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ORIGINAL ARTICLE

Utility of Microhemorrhage as a Diagnostic Tool in Distinguishing Vestibular Schwannomas from other Cerebellopontine Angle (CPA) Tumors

G. Saigal[1] · L. Pisani[2] · E. Allakhverdieva[1,4] · J. Aristizabal[3] · D. Lehmkuhl[1,4] · F. Contreras[1,4] · R. Bhatia[1] · C. Sidani[1] · R. Quencer[1]

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Abstract Although a majority of tumors in the Cerebellopontine Angle (CPA) are vestibular schwannomas (VS), other masses can also be seen in the region and differentiation of various CPA tumors, particularly meningiomas can be difficult on imaging alone. Treatment options may vary based on specific pathology of the CPA tumor. In this study, the presence of microhemorrhage (MH) and other imaging features such as size of lesion, cystic features and pattern of IAC extension, were evaluated as a tool in distinguishing VS from other CPA masses. A review of CPA masses in the last 11 years at our institution was performed. All the pathology proven tumors with at least 1 pre-operative MRI were considered for analysis. A T2* GRE or SWI sequence was used to assess presence of MH within the lesion. Pattern of IAC extension ('centric' versus 'eccentric') of tumor was also evaluated. A total of 147 patients were reviewed out of which 102 patients (with T2* GRE or SWI) were included for analysis of MH. 57 patients (56%) had VS as the final histopathological diagnosis and 45 patients (44%) had other types of tumor. A sensitivity of 82% and a specificity of 98% was noted for the presence of MH favoring the diagnosis of VS from other tumors ($p < 0.001$). All meningiomas with IAC extension (25/31) showed an 'eccentric' pattern of extension into the canal. Visualization of MH and pattern of IAC extension is useful in the differentiation of schwannomas from other CPA masses, particularly meningiomas.

Keywords Microhemorrhage · Vestibular schwannoma · Cerebellopontine angle tumor

Introduction

The cerebellopontine angle (CPA) region is the most common site for posterior fossa tumors [1]. The region is occupied by vital neurologic and vascular tissue and pathological masses originating in this region may result in

✉ G. Saigal
gsaigal@med.miami.edu

L. Pisani
leonardo.pisani@emory.edu

E. Allakhverdieva
aa.elvira@gmail.com

J. Aristizabal
aristizabal.baron89@gmail.com

D. Lehmkuhl
david.lehmkuhl@jhsmiami.org

F. Contreras
francisco.contreras@jhsmiami.org

R. Bhatia
rbhatia@med.miami.edu

C. Sidani
charif.sidani@gmail.com

R. Quencer
rquencer@med.miami.edu

[1] Department of Radiology, WW279, University of Miami Miller School of Medicine, 1611 NW 12th Avenue, Miami, FL 33136, USA

[2] Emory University, 1364 Clifton Road Northeast, Atlanta, GA 30322, USA

[3] University of Antioquia, Cl. 67 ##53-108, Medellín, Antioquia, , CO, USA

[4] Jackson Memorial Hospital, 1611 NW 12th Avenue, Miami, FL 33136, USA

significant symptoms related to compression of the underlying cranial nerves (CN), vessels and other posterior fossa structures [2]. Despite the high prevalence of vestibular schwannomas (VS), other masses can also be seen in this region. Although imaging is useful in differentiating various CPA masses, sometimes imaging features may overlap. In fact, 25% of meningiomas (2nd most common CPA tumor) can still be mistaken for VS [3]. The purpose of this study was to evaluate the presence of microhemorrhage (MH) as a distinguishing imaging feature for the differentiation of VS from other CPA masses.

