

# Vestibular schwannomas: A Review

Duy Nguyen, MBBS, and Lucy de Kantzow, MBBS

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**V**estibular schwannomas (VS) are benign tumors of the nerve sheath and the most common tumor in the cerebellopontine angle, accounting for 6-8% of all intracranial tumors and 80% of cerebellopontine angle (CPA) tumors, with an estimated prevalence of 0.02% and mean age of diagnosis at 58 years.<sup>1,2,3</sup> The sporadic form of VS makes up > 90% of cases; there is no predominance for the left or right side.<sup>4</sup> The remainder predominantly occur in neurofibromatosis type 2 (NF2); one of the diagnostic criteria for which is bilateral VS. NF2 is a rare autosomal dominant multiple neoplasia syndrome, occurring due to mutations in the NF2 gene located on chromosome 22q12, coding for the tumor suppressor Merlin.<sup>5</sup> Genetic studies have demonstrated loss of both wild-type copies in the NF2 tumor suppressor

gene as a common finding in sporadic VS as well NF2.<sup>6</sup>

This paper will review the clinical presentation, natural history, and pathology of vestibular schwannomas, as well as discuss the cystic subtypes and provide an overview of imaging diagnosis and measurement techniques.

## Clinical presentation

In a study of 1000 patients, Matthies et al found symptomatic cochlear nerve involvement in 95% of patients with two major symptoms present: hearing loss and tinnitus. Vestibular nerve dysfunction was present in 61% of patients, with a common finding of imbalance. Trigeminal nerve disturbances occurred in 17%. Major symptoms included facial numbness (paresthesia), hypoesthesia and pain.<sup>7</sup> Hearing loss can be evaluated on audiometry; however, audiometry results do not necessarily correlate with lesion site or tumor size.<sup>8</sup>

## Natural history

A systematic review on the natural history of VS performed by Yoshimoto et al showed a growth rate of 1.2 mm/year. Although there was a large varia-

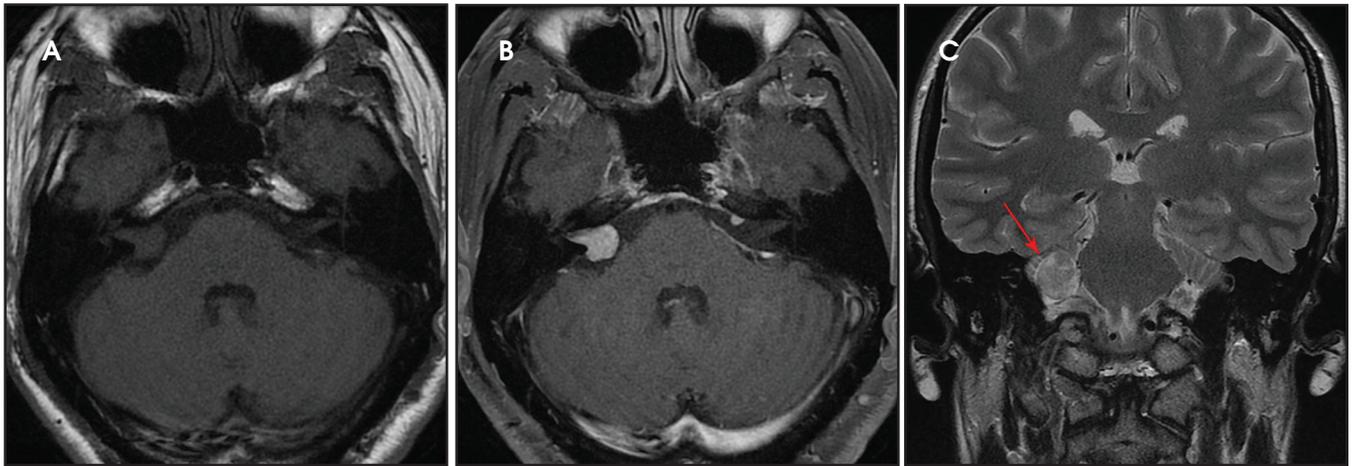
tion in the frequency of tumor enlargement over time (15 to 85%), the overall frequency of tumor growth was 46%, whereas the frequency of tumor regression was 8%.<sup>9</sup> A study performed by Hunter et al found 40.8% of tumors demonstrated a growth of >2 mm during a median observation period of 23 months. In addition, factors predicting growth or requirement of intervention were initial size at diagnosis and disequilibrium.<sup>10</sup>

