Original Article

Intratumoral microhemorrhage detection on susceptibility-weighted imaging can help in preoperative differentiation of cerebellopontine angle vestibular schwannomas from meningiomas: Correlation with pathology findings

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ABSTRACT

Objectives: In this study, we aimed to evaluate whether intratumoral microhemorrhage detection on susceptibility-weighted imaging (SWI) could help in preoperative differentiation of cerebellopontine angle (CPA) vestibular schwannomas (VSs) from meningiomas.

Patients and Methods: A total of 75 patients (32 males, 43 females; mean age: 45.5±16.7 years; range, 17 to 68 years) consisting of 61 VSs and 14 meningiomas located in the CPA cistern were retrospectively analyzed. All patients underwent contrast-enhanced magnetic resonance imaging (MRI) using the SWI sequence. All images in our study were obtained with a 12-channel phased-array head coil on a 1.5-Tesla clinical scanner. The presence of intratumoral microhemorrhages on SWI sequence was evaluated by demonstrating blooming artifacts as punctate hypointense regions. Both magnitude and phase-contrast images were used to verify microhemorrhages. All patients in our patient cohort underwent surgery and resected tumor specimens were evaluated by pathology.

Results: All VS cases in our cohort exhibited multiple hypointense small foci causing blooming artifact on magnitude and processed SWI images. In the meningioma population, typical MRI signal intensity characteristics, including an intense homogenous contrast enhancement, were observed. In all the meningioma cases, except for one, there was no blooming artifact due to intratumoral hemorrhage within the mass lesions on SWI images. In only one meningioma case, SWI revealed hypointense microhemorrhages within the mass lesion. Following surgical procedures and tumor resections, pathology specimens were evaluated and absence or presence of intratumoral microhemorrhages were detected. These results were significantly correlated with the SWI findings. We obtained 100% sensitivity, 92.8% specificity, and 98.6% accuracy in terms of differentiating VSs from meningiomas located in the CPA cistern by using the SWI sequence.

Conclusion: Meningiomas and VSs are the two most common masses of the CPA cistern and, in some cases, it seems to be difficult to reach an accurate diagnosis with conventional MRI sequences. The SWI can be helpful to solve this problem by demonstrating whether intratumoral microhemorrhages are present or not within mass lesions and, thus, can help to assume a probable accurate diagnosis prior to surgery.

Keywords: Cerebellopontine angle, magnetic resonance imaging, meningioma, susceptibility-weighted imaging, vestibular schwannoma.

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Susceptibility-weighted imaging (SWI) is a relatively new magnetic resonance imaging (MRI) sequence providing information about any substance that has a different susceptibility than its surrounding structures. These substances include deoxyhemoglobin, hemosiderin, iron, and calcium which can provide new sources of MRI contrast.[1] The SWI is based on a three-dimensional (3D), high-resolution, long time to echo (TE), fully velocity-compensated gradient echo (GE) imaging technique and has superiority to those of T2* GE sequences. The SWI sequence uses both magnitude and phase information and by combining these data an enhanced contrast magnitude image (i.e., SWI processed image) is obtained that is particularly sensitive to hemorrhage, iron, calcium and slow venous blood.[2] Deoxyhemoglobin is a paramagnetic substance used as an intrinsic contrast agent by SWI.

Vestibular schwannoma (VS) and meningioma are the most frequently seen mass lesions in the cerebellopontine angle (CPA) cistern and constitute approximately 85 to 90% of tumors found in this location.[3] Preoperative differentiation of VSs from meningiomas has a critical importance due to different surgical approaches that can be implemented to these tumors. On computed tomography (CT) and MRI studies, significant overlapping has been found between the imaging features of these two tumors. Therefore, in the present study, we aimed to solve this problem by determining intratumoral microhemorrhages within VSs by revealing a blooming artifact on SWI. However, in meningioma cases, microhemorrhage detection is not a usually expected finding on SWI sequence.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Şişli Hamidiye Etfal Training and Research Hospital, Department of Radiology between March 2014 and April 2020. All patients who were diagnosed with either VS or meningioma located in the CPA cistern at our Picture Archiving and Communication System (PACS Medical workstation, Siemens Medical Systems, Erlangen, Germany) were retrospectively analyzed. A total of 75 patients (32 males, 43 females; mean age: 45.5±16.7 years; range, 17 to 68 years) consisting of 61 VSs and 14 meningiomas located in this region were reached. All these patients underwent contrast-enhanced MRI examination including SWI sequence. We investigated the presence of intratumoral microhemorrhages on SWI sequence by demonstrating blooming artifacts manifested as punctate hypointense regions. Both magnitude and phase-contrast images were used to verify microhemorrhages, as the evaluation of phase-contrast images allows for the differentiation of paramagnetic microhemorrhages versus diamagnetic calcium. In left-handed MRI systems, hemorrhage appears bright due to a positive phase shift, whereas calcification exhibits low signal depending on the opposite shift effect.

