Rheumatoid Arthritis: Treatment Advances in 2014

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Outline
- Introduction
- Epidemiology
- Pathology
- Clinical Presentation
  - Joints
  - Associated conditions
- Diagnostic Criteria
- Treatment
  - Supportive
  - Pharmacological
  - Surgical

Rheumatoid Arthritis
- Prevalence ranges from 0.5% to 1%, affecting nearly 2.5 million Americans and 165 million people worldwide
  - Prevalence may be as high as 7% and as low as 0% in different ethnic groups
    - Up to 7% in certain American Indian tribes
    - Virtually 0% in Asia and southern Africa
  - Age of onset is typically between 25 and 50 years
  - Female-to-male ratio is approximately 3:1
- Annual incidence ranges from 14.3 cases per 100,000 in men to 35.9 cases per 100,000 in women

Risk Factors
- Genetic susceptibility
  - 50% of risk attributable to genetics
- Environmental factors
  - Higher smoking rates in patients with RA

Pathology
- A clinical syndrome spanning different disease.
- Basically multiple inflammatory cascades that lead to a common pathway
- Persistent synovial inflammation
- Damage to the cartilage joint surface
- Damage to the underlying bone

Pathogenesis
- Antigen mediated activation of T cells in susceptible host
- Cascade of events leading to endothelial cell activation
- Proliferation of synoviocytes
- Inflammatory cells from bone marrow
- TNF-α and IL-1
TNF-α and IL-1
- Proteases and autoantibodies
- Synovium transformed to a proliferative, invasive synovium (Pannus)
- Invades adjacent cartilage and bone
- Activation of osteoclasts
  - Periarticular erosions and osteopenia

TNF
- Activated T Cells, macrophages, neutrophils, mast cells
- Convergence point of cytokines
- Increased antigen presentation

Bone Erosion
- Pannus is key ingredient
- Osteoclasts possess tartrate resistant acid phosphatase
  - Digests inorganic compounds in bone matrix
  - RANK pathway

Autoantibodies
- Rheumatoid Factors are autoantibodies found in RA.
  - Present in as few as 50% of patients with early RA
  - Found in only 5% of healthy individuals
  - Not a good screening test
  - Better as prognostic tool
    - Positive RF associated with more aggressive RA

Rheumatoid Factor (RF)
- RF is a specific antibody in the blood.
- A negative RF does not rule out RA. The arthritis is then called seronegative, most common during the first year of illness and converting to seropositive status over time.

Anti-Citrullinated Protein Antibodies (ACPAs)
- Like RF, this testing is only positive in a proportion of all RA cases.
- Unlike RF, this test is rarely found positive if RA is NOT present, giving it a specificity of about 95%.
- Better predictor of poor prognosis such as progressive joint destruction
Clinical Presentation

- Insidious onset of fatigue over weeks to months
- Transient early on
- Joint inflammation
  - Warmth
  - Effusion
  - Tenderness
  - Loss of Function

Clinical Presentation

- Early morning stiffness
  - Greater than 60 minutes
  - Duration correlates with degree of synovial inflammation
- Improves with activity
- Symmetric polyarthritis
  - Wrists
  - MCPs
  - PIPs
- Structural damage within months by MRI

Rheumatoid Nodule

- Usually subcutaneous
- May be first manifestation of RA
- Inflammatory cells in nodule
- The nodule with central area of fibrinoid necrosis.
  - Accumulation of amorphous, proteinaceous material in the tissue matrix with a staining pattern reminiscent of fibrin.

Lungs

- Fibrosis of the of lungs
  - The formation or development of excess fibrous connective tissue.
  - A recognized response to RA. It is very rare, but a well identified consequence of therapy.

Kidneys

- Renal Amyloidosis
  - A progressive, incurable, metabolic disease characterized by abnormal deposits of protein in the kidneys.

Cardiovascular

Myocardial Infarction

Commonly known as a heart attack. Occurs when the blood supply to part of the heart is interrupted causing some heart cells to die.

Stroke

The rapid loss of brain function(s) due to disturbance in blood supply to the brain.

Atherosclerosis

The abnormal narrowing of an artery. The condition in which an artery wall thickens due to a build up of fatty materials such as cholesterol.
**Ocular**

- Episcleritis
  - Inflammation of the sclera or white of the eye

- Scleromalacia
  - An abnormal softening of the sclera.

- Keratoconjunctivitis Sicca
  - Dryness of the eyes.
    - Caused by the lack of tear production.
    - When severe, dryness of the cornea can lead to keratitis.
    - Inflammation of the cornea.
    - Loss of vision

**Hematologic**

- Anemia
  - The most common abnormality
  - Normal size and color but are lacking in number.

