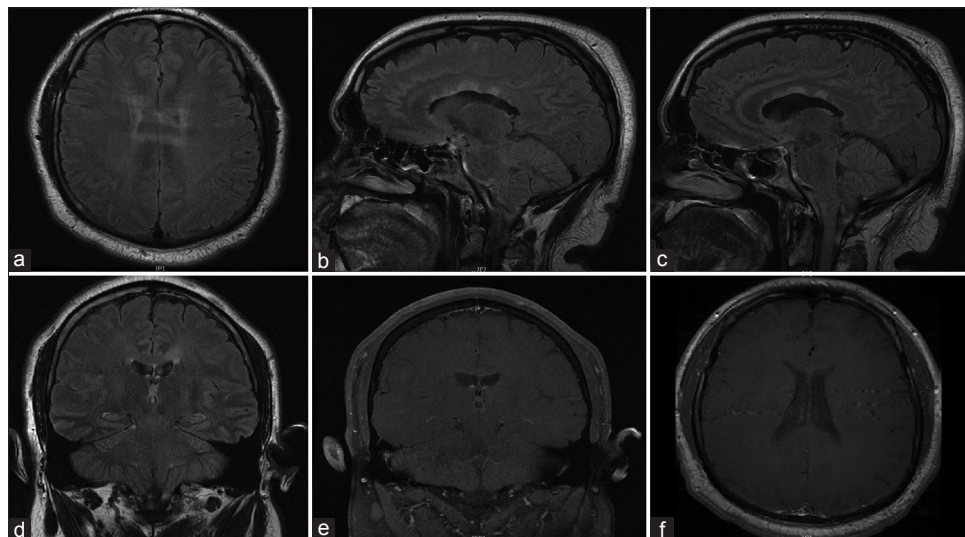


Figure 1: (a) Axial view showing corpus callosum lesions (b and c) sagittal T2 FLAIR images showing corpus callosal lesions and periventricular lesions oriented perpendicular to long axis of lateral ventricle (d) ovoid periventricular lesion (e and f) coronal T1 + contrast and axial T1 + contrast demonstrating absence of lesions.

On immunohistochemistry with Ki67, an average labeling index of about 30% was demonstrated. The tumor cells were positive for OCT3/4 [Figure 3d], CD117 (c-kit) [Figure 3e],

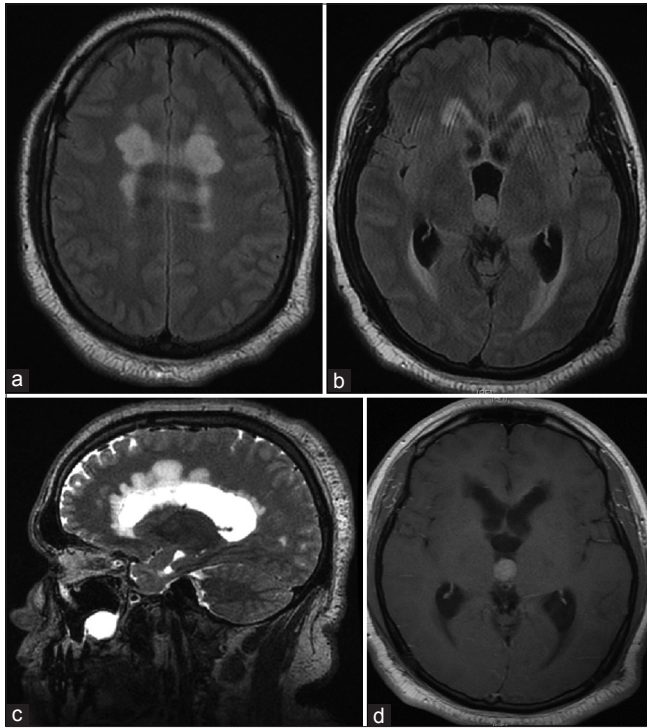


Figure 2: (a) Axial T2 FLAIR showing worsening of previously noted corpus callosum lesion (b) axial T2 FLAIR showing an ovoid 3rd ventricular mass, obstructive hydrocephalus, and periventricular T2 hyperintensity (c) sagittal T2 image showing worsening of previously noted periventricular lesions (d) T1 axial post contrast scan showing homogenous enhancement of 3rd ventricle mass.

