L2: Prolong fever

Tuberculosis

Learning objectives

At the end of this lecture, you should be able to:

- *Understand the common presentation of tuberculosis in children*
- *Approach to a child who is suspect to have tuberculosis through different diagnostic ways*
- *Describe drug regimens used in treatment of both pulmonary and extra pulmonary tuberculosis*
- *Discussion prevention methods to decrease incidence of TB*

Tuberculosis

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*. Tuberculosis continues to be an important cause of morbidity and mortality for children worldwide

Mycobacterium tuberculosis is the most important cause of tuberculosis(TB) disease in humans**,** The tubercle bacilli are non spore forming ,non motile , pleomorphic ,weakly gram-positive curved rod 1-5 µm long ,typically slender and bent ,the hallmark of all Mycobacterium is acid fastness

Mode of infection

- The infection is spread by the patient with tuberculosis, who discharges tubercle bacilli in his sputum or nasopharyngeal secretions during bouts of coughing or sneezing, etc. Such patients are open or infective cases.
- The usual mode of infection is through inhalation of droplets of infected secretions, This may be a source of infection through breathing
- Infection through ingestion of infected material is rare.
- Rarely infection may be transmitted through skin, mucous membrane or transplacentally.
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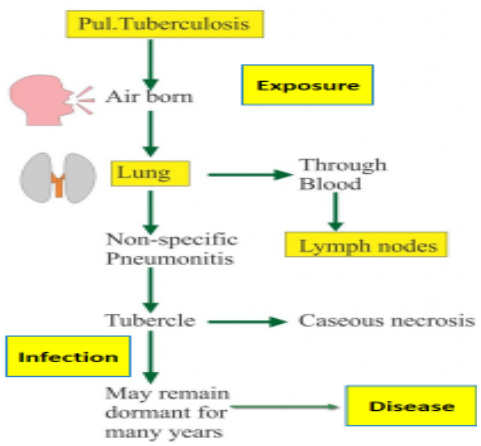
<u>The chance of transmission increases when the patient has:</u>

- ✓ Positive acid-fast smear of sputum
- ✓ An extensive upper lobe infiltrate or cavity
- ✓ Copious production of thin sputum, and severe forceful cough
- ✓ Environmental factors such as overcrowding, poor air circulation ,these factors enhance transmission.

- Most adults no longer transmit the organism within several days to 2 wk. after beginning adequate chemotherapy, but some patients remain infectious for many weeks.
- Young children with tuberculosis rarely infect other children or adults. Tubercle bacilli are sparse in the endobronchial secretions of children with pulmonary tuberculosis, and cough is often absent or lacks the tussive force required to suspend infectious particles of the correct size.

Pathogenesis

- **Primary complex (Ghon complex)** of tuberculosis includes local infection at portal of entry and the regional lymph nodes that drain the area
- lung is the portal of entry in 98%
- Mycobacterium tubercle bacilli cause damage by invading the macrophagic cells by Type IV hypersensitivity reaction.
- This bacteria leads to caseating necrosis and granuloma formation
- Viable tubercle can persist for decade



Clinical Stages

There are three major clinical stages of tuberculosis: exposure, infection, and disease

Exposure

- History of contact with TB patient
- Lack evidence of infection (no signs or symptoms)
- Negative tuberculin test and IGRA
- Normal chest x-ray

Infection(TBI), latent TB infection (LTBI)

- Occurs when the individual inhales droplet nuclei containing M. tuberculosis, which survive intracellularly within the lung and associated lymphoid tissue.
- The hallmark of TBI is a positive TST or IGRA result.
- In this stage the child has no signs or symptoms, a normal physical examination
- Chest radiograph is either normal or reveals only granuloma or calcifications in the lung parenchyma

Disease (Tuberculosis)

- Occurs when signs or symptoms or radiographic manifestations caused by M. tuberculosis become apparent
- Term tuberculosis usually referred to stage

- 10% of the latent TB develop active TB and its mainly occur when there is following risk factors::
  - Age of patient <5 year
  - Severe malnutrition
  - Immunosuppression
  - Enviromental factors
  - Intercurrent infection

Sites of Tuberculosis

- Primary infection most commonly occurs in the lung (pulmonary TB)
- It may also involve other organs including gut, skin CNS, bone and lymph nodes

Pulmonary TB:

Pulmonary TB course

- **Most cases** : resolving completely with appropriate treatment
- **Occasionally** : Residual calcification (6-12 month)
- **Progressive primary pulmonary TB :** (intra-pulmonary dissemination) is rare but serious complication of tuberculosis

Reactivation and post primary TB

This may present as local disease or may be widely disseminated **(miliary TB)** to sites such as bones, joints, kidneys, pericardium and CNS. In infants and young children, seeding of the CNS is particularly likely, causing **tuberculous meningitis**

Signs and symptoms suggest pulmonary TB

Symptoms

- **Persistent cough of 2 weeks or more** with or without Production of sputum which may be blood-stained not responding to non-specific treatment (including antibiotics with no anti-TB effect i.e. avoid Rifampicin, aminoglycosides and Quinolones)
- Fever for more than 2 weeks mainly at night.
- Night sweats
- Breathlessness
- chest pain
- loss of appetite and loss of weight
- History of contact sometimes could be detected.