Methods and Materials

Patient Selection

A retrospective review of the database at our institution for CPA masses, over the last eleven years (from January 2009 to January 2020) was performed. 292 cases of CPA tumors were found. A total of 190 patients were excluded, either due to lack of pathology (not operated), missing images or lack of specific MRI sequences. 4 cases of neurofibromatosis were also excluded, since the diagnosis of the CPA tumor would be known at the time of the evaluation. The final 102 patients who were evaluated, had at least one preoperative magnetic resonance imaging (MRI) study with either a T2* GRE or SWI sequence and a final pathological diagnosis of the resected mass. Two neuroradiologists (one with 17 years and the other with 19 years of experience) evaluated all of the studies independently for the presence or absence of MH. Both the reviewers were blinded to the clinical history and the final histopathological diagnosis. Other relevant imaging findings such as size of the extrameatal component of the CPA mass, extension of enhancing mass within the IAC, presence of cystic changes within the mass were also evaluated. 'Centric' or 'eccentric' type of extension into the canal was also evaluated.

Parameter Definition and Imaging Protocol

MH was defined as T2 hypointense foci (each < 5 mm in size) similar to the ones described for cerebral hemorrhages and were evaluated on T2-weighted gradient-echo (T2* GRE) or susceptibility weighted imaging (SWI) which were performed, depending on the MR scanner used for the study. Greatest axis was measured over the longest dimension of the extra-axial portion of the tumor. Histopathologic diagnosis of the tumors was obtained in all cases. Cases included, had imaging done both at our institution and other outside hospitals/imaging centers. Computed tomography (CT) was performed in most cases and was evaluated to exclude intratumoral calcification. Phase component from the SWI sequence, when performed, was used to confirm the presence of MH and differentiate from calcifications. MR sequences which were reviewed included standard brain imaging sequences such as Sagittal T1 and Axial T1, T2 and FLAIRand post contrast sequences in different planes. Depending on the type of sequence available, SWI or T2* GRE sequences were reviewed for susceptibility. Studies performed on both 1.5 and 3 T magnets were included and they were not separated based on the magnet strength. When available, dedicated imaging of the internal acoustic canal (IAC), which included three-dimensional (3D) constructive interference in steady state (CISS) T2 in the axial plane and thin section pre and post gadolinium T1-weighted imaging in the axial and coronal planes was reviewed.

Statistical Analysis

Continuous variables were reported as mean ±SD. Categorical variables were reported as proportions. Between groups, comparisons for continuous/ordinal variables were made with Student t test. Categorical variables were compared by chi-square. Significance was set at and the solid group (mean < 0.05, and all p values were based on 2-tailed tests. Statistical analysis was performed using IBM SPSS Statistics 25 (IBM-Armonk, NY).

Ethics Committee

This study was approved by the Institutional Review Board of the University.

Results

102 patients were included for primary analysis for having either T2* GRE or SWI sequences. 60 patients (58.9%) were evaluated with T2* GRE sequences and 42 patients (41.1%) were evaluated with SWI sequences. Mean age was 51.3±14.1 years. There were 46 males (45%) and 56 females (55%) (Fig. 1). 57 (56%) had VS as the final histopathological diagnosis, 31 patients (30%) had meningioma, 3 (3%) had metastasis and 12 (12%) had other types of tumor (Fig. 1).

Of the total 102 patients, 48 (47%) showed MH (Fig. 1). The presence of MH had 100% interreader agreement between the two independent neuroradiologists. MH was seen as multiple tiny foci of intratumoral susceptibility on the T2* GRE or SWI sequence (Fig. 2). Of the 48 masses which showed MH, 47 were VSs, resulting in a specificity of 98% and a sensitivity of 82%.. Of these, 47/48 cases of MH were pathologically proven to be VS (47 out of 57 VS) (Fig. 1). The only other case which showed MH, but was

not a VS, was a case of proven hemorrhagic metastatic melanoma in the CPA. Another case of a large CPA mass, demonstrated fluid blood levels and not discrete MH, and was proven to be an endolymphatic sac tumor (Fig. 3). Statistical analysis revealed a sensitivity of 82%, specificity of 98%, and positive predictive value of 98% and negative predictive value of 81% for presence of MH as test for distinguishing VS from other tumors in this population ($p < 0.001$).

Greatest axis size means of extrameatal extension between presence of MH group (25.0±9.8 mm) and absence of MH group (27.6±13.1 mm) showed no significant correlation ($p = 0.266$).

