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Editor: **S. Ather Enam,** M.D., Ph.D., Aga Khan University, Karachi, Sindh, Pakistan

Case Report

Neurocytoma mimicking macroadenoma

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Received: 05 November 18 Accepted: 28 November 18 Published: 21 January 19

Abstract

Background: Intraventricular and extraventricular central neurocytomas (CN) are equally frequent among 20–40-year-old men and women. However, sellar and suprasellar extraventricular CN are extremely rare, with only 12 reported cases.

Case Description: The authors report the case of a Brazilian 27-year-old man who presented with progressive vision loss during the last 4 years and serious bilateral keratoconus. We also review the epidemiological, clinical, radiological, pathological, and treatment features of the 12 reported cases. The patient developed left amaurosis and right temporal hemianopsia after undergoing bilateral corneal transplantation, which was detected during campimetry testing, and subsequently underwent magnetic resonance imaging, which revealed a huge hypophyseal tumor. Endocrinological evaluation revealed complete loss of pituitary function. The patient was referred to our department and underwent a two-step surgery (using transsphenoidal approach and cranio-orbital zygomatic approach) based on the diagnosis of an extraventricular central nervous system neurocytoma. Tumor removal was successful, and the patient was discharged at 3 weeks after admission to our department.

Conclusion: Although extraventricular neurocytomas of the brain are rare, careful preoperative consideration of its anatomy, pathophysiological features, and radiological features can enhance the treatment outcomes.

Key Words: Central nervous system, central nervous system neoplasms, central neurocytomas, neurocytoma

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/sni.sni_387_18

Quick Response Code:

How to cite this article: Nery B, Bernardes Filho B, Costa RA, Pereira LC, Quaggio E, Queiroz RM, *et al.* Neurocytoma mimicking macroadenoma. Surg Neurol Int 2019;10:8. http://surgicalneurologyint.com/Neurocytoma-mimicking-macroadenoma/

INTRODUCTION

Central neurocytomas (CN) are neuronal neoplasms with little aggressive behavior, which were initially described by Hassoun *et al.* in 1982 as an intraventricular tumor exhibiting histological similarities to oligodendrogliomas.[6] In 2000, the World Health Organization recognized the existence of extraventricular neurocytomas which received their own classification in 2007, although the intraventricular and extraventricular forms have strong cellular similarity and are both considered grade II tumors.[19] Approximately 0.1–1.0% of central nervous system neoplasms are CN, and approximately 10% of CN are considered extraventricular at presentation,[1] although there are <200 cases reported in the literature.[15] Thus, we report our experience with an extraventricular central nervous system neurocytoma, which occupied the sellar and suprasellar compartments in a young man and review the related literature.

CASE REPORT

History

A Brazilian 27-year-old man presented with a 4-year history of progressive bilateral vision loss caused by serious keratoconus. A neuro-ophthalmological evaluation revealed near-total left-eye amaurosis and moderate right-eye vision loss. The patient subsequently underwent bilateral corneal transplantation, although his condition progressed to left amaurosis and right temporal hemianopsia during the following 2 months. Thus, he underwent magnetic resonance imaging (MRI), which revealed a 79-cm^3 bulky solid expansive lesion that involved the sellar and suprasellar compartments. The lesion had well-defined lobulated margins and a heterogeneous appearance without cystic or calcified components. There was no edema in the adjacent brain parenchyma. The imaging also revealed invasion of the sellar floor, lateral displacement of both internal carotid arteries, medial obliteration of the cavernous sinus, and extrinsic compression of the optic chiasm, hypothalamus, and third ventricle [Figure 1]. Injection of a paramagnetic agent revealed diffuse and heterogeneous enhancement in the lesion. The preliminary diagnosis was a pituitary adenoma, and endocrinological evaluation revealed complete loss of pituitary function. Thus, the patient was referred to our department for evaluation and treatment.

Surgery

We initially selected the endoscopic endonasal approach, which revealed that the tumor was unexpectedly firm. We then sent a specimen for intraoperative pathological analysis. The results were inconclusive for macroadenoma, and we chose to stop the surgery until we received a conclusive result (approximately 60% of the tumor had been removed at that point). The patient did not experience any postoperative deficits during the 8 days until we received conclusive pathological diagnosis of CN without signs of malignancy. Immunohistochemical analysis revealed positive synaptophysin expression, a Ki-67 index of 0.8%, and negative AE1/AE3 expression [Figure 2]. Based on these results, we performed a second surgery through the right cranio-orbital zygomatic approach, which resulted in successful microsurgical total resection of the tumor.