## Histopathology

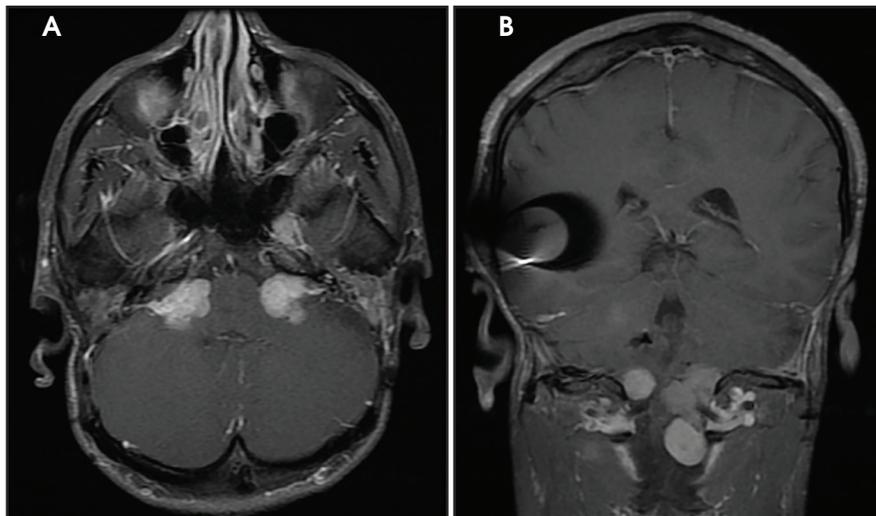
Historically known as acoustic neuromas, these tumors have been demonstrated not to involve the acoustic (cochlear) nerve in most cases, nor to be of neuroglial origin. Instead, they originate from Schwann cells,<sup>11</sup> and they can occur anywhere lateral to the glial-schwannian junction.<sup>10</sup>

Although commonly described in the literature as arising from the glial-schwannian junction, a systematic review of archival temporal bone collections by Roosli et al showed 40 tumors within the internal auditory canal, and 10 intralabyrinthine. Of those 40, 4 arose from the cochlear nerve and 36 from the vestibular nerve. Twenty-one tumors clearly

*Dr. Nguyen is a senior Radiology Trainee in the Medical Imaging Department, St Vincent's Hospital, Darlinghurst, NSW, Australia; and Dr. de Kantzow is an intern at Gosford Hospital, NSW, Australia. The authors have no conflicts of interest to disclose.*



**FIGURE 1.** Typical MRI appearances of a vestibular schwannoma. (A) Axial T1-weighted image of a 63-year-old male, showing an isointense tumor in the right internal auditory meatus with extension into the cerebellopontine cistern, without brainstem compression (Koos grade III/Hanover T3a). (B) Fat-suppressed, post-gadolinium T1-weighted image of the same patient, showing avid homogeneous contrast enhancement of the tumor. Note the acute angle formed between the posterior margin of the tumor and the petrous bone. (C) Coronal T2-weighted image of a 39-year-old female, showing the cysternal component of a vestibular schwannoma (arrow). The T2 signal is heterogeneously hyperintense.



**FIGURE 2.** Example of neurofibromatosis 2. (A) Axial fat-suppressed gadolinium-enhanced T1-weighted image of a 28-year-old male with bilateral vestibular schwannomas, showing typical avid contrast enhancement. (B) Coronal fat-suppressed gadolinium-enhanced T1-weighted image of the same patient showing enhancing extra-axial tumors, likely nerve sheath tumors, in the foramen magnum

arose lateral to the glial-schwannian junction, whereas only 3 were located in the medial one third. Of the tumors involving the vestibular nerve, they occurred roughly equally in the superior and inferior divisions as well as their common trunk.<sup>11</sup> This is in contrast to a prospective study of 200 consecutive cases that showed the origin of 91.4% of schwannomas to be from the inferior vestibular nerve. This study also reported an increased incidence of involvement of the inferior vestibular