All patients in our patient cohort underwent surgery and the resected tumor specimens were evaluated by an experienced neuropathologist. All images in our study were obtained with a 12-channel phased-array head coil on a 1.5-Tesla clinical scanner (Avanto- SQ Engine, Siemens, Erlangen, Germany) The SWI sequence parameters were as follows: repetition time (TR), 49 ms; TE (echo time), 40 ms; NEX (number of excitations), 1; flip angle (FA), 150; bandwidth, 80 kHz; slice thickness, 4 mm; Gap, 0.8; and matrix size, 256×142. We used a TE value of 40 ms to avoid phase aliasing. Also, a flip angle of 150 was chosen to avoid nulling of the signal from pial veins within the cerebrospinal fluid. The acquisition time was 1.36 min using an iPAT factor-3. After post-processing, 9 to 12-mm thick minIP slabs were generated.

Statistical analysis

Statistical analysis was performed using the SSPS for Windows version 15.0 software (SPSS Inc., Chicago, IL, USA). Fischer's exact test was used in the discrimination of CPA masses on SWI sequence. The intersection value was determined by receiver operating characteristic (ROC) curve analysis and sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated.

RESULTS

Of 14 meningioma cases, 12 were females and two were males. Of 61 VSs cases, 31 were females and 30 were males. As expected, meningioma