Postoperative course

The patient was successfully treated for postoperative insipidus diabetes during a 1-week stay in the intensive

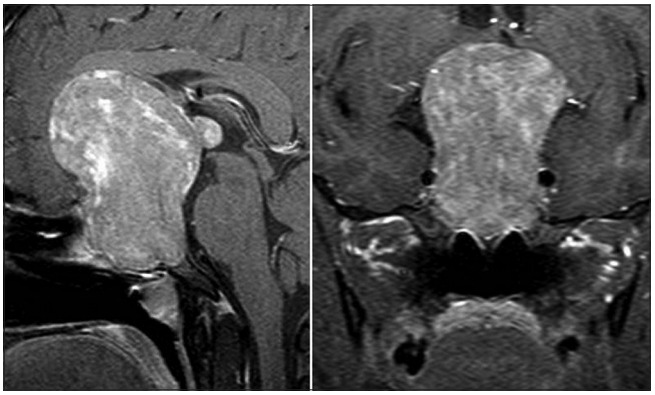

Figure 1: Sagittal (left) and coronal (right) results from gadolinium-enhanced T1-weighted magnetic resonance imaging

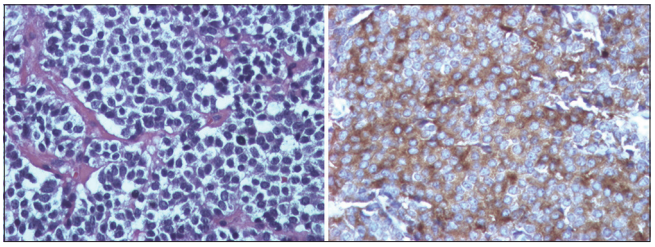

Figure 2: Histological sections show solid neoplastic cell proliferation, as well as noncohesive monomorphic small cells with round nuclei, fine chromatin, and well-distributed micronucleoli. The cytoplasm is poorly defined and a fine smooth granular vascular network is observed in the absence of necrosis or mitotic figures. Left: Hematoxylin and eosin staining (×400). Right: Immunohistochemical analysis revealed positive synaptophysin expression, a Ki-67 index of 0.8%, and negative AE1/AE3 expression (×400). Color versions are available as an online supplementary resource

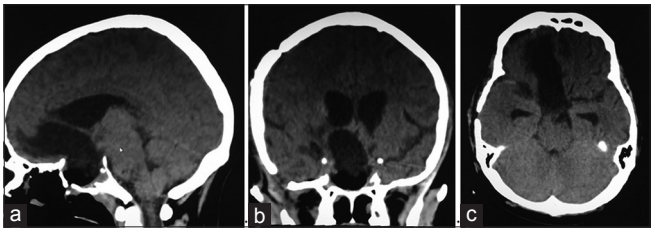

Figure 3: Gross total resection of the tumor was confirmed based on the sagital (a), coronal (b), and axial results (c) from the postoperative computed tomography

care unit. He was subsequently discharged at 3 weeks after his admission to our department without any new neurological deficits and with improvement of the right-eye hemianopsia. Computed tomography (CT) at 1 week after the surgery revealed gross total resection of the tumor and mild ventricular dilation, without any manifestations of hypertensive hydrocephalus that required further treatment [Figure 3]. Close outpatient follow-up was performed for 18 months, and the endocrinological workup revealed no improvement of pituitary function, although the patient did not experience any motor, sensory, or autonomic deficits. He continues to receive hormone replacement using testosterone, thyroid hormones, cortisol (prednisone), and exogenous vasopressin (desmopressin). The MRI scans from the 4-month and 18-month follow-ups revealed a hyperintense central sellar mass, which was compatible with an autologous fat graft that was used during the surgery to prevent fistula. These scans also revealed sellar contrast enhancement in both approaches, which was probably related to fibrosis [Figure 4]. Thus, if any residual tumor was present, it did not grow during the last year of follow-up.

