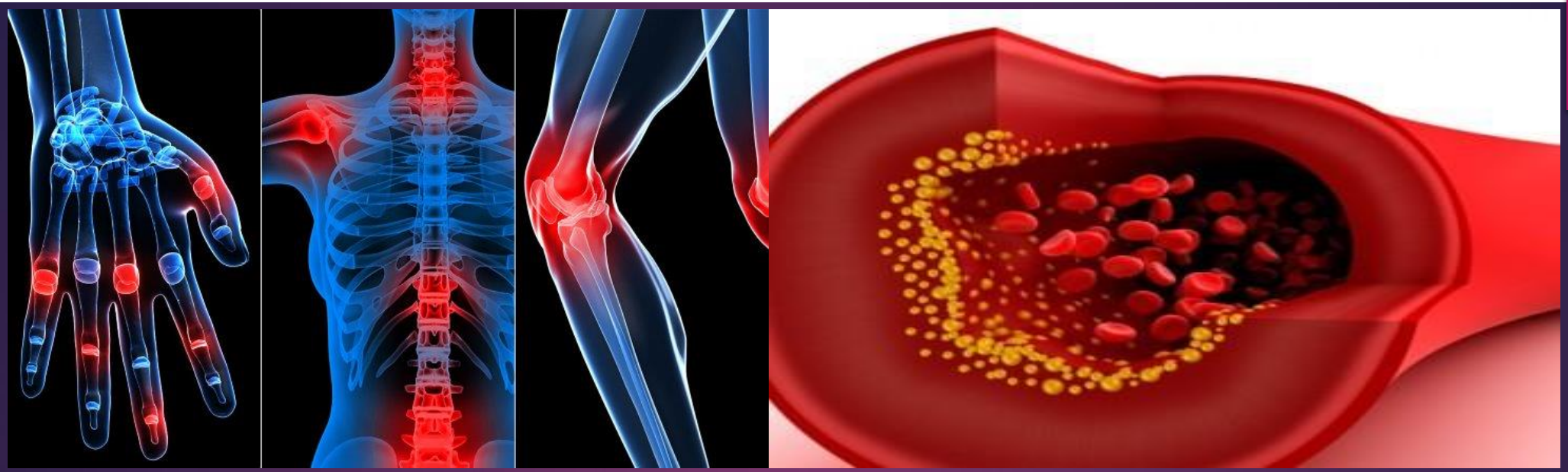

Accelerated Atherosclerosis in Rheumatic Diseases

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Accelerated atherosclerosis in rheumatic diseases :

- The relation between syst.inflam disease & accelerated atherogensis is always under investigation .
- This effort advanced our understanding of → pathogenic mechanisms & epidemiology .
- Current priorities include → identification of patient at risk & developing preventive strategies .

Accelerated atherosclerosis in rheumatic diseases :

- Evidence of this relation is best developed for → rheumatoid arthritis and systemic lupus erythematosus
- Underlying inflame.disease should be suspected in → young patient with unexplained angina
- Patients with a rheumatic D. who suffer M.I → have worse outcomes

Endothelial dysfunction and vascular injury :

- Homeostatic mechanisms ⟶ control vasodilatation & permeability
- Prolonged syst.inflam. (RA,SLE) ⟶ promote endothelial injury & impair vasomotion
- Inflammation may exacerbate ⟶ the effect of classical R.Fs

Endothelial dysfunction and vascular injury :

- Patients with syst. Inflam.D. exhibit → End.dyfun. & aortic stiffness
- Effective treatment of inflam → may not always reverse endothelial dysfunction
- Systemic inflam. environment may → ↑ plaque instability & rupture

Endothelial dysfunction and vascular injury :

- BOTH ↑ plaque burden & ↓stability → lead to premature C.V events .
- Various molecular mechanisms → ↑risk of atherosclerosis & C.V events
- Disease related factors like TNF & interleukin → share in pathogenesis
- other factors include → Endo.cell apoptosis, ↓ capacity of repair

→ autoantibodies , genetic polymorphism , deleterious effect of drugs .

Rheumatoid Arthritis

- R.A. → Auto Immune, Systemic, Inflammatory Polyarthritis.
- Male/ Female ratio 3/1.
- Affect 1% of the population.
- Age of onset → between 30 - 50 years.
- 80% of patients → +ve R. F. & CCP
- Systemic Inflammatory Response is evident.

Atherosclerotic Disease in R. A.

- A Variety of studies showed → Subclinical arterial D. with ↑ IMT.
- The precise mechanistic relationship → remains unknown.
- Studies showed → abnormal Myoc. Perfusion & coronary flow reserve.

Atherosclerotic Disease in R. A :

- The classic CV. RFs → influence endoth. function → > inflammation.
- Abnormalities in vasc. function → may occur before R.A. symptoms.
- Chronic inflammation → may promote atherogenesis .

Atherosclerotic Disease in R. A :

- Syst. inflam. environment ⟶ can promote C.V. events .
- Pts with RA have ⬆ classical RFs → smoking , dyslip. & insulin resist.
- The risk of M.I. ⟶ is similar to those with D.M.

Atherosclerotic Disease in R. A :

- Heart attack & stroke → occur at an earlier age & cause 50 % of mortality
- Excess mortality is associated with → disease activity
- Pts. with RA who suffer MI → less likely to receive reperfusion

Treatment :

- Drug therapy for RA ⟶ undergone remarkable evolution
- Current focus ⟶ biological therapies & management of early disease
- Whether drugs which control arthritis ⟶ confer vascular protection ??
- Methotrexate ⟶ most used disease modifying anti rheumatic .D, (DMARD)
- In the same category are ⟶ sulfasalazine & hydroxy chloroquine

Treatment :

- Patients who don't respond to DMARD → should switch to biological therapy .
- This group include → agent targeting TNFa & IL6 receptor .
- An aggressive disease modifying approach → ↓ the need for NSAID
- Corticosteroid therapy may adversely effect traditional R.Fs .
- NSAID although effective → can ↑ BP & Thrombotic CV events .