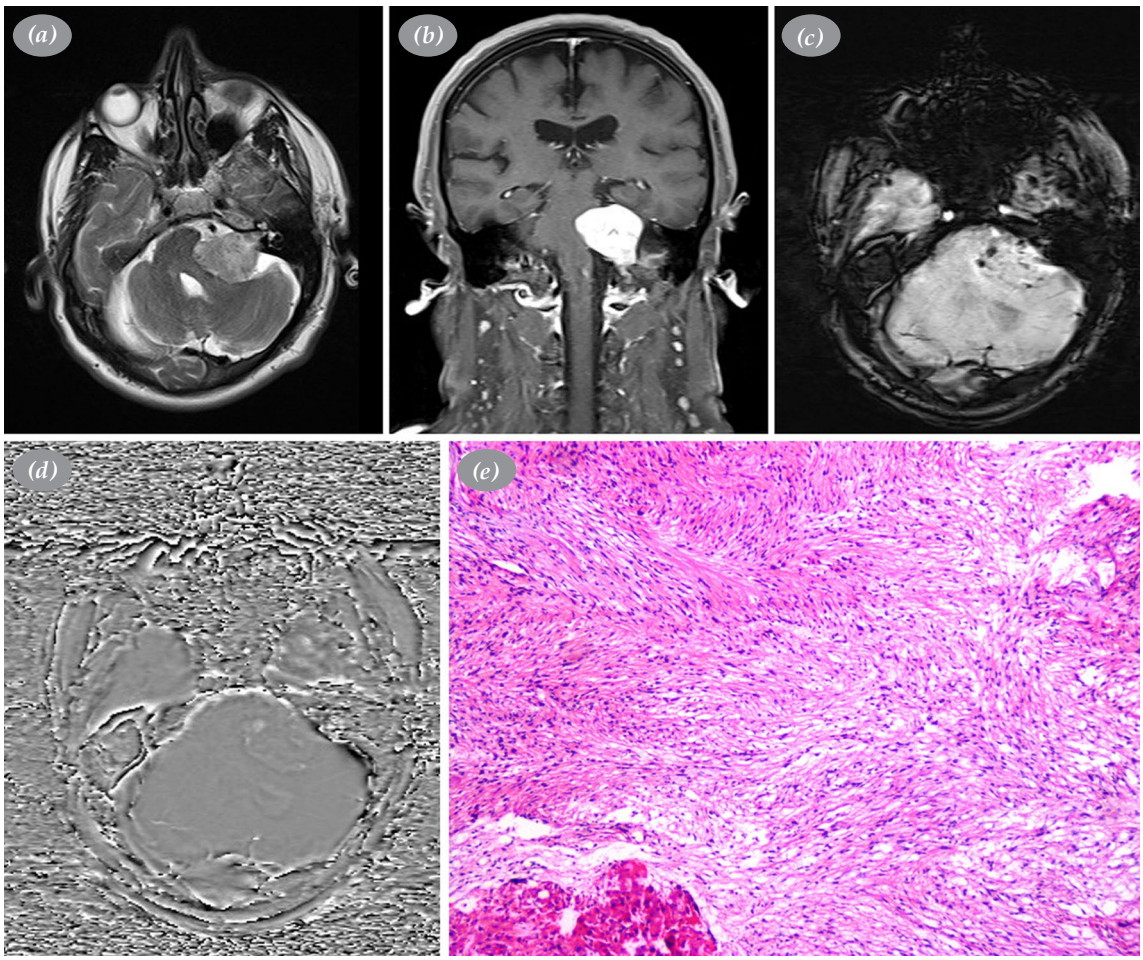

Figure 1. ***(a)*** *A 58-year-old man complaining of left-sided tinnitus. An axial T2-weighted fast spin echo image shows a 35×30-mm mass lesion in the left CPA cistern extending into the internal acoustic canal. It has a slightly heterogenous hyperintense signal intensity and compresses the brain stem.* ***(b)*** *Coronal post-contrast T1-weighted image, an intense contrast enhancement is seen.* ***(c)*** *The SWI magnitude image reveals punctate microhemorrhages within the mass causing a blooming artifact.* ***(d)*** *The SWI phase-contrast image demonstrates a positive shift effect due to paramagnetic susceptibility of hemorrhage in left-handed MRI system.* ***(e)*** *Pathology specimen reveals microhemorrhagic foci within the VS, HE x100.*

CPA: Cerebellopontine angle; SWI: Susceptibility-weighted imaging; MRI: Magnetic resonance imaging; VS: Vestibular schwannoma; HE: Hematoxylin-eosin.

cases were mostly middle-aged women. All VS cases composing our patient cohort exhibited multiple hypointense small foci causing a blooming artifact on magnitude and processed SWI images (Figures 1 and 2) which were considered intratumoral microhemorrhages, as on left-handed MR machines, they showed a hypointense signal intensity on magnitude and processed final SWI images, leading to an opposed signal intensity on phase-contrast SWI images. Among the meningioma cases, typical MRI signal intensity characteristics including intense homogenous enhancement were observed. In all cases except for one, there was no blooming artifact due to intratumoral hemorrhage within the mass lesions on SWI images (Figure 3). In one meningioma case, SWI revealed punctate hypointense microhemorrhages within the mass lesion (Figure 4). Following surgical procedures and tumor resections, pathology specimens were evaluated and absence or presence of intratumoral microhemorrhages were detected.