DISCUSSION

Intraventricular and extraventricular CN are equally frequent in 20–40-year-old men and women.[4,6,15] The symptoms of extraventricular CN are generally nonspecific, including headache, dizziness, nausea, vision changes, and symptoms related to focal compression or intracranial hypertension.[4,6,7,13,15] The most common sites of extraventricular CN are the frontal lobe (30–46%), parietal lobe (11–23%), temporal lobe (13–20%), occipital lobe (2–11%), and cerebellum (6–9%).[2,7,11,13,15] Other less common locations include the thalamus, corpus callosum, sella, hypothalamus, pineal region, pons, spinal cord, and sphenoid wing.[1,4,15,19] Extraventricular CN usually appear as large solitary solid formations and may contain cystic components (40–71%), small calcifications (10–46%), or hemorrhagic foci (20–33%),[2,7,11,13] whereas CT usually reveals discreetly hyperdense solid portions, compared to the gray matter.[8,15] The preferred diagnostic modality is MRI as extraventricular CN can have discrete iso/hyperintense signals in both the T1- and T2-weighted images, and signs of restricted water diffusion may also be present. An intense and often heterogeneous enhancement is observed when using intravenous contrast agents, although 5–10% of cases do not exhibit enhancement. Spectroscopy reveals elevated levels of choline and reduced levels of N-acetyl-aspartate.[5,8,11,13-15,19]

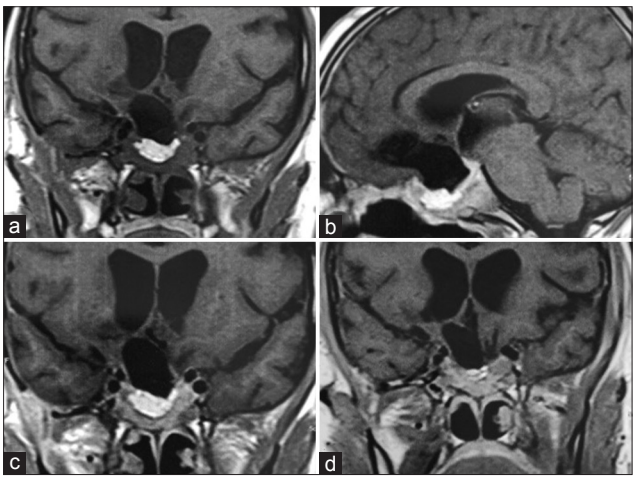

Figure 4: Four-month follow-up axial (a) and sagittal results (b) from T1-weighted magnetic resonance imaging revealed a hyperintense sellar mass, which was compatible with an autologous fat graft that was used to prevent nasal fistula. Findings from T1-weighted gadolinium-enhanced magnetic resonance imaging after 4 months (c) and 18 months (d)

The CN lesions can be grade III malignant variants (20–27%), which occur more often in older patients and typically exhibit greater infiltrative behavior, metastatic behavior, and unresectability. These lesions also frequently exhibit atypical cells, marked mitosis, vascular proliferation, necrosis, an MIB1 index of >2%, and a Ki-67 index of >2%.[1,2,5,7-9,11,13,15] The treatment of choice for extraventricular CN is total tumor excision, with adjuvant radiotherapy in cases of incomplete or questionable resection. However, there is lack of evidence regarding the ability of adjuvant radiotherapy to prevent recurrence or mortality in these cases.[2,5,7,9,11,13,15] The typical recurrence rates are 28% for intraventricular CN and 36% for extraventricular CN, with combined mortality rates of 4–6%. However, the atypical variants of intraventricular and extraventricular CN have a two-fold higher rate of unresectability, compared to typical CN, with mortality rates of 20–30% for intraventricular CN and 44% for extraventricular CN.[2,5,7,9,15]

Sellar and suprasellar extraventricular CN are extremely rare, and only 12 reported cases[4,5,10-12,14,16-19] were identified during our review of the PubMed and Bireme databases using the following keywords: neurocytoma, central, extraventricular, sellar, suprasellar, pituitary, and hypophysis. The clinical, radiological, pathological, and treatment features of these cases are shown in Table 1. The overall age range was 23–64 years, with a higher incidence at the ages of 40–60 years (mean: 49.75 years, median: 50 years), although no sex-specific tendency was observed. Reduced visual acuity was the original complaint in 91.7% of the cases (the symptoms at presentation were not described in one case), with bitemporal or asymmetrical hemianopsia. Half of the reported cases had an interval of 2–12 months between their symptom development and diagnosis, although only six reports described the patient's hormonal status and only 66% of those patients had a slight increase in prolactin levels.

