Rheumatic conditions in Human Immunodeficiency Virus infection

Dr G. Omondi Oyoo FACR
CONSULTANT PHYSICIAN AND RHEUMATOLOGIST,
SENIOR LECTURER, DEPARTMENT OF CLINICAL MEDICINE
AND THERAPEUTICS, SCHOOL OF MEDICINE; UNIVERSITY OF NAIROBI,
NAIROBI, KENYA.
Chairman, Association for Arthritis and Rheumatic Diseases of Kenya (AARD),
Chairman, Kenya Society for Rheumatology (KSR)
President-elect, African League of Associations for Rheumatology (AFLAR).
Country coordinator, Bone and Joint Decade (BJD), Kenya.
There are two primary choices in life, to accept conditions as they exist, or to accept the responsibility for changing them.

Denis Waitley
ASSUMPTIONS IN PREPARING THE TALK

- AUDIENCE IS PREDOMINANTLY NON RHEUMATOLOGISTS

- SINCE THE TALK IS IN THE AFTERNOON JUST BEFORE LUNCH, THE AUDIENCE IS PHYSICALLY AND MENTALLY EXHAUSTED

- TALK WILL BE MORE QUALITATIVE AND WILL STRESS KEY CONCEPTS
Introduction

- Increased musculoskeletal pathology in HIV infections
- Pre HAART era: 11% to 72%
- HAART era: Significant decline; New manifestations
Laboratory abnormalities

- Autoimmune phenomenon:
  - Polyclonal stimulation of B cells
  - Homeostatic expansion of T-Cells after initiation of HAART

- Presence of:
  - RF
  - Cold agglutinins
  - ANA
Laboratory abnormalities

- Anti-centromere antibodies
- Circulating immune complexes
- ANA
- ANCA
- aCL
- aPL
- anti-β2 glycoprotein 1
Overview of rheumatic manifestation in HIV infection

- Athralgia
- Arthritis
- Myalgia
- Rhabdomyolisis
- Muscle weakness
- Osteonecrosis
- Osteopenia/osteoporosis
- osteomalacia
- Osteomyelitis
- Vasculitis
- DILS
- Sarcoidosis
- Parotid lipomatosis
- SLE
Arthralgia

- Intermittent painful articular syndrome
- Occurs in 4-45% of cases
- Affects Knees, shoulders and elbows
- May require opioid analgesics
Arthritis

- HIV associated arthritis
- Reactive arthritis
- Psoriasis
- Gout

- Septic arthritis
- Articular complications of ARV therapy
- Cryoglobulinemia
HIV-Associated arthritis

- Non-erosive oligoarthritis of lower extremities
- Described in 10-12% of HIV patients
- Self-limited and lasts < 6 weeks
Reactive arthritis

- Asymmetric oligoarthritis
- Enthesopathy
- Sacroilitis
- Conjunctivitis, circinate balanitis, urethritis and Keratoderma blennorhagicum
- Occurs in 0.4-10 % of HIV infected subjects
- SSZ successfully used
- Dramatic improvement with effective HIV suppression or anti-TNF-α biologics
Psoriasis and PsA

- PsA incidence is 1-5-2%
- Severity of psoriasis parallels impairment of immune system
- HIV associated psoriasis improves with ARVs
- anti-TNF-α biologics have been successfully administered
Psoriasis
Septic arthritis

- Observed in 1% of HIV-infected individuals
- No clear association with CD4+ counts
- Risk factor is simultaneous intravenous drug abuse
- Affects young men
- Common in large weight bearing joints of the lower extremities and sternoclavicular joint
- CD4+ cells >250/µl-pyogenic organisms
- CD4+ cells <100/µl-opportunistic pathogens
Articular complications of anti-retroviral therapy

- Indinavir
  - Arthralgia
  - Monoarthritis
  - Oligoarthritis
  - Adhesive capsulitis
  - Crystal arthropathy

- Ritonavir & saquinavir
  - Joint pains
Gout in HIV infection

- Hyperuricaemia occurs in up to 42% of HIV infected patients
- Gout incidence is 0.5% (higher than normal population)
- Hyperuricaemia in HIV:
  - Increased cell turnover
  - ARVs
  - Saquinavir and didanosine (mitochondrial toxicity)
Prevalence of articular disease in HIV infection at KNH (n:193)

- **Articular disease 17% of total**

- **Types:**
  - HIV associated arthritis 0.5%
  - Undifferentiated spondyloarthropathy 1.0%
  - HIV associated arthralgia 15.6%

Etau et al 2008
Muscular complications

- Rhabdomyolysis
- Zidovudine myopathy
- HIV associated polymyositis
- Dermatomyositis
- Inclusion body myositis
- Nemaline rod myopathy
- Wasting syndrome
- Pyomyositis
Rhabdomyolysis

- Primary HIV infection
- Drug interactions
  - PI and statins
  - Abacavir hypersensitivity
  - Tenofovir
Zidovudine

- Interferes with replication of mitochondrial DNA
- Muscle weakness
- Normal serum CK
- Histology:
  - Ragged fibres in the Gomori Trichrome stain
- Histochemistry and electron microscopy:
  - High frequency of cytochrome c-oxidase negative fibres
- Prevented by uridine supplementation
- Resolves within months after drug cessation
HIV associated polymyositis