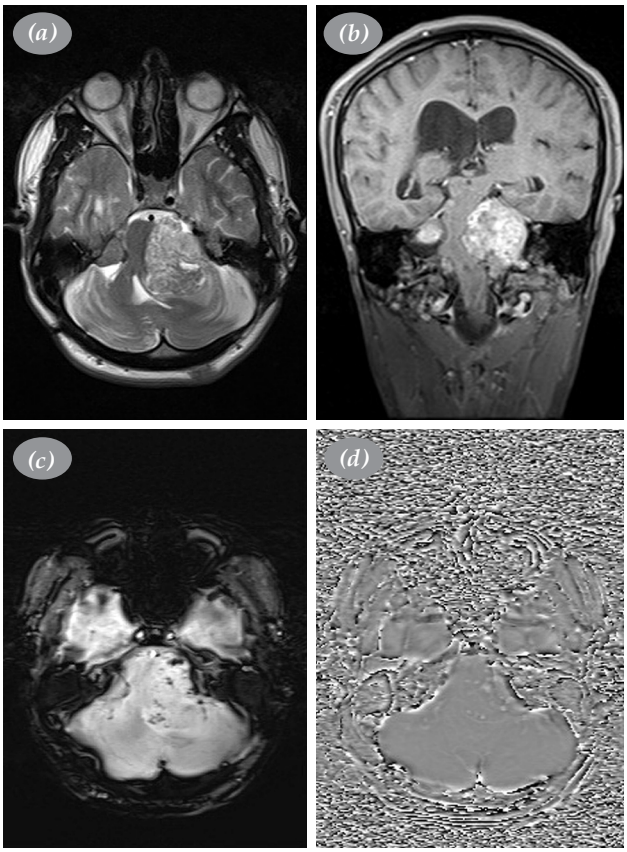

Figure 2. ***(a)*** *An 18-year-old man complaining of bilateral tinnitus. An axial T2-weighted fast spin echo image demonstrates bilateral mass lesions in both CPA cisterns measuring 16×11 mm in diameter on the right and 43×34 mm in diameter on the left. Both show mass effect on the brain stem.* ***(b)*** *Coronal post-contrast T1-weighted image, heterogenous intense contrast enhancement is present for both lesions.* ***(c)*** *The SWI magnitude image reveals punctate microhemorrhages within the mass lesions presenting with blooming artifacts indicating bilateral VSs.* ***(d)*** *The SWI phase-contrast image again shows a positive shift effect due to paramagnetic susceptibility of hemorrhage.*

CPA: Cerebellopontine angle; SWI: Susceptibility-weighted imaging; MRI: Magnetic resonance imaging; VS: Vestibular schwannoma; HE: Hematoxylin-eosin.

These results were substantially correlated with our SWI findings. We used the Fischer's exact test in the discrimination of VS versus meningioma based on the detection of blooming artifact on SWI sequence and found a statistically significant difference ($p<0.0001$). We obtained 100% sensitivity, 92.8% specificity, 98.4% positive predictive value (PPV), 100% negative predictive value (NPV), and 98.7% accuracy for SWI sequence in predicting microhemorrhages of the histopathologically-confirmed VS cases.

DISCUSSION

The two most common extra-axial tumor in the CPA cistern are VS (80 to 90%) and meningioma (10 to 15%).[3,4] Accurate preoperative differential diagnosis of VS from meningioma carries an utmost importance, as the prognosis and surgical approach for treatment may show a difference between the two entities.[4] Although the recurrence rate is higher in meningioma cases, hearing preservation seems to be better in schwannoma cases following surgery. This is possibly due to less injury occurring in the cranial nerves VII/VIII.[3,4]

The CT and MRI can reveal some characteristic imaging findings which enable us to reach an accurate diagnosis for both tumor types. In VS cases, tumor involvement and dilatation of the internal auditory canal and relatively heterogenous type contrast enhancement are typical imaging findings. Nevertheless, intratumoral calcification, hyperostosis of the adjacent bone, homogenous type intense contrast enhancement and dural tail sign are in favor of a meningioma diagnosis.[5,6] However, significant overlapping in these imaging features has been shown in many cases and, therefore, differential diagnosis between these two entities can sometimes be very challenging. In a study performed by Grey et al.,[7] 25% of CPA cistern meningioma cases were misdiagnosed as VSs. In recent years, to enlighten this issue, some studies based on T2* GE sequences have been performed.[8]

Although meningiomas are known to be highly vascular tumors, hemorrhage is an uncommon finding. In some cases, hemorrhage may be detected within these tumors and is usually seen in a macroscopic form, instead of multiple small foci.[9] Nevertheless, the presence of microhemorrhage is considered a characteristic histological feature of VS cases.[10] It is considered to be arising from the spontaneous thrombosis of abnormal vascular channels found in the tumor.

