

Lepra reactions

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Learning objectives

- Definition and types of reactions
- Etio-pathogenesis and precipitating factors
- Clinical features
- Differentiating between mild and severe reaction
- Differential diagnosis
 - A note on relapse
- Management of reactions

Definition

Acute episodic inflammation during the course of the illness

Due to abrupt change in immunological response of the body against *M. leprae*

It depends on Bacterial load in the body of PAL and
Strength of immunological response of the PAL

Time of onset

Before starting / During /After completion of the treatment

Sometimes reaction itself is a clinical presentation which helps in diagnosis.

- ❖ Diagnosis and Management of reactions is very important as Patients developing reactions are at a higher risk of developing disabilities and deformities compared to others.

Risk of reaction

- Multiple lesions (LL with skin infiltration)
- BI >4+
- Age <40
- Lesion close to the peripheral nerve
- Lesion on the face
- Patient with nerve thickening with/without NFI

Precipitating factors

- Infection and infestation
- Anti leprosy drugs except CLF
- Vaccination
- Hormonal changes : Puberty, Pregnancy and Childbirth
- Psychological stress

Types

1. Type 1 reaction or reversal reaction
2. Type 2 reaction or Erythema Nodosum
Leprosus

Type 1 reaction

- Also called as Reversal Reaction and can occur in any patient with unstable CMI .

Etiopathogenesis :

- It is the Increased activity of cell mediated immune response fighting the leprosy bacillus or remnants of dead bacilli.
- A kind of type 4 hypersensitivity reaction.

Clinical features:

Inflammation of skin lesions – red, prominent, swollen and sometimes painful.

Appearance of new skin lesions.

Sudden Increase in size of the existing lesion.

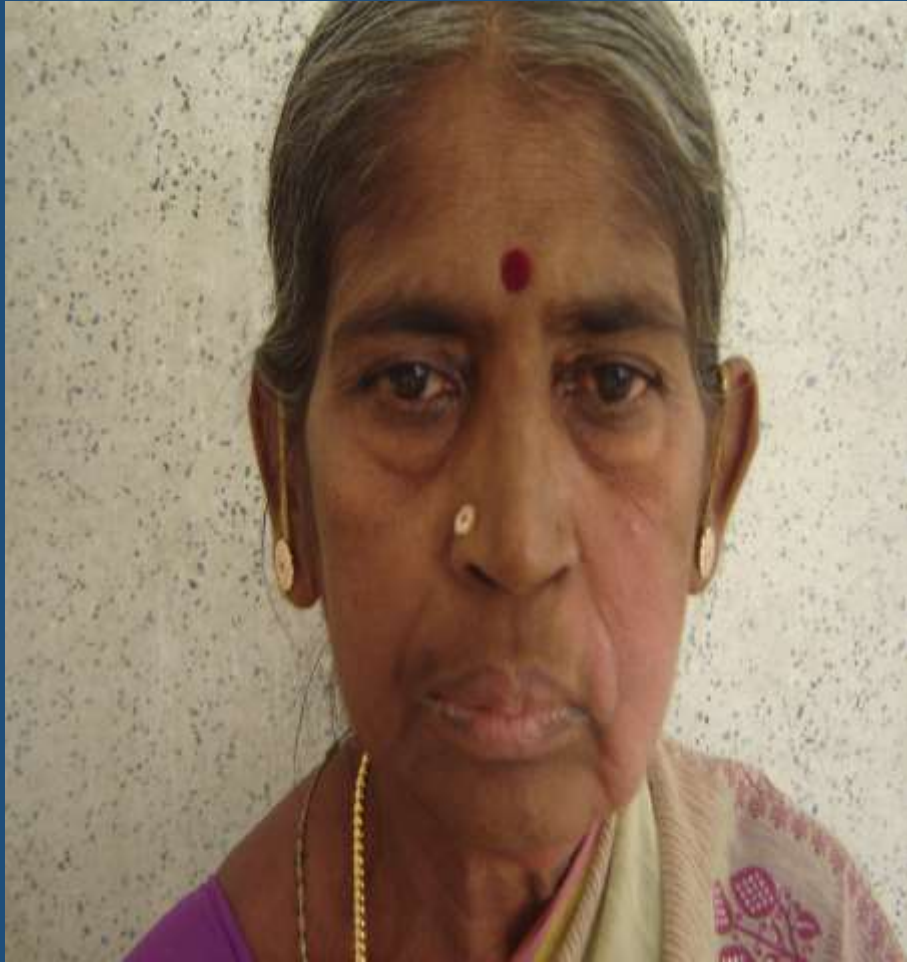
Involvement of nerves:

Acute neuritis- sometimes leads to nerve abcess.

