Genitourinary Tuberculosis

VGH Grand Rounds
March 2, 2005

Case Presentation

- 41 yo asian male
- Nocturia, frequency, gross hematuria X 6 mo’s
- Hx of urolithiasis
- U/A: RBCs, WBCs, protein (1g/L)
- Urine C&S = no growth

Non - Contrast CT : Feb 2004
Case Presentation

- urine $\rightarrow$ AFB positive
- $\rightarrow$ *M. tuberculosis* cultured
- Started on 4 drug Rx

Tuberculosis: History

7000 BC – 1800 AD

- "Consumption"
- "Phthisis"
- "Scrofula" – King’s Evil
- Endemic in 1700- 1800’s
- 25% of deaths in England
- Infectious nature determined 1860s

1882 Koch’s postulates

1. Organism in diseased animals
2. Organism grown in lab media
3. Innoculation $\rightarrow$ cause disease
4. Re-isolation

Armand Frappier fights “La Tuese de Maman”
Tuberculosis: Epidemiology

**TB Epidemiology**
- 1/3 world's population infected
- 8.3 million new cases in 2000
- 1.8 million died of TB in 2000
- Drug resistant Tuberculosis

**Epidemiology – Developing World**

**WHO estimate : TB Mortality**

**The Spread of TB : contributing factors**
- Growth of world's population
- Catalytic effect of HIV
- Poor control programmes
- Drug resistance
- Lack of political will and necessary resources

**Statistics Canada – 1926 → 1990**
Declining Mortality

- 1944 Streptomycin
- 1952 Isoniazid
- 1961 Ethambutol
- 1966 Rifampin
- 1975 Pyrazinamide

Declining Mortality: Canada

Epidemiology – British Columbia

People at risk

- Populations at risk for infection
  - Resource-poor countries
  - HIV

- Populations at risk for active TB disease
  - Immunocompromised - AIDS, malignancy, medications, Tx

- Risk factors for MDR TB
  - Hx of TB treatment, poor compliance, country of origin

TB and HIV

- TB = most common cause of death in HIV Px in developing world

- Lifetime risk of TB following infxn ~ 5-10% in immunocompetent individual

- HIV Px infxn → virtually all get TB
**Genitourinary TB**

- 1.2-2.6% of TB in 1st world
- 15-20% in developing countries

**Microbiology**

- Mycobacterium species:
  - *M. tuberculosis*
  - *M. bovis*
  - *Mycobacterium microti*
  - *Mycobacterium africanum*
  - *Mycobacterium avium*
  - *Mycobacterium intracellulare*
  - *Mycobacterium leprae*

*M. tuberculosis* – human only host

**Pathogenesis of M. tuberculosis**

- Invasion of host macrophages
- Dormant host cellular response

- Fibrosis
- Calcification
- Caseating granulomas

- 5-10%

- Reactivate

**Tuberculosis: Microbiology**

- *M. tuberculosis*:
  - Aerobic bacillus
  - Non-spore forming
  - Non-motile
  - Generation time 15-20hrs
  - 3-6wks to culture in media
GU TB: Clinical Presentation

Male (2:1), 20-40 y.o.

LUTS: storage symptoms, nocturia, frequency
Sterile pyuria, 20% w/out pyuria
10% gross hematuria, 50% microhematuria

Diagnosis

PPD skin test
AM urine ➔ AFB
Urine ➔ TB culture
Urine PCR
CXR

Caseating Granuloma

Clinical Presentation

PPD

48 hrs
Tuberculin skin test

- Intradermal injection of purified protein
- Inflammatory reaction develops @ site
- Measure of induration @ 48-72h
- Three cut-off points for induration
- Indication of previous exposure NOT active infection

Endoscopy

- Little role in establishing diagnosis
- Monitoring response
- Ureteroscopy to assess ureteral anatomy
- Bladder biopsy contraindicated in the presence of acute tuberculous cystitis

BCG Vaccine

- Attenuated strain of *M. bovis*
- Not used in most developed nations:
  - Offers variable protection
  - Risk of BCGitis

Renal Tuberculosis

Pathophysiology of Renal TB

- Tuberculi dormant in blood vessels
- Activation → immune Rx → caseation, fibrosis & Ca^{2+}
  - Papillary sloughing
  - Fibrosis & stricture
  - Viable bacteria w/in Ca^{2+} fibrotic tissue

Renal Tuberculosis: Radiology

- Early parenchymal TB
- Wedge-shaped hypoperfused segment of kidney
- Similar to bacterial pyelonephritis
Renal Tuberculosis: Radiology

- TB of the collecting system
- Infundibular stenosis
- Uneven caliectasis

Renal Tuberculosis: Radiology

- "putty kidney"
- Dystrophic calcification
- Result of poor Rx

Adrenal Tuberculosis: Radiology

- Can \(\rightarrow\) adrenal failure
- Post Rx\(\rightarrow\) calcification

Renal TB: pathology

- Organisms settle in medulla
- epithelioid granuloma w/ caseous necrosis + tissue destruction
- Spread to renal pelvis
- calcification, scarring

Renal TB: pathology

- Inflammation down ureter
- Destructive process \(\rightarrow\) autonephrectomy
- Local spread
- Squamous metaplasia

Renal TB \(\rightarrow\) renal failure

- Can be associated w/ GN & amyloidosis
- Associated w/ atypical interstitial nephritis
- 4.5% Px on dialysis in Greece
TB Ureter, Bladder & Urethra

