SNI SURGICAL NEUROLOGY INTERNATIONAL

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Case Report

Bilateral internal auditory canal gangliogliomas mimicking neurofibromatosis Type II

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Received: 22 May 14 Accepted: 16 February 16 Published: 13 April 16

Abstract

Background: Gangliogliomas are rare low grade, typically well-differentiated, tumors that are composed of mature ganglion cells and neoplastic glial cells. These tumors can appear at virtually any location along the neuroaxis but classically occur in the temporal lobe of young patients. In a small number of cases, gangliogliomas have presented as masses in the brainstem or involving cranial nerves. With the exception of vestibular schwannomas, bilateral tumors in the region of the internal auditory canal (IAC) or cerebellopontine angle (CPA) are exceedingly rare.

Case Description: We report a case of a 58-year-old male who presented with hearing loss, tinnitus, and vertigo. Initial magnetic resonance imaging revealed bilateral nonenhancing IAC/CPA tumors. Based on this finding, a presumptive diagnosis of neurofibromatosis Type II was made, which was initially managed conservatively with close observation. He returned for follow-up with worsening vertigo and tinnitus, thus prompting the decision to proceed with surgical resection of the symptomatic mass. Intriguingly, pathological study demonstrated a WHO Grade I ganglioglioma.

Conclusion: This is the first reported case of bilateral IAC/CPA gangliogliomas. When evaluating bilateral IAC/CPA lesions with unusual imaging characteristics, ganglioglioma should be included in the differential diagnosis.

Key Words: Bilateral, cerebellar-pontine angle, gangliogliomas, internal auditory canal, tumors

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.180300

Quick Response Code:

INTRODUCTION

Gangliogliomas are relatively rare tumors accounting for only 1% of all intracranial neoplasms. These tumors are composed of a combination of both neuronal and glial cell types and are typically benign, low-grade, and well differentiated.[22] Classically, these tumors occur within the temporal lobe of children and young adults and present clinically with seizures. However, gangliogliomas have also been reported throughout the central nervous system including the posterior fossa, brainstem, spinal cord, and cranial nerves.[10,13,22,24]

Bilateral internal auditory canal (IAC)/cerebellopontine angle (CPA) tumors are virtually pathognomonic

How to cite this article: Hooten KG, Oliveria SF, Sadrameli SS, Gandhi S, Yachnis AT, Lewis SB. Bilateral internal auditory canal gangliogliomas mimicking neurofibromatosis Type II. Surg Neurol Int 2016;7:39.
http://surgicalneurologyint.com/Bilateral-internal-auditory-canal-gangliogliomas-mimicking-neurofibromatosis-Type-II/

for vestibular schwannomas in the setting of neurofibromatosis Type II (NFII).[1] Descriptions of bilateral nonschwannomatous IAC/CPA tumors are limited to case reports. We present a case of a 58-year-old male with unusual bilateral IAC tumors who was initially referred to our practice carrying the diagnosis of NFII. To the best of our knowledge, this is the first reported case of bilateral gangliogliomas of the IAC/CPA region.

CLINICAL PRESENTATION

A 58-year-old male presented with new onset vertigo and chronic asymmetric hearing loss, which was worse in the left than the right ear. The patient also complained of mild left-sided tinnitus. Over 3 months he developed progressively worsening balance causing him to fall, typically to his right side. Neurological exam was unremarkable except for bilateral sensorineural hearing loss. His initial audiogram confirmed the finding of bilateral sensorineural hearing loss, with profound loss of hearing in the higher frequencies that were most prominent on the left side. Magnetic resonance imaging (MRI) of the brain revealed bilateral nonenhancing IAC/CPA masses [Figure 1a and b]. The lesion on the left measured 4.5 mm × 4.5 mm × 5 mm; the lesion on the right was slightly larger, measuring approximately 8 mm × 8.3 mm × 8.2 mm with a 4 mm intracanalicular portion. Given the small size of these masses at presentation, the patient was initially managed conservatively with close follow-up. A repeat MRI of the brain 3 months later revealed no change in the size of either mass. During this time, the patient underwent occupational therapy and tried multiple medications for symptomatic relief.

At his 1 year follow-up visit, the patient reported worsening left-sided hearing loss, tinnitus, and otalgia and had begun taking a benzodiazepine to alleviate his symptoms. Repeat MRI of the brain at this time demonstrated the modest growth of both IAC/CPA masses, which remained nonenhancing. The mass on the left measured 6 mm × 5 mm × 4 mm; the right-sided mass measured 10 mm × 8 mm × 7 mm with growth of the intracanalicular portion to 8 mm in length [Figure 2a and b]. Based on evidence of tumor growth and progressively worsening symptoms, the patient elected to pursue surgical resection of the left-sided tumor. Radiosurgery was not considered a viable option since the patient's age and unusual radiographic findings made the tissue diagnosis uncertain.

