Rheumatoid Arthritis
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- Multisystem disease of unknown etiology
- Persistent Inflammatory synovitis of Peripheral joints in Symmetric distribution
- Variable course but potential for cartilage damage and bone erosions
Epidemiology

- Women : Men = 3 : 1
- Onset $\rightarrow$ 4th decade (35 - 50 yrs)
- Genetic pred. $\rightarrow$ in first-degree relatives in monozygotic twins
  - role of HLA - DR 1, DR 4, DRB1 alleles
- ? Environ. Factors $\rightarrow$ Smoking, Urbanizations
Etio-pathogenesis

- Infectious agent in genetically susceptible host
- ? Mycoplasma ? EBV / CMV / Rubella / Parvo

Persistent infxn revealed antigenic cross-peptides (collagen, reactiv microbial products heat-shock protein

Or retention of
Etio-pathogenesis

- RA synovitis $\rightarrow$ Hyperplasia (Pannus) +
  Microvascular Injury (CD4+)
  (edema, thrombosis, neovascularisation)

- IL-1, TNF-α & IL-6 (also involved in systemic manifestations n potential anti-cytokine therapy)

- Ac. Inflam. process in synovial fluid overriding Chr. Inflam. in synovial tissue
Clinical Manifestations

- Non-sp. gradual onset (fatigue, anorexia) in 2/3\(^{rd}\) of patients until overt synovitis

- 10% have acute presentation with polyarthritis, fever, lymphadenopathy and splenomegaly
Clinical Manifestations

- Articular manifestations:
  (arthritis n deformities)
  - Inflam. Arthritis with Morning Stiffness
  - Symm. Pattern
  - Joint swelling $\rightarrow$ ↑ synovial fluid, synovial hypertrophy, thickened joint capsule
  - PIP, MCP, Wrist joint
  - DIP rarely involved
  - Baker’s cyst
  - Upper cervical spine (never Lumbar spine)
Clinical Manifestations

- Articular manifestations:
  (arthritis and deformities)

  - Z deformity → radial deviation at Wrist
    + ulnar dev. at MCP
    + palmar subluxation at PIP

  - Swan neck deformity → hyperextension at PIP
    + flexion at DIP

  - Boutonniere deformity → flexion cont at PIP
    + Ext at DIP
Clinical Manifestations

- **Articular manifestations**: (arthritis and deformities)
  - Hyperextension at 1st (thumb) IP joint and flexion at 1st MCP joint (loss of pinch)
  - Foot deformities - hallux valgus
    - Eversion (subtalar joint)
    - Plantar subluxation of metatarsals
Clinical Manifestations

Extra-Articular manifestations:

- Periarticular Rheumatoid nodules → usually on extensor surfaces like olecranon bursa, achilles tendon, occiput (MTX îses number)

- Skeletal muscle atrophy (asa 3 weeks)

- Osteoporosis (often compounded by steroid therapy)
Clinical Manifestations

- Extra-Articular manifestations:
  - Rheumatoid vasculitis - polyneuropathy, mononeuritis multiplex, digital gangrene, visceral infarction
  - Pleuro-pulmonary ds. - Pleural effusion, pleural fibrosis, ILD, pneumonitis, Caplan syndrome (Pulm Rh. nodule + Pneumoconiosis)
  - Felty’s syndrome - RA + Splenomegaly
    + Neutropenia (<1500/µL)
Clinical course and Prognosis

- Variable course, difficult to predict in an individual patient
- 15% have short-lived inflammatory process that remits without major disability
- Sustained ds activity for >1 yr portends poor outcome
- Most rapid rate of functional disability within first 2 yrs
- High RF titers, high ESR, > 20 joints involved
  Rh. Nodules → progressive disease
Lab Investigations

- **Rheumatoid Factor**: Ig M against Fc portion of Ig G
  - also + in 5% healthy population, CLD, Hep B, SABE, Malaria, Syphilis, Leprosy, ILD
  - high titers → progressive disease

- **ESR and Ac phase reactants (CRP, Ceruloplasmin)**

- **Radiological eval.**: Juxta-articular osteopenia, bone erosions etc.
Diagnosis