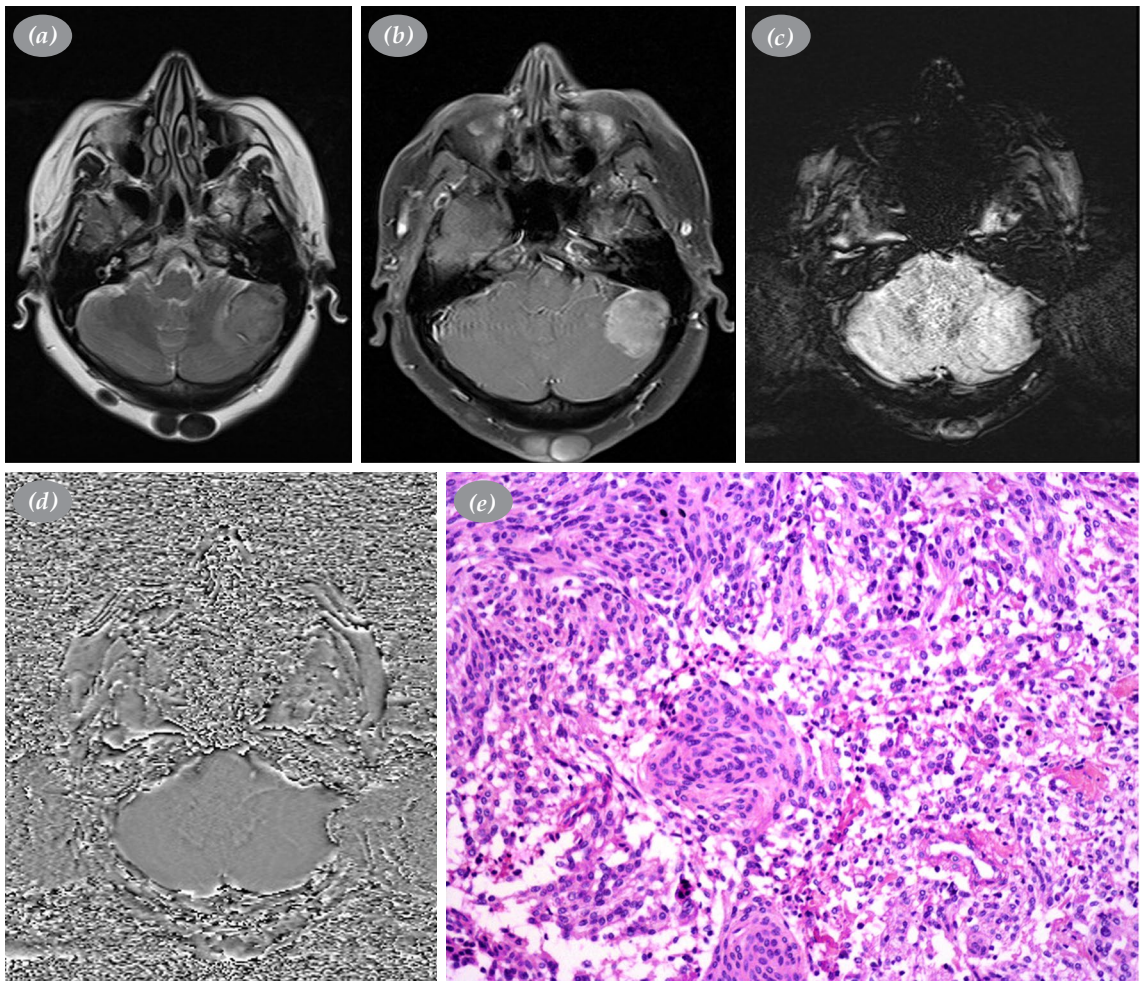

Figure 3. ***(a)*** *A 57-year-old woman with severe headache and left-sided tinnitus. An axial T2-weighted fast spin echo image demonstrates a 32×30-mm extra-axial mass lesion exhibiting isointense signal intensity with the brain parenchyma in the left CPA cistern.* ***(b)*** *Axial post-contrast T1-weighted image shows a mass with intense homogenous contrast enhancement.* ***(c)*** *The SWI magnitude image shows no blooming artifact within the mass lesion.* ***(d)*** *The SWI phase-contrast image shows a positive shift effect, due to the absence of paramagnetic susceptibility.* ***(e)*** *Pathology specimen show solid tissues of meningioma not containing hemorrhagic foci, HE, ×100.*

CPA: Cerebellopontine angle; SWI: Susceptibility-weighted imaging; MRI: Magnetic resonance imaging; HE: Hematoxylin-eosin.