One of the subsets evaluated, were tumors with cystic components. Of the total 102 patients, 23 showed cystic features (22.5%) and 79 were solid (77.4%). 18/23 cystic tumors were proven to be VSs. MH was noted in 17/23 cystic tumors. All the 17 cystic tumors that showed MH were proven to be VSs (specificity of 100% $p < 0.001$).

Of the patients with VS, 18/57 presented with cystic pattern and 39/57 showed solid pattern. There was no statistical significance between ($p = 0.05$) the cystic group (mean 27.3 mm ±9.3) and the solid group (mean 21.5 mm ±10.2).

Out of 102 patients included in the study, 38 had CT scans performed to evaluate for tumor calcifications, 4 of which were positive. Positive cases included chordoma, cholesteatoma, meningioma and choroid plexus papilloma None of the VS, showed any calcification. SWI sequences were available in 42 and T2* GRE imaging was available in 60 patients. In patients with positive findings on the SWI sequence (17 in number), phase imaging, if available, was used to differentiate between calcification and MH. MH was confirmed on all the cases of VS on phase imaging, when available.

IAC extension of enhancing component of all the CPA masses was also evaluated. Of the 102 CPA masses 84 (82.4%) showed IAC extension. When seen, 'centric' versus 'eccentric' extension of the IAC component was evaluated. All meningiomas (31/31) showed IAC extension. Dural enhancement along the canal was considered as a positive and 'eccentric' type of IAC extension. Of the meningiomas with IAC extension 81% (25/31)showed an 'eccentric' type of extension into the IAC. 'Eccentric' pattern of extension was 100% specific for meningiomas. All the schwannomas with IAC extension(53/84), showed a 'centric' pattern of extension. The extent of involvement of the mass in the IAC was not evaluated. Widening of the IAC could not be evaluated, as since many of the cases, did not have corresponding CT's.

Discussion

The differential diagnosis for a CPA mass is broad, with VS being the most common (80%) [1]. Other tumors in this region include meningiomas, dermoids, arachnoid cysts,

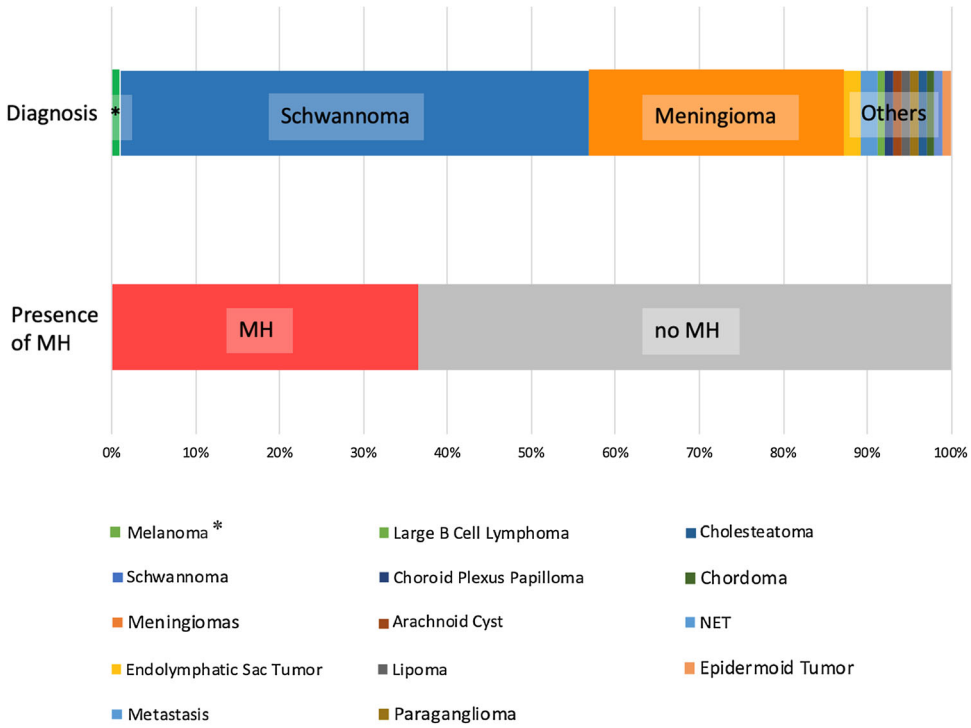

Fig. 1 Chart demonstrating the male to female distribution of the cerebellopontine angle tumors. The presence (or absence) and distribution of microhemorrhage across all tumor types is shown. All lesions (except one of the metastases*)—showing microhemorrhage were proven to be vestibular schwannomas,. Not all vestibular schwannomas however showed microhemorrhage. The incidence and different types of CPA tumors, which were seen is shown at the bottom of the chart. The only tumor which showed microhemorrhage other than vestibular schwannoma, was a metastatic melanoma*