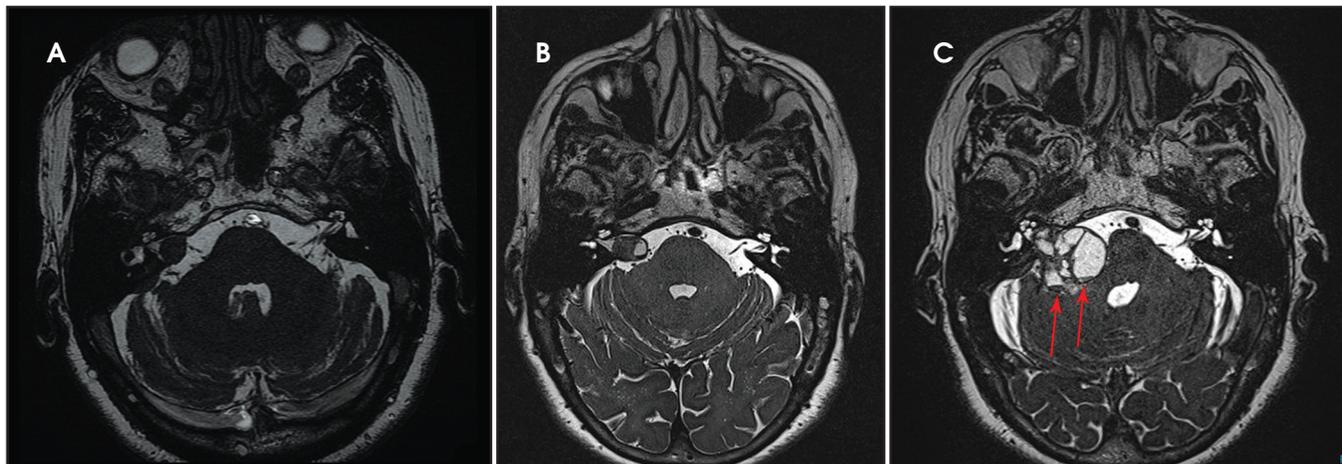
nerve corresponding to an increase in tumor size.<sup>12</sup>

Two different tissue types may be present in vestibular schwannomas: Antoni type A tissue, which is compact and ordered with a palisading architecture, and Antoni type B tissue, which is myxoid and loose.<sup>12</sup> Histological studies have shown no correlation between dominance of Antoni A or B tissue in either cystic or solid vestibular schwannomas.<sup>14</sup>