- B/L Symm. Inflam. Polyarthritis involving small and large joints of both UL n LL with Sparing of axial skeleton (except for cervical spine)
Diagnosis

- ACR criteria, 1987 (4/7)
  - Morning stiffness (> 1 hr)
  - 3 or more joint area
  - Hand joints
  - Symmetric distribution
  - Rheumatoid nodules
  - RF
  - Radiographic changes
Treatment

Treatment goals:
- Relief of Pain
- Reduction of Inflamm. N protection of articular surfaces
- Control of Systemic features
- Maintenance of functional status

● All therapeutic interventions are palliative and none is curative
Treatment

- NSAIDs
- DMARDs
- Steroids
- Anti-Cytokines
- Immuno-suppressants
NSAIDs

- Relief of pain, reduces swelling
- Rest and splintage ameliorates symptoms
- Rapidly effective in mitigating signs and symptoms
- However, no effect on disease progression
- Coxibs n classical NSAIDs equally effective but lesser S/E like gastritis
- S/Es: gastritis, azotemia, platelet dysfunc.
DMARDs

- Reduce levels of Ac. phase reactants and can modify inflammatory process but....
- Can not induce true remission and onset of action is delayed
- Options: - MTX
  - D-penicillamine
  - Antimalarials (HCQ)
  - Sulfasalzine
  - Gold compounds
DMARDs

- **Methotraxate**: DMARD of choice
  - relatively rapid onset of action and sustained improvement with ongoing therapy
  - 7.5 to 30 mg/week
  - maximal improvement by 6 months (thereafter negligible)
  - S/Es \( \rightarrow \) hepatic dysfunction, oral ulcerations, gastritis... give Folic Acid
Glucocorticoids

- Additive therapy both for acute flare-ups as well as chr. low dose maintenance therapy (< 7.5 mg/day)

- Monthly pulse high dose glucocorticoids?

- Intra-articular steroids when systemic medical therapy not effective

- S/Es → Osteoporosis, gastritis (++NSAIDs)
Anti-cytokine agents

- **Anti-TNF α therapy:**
  - TNF receptor bound to Ig G (Etanercept)
  - Chimeric monoclonal Ab to TNF (Infliximab)
  - Humanised monoclonal Ab (Adalimumab, Golimumab)

- **Effective in DMARD failure and DMARD naïve patients as well**

- **Issues** → Cost, Parenteral admin., TB, AntiDNA Ab, CNS demyelination
Anti-cytokine agents

- IL-1 Receptor antagonist (Anakinra)
- Monotherapy or in combination with MTX
- Injection site reactions a major S/E

- CTLA4 bound to Ig G (Abatacept)
- Inhibits co-stimulation of T-cells by preventing surface receptor interaction CD28-CD80
Immunosuppressive therapy, Surgery and Rehabilitation

- Not more effective than DMARDs
- More serious S/E profile
- Reserved for clearly failed DMARD and Anti-cytokine therapy
- Options → Azathioprine, leflunomide, cyclophosphamide
- Surgery → Arthroplasty, Joint Replacement, Synovectomy, Orhtotic and Assistive devices, Exercise
Approach to patient

Risk factors for disability/erosions?
- Rheumatoid factor
- Anti-CCP antibody
- Multiple swollen joints
- Elevated acute-phase reactants
- DR4+ (Shared epitope)
- Erosions on x-ray
- Disability

Early aggressive therapy

MTX or Combination DMARD therapy
- Methotrexate w/wo HCQ w/wo SSA with low-dose glucocorticoids

Coxib or hydroxychloroquine w/wo low-dose glucocorticoids

Responders
- Continue

Nonresponders
- Leflunomide TNF blocker
  - Add: Leflunomide TNF blocker
  - Switch: Leflunomide TNF blocker
  - Nonresponder or toxicity
    - Consider abatacept, rituximab, cyclosporine

Partial responders
- Add: Leflunomide TNF blocker

Toxicity
- Switch: Leflunomide TNF blocker

Persistent synovitis for >12 weeks
The End
(0f RA1 &2)