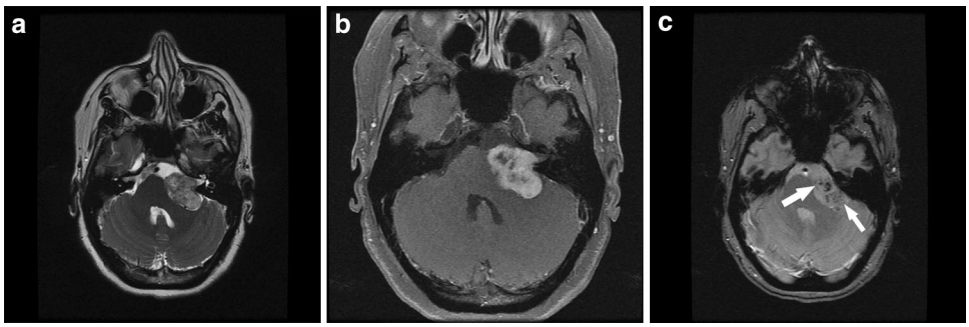

Fig. 2 Axial T2W (**a**) and T1W post contrast, (**b**) images demonstrate a large, lobulated left cerebellopontine angle mass with internal auditory canal extension, demonstrating heterogeneous enhancement consistent with a vestibular schwannoma. Mass effect on the left side of the brainstem is noted. T2* GRE image, (**c**) through the mass, demonstrates numerous tiny foci of susceptibility within the mass (white arrows), consistent with microhemorrhage

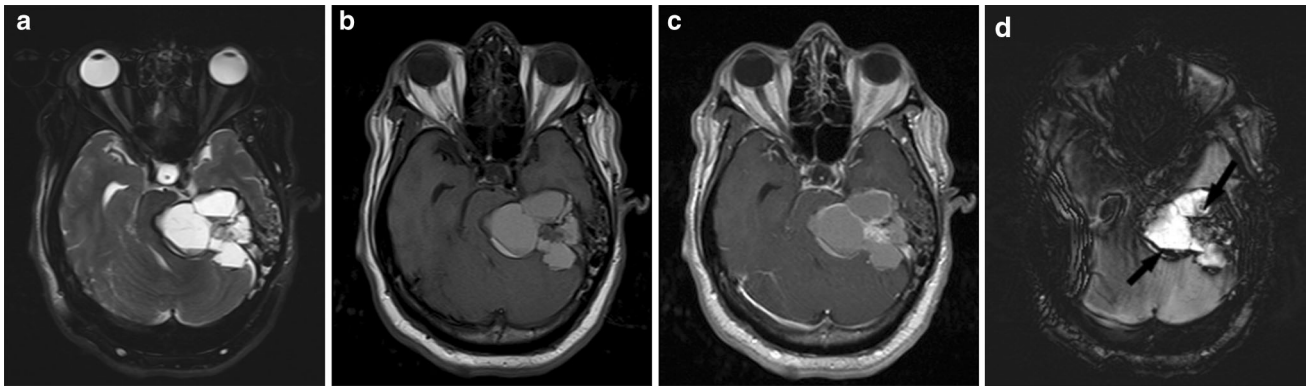

Fig. 3 Axial T2W (**a**) and T1W pre and post contrast, (**b, c**) images demonstrate a large multiseptated, multicystic mass in the left cerebellopontine angle, causing significant mass effect on the left brainstem. The mass demonstrates underlying T1 hyperintensity and multiple fluid blood levels (arrows), best seen on the SWI image (**d**). No microhemorrhage was noted. At pathology, mass was proven to be an endolymphatic sac tumor

lipomas, endolymphatic sac tumors, metastases, paragangliomas and other exophytic masses [1, 2].