INTERVENTION

The patient underwent a left retrosigmoid craniotomy for tumor resection. A small lesion involving the intracanalicular portion of the eighth nerve complex was encountered and completely resected.

The excised tumor was an oval, well circumscribed, gray-tan, nodule that measured 0.5 cm × 0.5 cm × 0.4 cm. One-half was submitted for intra-operative consultation, which yielded a diagnosis of "ganglioneuroma versus ganglioglioma." Examination of formalin-fixed, paraffin-embedded tissue sections reveled circumscribed neuroglial tissue composed of mature ganglion cells existing in a background of low-grade astrocyte-like cells with coarse processes [Figure 3a-d]. Ganglion cells contained Nissl substance and vesicular nuclei with prominent nucleoli and were randomly distributed in a haphazard fashion without polarization of cell processes [Figure 3a].

Neurofilament protein was strongly immunoreactive in the ganglion cells and revealed un-oriented cells' processes extending into the glial stroma [Figure 3b]. Glial fibrillary acidic protein (GFAP) was strongly reactive in abundant astrocytic cell processes [Figure 3c]. Only weak reactivity for neuronal nuclear antigen was observed in the ganglion cells while granular synaptophysin reactivity was associated with ganglion cells and the stroma. S-100 was strongly and diffusely reactive in the lesion. The background stroma was distinctly astrocytic as demonstrated by strong GFAP-immunoreactivity of the cell processes. There were no areas of schwannoma-like

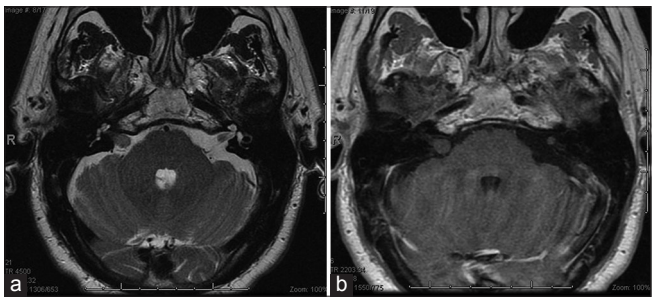

Figure 1: Axial T2 (a) and postcontrast axial T1 (b) magnetic resonance imaging sequences at initial patient presentation, demonstrating bilateral cerebellopontine angle masses extending into the internal auditory canal

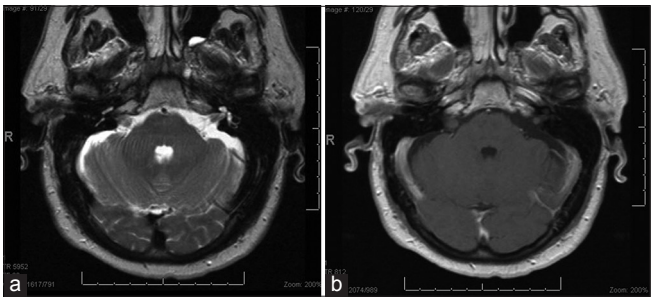

Figure 2: Axial T2 (a) and postcontrast axial T1 (b) magnetic resonance imaging sequences 1 year after initial patient presentation, demonstrating slight growth of bilateral internal auditory canal/cerebellopontine angle tumors

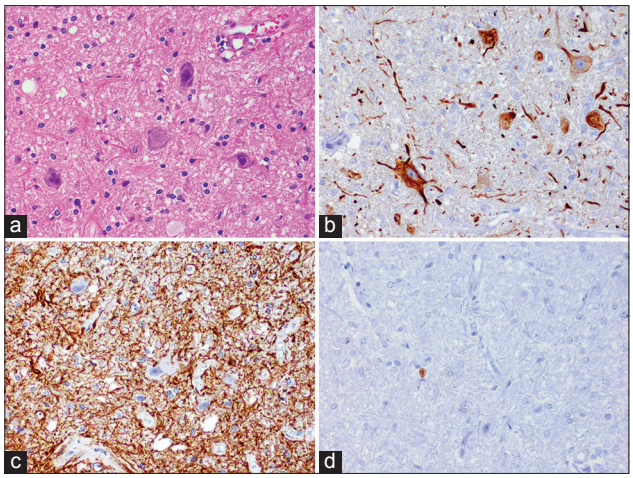

Figure 3: Surgical pathologic studies consistent with ganglioglioma. (a) H and E staining. Several ganglion cells, with cytoplasmic Nissl substance and smudgy nuclei, exist within a low grade appearing glial stroma. (b) Ganglion cells within the tumor show strong neurofilament protein immunoreactivity and haphazardly oriented cell processes. (c) Glial fibrillary acidic protein is strongly immunoreactive within a background astrocyte-like cell processes. (d) Only a rare cell was immunoreactive for Ki-67 (MIB-1)

morphology with Antoni A or B histology and no Verocay bodies. The tumor was mitotically quiescent and the Ki-67 labeling index <1% [Figure 3d].