Silent neuropathy /quiet nerve paralysis

Swelling of hands and feet rarely

Type 1 reaction





Nerve abscess







Difference between mild and severe Type 1 reactions

Mild type 1 reaction

- Occurs in some of the pre-existing skin lesions only (**Other than those on face**)
- Erythema and swelling of skin lesions **without ulceration**
- **Nerves** are not affected
- No constitutional symptoms
- No edema of hands and feet

Severe type 1 reaction

- An erythematous, swollen skin patch **on the face** around the eye
- Red, painful, inflamed skin lesions **with ulceration**
- Pain or tenderness in one or more nerves with or without loss of nerve function
- Skin lesion overlying major nerve trunk
- Constitutional symptoms
- edema of the hands, feet or face
- Clinically mild reaction not responding to NSAIDs for a period of 2–4 weeks

Differential diagnosis of type 1 reaction

- Acute urticaria
- Erysipelas
- Cellulitis
- Insect bite reaction
- Relapse confusing with late reversal reaction

Type 2 reaction

- Also called as Erythema Nodosum Leprosum (ENL) and occurs usually in patients with MB Leprosy having a heavy load of bacilli.

ETIO-PATHOGENESIS :

- Antigens from the dead bacilli provoke an arthus type allergic reaction producing antigen antibody immune complexes in the presence of complement system.
- Immune complexes are precipitated in the tissues (skin, eyes, joints, lymph nodes, kidneys, liver, spleen, bone marrow, endothelium and testes) as well as in the circulation. A kind of type 3 hypersensitivity reaction. Therefore it can involve multiple organs and systems.

Clinical features

Type 2 reaction can involve multiple organs & systems, causing generalized symptoms like fever, headache and body ache appear before or along with the characteristic nodules that appear on the skin.

Skin lesions- red, firm, painful, tender cutaneous and subcutaneous **nodules** (about 1–2 cm across) and variable sized **plaques** appear in crops. Usually multiple, they tend to be distributed bilaterally and symmetrical. Some times break down and suppurate / necrose producing ulcerative ENL(**Erythema Nodosum Necroticans**).

Swelling of hands and feet: Often there is oedema of face, hands and feet

- Nerves may also get affected in type 2 reactions
- Iritis or iridocyclitis (inflammation of the iris and ciliary body)
- Impairment of vision. Eye becomes red, watery and painful
- Photophobia (pain in the eye when it is exposed to light)
- Periosteal pain (especially tibia) and muscle pain Arthritis, tendinitis, rhinitis, epistaxis
- Painful dactylitis, lymphadenopathy
- Acute epididymo-orchitis
- Hepato-splenomegaly with hepatitis
- Endocarditis with/without arrhythmia
- Glomerulonephritis







Pustular ENL



Difference between Mild Type 2 and Severe Type 2 Reactions

Mild type 2 reaction

- Intermittent crops of **few nodules**
- Nerves are **not affected**
- **Mild fever** (less than 100 F) may or may not be present
- **No other organs involved**

Severe type 2 reaction

- Red, painful, multiple nodules in crops
- Pain or tenderness in one or more nerves with or without loss of nerve function
- ENL that becomes ulcerated
- Accompanied by a high fever (>100 F)
- Pain and/or redness of the eyes with or without loss of visual acuity (Involvement of eye)
- Generalized symptoms with painful swelling of the small joints with fever
- Recurrent ENL (more than four episodes in a year)
- Clinically mild reaction not responding to NSAIDs and/or within 2–4 weeks.
- Enlargement of Lymph glands/testes with pain, Involvement of other vital organs is seen

Note :

- ENL reaction may become **chronic** (when the condition persist for more than **three months** in spite of adequate treatment) or
- May become **recurrent** (when more than **four** episodes are observed in a year)

Lab tests

These are used to assess the severity of the reaction

- CBC-Leukocytosis
- ESR increased
- CRP elevated
- LFT- may be mildly increased
- RFT
- Urine analysis

	Signs		Type 1		Type 2	
Type of reaction			Cell mediated Delayed Hypersensitivity		Antigen antibody (Immune complex), reaction	
Inflammation of the skin			Skin lesions suddenly becomes large/reddish, swollen, warm, painful and “fresh” lesions may be noticed		Red, painful, tender, cutaneous/subcutaneous nodules appear . ENL may appear commonly on face, extensor surfaces of arms and legs.	
Nerve involvement			Early, common, severe		Nerves may be affected .	
General condition (Constitutional symptoms)			Good		Poor, with prominent fever and general malaise	
Eye involvement			Lagophthalmos , sensory impairment of cornea		Internal eye disease (iritis, iridocyclitis) occurs, lepromatous nodules are seen.	
Other Organs/Tissues			Not affected		May be affected	

