Sjögren’s Syndrome: The Cavities You Can’t Cry About

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Sjögren’s Syndrome

- History
- The Disease
- Characteristics
- Pathogenesis
- Genetic Predisposition
- Treatment / Therapy
- Future Research
History: The year 1888

- Conan Doyle published his first Sherlock Holmes story
- The affordable Kodak camera was invented
- First clinical observations of Sjögren’s Syndrome
History: Henrich Sjögren (1930)

- Stained corneal lesions with Rose Bengal stain
- First pathologic studies, classified the disease as a Systemic Disorder
- Coined “Keratoconjunctivitis sicca”
Sjögren’s Syndrome

- White Blood Cells invade moisture producing glands
- Xerophthalmia (dry eyes)
- Xerostomia (dry mouth)
  - Saliva’s important roles
  - Saliva deficiency
- Females ages 30-40
Sjögren’s Syndrome

- Lymphoid Cell Accumulations in exocrine glands
- Loss of secretory activity
- Production of autoantibodies
Diagnostic Tests

- **Schimer’s Test**
  - Measure the amount of wetting in 5 min.

- **Rose-Bengal Dye**
  - Examines damaged epithelium in eye

- **Salivary gland biopsy**
  - Examined for inflammatory infiltrates
Characteristics: Primary Antigen

α-Fodrin
- Observed in primary, secondary Sjögren’s
- Sub-unit in cortical cytoskeleton
- Activated by calpain (a Calcium activated protease)
- Unknown Protease activation
Characteristics: Antibodies

- **Anti-Ro**
  - Commonly found in Sjögren’s patients

- **Ro protein**
  - 84-112 bases, 2 conserved sequences
  - Major sub-unit is 60 kDa
    - Leucine zipper, zinc finger
  - Target of autoimmunity
  - Function? - discard pathway for 5s RNA
Characteristics: Antibodies

- **Anti-La**
  - Common, mostly found with anti-Ro

- **La polypeptide**
  - 408 amino acids 46.7 kDa
  - Many functions in cell binding virus RNA’s
    - Shuttle protein
    - Termination factor
  - Connection to immune response unknown
Pathogenesis

- Role of CD4$^{+}$CD28$^{\text{low}}$ T cells
  - Normal function
    - activated by autoantigen
    - Expresses cytokine genes with a regulatory function in immune response
  - IL-10, TGF-β are regulatory in immune response

- Unknown Pathway
Pathogenesis

- Apoptosis and defects in Apoptosis
  - Lymphoid cell accumulation
  - Loss of secreting epithelium
  - Destruction of components might induce autoantibody production

- Fas and FasL polymorphisms
  - No connection between patients and controls

- Pathogenesis Remains Unclear
Genetic Predisposition

- Major Histocompatibility Complex
  - Region of genetic involvement in HLA class II proteins
  - Gene alleles associated with Sjögren’s
    - DRB1*15 - DRB1*0301
    - TAP1, TAP2 genes candidate

- Association between DRB1 and TAP
Treatment / Therapy

- Unknown pathway - treat the symptoms
- Drugs to control symptoms
- Fluoride Treatments
- Gene Therapy
  - Insert cytokines
  - Gene transfer
  - Artificial Salivary Glands
Future Directions

- Pathogenic role of transcription factors and signaling
- Role of individual contribution of HLA sequences
- Oncogenes and autogenes
- Understanding pathway / relationship of auto-immune response to antigens
Resources