Physical signs

- Physical signs are non-specific and may not be helpful in confirming the diagnosis
- Chest – there may be crackles in the lung apices more pronounced on deep breathing; localized wheeze in local obstruction or pressure: dullnes

➢ **Non-resolving pneumonia and LN enlargement**

Recommended approach to diagnose TB in children :

- Careful history including history of TB contact and symptoms consistent with TB
- Clinical assessment include growth assessment
- Radiological evaluation
- Bacteriological confirmation of AFB
- TST,IGAR,PCR

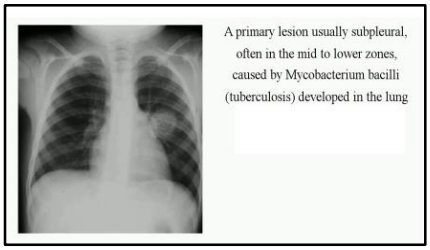
Bacteriological confirmation through

- **Sputum**
- **Gastric washings on three consecutive mornings :**
  Is required to obtain and culture acid fast bacilli that originate from lung , and its done through NG tube that passed and secretion are rinsed out of the stomach with saline before food

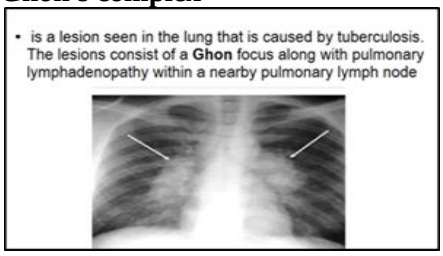
Radiological diagnosis

- **CXR**
  Hilar lymph node enlargement
  Parenchymal opacification
  Pleural effusion

Ghon focus



Ghon's complex



- **Chest CT scan**

TST (Tuberculin skin test) (Mantoux skin test)

- Intradermal injection of 0.1 ml PPD (Purified Protein Derivative)
- Only the induration should be measured (not the surrounding erythema) after 48-72 hours
- **Interpretation of Mantoux test :**

Size of induration	Interpretation
<5mm	Negative; no active disease
5-10 mm	Borderline; consider positive in immunocompromised host; contact with adult patient with sputum AFB positive tuberculosis
≥10 mm	positive; suggests disease in presence of clinical features

False positive TST

- Cross reaction with non tuberculous mycobacteria.
- Previous BCG vaccination

False negative TST

- Improper tech. and misreading
- Very young age
- Malnutrition
- Disseminated TB
- Steroid therapy
- Immunocompromised patient

Interferon-γ Release Assays (IGRAs)

- T– Cell based assay
- Advantage of IGRAs is the lack of cross reaction with BCG vaccination and most other mycobacteria

Treatment

- **6 month regimen** : of INH & Rifampicin with Pyrazinamide and ethambutol in the 1st 2 months then continue on INH & Rifampicin for the last 4 month
- Same regimen of treatment for **extra pulmonary TB** with long duration **9-12mo.**
- **TB Lymphadenitis**, is the same as for pulmonary TB regimen and duration.
- **The main TBI treatment regimens** used in children include 6-9 mo of isoniazid (daily, or twice weekly by DOT).

Directly Observed Therapy(DOT)

- Directly Observed Therapy is the World Health Organization (WHO) standard for treatment of Tuberculosis disease or LTBI
- DOT by definition means watching patient swallow each dose of anti-TB medication
- DOT has been shown to reduce the risk of drug resistance and to provide better treatment completion and compliance
- When DOT therapy is used, intermittent (twice or thrice weekly) administration of drugs after an initial period as short as 2 wk. of daily therapy, is as effective in children as daily therapy for the entire course.

Treatment

Drugs	Dose (mg) Daily/wk.	Dose(mg) Twice/wk. (DOT)	Side effects
Isoniazid(INH)	10-15	20-30	Mild hepatic enzyme elevation, peripheral neuritis, hypersensitivity
Rifampin	10-20	10-20	Orange discoloration of secretion or urine ,Hepatitis ,flu like reaction .pruritis, thrombocytopenia
Ethambutol	20	50	Optic neuritis ,GIT disturbances ,hypersensitivity
Pyrazinamide	30-40	50	Hepatotoxic effects,artheralgias,GIT disturbances,hyperuricemia

Role of Steroid in management of TB:

- Prednisolone 1-2 mg/kg/ day for 4-6 weeks are indicated in:
  - Meningeal and CNS TB.
  - Miliary TB
  - Endobronchial TB
  - Sever pleural effusion.

Prevention

- **Case finding& treatment.**
- **BCG Vaccination:**
  - **Vaccine Efficacy**: BCG is only 50% effective to prevent pulmonary TB. and 50-80% effective to protect against disseminated and meningeal TB.

Prevention of Perinatal Tuberculosis:

- If the mother has suspected tuberculosis at the time of delivery, the newborn should be separated from the mother until the chest radiograph is obtained:

  - If the mother's chest radiograph is abnormal, separation should be maintained until the mother has been evaluated thoroughly, including examination of the sputum. If the mother's chest radiograph is abnormal but the history, physical examination, sputum examination, and evaluation of the radiograph show no evidence of current active tuberculosis, it is reasonable to assume that the infant is at low risk for infection. The mother only should receive appropriate treatment

  - If the mother's chest radiograph or AFB sputum smear shows evidence of current TB disease, additional steps are necessary to protect the infant. Isoniazid therapy for newborns has been so effective that separation of the mother and infant is no longer considered mandatory. Isoniazid treatment for the infant should be continued until the mother is sputum culture negative for ≥3 mo. At that time, a Mantoux TST should be placed on the child:
    - If the test is positive, isoniazid is continued for a total duration of 9-12 mo.
    - If the test is negative, isoniazid can be discontinued.

- Once the mother and child are taking adequate therapy, it is usually safe for the mother to breastfeed, because the medications, although found in milk, are present in low concentrations.