Table 1: Clinical, radiological, pathological, and treatment features of the 12 reported cases

	Yang GF *et al.* (2009)	Chen H *et al.* (2011)	Yuen Wang Y *et al.* (2012)	Kaimal N *et al.* (2012)	Liu K *et al.* (2013)	Wang Y *et al.* (2013)	Kawaji H *et al.* (2014)	Xiong Z *et al.* (2015)	Makis W *et al.* (2015)	Peng P *et al.* (2015)	Chen S *et al.* (2016)	Chen S *et al.* (2016)
Clinical features												
Age (years)	46	52	50	50	40	23	48	56	64	56	50	62
Sex	Female	Male	Female	Female	Male	Female	Male	NA	Female	Male	Female	Male
Duration of symptoms (months)	12	6	2	NA	NA	4	3	NA	NA	NA	2	NA
Initial symptoms	Visual impairment	Blurred vision	Bitemporal hemianopsia	Blurred vision in left eye	Visual impairment	Bitemporal visual deficit and headache	Visual impairment	NA	Bitemporal hemianopsia	Bitemporal hemianopsia	Decreasing vision in left eye and diplopia	Homonymous hemianopsia, temporal both eyes
Endocrine evaluation	NA	NA	Prolactin 980 mU/L and estradiol <40 pg/mL	SIADH and prolactin 980 mU/L	NA	Prolactin 1,003 mU/L, others normal	Mildly elevated prolactin and decreased estradiol	NA	NA	Mildly decreased cortisol, others normal	Normal	Decreased testosterone and progesterone
Radiological features												
Topography	Sellar/ suprasellar	Sellar	Sellar/ suprasellar	Sellar/ suprasellar	Sellar/ suprasellar	Sellar/ suprasellar	Sellar/ suprasellar	Suprasellar	Sellar/ suprasellar	Sellar/ suprasellar	Sellar/ suprasellar	Sellar/ suprasellar
CT calcification	Yes	No	Yes	NA	No	No	NA	NA	NA	NA	No	NA
MRI T1	Hypo	Iso	Iso	NA	Iso	Iso	NA	NA	NA	Iso	Iso	NA
MRI T2	Hyper	Hyper	Iso	NA	Iso	NA	NA	NA	NA	Hyper	Iso	NA
Contrast enhancement	High	High	High	NA	High	High	High	NA	High	High	High	High
Enhancement	Heterogeneous	Heterogeneous	Heterogeneous	NA	Heterogeneous	Homogeneous	Heterogeneous	NA	Heterogeneous	Heterogeneous	Heterogeneous	Heterogeneous
Cystic component	Present	Absent	Present	NA	Present	Absent	Absent	NA	NA	Absent	Present	NA
Cavernous sinus Invasion	Yes	NA	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes
Pathological and immunohistochemical features												
Typical/atypical	Typical	Typical	Typical	Typical	Typical	Typical	Atypical	Typical	Atypical	Typical	Typical	Typical
Synaptophysin	NA	Yes	Yes	NA	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Neurofilament	NA	NA	Yes	NA	NA	Yes	Yes	NA	No	NA	Yes	Yes
NSE	Yes	NA	No	NA	NA	NA	NA	Yes	NA	Yes	NA	NA
CgA	NA	Yes	Yes	NA	NA	Yes	NA	NA	NA	Yes	NA	Yes
Vimentin	Yes	Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA	Yes
NeuN	NA	NA	NA	NA	NA	NA	Yes	No	NA	NA	No	Yes
GFAP	No	No	NA	NA	NA	No	No	No	NA	No	No	No
Olig2	NA	NA	NA	NA	NA	NA	NA	No	NA	NA	NA	NA
Treatment and follow-up												
Craniotomy	NA	NA	No	No	NA	No	Yes	NA	NA	Yes	Yes	Yes
Endoscopic approach	NA	NA	Yes	Yes	NA	Yes	No	NA	NA	No	Yes	No
Prior craniotomy	NA	No	No	No	NA	No	No	NA	NA	No	No	No
Prior endoscopic surgery	NA	No	No	No	NA	No	No	NA	NA	No	No	Yes

Contd...

Table 1: Contd...