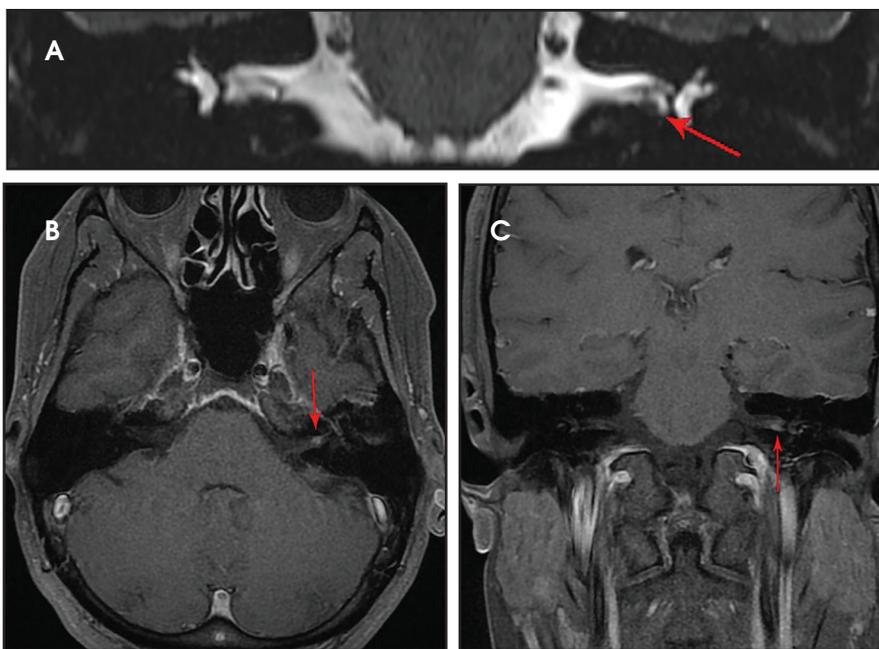
### Cystic vestibular schwannoma

Cystic VSs represent a subtype of VS. Incidence on previous publications has been reported from 5.7% to 48%; however, the former study had the largest cohort, consisting of 773 patients and is therefore most likely closest to the true incidence.<sup>15,16</sup> Cystic VSs tend to be large at diagnosis; they can demonstrate rapid and unpredictable growth, with a significantly shorter duration of symptoms.<sup>17,18,19</sup> The rapid growth of cystic VS is attributed to expansion of the cystic component. On histological studies, the Ki-67 index of cystic VS is either lower or not significantly different to that of solid VS.<sup>18,20</sup> Ki-67 is a nuclear antigen appearing in certain phases of the nuclear cycle and is an indicator of the rate of cell proliferation.<sup>21</sup>

Benech et al reported an increased incidence of adherence to the brainstem; however, they found no significant difference in other postsurgical complications, such as CSF leak, cranial nerve impairment or symptomatic post-operative hemorrhage.<sup>19</sup> In the immediate post-operative period, facial nerve complications exceeded that of solid VS. Long-term postsurgical facial nerve outcomes, however, are not significantly different between solid and cystic VS when taking into account the size of the tumor.<sup>1,22</sup>



**FIGURE 3.** Example of cystic change. (A) Axial 3D FIESTA image in a 73-year-old female showing a Koos grade II/Hannover T2 vestibular schwannoma displacing the adjacent seventh and eighth nerve complexes, with widening of the internal auditory canal. (B) Axial 3D SPACE image three years after the initial MRI showing development of cystic change in the medial component, with progressive enlargement. (C) Axial 3D SPACE image five years after the initial MRI showing marked enlargement of the cystic component, with fluid-fluid levels (arrows). There is progressive widening of the internal auditory canal and now compression of the brainstem, with distortion of the fourth ventricle without stenosis (Koos grade IV / Hannover T4b).



**FIGURE 4.** Example of a small intrameatal vestibular schwannoma. (A) Coronal 3D SPACE image demonstrating a 4 mm Koos grade I/Hannover T1 vestibular schwannoma in the inferior aspect of the internal auditory canal adjacent to the fundus (arrow). (B, C) Axial and coronal fat-suppressed gadolinium-enhanced T1W images demonstrating avid contrast enhancement in the same lesion (arrows). A lesion in such a location may be missed if using the T2 sequence alone, however is easily detected following the administration of contrast.

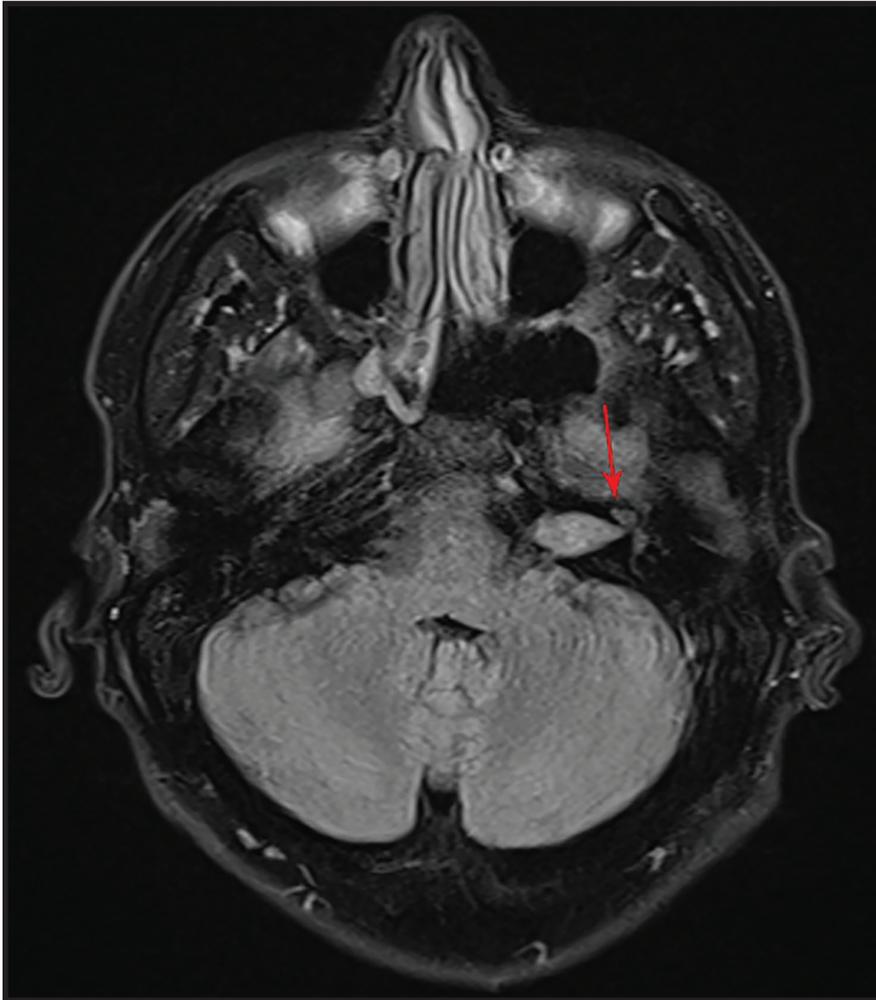
Erratic growth of the cystic component following radiosurgery has been reported.<sup>23</sup> Therefore, conservative management or radiotherapy may have unfavorable outcomes, leaving surgery as the main therapeutic option.<sup>24</sup> Several mechanisms by which the cystic