- In up to 2-7% HIV positive patients
- CD8+ T-lymphocyte infiltration
- Indistinguishable from idiopathic polymyositis
- Responds well to immunosuppressive therapy
- May resolve spontaneously
Dermatomyositis and inclusion body myositis

- Rarely observed in HIV infection
Nemaline rod myopathy

- Rare
- Progressive painless muscle weakness and wasting
- Elevated CK
- Muscle biopsy:
  - atrophic type I fibres
  - Intracytoplasmic nemaline rods
- Response to prednisone or plasmapharesis
Wasting syndrome in HIV

- Involuntary weight loss of at least 10% of body weight
- Persistent diarrhoea, weakness or fever
- Muscle biopsy:
  - Diffuse or type II fibre atrophy
  - Mild neurogenic atrophy
  - Thick filament loss
  - No inflammation
- Responds to ARVs
Pyomyositis

- Rare
- Male patients with low \(\text{CD4}^+\) cells
- *Staphylococcus aureus* most frequently isolated
Bone complications

- Osteonecrosis
- Bone mineral loss
- Osteomalacia
- Osteomyelitis
Osteonecrosis

- 100 fold risk of osteonecrosis in HIV infection
- Annual incidence-0.3 (symptomatic) to 0.7 % (asymptomatic)
- 4.4% hip joint—often bilateral, require hip replacement
- Due to:
  - Chronic inflammation
  - Corticosteroids in immune reconstitution
  - aCL
Bone mineral loss

- Osteopenia and osteoporosis
- Multifactorial causes:
  - HIV mediated immune activation
  - Cytokine release
- Respond to bisphosphonates
Osteomalacia

- Hypophosphatemia and elevated alkaline phosphatase
- Skeletal Scintigraphy: pseudofractures (Looser’s zones)
- Due to tenofivir toxicity
- Improve on discontinuation of tenofovir and supplementation of phosphates
Osteomyelitis

- Occur at lower CD4+ counts
- *Staphylococcus aureus* most frequently observed pathogen
- Polymicrobial infections are observed
Multisystem manifestations

- Vasculitis
- DILS
- Sarcoidosis
- SLE
Vasculitis

- Non-specific neutrophilic or monocytic vascular inflammation:
  - Heterogenous clinical features
    - Cutaneous rash
    - Peripheral neuropathy

- Cryoglobulinemia:
  - Palpable pupura, mononeuritis multiplex, arthralgia, nephrotic range proteinuria
  - Declines with HAART therapy
Vasculitis

- Polyarteritis nodosa
- Behcet’s disease
- Coronaritis
- Large vessel vasculitis with multiple aneurysms
- Cerebral vasculitis
  - Stroke-13% have vasculitis
  - Granulomatous angitis of CNS
DILS

- Bilateral painless parotid gland enlargement
- Lacrimal gland enlargement
- Sicca symptoms
- CD8+ lymphocytosis and CD8+ T cell infiltration of multiple organs
- Lymphoid interstitial pneumonitis
- ARVs therapy effective
Sarcoidosis

- Marked increase of CD4+ cells under HAART
- CD4+ lymphocytosis >200µl

- Improve with immunosuppression and discontinuation of HAART
SLE

- SLE improves in untreated HIV infection
- SLE flare with immune recovery under HAART
- SLE/HIV: clinical and laboratory similarities:
  - Oral ulcerations, sicca syndrome, alopecia, arthritis, fever and neuropathies
  - Leucopenia, lymphopenia, thrombopenia, ANA, hypergammaglobulinemia and aPLs
  - Anti HIV antibodies
Anti-rheumatics in HIV-infected individuals

- Indomethacin inhibit HIV replication
- SSZ used in SpAs ,does not adversely promote HIV replication
- MTX used with careful monitoring of HIV viral loads and CD4+ counts
- HCQ effective in HIV associated arthopathies
- HCQ in a dose of 800mg equal to zidovudine in controlling viral replication
Anti-rheumatics in HIV-infected individuals

- Anti TNF-α:
  - Good response in ReA, PsA and AS
  - No deterioration due to HIV disease
  - Safe in Hepatitis B and C co infection
  - Problem: intercurrent infections
Rheumatology Key messages

- HIV infection can underlie autoimmune disease
- DMARDs can be used in HIV patients with autoimmune disease
- Prospective data about the incidence of rheumatic conditions in HIV patients are needed
AFLAR: African League of Associations for Rheumatology

- 3rd Regional Rheumatology symposium and workshops
  - October 4 to 9, 2009
  - Lenana House conference centre, Nairobi, Kenya.

- 6th AFLAR Congress, Nigeria 2011
  - Details to be announced soon

- www.aflar.org
You have reached the pinnacle of success as soon as you become uninterested in money, compliments, or publicity

O. A. Battista
TIME TO WAKE UP
Shukran

- 감사합니다 (Korean)
- 感謝 (Chinese)
- Thank you (English)
- ありがとうございます (Japanese)
- Asante (Kiswahili)
- Gracias (Spanish)
- Merci (French)
Shukran

- Shukran (Korean)
- 謝謝 (Chinese)
- Thank you (English)
- ありがとう (Japanese)
- Asante (Kiswahili)
- Gracias (Spanish)
- Merci (French)
- Erokamano (Dholuo)
THE END