Treatment :

- Other evidence suggest that → their anti inflammation effect , predominate
- Agents targeting TNFa → improve endothelium function & plaque stabilization
- Other new studies → disagree about this concept
- British society of rheumatology → anti TNFa agents → ↓M.I significantly
- Treat of RA activity → should be combined with tight control of RFs

Systemic lupus Erythematosus (SLE) :

- SLE is ⟶ AN Autoimmune disease and predominate in ♀ (9:1) .
- Prevalence varies from ⟶ (4-280) per 100,000 .

Systemic lupus Erythematosus (SLE) :

- Constitutional symptoms include → night sweats , malaise and ↓ WT.
- Muco-cutaneous features include → butterfly facial rash , oral ulcer & alopecia
- Life threating complications include → G.Nephritis , CNS & shrinking lung syndrome

Systemic lupus Erythematosus (SLE) :

- Hematological involvement ⟶ lymphopenia , hemolytic anemia & thrombocytopenia .
- Cardiac involvement (rare) ⟶ pericarditis , endocarditis and coronary arteritis .

Systemic lupus Erythematosus (SLE) :

- Pathogenesis ⟶ generation of autoantibodies & immune complexes

⟶ activation of complement & tissue injury .

Lab investigations ⟶ ⬆ ANA & ds : DNA , ⬆ ESR & normal CRP ?

Atherosclerotic disease in SLE :

- Bimodal peak in SLE related mortality → Early infection complication
  → Late- CAD .

- Risk of MI & stroke → from 2-50 fold > general population .
- The young ages & ♀ incidence → SLE accelerate arterial disease.

Atherosclerotic disease in SLE :

- In one **study** → 97 vascular event within 8 y ⟶ 31 from atherosclerotic.D
- In patients With CAD ⟶ the plaque is more vulnerable .
- Patients has worse prognosis after M.I ⟶ reluctance to treat aggressively.

Atherosclerotic disease in SLE :

- HTN due to ⟶ renal disease & use of corticosteroids
- M.S ⟶ associated with renal impairment & corticosteroid use
- Lipid abnormality ⟶ ⬆TG & ⬇HDL & normal LDL

Treatment :

- Mild SLE can be treated with → analgesics , NSAID , +_ hydroxychloroquine
- Organ involvement require → prednisone , immunosuppressant (methotrexate)
- Life threating complications → cyclophosphamide & high dose corticosteroids
- Mycophenolate mofetil (MMF) instead of cyclophosphamide (infertility)

Treatment :

- Rituximab ⟶ is an effective treatment of sever SLE
- variety of regimens ⟶ combination of rituximab , prednisone & cyclophosphamide
- Belimumab a monoclonal antibody ⟶ modest disease modifying effect

Treatment :

- Strategies for prevention of CVD need → long term prospective trial
- Persistently active disease → associated with accelerated atherosclerosis
- Individualized immunosuppressive therapy → minimize CV complications
- Hydroxychloroquine → ↓ LDL & lower mortality from CVD
- Aggressive management of traditional RFs → are highly indicated

Atherosclerosis associated with other rheumatic disease :

- Many rheumatic .D. ⟶ associated with premature & ↑ CV risk
- This is because of the relation ⟶ between inflammation and atherogensis

Important current clinical challenges include :

- 1- which rheumatic .D. ⟶ pose the great cv threat
- 2- a means of identifying ⟶ subset of patients most at risk
- 3- preventative strategies ⟶ to minimize CV events .

- Most common rheumatic .D.associated with atherosclerotic.D. ⟶ are ankylosing spondylitis , psoriatic arthritis & gout

Hyperuricemia:

- Hyperuricemia → is independent predictor of CVD
- Patients with gout often have → HTN , DM , obesity and dyslipidemia
- Many cardiovascular drugs ↑ uric acid like → diuretic, BB and aspirin
- in contrast losartan ,atorvastatin and fenofibrates → ↓ urate level
- Allopurinal → ↓ risk of CHF & CV related death
- Pts. with gout should receive → diet advise , aggressive ↓ of RF + medications .

Psoriatic arthritis (P.A):

- PTS.with PA have ⟶ ↑ RFs , End,dysfun ,A stiffness

Subclinical atherosclerosis .

- Suppression of inflam. activity ⟶ improve end.dysfun and carotid IMI .

Ankylosing spondylitis (AS):

- Patients with A.S has ⟶ Endo.dysfun , ⬆carotid IMT ,⬆Pulse wave velocity
- The role of Anti-TNFa therapies ⟶ are under investigations .

Conclusion :

- Inflam. rheumatic .D. → Have a long recognized relationship with the CV system
- Both the treat & survival rate of rheumatic.D. → ↑ significantly over the last 15 years .
- Patients with multisystem rheum.D. → may initially be evaluated by CV specialist .
- The vasculature is → primary target organ for rheumatic disease.

Conclusion :

- Rheumatoic disease also has ⟶ secondary effect on CV system .
- Chronic syst.inflam. ⟶ End.dysfun . & arterial stiffness ⟶ atherosclerosis
- Rheumatic Ds are ⟶ important cause for premature MI & stroke
- Many clinical challenges remain like ⟶ early recognition , underlying molecular mechanisms & preventive strategies .

THANK YOU