component grows have been proposed: extravasation of serum proteins from impaired blood-tumor barrier; protein secretion from tumor cells; isolated or repeated intratumoral microhemorrhage; hyaline, fatty and mucinous degeneration; and microcystic changes.<sup>18</sup>

### Imaging diagnosis

Magnetic resonance imaging (MRI) is the gold standard of imaging diagnosis, owing to excellent soft tissue contrast. Tumors are typically round, ovoid, or lobulated. If there is extension into the cerebellopontine cistern, the angle formed between the tumor and the petrous bone is usually acute. Vestibular schwannomas on MRI are typically T1 isointense or hypointense to adjacent brain tissue and show avid, homogeneous contrast enhancement. Some tumors may show heterogeneous contrast enhancement, which can be due to cystic change.<sup>25</sup> On T2 imaging, tumors are most commonly hyperintense, with a small portion showing heterogeneous signal intensity (Figures 1, 2).<sup>26</sup> Cystic VS will show T2 hyperintense cysts, which are hypointense on T1W imaging.<sup>25</sup> Intratumoral hemorrhage may result in T1 hyperintensity and susceptibility on T2\* sequences (Figure 3).<sup>3</sup>

Heavily T2-weighted sequences such as CISS (Constructive Interference in Steady State, Siemens Healthcare, Erlangen, Germany), SPACE (three-dimensional Sampling Perfection with Application-optimized Contrasts using different flip angle Evolutions, Siemens Healthcare, Erlangen, Germany) and



**FIGURE 5.** Axial FLAIR image of a 27-year-old male showing a slightly hyperintense left vestibular schwannoma, extending from the fundus to just beyond the porus acusticus, widening the internal auditory canal, as well as increased cochlear signal (arrow).

FIESTA-C (Fast Imaging Employing Steady-state Acquisition Cycled Phases) on GE (General Electric, Milwaukee, USA) are commonly used in MR cisternography, offering high contrast between cerebrospinal fluid and adjacent structures.<sup>27</sup>

CISS is highly sensitive and specific in the detection of small VS, approaching that of gadolinium-enhanced T1. However, there was an increased risk of missing VS using CISS alone if the tumor was intralabyrinthine in location or < 3 mm in size (Figure 4).<sup>28</sup> Despite this limitation, CISS avoids the risks of gadolinium-based contrast agents (GBCA) which are well-known and include hypersensitivity reactions and nephrogenic systemic fibrosis in patients with severe renal dysfunction (glomerular filtration rate < 30 ml/min).<sup>29</sup> Additional drawbacks of using GBCA include increased cost and scanning time. On computed tomography (CT) imaging, VS is usually isoattenuating to the adjacent brainstem and demonstrates avid, homogeneous contrast enhancement. The cystic variant will show hypoattenuating cysts, which do not enhance. CT also offers superior assessment of bony anatomy, which can reliably appreciate widening of the internal auditory canal.

