Autoimmune Inner Ear Disease

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Grand Rounds Presentation
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Background

- Lenhardt 1958
- McCabe 1979
- Harris 1990

Lenhardt - 1958 anticochlear antibodies- hypothesis
Immune Function of Inner Ear

- blood-labyrinthine barrier
- maintenance of homeostasis
- little lymphatic drainage
- immunoglobulins 1/1000th of serum
- immune responsiveness

NOTES:
- Blood-labyrinthine barrier similar to blood-brain barrier
- limited immunosurveillance
- maintains ionic characteristic of cochlear fluids
- lack of significant lymphatic drainage in inner ear
- perilymph has immunoglobulins at concentrations 1/1000th of serum
- IgG > IgM > IgA
- Harris antigen in inner ear, middle ear and peritoneum
- systemic immunization led to inner ear immune response when antigen presented within inner ear - inner ear is subject to immune surveillance
- cellular infiltration, inflammation, cochlear damage, inc antibody titers, local antibody production
Endolymphatic Sac

- Resident lymphocytes
- immunoglobulin production
- systemic lymphocyte entry
  - spiral modiolar vein
  - intercellular adhesion molecule

- Immune response decreased when sac or duct destroyed
- normal cochlea no lymphocytes and those present in immune response do n’t come from ELS
- lymphocytes enter by SMV after stimulation by ICAM
- antigens from inner ear migrate to ELS which stimulates lymphocytes to produce antibodies
- Darmstadt showed that cochlear from viral labyrinthitis reduced with immunosuppressive meds
- injury to cochlea secondary to uncontrolled immune response or is immune reaction directed at inner ear tissues
Type I Hypersensitivity

- IgE
- mast cells
- histamine
- vasodilation
- ? Hydrops
  Meniere’s
- inhalant allergy

See notes next slide
Type I Hypersensitivity

- Gell and Coombs Hypersensitivity types I-IV
- IgE on mast cells recognizes antigen causing histamine release which in turn leads to vasodilation and immune activation
- ? Interruption of ionic transport and hydrops
- inhalant allergy and anaphylaxis
Type II Hypersensitivity

- Antibodies
- complement activation
- anti-68kDa protein antibody
- SLE, Goodpasture’s

- Antibodies directed toward specific antibody
- anti DNA and anti nuclear Abs in SLE
- anti-basement membrane in kidney dz in Goodpasture’s
- Meniere’s pts - 34% with antibodies that react toward inner ear preps from guinea pigs
- serum from Meniere’s pts reacts with protein 68kDa from bovine ear preps
- Meniere’s patients with reactivity toward type II collagen (otic capsule and tectorial membrane)
Type III Hypersensitivity

- Immune complex
- Ig deposition
- Tissue injury
- Wegener’s, ?Meniere’s

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- Anti DNA and anti nuclear Abs in SLE
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Type IV Hypersensitivity

- T-cell mediated
- direct lysis
- lymphokine production
- lymphocyte transformation test
- Cogan’s syndrome

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Clinical Picture

- Middle-aged women
- progressive SNHL, weeks to months
- dizziness, aural fullness
- bilateral 79%
- \( \checkmark \) no vestibular symptoms
- systemic autoimmune disease in 29%
Diagnosis

- Clinical
- LTT - 93% specific, 50-80% sensitive
- Western blot for anti-68kDa protein (hsp70)
  - 95% specific
  - insensitive
  - predictor of steroid response
Diagnosis

- ESR
- CRP
- C1q binding assay
- anti-cardiolipin
- ANCA
- syphilis testing
- Lyme titers

- CBC
- chemistries
- thyroid functions
- imaging
Polyarteritis Nodosa

- Vasculitis of small and medium-sized arteries
- Renal and visceral
- Ischemia ☑ osteoneogenesis ☑ fibrosis
- Hearing loss rare
Cogan’s Syndrome

- Interstitial keratitis
- Vertigo, tinnitus, SNHL
- Positive LTT to corneal antigen
Vogt-Koyanagi-Harada (VKH) Syndrome

- SNHL, vestibular signs, uveitis
- periorbital hair loss, depigmentation
- aseptic meningitis
- ?autoimmunity to melanocytes
Wegener’s Granulomatosis

- Necrotizing granulomata
- Vasculitis
- Respiratory tract and kidneys
- Serous OM
- cANCA 90% specific
Behçet’s Disease
Relapsing Polychondritis

- Recurrent inflammation of ear, nose, trachea, larynx
- Autoantibodies to cartilage II & IX
- NSAIDs, steroids, dapsone
Systemic Lupus Erythematosus

- Anti-nuclear, anti-DNA antibodies
- Numerous systemic manifestations
- COM with vasculitis, SNHL, dysequilibrium
Rheumatoid Arthritis

- Small joints of hands and feet
- Vasculitis, muscle atrophy, subcutaneous nodules, splenomegaly
- IgM 19S and 7S, IgG 7S 75%
- 44% bilateral SNHL
Meniere’s Disease

- Fluctuating SNHL, episodic vertigo, aural fullness
- ? Autoimmune etiology
  - 97% with CICs (Derebery)
  - response to immunotherapy
  - 32% with anti-68kDa antibody
Treatment

- Steroids
- Cyclophosphamide
- Plasmapheresis
- Methotrexate
  - dihydrofolate reductase inhibitor
## Complications of therapy

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<tr>
<th>Corticosteroids</th>
<th>Cyclophosphamide</th>
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<tr>
<td>Sodium retention</td>
<td>Nausea-vomiting</td>
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<tr>
<td>Potassium loss</td>
<td>Alopecia, skin rash</td>
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<td>Fluid retention</td>
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<td>Congestive heart failure</td>
<td>Interstitial pulmonary fibrosis</td>
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<td>Hypertension</td>
<td>Hemorrhagic cystitis</td>
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<td>Muscle weakness</td>
<td>Hemorrhagic myocardiitis</td>
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<td>Myopathy</td>
<td>Carcinogenesis (urinary bladder, myeloproliferative malignancies)</td>
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<td>Osteoporosis</td>
<td>Sterility</td>
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<td>Aseptic necrosis of femoral and humeral heads</td>
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<td>Peptic ulcer perforation, hemorrhage</td>
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<td>Glaucoma</td>
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<td>Increased intraocular pressure</td>
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<td>Cataracts</td>
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<td>Increased intracranial pressure</td>
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<td>Manifestations of latent diabetes mellitus</td>
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<td>Cushingoid state</td>
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<td>Pituitary, adrenocortical insufficiency</td>
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<td>Insomnia</td>
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Case Study

- 45 year old female
- right sided hearing loss and aural fullness, dysequilibrium progressive over 2 months time
- physical normal except Weber AS, Rinne positive AU
Case Study, continued

- CBC, chemistries, TFTs, RPR, ESR normal
- MRI acoustic protocol normal
- low salt diet, Dyazide
Case Study, continued

- At follow-up, AD hearing worse
- Prednisone 30 mg BID
- anti-68kDa protein positive
Case Study, continued

- Hearing improved
- Steroids tapered
- One relapse, again with improvement on steroids

Hearing better - steroids tapered, one relapse requiring increase in dose that again responded, hearing stable now
Conclusion

- Elusive etiology, diagnosis and treatment
- Potentially treatable cause of progressive SNHL
- Need less toxic therapy