placental alkaline phosphatase, cytokeratin AE1/AE3, and cytokeratin 7. The tumor cells were negative for H3 K27M [Figure 3f], glial fibrillary acidic protein, Olig2, IDH1-R132H, synaptophysin, Sox10, Melan-A, CD30, thyroid transcription factor 1, and thyroglobulin. The tumor cells were also positive for BAF47 (INI1) indicating no loss of INI1 gene. A diagnosis of germinoma was made based on these characteristics.

Postoperative course

The patient’s neurologic exam was normal postoperatively and he was discharged home after a 2-day hospital stay. Two months after surgery, the patient was started on carboplatin + etoposide to attempt cytoreduction before radiation therapy to treat intracranial germinoma. Interestingly, brain MRI 4 months after surgery showed resolution of hydrocephalus, periventricular T2 hyperintense changes (thought to possibly be related to trans-ependymal flow initially) and decrease in size of corpus callosum plaques [Figure 4]. To rule out paraneoplastic optic neuritis, serum studies were performed and common markers for the disease, anti-CRMP-5, and anti-amphiphysin, were both negative.^[11] At the time of this manuscript, the patient had not undergone adjuvant radiation treatment nor started disease modifying treatment for MS as this was held secondary to initial focus on oncologic treatment after discussion among the patient’s treating physicians.

DISCUSSION

Primary intracranial germinomas generally present with clinical symptoms that include headaches and vision changes

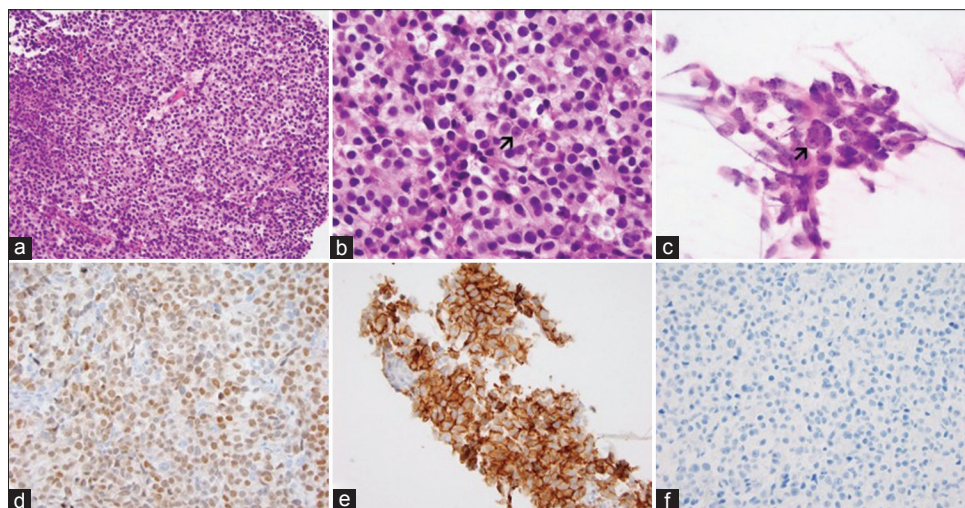


Figure 3: (a and b) are low- and high-magnification. (c) is cytologic preparation during intraoperative consultation. Prominent nucleoli are highlighted by arrows in (b and c). (d-f) are immunohistochemistry for OCT3/4, CD117, and H3 K27M respectively. Original magnification for (a) is ×20, (b) and (c) are ×60, (d) to (f) are ×40.