In approximately 20% of meningioma cases, calcification may occur within the tumor and, although it has a course and nodular appearance, this may lead to a confusion due to the susceptibility effect on SWI in certain cases. Phase-contrast images can solve this problem, since diamagnetic calcium has a negative shift effect, contrary to the positive shift effect of paramagnetic deoxyhemoglobin in left-handed MRI systems. Hence, calcium would appear as dark on these images, whereas blood would be bright. Besides, on CT images, calcium can be identified as very high-attenuated regions presenting with elevated Hounsfield units (HU).

The T2-weighted MRI sequences have been previously used to determine microhemorrhages within VS cases. Park et al.[11] in their study showed microhemorrhages in only 35% of cases of their VS patient cohort using T2-weighted sequences. Similarly, despite the

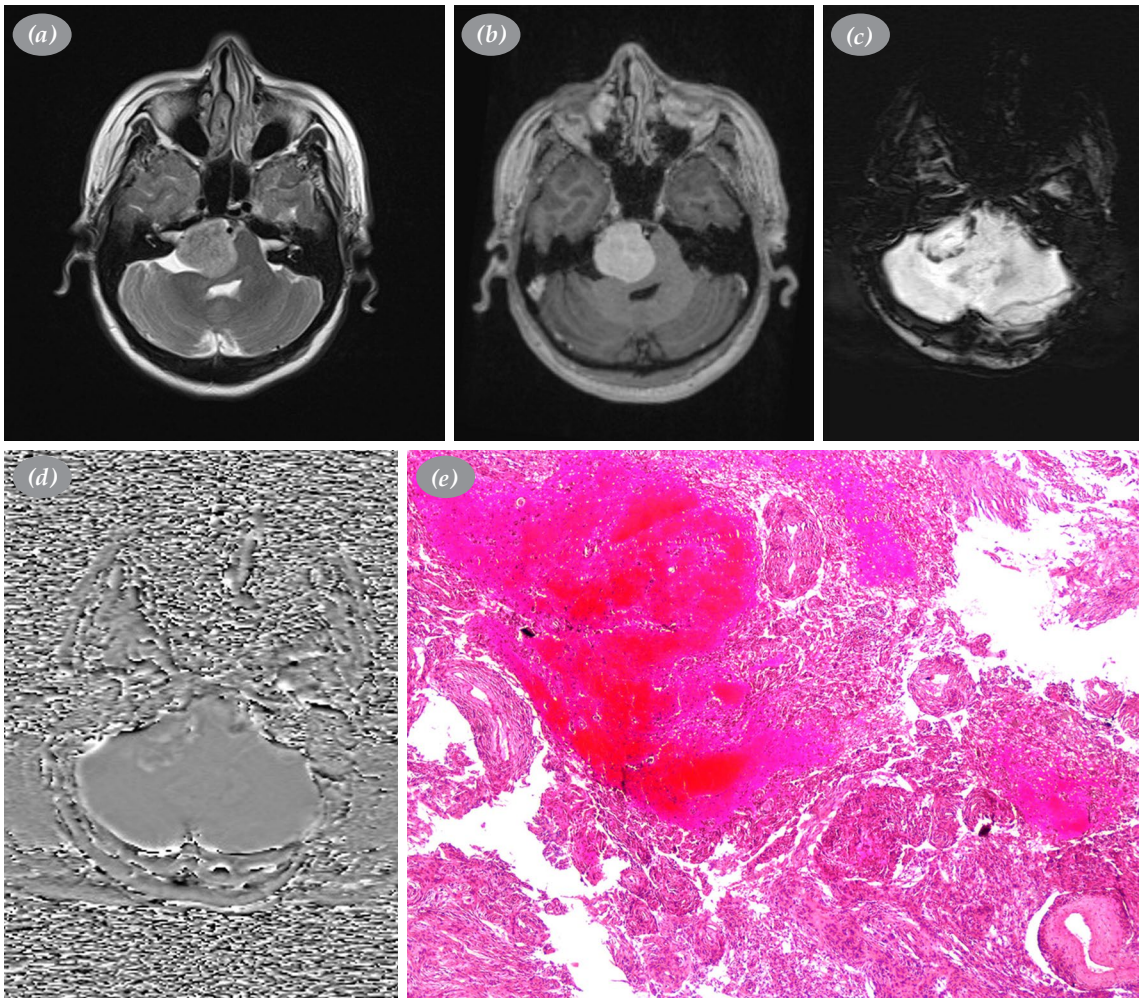

Figure 4. ***(a)*** *A 51-year-old woman complaining of headache and right-sided tinnitus. An axial T2-weighted fast spin echo image shows a 31×29-mm extra-axial mass located in the right CPA cistern. It has lobulated contours, compressing on brain stem and slightly hyperintense than the brain parenchyma.* ***(b)*** *Axial post-contrast T1-weighted image shows intense homogenous contrast enhancement.* ***(c)*** *The SWI magnitude image punctates hemorrhagic foci within the mass causing blooming artifact.* ***(d)*** *The SWI phase-contrast image shows a positive shift effect due to the absence of paramagnetic susceptibility.* ***(e)*** *Pathology specimen show solid tissues of meningioma containing hemorrhagic foci, HE, ×100.*

CPA: Cerebellopontine angle; SWI: Susceptibility-weighted imaging; MRI: Magnetic resonance imaging; HE: Hematoxylin-eosin.

histopathological confirmation of hemosiderin deposition, Ischii et al.[12] could only detect microhemorrhages in five of 12 VS cases based on T2-weighted imaging in their study. Inadequate achievement of T2-weighted MRI sequences in the detection of microhemorrhages within VS cases, a more sensitive sequence to hemorrhage called as T2*-weighted GE imaging has been utilized to solve this problem. Thamburaj et al.[8] performed a study by using T2* GE imaging to be able to increase the visibility of these hypointense microhemorrhages. In their patient cohort, they were able to demonstrate microhemorrhages in 15 out of 16 VS cases, whereas a total of five meningioma cases in the CPA cistern did not show any microhemorrhage. Tomogane et al.[13] also used a new MRI technique called the principles of echo-shifting with a train of observations (PRESTO), which was originally developed for functional MRI studies. This technique can also effectively detect susceptibility changes. In their study,