Tuberculous ureteritis
- Result of renal TB
- Most common @ UVJ
- Edema, bullous granulation, ulcers

Tuberculous cystitis
- Chronic changes
- Fibrosis & fistulae
- "golf-hole" orifice

TB Urethra
- 16 cases reported
- Acute: purulent discharge
  - Medical Rx
- Chronic: urethral obstruction
  - DVIU followed by medical Rx

TB Epididymitis
- Inflamed scrotum, discharging sinus, infertility
- Men 20-40 yrs old
- >80% have extragenital TB
- Pulmonary ~80%, renal ~50%
- Mechanism of spread: direct, via GU tract, hematogenous? Sexual transmission

Genital Tuberculosis
- Epididymis
- Prostate
- Seminal vesicles
- Rarely testis
**TB Epididymitis**

- **DDx:** epididymo-orchitis vs GCT
- Often urine AFB negative
- Initial Rx vs STD
- ➔ Rx TB
- 3 wks no improvement ➔ inguinal exploration

**TB Epididymitis: Management**

- Medical Rx initially
- Intervention:
  - abscess
  - Sinus
  - R/O malignancy
  - Symptoms

**TB Testis & Prostate**

- TB testis secondary to TB epididymitis
- Difficult to differentiate from tumor
- Majority have extragenital TB as well
- "watering-can" penis & perineum

**King Edward Sanatorium, BC**
TB Treatment

Management of GU TB

1. Multimodal medical therapy
   - All pts receive chemotherapy for 6-9 months
     - Rifampicin 450 mg OD
     - INH 300 mg OD
     - Pyrazinamide 25mg/kg OD
     - Prednisolone 20 mg TID if edema, obstruction, cystitis
     - Rifampicin 900 mg + INH 600mg continuously, 3x week, or 2x week

Isonicotinic acid hydrazide (INH)

- Inhibits mycolic acid synthesis
- Bactericidal, caseous material
- 10-20 % hepatitis
- Peripheral neuropathy
- Require pyridoxine suppl

Rifampin

- Lipid soluble, bactericidal
- Inhibits RNA polymerization
- Significant drug interactions
- Hepatotoxic, flu-like Sx

TB Drugs

- **Streptomycin** – inhibits protein synthesis
  - Ototoxic, nephrotoxic
- **Pyrazinamide** – inhibits fatty acid synth
  - Hepatotoxic, hyperuricemia
- **Ethambutol** – bacteriostatic, cell wall inhib
  - Optic neuritis
TB: Surgical Treatment

Surgery for GU TB: Nephrectomy

- Indications for Nx:
  1. Nonfunctioning kidney +/- calcification
  2. Extensive disease with HTN and UPJO
  3. Coexisting renal carcinoma

Surgery for GU TB: Nephrectomy

- Non-functioning units → problems
  - Gow et al (1980) n=300 cases GU TB
  - N=73 w/ non-functioning units
  - N=4 Px managed w/out Nx
    - ¾ developed abscesses, sinus & HTN
- Non-functioning units harbour residual bacteria
  - Osterhage (1980) 50% of Px Rx’d for GU TB had residual Mycobacterium despite sterile urine

Partial Nephrectomy

- Rarely indicated w/ effective meds
- Two indications:
  - Localized polar calcified lesion that has failed intensive 6wk Rx
  - Area of calcification that slowly increasing in size → progressing to destroy kidney

Surgery: UPJ Strictures

- UPJ stricture late event
- Relief of obstruction: JJ stent or perc
- Antegrade instillation of TB meds
- If no resolution of UPJO w/ meds
  → surgery
- Pyelostomy essential

Surgery: Mid & distal strictures

- Mid ureteric strictures v. rare
  - JJ stenting w/ medical RX
  - Davis intubated ureterostomy
- Distal strictures
  - Medical Rx for 3 wks
  - If no change then corticosteroids for 3wks
  - If no change then dilatation or re-implantation
Stents: Mid & distal strictures

- Evidence that JJ stenting during medical Rx improves renal salvage
- Park et al (n=77) ureteral strictures
  - Meds plus stenting (n=28)
  - Meds alone (n=37)
  - Meds w/ PCN (n=19)
- Nx rate 73% w/out stent, 9% w/ stent

J Endourol. 2002 Dec;16(10):755-8

Dilatation: Distal Ureter

- Murphy et al (1982) n=97 distal ureteric strictures
  - 64% success initially
  - Dilation repeated until disease stable
  - Mean # dilations/Px = 4
  - Dilation requires anesthetic
  - Dilation not advocated

Distal Ureteric stricture

- Usu ~5cm, starting @ u.o.
- Pyelography used to assess muscular integrity of proximal ureter
- Distal resection @ re-implantation into unaffected area of bladder
- +/- Boari flap & psoas hitch, TUU

Bladder Augmentation

- Indications:
  - Intractible storage Sx
  - capacity <100cc’s
  - Creatinine clearance > 15ml/min
- Contra-indications:
  - Incontinence
  - Psychiatric disturbances

Epididymectomy

- Rarely indicated
- Two indications:
  - Caseating abscess not responding to medical Rx
  - Firm expanding mass despite medical Rx

Case Presentation
Case Presentation

- Ongoing frequency 15-25X/day
- Dec 12 2004 CT abdo
  - Increasing R hydro
  - Thickened R ureter fr sacral promontory → UVJ
Contrast CT w/ 10min delay
Conclusion

- Diagnosis requires high index of suspicion
- Many manifestations of disease
- Medical treatment prior to surgery