Fevers & Rheumatic Diseases lecture

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Clinical Problem
Solving
FEVERS
and Rheumatic Diseases
Introduction

- **Pyrexia** alone as a clinical presentation of rheumatic diseases - PUO differential diagnosis
- The investigation and differential diagnosis of fever presenting with **musculoskeletal** symptoms or signs
- MSc relevance - **Clinical practice and problem solving**
Agenda

- **Fever** - Aetiopathogenesis
- **Fever** - Periodicity and rheumatic disease: Childhood fevers
- **Fever** - PUO and the rheumatic diseases
- **Fever** - and vasculitis - A simplified Guide to Investigation
Agenda

Fever - Aetiopathogenesis

Fever - PUO and the rheumatic diseases
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FEVER

- Hypothalamic control
- **Cooling** - accelerated activity of skeletal muscle / Reduction of peripheral blood flow
- **Heat** - Reduced muscle activity / Peripheral vasodilation and sweating

- **Endogenous Pyrogens**
  - PMN / Macrophages but not lymphocytes
  - TNF / INF alpha / IL1 / IL6 found in many rheumatic diseases

- **Exogenous pyrogens**
  - Bacterial cell wall, LPS, drugs
LIPOPOLYSACCHARIDE

- Endotoxin on surface of bacterial cell wall
- Lipid A as active component
- “Shock toxin”: Hypotension, peripheral shutdown
- Leucopaenia
- Activation of kinins and complement cascade
- Activation of macrophages and monocytes
- Inhibition of macrophage migration
- Inhibition of PMNs
- Vascular leakage and inflammation
Agenda

Fever - aetiopathogenesis

Fever - PUO and the rheumatic diseases

Fever - Periodicity and rheumatic disease: Childhood fevers

Fever - and vasculitis - A simplified Guide to Investigation
Fever as a symptom

- Pyrexia
- Joint and back pain
- Myalgia
- Weight loss
- Normochromic normocytic anaemia
- Skin rash
- Lympadenopathy
PUO

- Prolonged obscure fever > 3 weeks usually represents an atypical presentation of a well-known condition
- Pattern and periodicity rarely aid diagnosis
- Aggressive diagnostic efforts are usually justified - treatment
PUO without localising signs

INFECTION
NEOPLASIA
IMMUNOGENIC
INFLAMMATION
PUO - Don’t Forget...

- Factitious
- Drug induced (anti-TB, cyclophosphamide)
- Recurrent PEs
- Chronic granulomatous hepatitis
- Sarcoidosis
- Occult bowel inflammation
PUO without localising signs- 

Infection

Viral longterm infection: EBV CMV Chronic

Pyogens and Granulomatous triggers:

TB

Fungi (Candidiasis, histoplasma, actinomyces, coccidioidomycosis)

Tropical diseases and parasites (Malaria, Toxoplasmosis etc etc)
PUO with rheumatological signs - Infection

JOINTS -
Septic arthritis: Septic bursitis.
Aspirate and Culture for;
- Bacteria
- Fungi
- Parasites

BONES -
Osteomyelitis acute or chronic. Culture and biopsy with stains for;
- Bacteria including TB
- Fungi
- Parasites especially in HIV
PUO - “Arthritogenic” Bacteria with few localising signs

- TB
- Salmonella
- Brucella
Bacterial Endocarditis

- Systemic vasculitis
- Mimic of immunogenic disease
- Complement consumption and elevated ESR CRP
- Urinary RBC
- Disclosed by positive blood cultures except with difficult germs (Q fever, aspergillus)
BACTERIAL ENDOCARDITIS and Rheumatic Disease

- Infectious endocarditis has a higher incidence in SLE (infected Libmann-Sachs)
- Antibiotic prophylaxis of SLE patients pre-surgery
- Endocarditis in patients with RA and AS with aortic involvement
Fever, Infection and Rheumatic disease - ? A sterile joint

Viral septic arthritis (hepatitis B, AIDs) and reactive arthritis (parvovirus, measles etc)
Reiter’s Syndrome (sexually transmitted and GI infection)
Lyme disease
Venereal diseases (Syphilis, GC)
Mycoplasma
Fungal and protozoal (joint and bone)
Back Pain and fever

- Fever as an alert sign with back pain

**X RAY:FBC:CULTURE:SCAN:BIOPSY**

- **SPINAL** - Infected disc and vertebral lesions: TB 40%: Gram neg 20%: Staph 20%: Strep 20%.

- **PARASPINAL** - Psoas abscesses usually secondary to vertebral OM
PUO with arthralgia, myalgia and vasculitis - Neoplasia

- Lymphoma - endogenous pyrogens from Hodgkins LNs
- Leukaemia - Usually due to infections
- Solid Tumours - Hypernephroma, Pancreatic carcinoma, GI carcinoma (tissue necrosis and release of LPS)
PUO - Immunogenic

- Rheumatic fever
- RA - Adult Stills
- SLE
- Systemic Vasculitides
- JIA
- GCA - 15% PUO >65 years
Rheumatic Fever

MAJOR
- polyarthritis
- chorea
- carditis
- erythema marginatum
- sc nodules

MINOR
- fever
- arthralgia
- ESR
- CRP
- PR prolonged
Fever and RA

- RA - Activity
- RA - Infection - Beware the septic joint replacement
- RA - Vasculitis
- RA - Amyloid
- RA - Drugs
SLE and **Fever** - The usual diagnostic dilemma

**Activity OR Infection**

Clues to infection

- Clinical (Urinary frequency, CXR, Diarrhoea and rigors)
- Elevated CRP, leucocytosis, dsDNA titre low
- Lab tests (Cultures, Urinary sediment)

Consider **drug-induced, PEs, Malignancy**
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Childhood fevers and Arthritis

- Infection: Viruses and Streptococci
- Post-Viral reactive arthritis
- Post - Viral vasculitic syndromes
- JIA and Stills disease
Familial Mediterranean Fever

- Genetic: autosomal recessive Sephardic Jews and ethnic Armenians: Short arm of chromosome 16
- Childhood or early adolescence
- Brief high fevers at irregular intervals
- Peritonitis, arthritis and pleuritis
- Amyloid AA systemic as nephropathy
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Fever - and vasculitis -
A simplified Guide to Investigation
ABC of PUO - ? Vasculitis

A - Acute phase Proteins (ESR, CRP)
B - Blood tests - Other (U and E, LFT, CPK, ANA, ANCA, C3 and C4)
C - Cultures (Blood, MSU, throat swab, Stool)
D - Dipstix urinalysis and renal function
E - ECG/Echocardiogram
F - Films (CXR)
ABC of Vasculitis Investigation

More complex serology
Biopsy - liver, BM, Temporal artery
HIV
Cryoglobulins
Hepatitis serology
CSF
Neuroelectric
Summary

- Pyrexia is common in disease and does not usually aid diagnosis
- Do not ignore fever - investigate as it normally represents pathology
- Exclude infection especially SBE
- After investigation consider alternatives such as drug induced fevers/PEs
- Basic vasculitis work up