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Learning Objectives:

Introduction: Cisplatin (CDDP) is a widely used chemotherapeutic drug with important side-effects, such as ototoxicity. CDDP ototoxicity affects individuals variably, which is mostly due to individual genetic factors. Aim of this study is to analyse the genetic background of the patients in which severe ototoxicity occurred.

Methods: 72 children who received CDDP chemotherapy between January 2013 and March 2015 were included in the study. Audiological evaluations were performed before and minimum three months after the therapy. Ototoxicity was evaluated using Muenster, Brock classifications. During routine controls, 5cc of peripheral blood samples were taken into EDTA-coated tubes. Peripheral blood mononuclear cell and subsequent DNA isolations were performed. In order to analyze the genetic background of patients, we performed comparative genomic hybridization (CGH) arrays for 5 patients with the most severe ototoxicity (Grade 3 and 4), among the studied 72 patients. Results were evaluated statistically by using "Agilent CytoGenomics Software".

Results: CGH analysis showed some common genetic differences among evaluated patients. Chr8.p23.1 (Defensin-family genes) deletion was seen in 3 patients. Chr11.q13.2 (NDUFV1) gain was observed among 4 patients. Chr14.q32.33 (ADAM6) amplification, Chr2.p21 (SIX3) amplification and Chr11.p15.5 (H19) gain were common in all patients. Chr20.q13.32 (GNAS) gain was also seen in 3 patients and this chromosomal region was deleted in one patient. Further assessments may be important to understand the roles of these genes in CDDP induced ototoxicity.

Conclusion: In order to minimize the risk for CDDP ototoxicity, identification of genetic differences is of great importance. Further studies on new candidate genes such as Defensin-family genes, ADAM6, SIX3, GNAS, NDUFV1, and H19 should be performed to better understand their effect on CDDP ototoxicity.

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Free Papers (F866)

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Network analysis of Innate Immune Interaction in Cholesteatoma

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Learning Objectives: Innate Immunity, Cholesteatoma, Network Analysis, Regulatory Network.

Introduction: The etiopathogenesis of Cholesteatoma is controversial, but it is associated with recurrent, persistent ear infections and bacteria. Thereby the interaction between pathogen susceptibility and innate immunity is relevant. Toll-like (TLRs) and Nod-like receptors (Nods) are known to be important participants in the innate immune response to pathogens at other sites, via elaboration of inflammatory cytokines. We explored the network of Innate Immune Receptor-signalling and cytokine production in cholesteatoma.

Methods: Cholesteatoma and control tissue of the external auditory canal skin (EAS) from patients undergoing surgery were evaluated for innate immune pattern and molecules. Cholesteatoma thickness and cellular infiltration were evaluated histologically. mRNA expression of receptors and downstream molecules were evaluated by microarray, real-time PCR, while protein levels were determined by Immunohistochemistry and bioinformatical network analysis.

Results: A subset of receptors involved and downstream molecules in Innate Immunity such as TLRs, Nods and TNF are expressed in cholesteatoma. NOD2 mRNA and protein, but not TLRs or Nod-receptors were significantly induced compared to control samples of the external auditory canal skin (EAS). Moreover, regulation of genes in an interaction network of the RIPK2 was detected. In addition to NOD2, NLRC4, PYCARD, the downstream molecules IRAK1 and anti-apoptotic regulator CFLAR, showed significant upregulation, whereas SMAD3, a pro-apoptotic inducer, was significantly downregulated.

Conclusions: The network interaction of innate immune regulation is important in the etiopathogenesis and growth of cholesteatoma.

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Endoscopic Ear Surgery: Concept and Technique 2 (V867)

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Teaching Videos of Endoscopic Middle Ear Anatomy: A Free Educational Resource

Presenting Author: **Alexander Saxby**

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Learning Objectives: Teaching the complex anatomy of the middle ear has always been a challenge. Textbook drawings and diagrams often fail to show the intricate 3D relationships of the various structures.

The Sydney Endoscopic Ear Surgery (SEES) Research Group has produced a series of videos looking specifically at the anatomy of this region, as visualized with new endoscopic techniques. The endoscope enables an incredible view of areas, such as the retrotympaanum, previously hidden by microscopic techniques.

Each video looks at a specific area of the middle ear and describes its anatomical relationships and clinical correlation. The videos will be available as a free online resource to anyone wishing to use them.

This presentation will demonstrate key parts of the video series and discuss in a broader context how the endoscope has improved trainee education of ear anatomy.

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Endoscopic Ear Surgery: Concept and Technique 2 (V867)

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Transcanal Endoscopic Ear Surgery for Lateralized Tympanic Membrane and Medial Meatal Fibrosis

Presenting Author: **Tsukasa Ito**

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Learning Objectives: Techniques for surgical treatment of LTM and MMF with TESS.

Introduction: The lateralized tympanic membrane (LTM) and medial meatal fibrosis (MMF) are conditions in which the visible surface of the tympanic membrane (TM) is located lateral to the bony annular ring. While the TM is out of position in each condition, the causes differ for the lateralization and the final position of the TM layers. Specifically the LTM loses contact with the ossicular chains while MMF is characterized by acquired atresia with fibrous tissue in the medial part of external auditory canal. Treatment of LTM and MMF presents challenges, in part due to difficulties in visualizing the affected site. Our unit has worked on developing a treatment protocol which incorporates and extends current treatment approaches as well as incorporates the use of the endoscope to achieve a less invasive approach with improved visualization of the affected site.

Methods: Transcanal endoscopic ear surgery (TEES) was used to treat both LTM and MMF using a rigid endoscope with an outer diameter of 2.7 mm coupled to a full HD system. A cross-shaped incision is made across the TM surface and four skin flaps are elevated to exposure the pathology. LTM is treated by removing the mucosa from the ear

canal wall and grafting the TM perforation with fascia to the anterior part of tympanic annulus using the underlay technique. MMF is treated by removing the fibrous tissue from the bony ear canal and the TM lamina propria. The lamina propria and denuded bone is covered with split-skin grafts. Both conditions require canalplasty using a curved bur for complicated bony canal stenosis.

Results: Endoscopes allow for greater overall visualization which is a significant advantage in the surgical treatment of LTM and MMF particularly around the tympanic annulus.

Conclusions: Surgical treatment for LTM and MMF via TEES is an effective and less invasive procedure.

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The Diagnosis and Treatment of Middle Ear Cholesteatoma with Tuberculous Otitis Media Co-infection: A Series of 11 cases

Presenting Author: **Franco Louie Abes**

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Introduction: Tuberculosis is thought to be an endemic disease in the Philippines wherein there have been a number of documented tuberculous otitis media (TOM) cases. The suspicion of TOM co-infection among patients with cholesteatoma of the middle ear (CME) has led to this investigation.

Objectives: 1.) To describe the clinical features and the treatment outcomes of patients with CME and co-existent TOM. 2.) To compare the features of TOM with CME to that of TOM without cholesteatoma.

Study Design: Retrospective review of cases.

Setting: Tertiary private hospital.