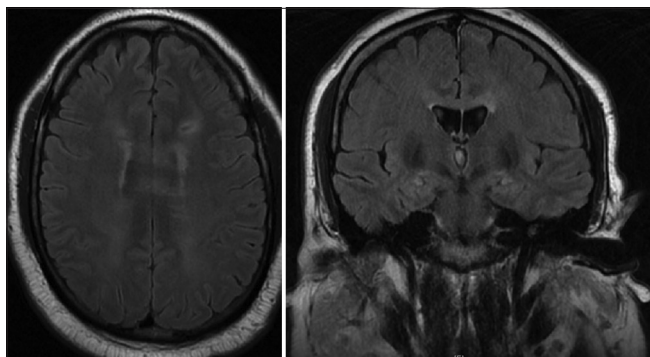


Figure 4: Axial and coronal T2 FLAIR showing corpus callosum and periventricular lesions which are decreased in size as compared to Figure 2 and resolution of hydrocephalus.

and are definitively diagnosed with an abnormal MRI and brain mass biopsy.^[6] MS is mainly a diagnosis of exclusion, and relies on a pattern of clinical presentation, MRI and CSF findings.^[5] Because these two diseases can present in a similar fashion, there have been a few reports in the literature detailing misdiagnosis of MS in CNS germinoma patients.^[2,7,8] To the best of our knowledge, no instance of true simultaneous presentation of CNS germinoma and MS in the same patient has been described in the scientific literature.

The patient's presentation with a clinically isolated syndrome of bilateral optic neuritis, lesional demyelination on MRI, and intrathecal oligoclonal bands all fulfill the McDonald criteria for an MS diagnosis.^[10] The CNS germinoma appeared on imaging 3 months after MS diagnosis, and the etiology of this tumor was confirmed with biopsy. Timing of the earliest MRI demonstrating only demyelinating plaques with no sign of an intraventricular mass indicates the demyelination caused by MS occurred before development of the CNS germinoma. Therefore, this provides evidence to support the concurrent presentation of MS and CNS germinoma. Due to the rarity of this dual diagnosis, a broad differential was considered including paraneoplastic optic neuritis, and germinoma as an MS mimic amongst others.

Paraneoplastic optic neuritis induced by the CNS germinoma was considered as an explanation for the patient's bilateral optic neuritis. This rare, autoimmune reaction can cause optic neuropathy in CNS tumors.^[11] Markers for this disease including anti-CRMP-5 and anti-amphiphysin were both negative.^[11] In addition, the timing of optic neuritis onset, 2 years before tumor presentation, rendered this diagnosis unlikely.

There have been a few reports where intrathecal oligoclonal bands were reported in germinoma patients.^[2-4,7,8] In each case, an enhancing lesion on MRI and oligoclonal bands in CSF were observed, but biopsy later confirmed a germinoma diagnosis. The key difference between these and the current case is the timing of diagnosis. The few reports in the

literature indicate discovery of the enhancing lesion occurred just before biopsy and subsequent germinoma diagnosis,^[2-4,7,8] while our patient exhibited T2 hyperintense demyelinating lesions in the corpus callosum (Dawson's Fingers) months before presenting with an intraventricular mass precipitating obstructive hydrocephalus.

The treatment plan for this patient focused on addressing the CNS germinoma first before managing the MS. The patient completed four cycles of carboplatin + etoposide with near complete response of the ventricular germinoma and no evidence of disease in the spine. Shortly thereafter, the patient is slated to begin radiation therapy. He is scheduled to start IVIG therapy following radiation treatment which has been shown to slow vision loss in MS.^[1]

At the time of writing this manuscript, the patient's headaches have improved significantly since completion of chemotherapy. Future IVIG therapy will hopefully slow vision loss due to optic neuritis caused by MS.

CONCLUSION

Concurrent presentation of MS and CNS germinoma is exceptionally rare. However, after careful consideration of the clinical presentation of our patient, combined with imaging and biopsy, a final dual diagnosis was made. Development of a treatment plan for coexisting MS and CNS germinoma is complex, but the emphasis was ultimately placed first on treating the CNS germinoma, to be followed with targeted MS therapy. For now, the current treatment appears to have addressed the patient's tumor-related symptoms. Future radiation and IVIG therapy will hopefully prevent further vision loss due to MS.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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