they investigated the utility of this sequence in the discrimination of CPA cistern VSs versus meningiomas. They demonstrated spotty signal voids on PRESTO images representing hemosiderin deposits within the intratumoral microhemorrhages belonging to VS cases and, thus, were able to differentiate them from those of meningioma cases.

The SWI sequence has been recently introduced and replaced T2* GE imaging. It has been proven to be more sensitive than T2* GE imaging in demonstrating blood products. Hence, it is capable of picking up microhemorrhages that occur in various pathological conditions. Mubarak et al.[14] reported a case with a right trigeminal melanotic schwannoma and showed the usefulness of SWI sequence in the diagnosis. The lesion exhibited a blooming artifact due to significant signal intensity loss on these images, compatible with the melanotic contents of the tumor.

In the literature, we encountered only one study using SWI sequence to identify microhemorrhages within VS cases. In this study performed by Mishra et al.[15] consisting of 59 VS and 14 meningioma cases in the CPA cistern, the authors attempted to differentiate between these two tumors by utilizing SWI sequence and revealed microhemorrhages, causing a blooming artifact on SWI, which were correctly diagnosed in all VS cases. In 13 of 14 meningioma cases, no blooming artifact due to microhemorrhage was detected. It was found in only one meningioma case, due to the calcification which was confirmed on both phase-contrast and CT images. The authors obtained a sensitivity of 100%, a specificity of 92%, a PPV of 98.3%, and a NPV of 100% for SWI sequence. They concluded that SWI can be used as a problem-solving tool in the differentiation of VS versus meningioma of the CPA cistern and can enlighten this dilemma with a high accuracy.

In our study, we used almost same number patient population with Mishra et al.'s[15] study and obtained similar results. We were able to show all microhemorrhages in our VS population by revealing the blooming artifact within these tumor types with 100% sensitivity. In the meningioma group, only one patient exhibited microhemorrhage within the tumor and was mistakenly diagnosed as VS and, therefore, caused a decrease of 92.8% in our specificity.

In conclusion, VSs and meningiomas are the two most common masses of the CPA cistern and, in certain cases, it is difficult to reach an accurate diagnosis with conventional MRI sequences. However, SWI can solve this problem by demonstrating whether intratumoral microhemorrhages are present or not within the mass lesions and, thus, can help to achieve an accurate diagnosis prior to surgery. Hence, the SWI sequence can show a positive impact on both the preferred surgical approach and the prediction of prognosis about these tumors.

Declaration of conflicting interests

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