Internal auditory canal involvement and extension, an acute angle with the bone and hyperintensity on T2WI has been reported to be suggestive of VS, whereas a broad base, dural tail, hyperostosis, and calcification favor the diagnosis of meningioma [5]. Although differentiation between a majority of the entities in the CPA can be made based on clinical history and characteristic imaging findings, imaging features may sometimes overlap, making it difficult to differentiate between these entities all the time [5]. Differentiation between the two commonest entities in the CPA i.e. meningiomas and VSs, is of particular importance, since surgical approaches may differ depending on the tumor type. Radiation treatment doses can also be different based on the type of tumor. Often differentiation must be made on imaging alone since biopsy may be difficult due to the close proximity of the tumor to vital cranial nerves and vascular structures. Post-operative hearing preservation tends to be better and the incidence of recurrence is higher in patients with meningioma compared to VS [3, 4, 6].

Presence of MH has been reported in VSs and the pathophysiology is thought to be due to the abnormal vascularity in the VS, which predisposes to spontaneous thrombosis, necrosis and formation of MH in the tumor [7]. On MR imaging, MHs were first described after the clinical use of gradient echo imaging and are defined as rounded foci, < 5 mm in size that appear hypointense and distinct from vascular flow voids, leptomeningeal hemosiderosis, or nonhemorrhagic subcortical mineralization [8]. Studies somewhat similar to ours have been performed and reported in literature [9–12]. These studies are limited however, due to a smaller number of patients. For example, Thamburaj et al. made a similar conclusion about the significance of intratumoral MH on T2* weighted GRE images in differentiating VS from meningiomas. [9]. In their study of 20 patients, GRE images revealed 100% specificity and 94% sensitivity, which provided a relatively reliable tool for the radiologist in helping establish the

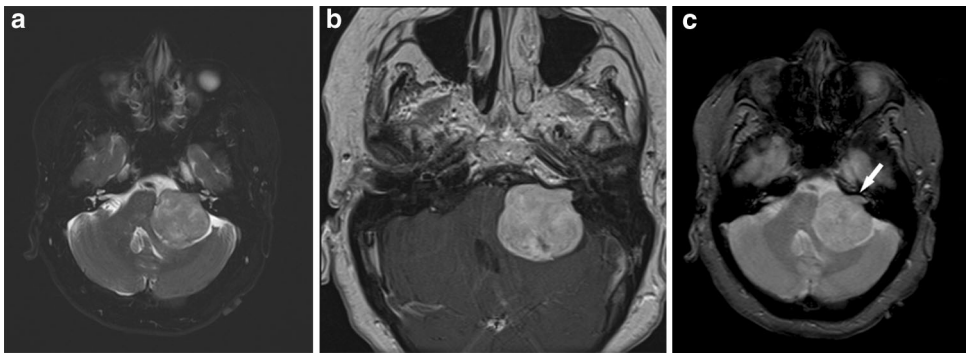

Fig. 4 Axial T2W (**a**) and T1W post contrast, (**b**) images demonstrate a left cerebellopontine anglemass demonstrating internal auditory canal extension (white arrow). Significant mass effect on the left brainstem resulting in adjacent brainstem edema is noted. The mass could be mistaken for a vestibular schwannoma given the internal auditory canal extension, however, note that there is no microhemorrhage noted on the T2* GRE image (**c**). At pathology, mass was proven to be a meningioma