Postoperatively, the patient's complaints of tinnitus improved. Postoperatively, his hearing remained stable and his House–Brackman grade was 1/6 bilaterally.

DISCUSSION

Gangliogliomas are rare, mixed glioneuronal tumors comprising only 1.3% of all brain tumors.[22] The average patient age ranges from 8.5 to 25 years, but cases have been reported in infants as well as the elderly.[12,13] The origin of gangliogliomas is believed to be from a hamartomatous glioneuronal lesion that evolves into neoplastic neuronal and glial cells.[2] These tumors are typically classified as benign, WHO Grade I; however, some gangliogliomas display anaplastic (WHO III) features.[8,23] Criteria for Grade II tumors are not established.

Classically, these tumors arise in the temporal lobe with seizures being the most common presenting symptom. Gangliogliomas have nevertheless been reported in all regions of the neuroaxis including the spinal cord, brainstem, cerebellum, ventricular system, cranial nerves, pituitary and pineal glands, with varying clinical presentations dependent on location.[10,12,13,22,25] Rarely, gangliogliomas affect the cranial nerves, the most commonly affected being the optic nerve.[15,26,30,33] Trigeminal nerve involvement has been reported in four cases, including one case of bilateral trigeminal nerve gangliogliomas on autopsy.[13] A single case of a unilateral CPA ganglioglioma has also been previously described.[20] However, this report represents the first known case of bilateral IAC/CPA gangliogliomas.

Bilateral IAC/CPA masses are characteristic of NFII with bilateral schwannomas occurring on either the vestibular or less commonly facial nerves.[1] The occurrence of bilateral nonschwannomatous IAC/CPA tumors is rare, and their description has been limited to individual case reports only. Bilateral tumors in the IAC/CPA that do not have classic radiologic findings typical of schwannoma can be a diagnostic dilemma. Reported bilateral tumors of the IAC/CPA include: Cartilaginous tumors,[5] xanthogranulomas,[17] choroid plexus papillomas,[6] endolymphatic sac tumors,[18] metastatic tumors including adenocarcinoma and melanomas,[11,14] meningiomas,[32] and lipomas.[9] For atypical IAC/CPA masses, emphasis should be placed on imaging characteristics as these may aid in diagnosis before surgical intervention. The precise site of origin of masses in this region may differentiate among the spectrum lesions that can occur here.[4] Imaging characteristics of IAC/CPA gangliogliomas are variable.[3,13,20] Computed tomography findings are not specific, with calcifications being noted only infrequently. MRI may demonstrate either an iso- or hypo-dense signal on T1 or a hyperintense signal on T2. In the case described, the patient's bilateral gangliogliomas appeared isointense to the brain on both T1 and T2 sequences. Gadolinium enhancement has been reported but is not universal.[3,13,20] In this report, the patient's tumors were distinguished from the more common schwannomas and meningiomas that occur in this location by the absence of contrast enhancement, which is typically avid for these more common tumors.[4,31]

The desired surgical treatment strategy for gangliogliomas is gross total resection when feasible. Adjuvant chemotherapy or radiation is not typically recommended for low-grade tumors (WHO I), but may be appropriate for select patients.[7,21,28,29] The role for adjuvant therapy is not well defined for WHO Grade III and IV gangliogliomas but is generally recommended, particularly in the setting of subtotal resection.[27] Radiosurgery for gangliogliomas has also been reported to be effective but has not been thoroughly studied as a primary treatment modality.[16,19] In this case, gross total resection was achieved for the left sided tumor. Based on the low grade of the left-sided tumor and minimal symptoms associated with the right-sided tumor, the patient is being followed closely with regular hearing monitoring and serial imaging. For chronic and/or benign lesions, it is paramount to approach the patient conservatively, focusing on preservation of hearing, and facial nerve function.

CONCLUSION

Gangliogliomas are rare and typically benign tumors that may occur at any location along the neuroaxis. Clinical

course and MRI can aid the diagnosis of gangliogliomas affecting cranial nerves before surgery. When evaluating bilateral IAC/CPA lesions with unusual imaging characteristics, ganglioglioma should be included in the differential diagnosis.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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