- Neutropenia
  - Low white blood cell count.
    - Normally only occurs when the patient has an enlarged liver or spleen.

- Thrombocytosis
  - Increased platelet count.
    - Occurs when inflammation is uncontrolled.

**Peripheral Neuropathy**

- Carpal Tunnel Syndrome
  - Compression of the median nerve as it passes under Transverse Carpal Ligament

**Spinal Cord Compression**

- Atlanto-Axial Subluxation
  - Erosion of the odontoid process and/or transverse ligaments in the cervical spine’s connection to the skull.

- Subaxial instability
  - Below C2
  - Vertebrae begin slipping over one another and compress the spinal cord.
    - Clumsiness is initially experienced, but without due care this can progress to quadriplegia.
    - Quadriplegia

**Disease Morbidity**

- Increased morbidity for patients with RA
  - Twice as likely to develop a myocardial infarction (MI)
  - 70% more likely to suffer a stroke
  - 70% more likely to develop an infection

- Increased risk of lymphoma
  - Up to 26-fold higher risk, depending on severity of disease and exposure to immunosuppressive drugs, including methotrexate

**Disability**

- Daily living activities are impaired.
  - After 5 years of disease, approximately 33% of sufferers can no longer work.
  - After 10 years of disease, approximately 50% of sufferers have substantial functional disability.

- Some people have mild or short-term symptoms, but in most cases, the disease is progressive for life.
Mortality Rates

- 27% higher than in the general population (41% higher for women)
- Life expectancy in patients with RA is reduced by as much as 18 years compared to age- and sex-matched controls without RA.

Diagnostic Criteria

ACR/EULAR 2010 criteria

1. Morning stiffness (at least 30min)
2. Two or more joints affected
3. 1 joint with swelling and tenderness
4. 1 joint with an obvious deformity
5. Elev.s of CRP or ESR

Pharmacological Therapy in RA

- No Cure… Just going for remission
- NSAID’s and analgesics
- Disease Modifying Antirheumatic Drugs (DMARD’s)
  - Outcome improved if instituted with 90 days or dx (based on x-rays at 5 years for bony erosion)
  - “Window of Opportunity”
- Important to institute early and maintain disease suppression to avoid permanent joint damage

DMARD’s

- Currently the mainstay of therapy
- Reduce inflammation
- Acute phase reactants
- Erosion scores
- Decrease long-term disability

DMARD’s

- Corticosteroids
- Methotrexate- May be most effective in lowering mortality
- Hydroxychloroquine
- Sulfasalazine
- Gold
- Cyclosporine
Corticosteroids

- Side effects
  - Thinning of skin
  - Cataracts
  - Osteoporosis
  - Hypertension
  - Hyperlipidemia
- Consider
  bisphosphonates, calcium, vit D

Biological Agents

- Anti TNF-α Drugs
  - Etanercept, Infliximab, Adalimumab
  - Immunosuppression
  - Reactivation of mycobacterial infection
- Anti IL-1 Drugs
  - Anakinra
  - Less reduction of inflammation vs. the anti-TNF-α drugs
  - Better safety profile
- Cost up to $15,000 per year

Biological Agents

- No consensus on surgery
- Some surgeons have patients stop before the surgery and resume 2 weeks later
- This may lead to flare up in periop period

Glucocorticoids and NSAIDs

- Glucocorticoids
  - Fast onset
  - Low cost
  - No disease modifying benefit
- NSAIDs
  - Patients with RA more prone to PUD than OA patients

Corticosteroid Injections

- Corticosteroid preparations
- Highly effective
- Risk of sepsis 1:10,000

Outcome of Current Treatments
Adjunct Treatment Modalities

- Support Groups/Psychological
- Weight Loss
- Podiatric Management
- Occupational Therapy
- Physical Therapy
- Acupuncture

Surgical management of joints with RA

- Arthroscopic and open surgical synovectomy
- Joint Arthroplasty
  - Rates are unchanged or going down while going up in osteoarthritis
- Be aware of multiple joint involvement
  - Treat upper extremity first
  - Staged procedures to avoid long hospitalizations

Surgical Management of RA

- Decrease or eliminate pain
- Improve Function

Summary

- Rheumatoid Arthritis is a systemic autoimmune disease
- Fundamental finding of activated synovial pannus leading to joint and bone degradation
- Multiple systemic effects in other organs
- Mainstay of treatment is medical

Summary

- New drugs are having significant effect on degree of pain and joint destruction
- These drugs are expensive and have high rate of other complications such as infection
- Total joint replacement is the mainstay of surgery for RA
- Overall, the rate of surgery for RA is remaining the same or decreasing
Thank You