Cystic vestibular schwannoma

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The definition of cystic vestibular schwannomas was based on the following criteria: preoperative identification of cystic components; occurrence of the hypodense/hypointense areas on computed tomography (CT) and/or magnetic resonance (MR); and histological verification of S-100 protein membrane-like structures. [1)]

Epidemiology

In a study of 773 Danish patients with vestibular schwannomas, 44 (5.7 per cent) displayed cystic components.

Mechanism

To elucidate the underlying potential genetic mechanisms in the cystic formation of VS, Yan et al., compared differences in gene expression between solid VS (SVS) and CVS via a bioinformatics analysis. The cDNA microarray method and MicroRNA sequencing were performed on 29 representative VSs (17 CVSs and 12 SVSs). A differential expression analysis was used to identify differentially expressed mRNAs (DEmRNAs) and MicroRNAs (DEMicroRNAs). Then, MicroRNA-mRNA regulatory networks were constructed. Gene ontology (GO), a KEGG pathway enrichment analysis, and the protein-protein interaction (PPI) were used to analyze the co-differentially expressed DEmRNAs at the functional level. From the differential expression analyses, 1304 DEmRNAs, 55 DEMicroRNAs, and hub genes including PTEN, FOXO1, FOXO3, VEGFA, and SIRT1 were identified. Histological evidence is presented to confirm the makeup of the hubs, which corresponded with the cDNA microarray. This analysis revealed that the maps of apoptosis, cellular response to hypoxia, and the PI3K-Akt, AMPK, FOXO, and chemokine signaling pathways were significantly enriched. In addition, the TUNEL assay, immunoblotting analysis, and transmission electron microscope revealed increased degenerative changes in CVS. These findings could be the foundation for understanding the potential role of differential genes in the cystic formation of VS and be helpful in exploring the potential biomarkers for the differential diagnosis, prognosis, and development of drug targets for CVS [2)].

The exact mechanism of the formation of these cysts is still controversial.

The most distinct finding was the presence of abundant abnormal sinusoid or telangiectasis-like vessels. Repeated small hemorrhages from these abnormal vessels, along with subsequent intratumoral changes, are the most probable cause of the formation of these cysts [3)].

Zhang et al collected tumor tissue and blood samples of 31 cystic vestibular schwannomas and 114 solid vestibular schwannomas. Mutation screening of NF2 was performed in both tumor and blood DNA samples of all patients. cDNA microarray was used to analyze the differential gene expression

between 11 cystic vestibular schwannomas and 6 solid vestibular schwannomas. Expression levels of top candidate genes were verified by quantitative reverse transcription PCR.

NF2 mutations were identified in 34.5% of sporadic vestibular schwannomas, with all mutations being exclusively somatic. No significant difference was found between the mutation detection rates of cystic vestibular schwannoma (35.5%) and solid vestibular schwannoma (34.2%). cDNA microarray analysis detected a total of 46 differentially expressed genes between the cystic vestibular schwannoma and solid vestibular schwannoma samples. The significantly decreased expression of four top candidate genes, C1orf130, CNTF, COL4A3, and COL4A4, was verified by quantitative reverse transcription PCR.

NF2 mutations are not directly involved in the cystic formation of vestibular schwannoma. In addition, the differential gene expression of cystic vestibular schwannoma reported in our study may provide useful insights into the molecular mechanism underlying this process [4)].

Diagnosis

The tumors were predominantly hypodense, corresponding to the cystic areas, but also iso- or hyperdense areas were observed, corresponding to other tissue types. Antoni type B tissue and xanthomatous areas were found in all 23 cases [5)].

Of the 16 acoustic schwannomas with MR evidence of intramural cysts, 11 tumors had single small cysts, and five had multiple intramural cysts of variable size. Intramural cysts in 11 of the 16 tumors exhibited higher signal intensity than that of cerebrospinal fluid; the remainder were isointense to cerebrospinal fluid on both T1- and T2-weighted images. All intramural cysts showed circumferential enhancement after contrast administration. Nine of the 16 cystic acoustic schwannomas also had MR evidence of extramural/arachnoid cysts. Six of the extramural/arachnoid cysts had epicenters away from the dural interface, and the other three cysts were broadly based against the dura. The incidence of cystic acoustic schwannomas was 11.3% and association with extramural/arachnoid cysts 7.5%.

The series suggests that cystic changes in acoustic schwannomas and the association with extramural/arachnoid cysts are not as rare as previously reported by other diagnostic methods. The high signal intensity of intramural cysts is probably related to necrotic material, blood, or colloid-rich fluid. The difference in the MR characteristics of extramural/arachnoid cysts associated with acoustic schwannomas and those of typical arachnoid cysts not associated with neoplasia may be related to higher protein and/or colloid contents secreted by the tumor. Most extramural/arachnoid cysts had epicenters between the tumor and brain, suggesting that the most likely mechanism of formation is peritumoral adhesions. It creates a pseudo-duplication caused by the trapping of fluid between the leptomeninges and the mass, resulting in an acquired type of arachnoid cyst [6)].

Treatment

The cystic variant of vestibular schwannoma (VS) presents a therapeutic dilemma. Several studies have previously demonstrated that the surgical outcome in this tumour entity is less favourable than that of solid tumours of comparable size. The “wait and scan” policy has not been recommended for

these tumours, as the cystic elements expand, causing displacement of the brainstem and compression of the 4th ventricle, resulting in hydrocephalus. The large tumour size at diagnosis and the cystic contents do not support the role of radiosurgery as a therapeutic option [7].

In the series of Bowden et al. SRS provided VS tumor control in >95% of patients, regardless of radiographic characteristics. Tumor volume regression was most evident in patients with cystic tumors [8].

Video

<html><iframe width="560" height="315" src="https://www.youtube.com/embed/gNH6Jc2oDYU" frameborder="0" allowfullscreen></iframe></html>

Outcome

The operative management of cystic vestibular schwannoma is more challenging.

Cystic VSs with fluid-fluid levels more frequently adhered to surrounding neurovascular structures and had a less favorable surgical outcome. A possible mechanism of peritumoral adhesion is intratumoral hemorrhage and consequent inflammatory reactions that lead to destruction of the tumor-nerve barrier. These findings may be useful in predicting surgical outcome and planning surgical strategy preoperatively [9].

The outcome of surgery on 44 cystic vestibular schwannoma (mean tumour size 39 mm) was evaluated and compared with that for 151 solid grant vestibular schwannoma (mean tumour size 49.8 mm). Preoperatively, a substantially higher adherence to different intracranial structures in the solid giant vestibular schwannoma compared with the cystic vestibular (95 per cent vs 70 per cent for brainstem, 91 per cent vs 59 per cent for trigeminal nerve, 85 per cent vs 45 per cent for cranial nerves X and XI, 67 per cent vs 32 per cent for dura). Nevertheless, the preservation of the facial nerve function was much better in patients with solid giant vestibular schwannoma compared with those with cystic vestibular schwannoma (House-Brackmann facial nerve dysfunction grade 6 (one year post-operative): 27 per cent vs 41 per cent, respectively $p < 0.04$).

Fundová et al. conclude that the cystic components in vestibular schwannoma are associated with a less favourable surgical outcome, probably due to the rapid tumour growth and symptoms caused by compression of the posterior fossa structures [10]

Case series

Cystic vestibular schwannoma case series.

Case reports

Cystic vestibular schwannoma case reports.

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