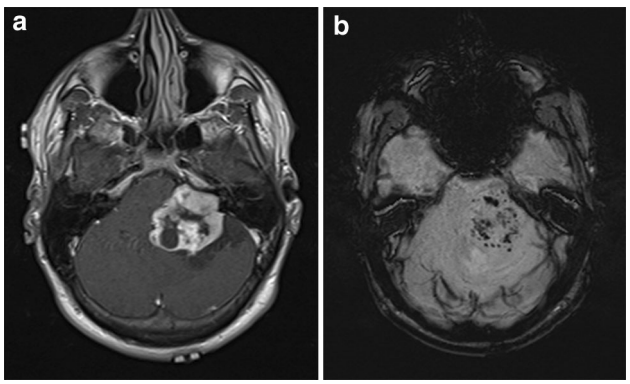

Fig. 5 Axial T1W post contrast image (**a**) demonstrating a heterogeneous enhancing cystic mass without internal auditory canalextension which does not have the characteristic appearance for a vestibular schwannoma. Axial SWI image, (**b**) demonstrating numerous foci of susceptibility consistent with microhemorrhage. At pathology mass was proven to be a vestibular schwannoma (cystic type)

correct diagnosis. However, the study was significantly limited by small sample size. Similarly, Mishra et al. used SWI imaging for the differentiation of VS and meningiomas in the CPA and showed similar results of MH being able to predict a VS, with a sensitivity of 100%, specificity of 92%(10). They had a relatively large sample size in their study but were limited by the evaluation of only meningiomas and schwannomas in the CPA. In our study, we offer a larger patient population sample size and more detailed evaluation of a variety of other tumors in the CPA. Besides VSs and meningiomas, there are several other masses which can occur in the CPA (as shown in this study), which were not included in that study. Our investigation builds on the prior study's observation with a much larger series (more than 100) of both VS and a variety of other CPA masses as well as highlights some important secondary findings.

Of the 102 patients with CPA masses, there were 57 VSs (56%) and 31 meningiomas (30%) and 14 others (Fig. 1). Several of the cases with CPA masses had to be excluded due to the lack of T2* GRE /SWI imaging. All of the excluded studies were performed in outside imaging centers/hospitals, where SWI/T2* GRE imaging of the brain was not routinely done. Of the 48 masses which showed MH, 47 were VSs (98% specificity and 82% sensitivity). The only mass which showed MH and was not a VS was a case of hemorrhagic metastatic melanoma. None of the other less common entities (except for the one case of hemorrhagic metastatic melanoma) demonstrated any MH. Based on the imaging findings alone, it would not have been possible to differentiate it from a VS, but history was known at the time of imaging, which helped in suggesting the diagnosis. Another case which demonstrated hemorrhage was an endolymphatic sac tumor; however, this mass demonstrated fluid blood levels, rather than MH (Fig. 3). In the meningioma group, one of the cases demonstrated multiple underlying T2 hypointensities; however, on careful assessment, these were confirmed as numerous flow voids (as they were all connected) rather than MH.

Of all the CPA masses 84 showed an enhancing IAC component. All meningiomas showed IAC extension. Traditional teaching is that the presence of IAC extension of a CPA mass, favors the diagnosis of a VS. An important secondary finding of this study is that meningiomas can demonstrate IAC extension, and therefore could be mistaken for a VS (Fig. 4). In our opinion, the presence of IAC extension should not be used when trying to differentiate meningiomas from VS. 'Centric' versus 'eccentric' extension of the enhancing component in the IAC was also evaluated to see if 'eccentric' pattern of extension favored the diagnosis of meningioma. 25 out of 31 (81%) meningiomas with IAC extension (25/31) showed an 'eccentric' pattern of extension. An 'eccentric' pattern of extension

was 100% specific for a meningioma. All schwannomas which demonstrated IAC extension (53/81) showed a 'centric' pattern of extension.

One of the subsets of the CPA masses evaluated were those demonstrating a cystic component. Of the 23 cystic CPA masses, 18 were found to be VSs. A high incidence of MH was seen in the cystic masses and all the masses with MH (17/23) were pathologically proven to be VSs (100% specificity) (Fig. 5). Also, VSs which were cystic, showed a higher incidence of MH, compared to solid tumors, suggesting a possible causative mechanism, which has been described in the literature [13, 14].

Limitations of the study include the low prevalence of tumors which were neither VS's nor meningiomas. This is, however, reflective of the lowincidence of such tumors, as reported in literature as well. Another limitation was the use of studies done both on the 1.5 and 3 T magnets as well the inclusion of both T2* and SWI in the evaluation. T2* GRE and SWI are different in sensitivity for MH and have differing artifact profiles., SWI in particular, is more prone to artifacts and aliasing in the base of the skull than T2* GRE imaging. In addition, artifacts from the petrous bone are significantly larger on SWI and at 3.0 T which can significantly limit evaluation of tumor tissue that is adjacent to bone, particularly within the internal auditory canal.