	Yang GF *et al.* (2009)	Chen H *et al.* (2011)	Yuen Wang Y *et al.* (2012)	Kaimal N *et al.* (2012)	Liu K *et al.* (2013)	Wang Y *et al.* (2013)	Kawaji H *et al.* (2014)	Xiong Z *et al.* (2015)	Makis W *et al.* (2015)	Peng P *et al.* (2015)	Chen S *et al.* (2016)	Chen S *et al.* (2016)
Resection	Partial/subtotal	Total	Partial/subtotal	Partial/subtotal	NA	Partial/subtotal	Partial/subtotal	NA	Partial/subtotal	Total	Partial/subtotal	Partial/subtotal
Adjuvant radiotherapy	NA	No	Yes	Yes	NA	Yes	Yes	NA	Yes	No	Yes	Yes
Recurrence	No	NA	No	NA	NA	NA	Yes	NA	Yes	No	No	No
Follow-up (months)	NA	NA	18	6	NA	18	6	NA	NA	NA	36	36
Spinal dissemination	No	No	No	No	No	No	Yes	NA	No	No	No	No

NA=Not available, NSE=Neuron-specific enolase, CgA=Chromogranin A, NeuN=Neuronal nuclear antigen, GFAP=Glial fibrillary acidic protein, SIADH=Syndrome of inappropriate antidiuretic hormone secretion

The reported cases were assessed using CT (66.7%) and/or MRI (100%), which revealed that the tumors were generally solid, bulky (a major axis of ≥3.0 cm), homogeneous, well-defined, and with limited or no swelling in the adjacent parenchyma. Two cases involved small-scattered calcifications, and four cases involved cystic components. All 10 patients with published imaging findings had invasion of the cavernous sinus. The CT scans commonly revealed discreetly iso/hyperdense tumors, and discrete iso/hyperintense findings were observed on approximately 58% of the T1- and T2-weighted images. All reported cases exhibited enhancement after the administration of an iodinated or paramagnetic intravenous contrast agent, with one-half of the results being prominent and nine cases exhibiting heterogeneous enhancement. Ten cases had detailed histological and immunohistochemical data, with generally positive results for synaptophysin expression (9/10 cases) and generally negative results for GFAP expression (8/10 cases). Two patients exhibited signs of malignancy (48 years and 64 years old), with MIB1 indexes of 3% and 4–10%, respectively. Only two patients had gross total tumor resection and eight patients had only partial resection, with 75% of those patients undergoing postoperative radiotherapy. Two patients with atypical extraventricular CN developed distant dural metastases or local recurrences. The main differential diagnosis was pituitary adenoma, especially the nonfunctioning type, which is usually isodense during CT, rarely contains calcification (5–7%) or hemorrhagic foci, and usually exhibits variable hypo/isointense signals during T1- and T2-weighted MRI. Furthermore, pituitary adenoma usually exhibits intense enhancement, but this is slightly slower than the rest of the pituitary gland.[3,20] Other diagnostic hypotheses include craniopharyngioma (more common in children, heterogeneous lesions, usually contains calcifications)[3,19,20] and meningiomas (more common in adults, homogeneous lesions, generally isodense during CT and isointense during T1-/T2-weighted MRI, can be calcified).[3,19,20] In all reported cases, an extraventricular neurocytoma was not suspected based on the preoperative imaging, which strongly indicated a giant pituitary tumor, as in the present case. Therefore, we believe that cases with a suspected huge pituitary lesion should always be screened based on the possibility that it is a sellar/suprasellar neurocytoma. We believe that total tumor resection should be the goal of surgical treatment, and that this goal is achievable using both craniotomy and endoscopic approaches.

In conclusion, we encountered a rare case of an extraventricular CN in the sellar/suprasellar region. Given the unusual nature of this case, we examined the 12 other reported cases and attempted to identify the features and signs that may help facilitate the diagnosis of these tumors in this region. Furthermore, we reported common histopathological characteristics and surgical approaches

from those cases. We strongly believe that total tumor resection must be the primary goal of the surgery, and that combined surgical approaches can help facilitate this outcome.

Acknowledgements
Not applicable.

Availability of data and materials
Not applicable.

Authors' contributions
BN, LCTP, RAFC, RMQ, LGA, EQ, LHC, ISTP, CHM, and FBF contributed to conception and design as well as the acquisition, analysis, and interpretation of data. RMQ, LGA, ISTP, and CHM contributed to acquisition and interpretation of imaging data. BN, LCTP, RAFC, RMQ, LGA, EQ, LHC, ISTP, CHM, and FBF documented the patient's status and contributed to analysis and interpretation of data. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their 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
There are no conflicts of interest.

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