**Table 1. A comparison of the Koos tumor grading system and Hannover tumor extension grading scale for vestibular schwannomas.**

Loos	Tumor description	Hannover	Tumor description
Grade I	Purely intrameatal (intraacanalicular)	T1	Purely intrameatal (intraacanalicular)
Grade II	Protrusion into the cerebellopontine cistern; no contact with the brainstem	T2	Protrusion into the cerebellopontine cistern without brainstem contact
Grade III	Occupying the cerebellopontine cistern without brainstem contact	T3a	Occupying the cerebellopontine cistern
		T3b	Occupying the cerebellopontine cistern and contacting the brainstem without compression
Grade IV	Large tumor with brainstem and cranial nerve displacement	T4a	Tumor compressing the brainstem
		T4b	Tumor compressing the brainstem with deformity of the fourth ventricle

Asymmetric increased ipsilateral cochlear fluid attenuation inversion recovery (FLAIR) signal relative to the brainstem is a known association, attributed to concentration of protein in the perilymphatic space (Figure 5).<sup>30,31</sup> Furthermore, relative cochlear signal abnormality tends to be greater in tumors of the CPA compared with purely intrameatal tumors.<sup>32</sup>

Commonly used tumor grading systems are the Koos grading system and Hannover tumor extension grading system (Table 1). Koos grade I – IV describes tumor size and location from being small and purely intrameatal through to large tumors causing displacement of the brainstem.<sup>33</sup> The Hannover tumor extension grading system also adds criteria that include CPA extension with and without brainstem contact (T3a and T3b) and brainstem compression with and without fourth ventricular deformity (T4a and T4b, Table 1).<sup>34</sup>

Some authors have proposed a classification system for the cystic appearance; eg, Piccirillo et al, who describe a system differentiating between central and thick-walled cysts (Type A) and peripheral and thin-walled cysts (Type B).<sup>35</sup> Other groups have classified cysts as either multiple, large, thin-walled cysts; multiple thick-walled cysts; a single, large, thin-walled cyst; a large, central, thick-walled cyst; or a mixed pattern of small and large cysts.<sup>22</sup> No single classification system has been widely implemented at the time of this review.

### Reporting measurements

Measuring VSs can be challenging, as these tumors often have an irregular shape, and linear measurements can suffer considerable interobserver variability. On follow-up studies, variation in scan technique and plane can also result in a miscalculation of growth rate.

The Consensus Meeting on Systems for Reporting Results in Vestibular Schwannoma described a standardized measurement technique which includes the following:<sup>36</sup>

- Size based on measurements in millimeters instead of volumetric measurements.
- Preoperative measurements based on MRI or CT if MRI is unavailable.
- Intrameatal and extrameatal portion of the tumor to be clearly distinguished.
- Only the maximum diameter of the extrameatal portion to be used.
- If the tumor is purely within the internal auditory canal, without extension through the porus acusticus, the term intrameatal should be used.
- It should be noted whether or not the fundus is empty or the tumor is cystic – if single or multiple cysts are present.
- The intrameatal tumor can be measured along the length of the internal auditory canal. The width is measured using a line perpendicular to the above. The size of the intrameatal portion should not be added to the extrameatal tumor size.

Varughese et al assessed growth of VS using a mm/year-based model, cm<sup>3</sup>/year-based model, and a volume-doubling time (VDT) based-model, concluding the VDT-based model was the most accurate in describing VS growth.<sup>37</sup> A literature review by Li et al also concluded linear measurement models are subject to reduced interobserver agreement and provide a poor estimation of tumor volume.<sup>38</sup> Volumetric measurements therefore have the greatest clinical utility, sensitivity and accuracy in measuring tumor size and growth.

### Conclusion

Vestibular schwannomas are the most common cerebellopontine angle tumor, commonly presenting with a constellation of symptoms related to cranial nerve deficits such as hearing loss. Most are slow growing; however, the cystic variant tends to have a rapid and unpredictable growth pattern, necessitating surgical management rather than a conservative approach. On MRI, VSs are typically

T1 isointense, T2 hyperintense, and avidly enhance with contrast. Heavily T2-weighted sequences offer high sensitivity and specificity in the detection of VS, unless the tumors are < 3mm in size or intralabyrinthine in location. The Koos or Hannover tumor extension grading system describe tumor extension from an intracanalicular location through to a large tumor compressing the fourth ventricle. Measurement techniques for VS and a system for classification of the cysts in the cystic variant have not been widely adopted at the time of this review.

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