In conclusion, when evaluating CPA masses, presence of MH is useful in making the diagnosis of VS, even if the mass is cystic in nature. However, the absence of MH does not preclude the diagnosis of VS. The higher incidence of MH in cystic VSs suggests a possible causative mechanism. A T2* GRE /SWI sequence is critical when evaluating CPA masses. Given the results of this study, the use of SWI/T2* GRE could be used to diagnose and differentiate VSs from other masses in other parts of the neural axis as well and this could be considered as an area for further exploration. CPA meningiomas show IAC extension and pattern of IAC extension (eccentric versus centric) is more helpful in differentiating a meningioma from a VS, rather than just extension alone.

Funding Retrospective study-so consent is not needed. IRB was applied for and approved by the institution.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent No funding was received for this study.

References

1. Bonneville F, Sarrazin JL, Marsot-Dupuch K, Iffenecker C, Cordoliani YS, Doyon D et al (2001) Unusual lesions of the cerebellopontine angle: a segmental approach. Radiographics 21:419–438
2. Heller RS, Silveira L, Heilman CB (2018) Cerebellopontine angle tumors. In: Principles of neurological surgery, 4th edn., pp 602–621
3. Grey P, Moffat DA, HardyDG, (1995) Surgical results in unusual cerebellopontine angle tumours. Clin Otolaryngol 21:237–243
4. Nakamura M, Roser F, Dormiani M, Matthies C, Vorkapic P, Samii M (2005) Facial and cochlear nerve function after surgery of cerebellopontine angle meningiomas. Neurosurgery 57(1):77–90
5. Tomogane Y, Mori K, Izumoto S, Kaba K, Ishikura R, Ando K, Wakata Y et al (2013) Usefulness of PRESTO magnetic resonance imaging for the differentiation of schwannoma and meningioma in the cerebellopontine angle. Neuro Med Chir 53:482–489
6. Samii M, Matthies C (1997) Management of 1000 vestibular schwannomas (acoustic neuromas): hearing function in 1000 tumor resections. Neurosurgery 40:240–260
7. McLendon R, Rosenblum M, Bigner D (2006) Russell & Rubinstein's pathology of tumors of the nervous system, vol 2, 7th edn. CRC Press, Cleveland
8. Viswanathan A, Chabriat H (2006) Cerebral microhemorrhage. Stroke 37(2):550–555
9. Thamburaj K, Radhakrishnan VV, Thomas B, Nair S, Menon G (2008) Intratumoral microhemorrhages on T2*-weighted gradient-echo imaging helps differentiate vestibular schwannoma from meningioma. AJNR Am J Neuroradiol 29(3):552–557
10. Mishra A, Thomas B, Kapilamoorthy TR (2017) Susceptibility weighted imaging—a problem-solving tool in differentiation of cerebellopontine angle schwannomas and meningiomas. Neuroradiol J 30(3):253–258
11. Seo M, Choi Y, Lee S et al (2020) diagnostic value of susceptibility-weighted mri in differentiating cerebellopontine angle schwannoma from meningioma. Investig Magn Reson Imag. 24(1):38–45
12. Saravanan K, Parthasarathy EA, Abubacker SF, Sridharan P, Gopalakrishnan AR (2018) Role of susceptibility weighted imaging in cerebellopontine angle schwannoma vs meningioma. Int J Contemp Med Surg Radiol 3(2):B20–B23
13. Park C, Kim DC, Park SH, Kim JE, Paek SH, Kim DG et al (2006) Microhemorrhage, a possible mechanism for cyst formation in vestibular schwannomas. J Neurosurg 105:576–580
14. Gagliardo C, Martines F, Bencivinni F, La Tona G, Lo Casto A, Midiri M (2013) Intratumoral haemorrhage causing an unusual clinical presentation of a vestibular schwannoma. Neuroradiol J 26(30):34