- Type 1 reaction must be differentiated clinically from T2R
- **Cutaneous drug reaction** : In some of these reactions the patients complain of itching or wheals formation that is not seen in Leprosy reactions.
- **Localized pyodermas**
- ENL lesions differ clinically from **erythema nodosum** seen in other conditions like **tuberculosis, streptococcal and viral infections and sarcoidosis**, by the fact that the lesions in other cases persist for longer duration (other lesions last up to 7 days) and requires longer therapy, whereas ENL lesions of lepra reactions do not last longer.
- **Relapse**: In relapse new lesions appear and are insidious not acute in appearance, not associated with pain/tenderness over old lesions.

- **Diabetes:** Diabetics are prone to infections as well as development of peripheral neuropathy. Therefore all patients should be screened for diabetes
- **Disk prolapse:** Patient may present with acute onset neuropathy of lower limbs. Patient usually gives history of straining the back or lifting heavy object before the onset.
- **Rheumatic fever:** Patients may develop fever with joint pains and **transient skin rash** usually in a young patient, ASO titre elevated.
- **Rheumatoid arthritis:** This condition can present in women of reproductive age group with skin eruptions, fever, joint involvement, deformities and multiple organ system involvement. RA factor is detectably raised or anti ccp may be positive.
- **Molluscum contagiosum**
- **Neurofibromatosis**
- **Histoid leprosy**

HISTOID LEPROSY



RELAPSE

- Relapse is defined as the re-occurrence of the disease at any time after the completion of a full course of treatment
- It can occur both in PB as well as MB cases
- Relapse is characterized by appearance of new skin lesions or nerve involvement where It should be differentiated from type 1 lepra reaction

PREDISPOSING FACTORS FOR RELAPSE:

1. Inadequate therapy- mis-categorisation
2. Irregular therapy – noncompliance from the patient part or defaulter
3. Monotherapy – chances of DRUG RESISTANCE
4. High initial B.I
5. Persisters –patients may have dormant organisms that have capacity to survive despite adequate therapy

Difference between relapse and lepra reaction

criteria	relapse	lepra reaction
Time since completion of treatment	appears usually later	usually early
History of type 1 reaction while on treatment	Variable	Usually positive
Progression of signs and symptoms	slow	fast
Site of skin lesions	Usually at new places	Usually over old patches
Skin-Pain, tenderness or swelling of patches	No	May be present
Nerve –Neuritis	Usually absent	May be present

MANAGEMENT OF REACTIONS

Principles of Management of reactions

For both type 1 and type 2 reaction :

- Anti leprosy drugs to be continued
- Counseling to relieve stress
- Treatment of intercurrent infection and infestation
- Anxiolytics

For neuritis : 1. Rest to the affected nerve using splint that is applied by involving joint in the vicinity of affected nerve
2. Surgery: surgical decompression of nerve.

Management of mild type 1 and type 2 reactions : NSAIDS, reassurance and treated symptomatically without steroids.

Management of severe type 1 and type 2 reactions :

Admission, Bed rest and watch vitals regularly

Analgesics

I.V fluids

Antibiotics

Prednisolone: drug of choice for severe reaction in both types.

Duration of treatment is 12 - 24 weeks

1.Tab. prednisolone dose at 1 mg/kg body wt/day, assess fortnightly,

In neuritis treatment may be prolonged.

2.After the reaction/inflammation is controlled, it is tapered.

Side effects of steroids

Edema and weight gain-cushingoid appearance

Gastritis

Diabetes

Hypertension

Glaucoma

Cataract

Flare up of Any infection

Osteoporosis

Avascular necrosis

❖ Recording of steroid treatment is very much necessary.

Alternative drugs for only type 2 reaction:

1. CLOFAZAMINE
2. THALIDOMIDE

These are second line drugs in treatment of ENL.

Indications:

Persons who suffer from

- persistent or chronic ENL.
- Recurrent ENL.
- Difficult to wean off from steroids.
- Developed severe side effects of steroids
- Requiring high doses of steroids for prolonged duration.

Clofazimine :

It is less potent than steroids and often takes 4 – 6 weeks to develop its full effect

Total duration of clofazimine therapy should not exceed 12 months

One capsule (100mg) 3 times a day x 12 weeks

One capsule (100mg) 2 times a day x next 12 weeks

One capsule (100mg) once a day x next 12 wks

S/E : Pigmentation, ichthyosis

Hepatitis

Pseudo intestinal obstruction- C/I in <7 years of age



THALIDOMIDE:

very effective in moderate to severe ENL

used as monotherapy or in combination with steroids

- TNF alpha blocking property
- It has rapid onset of action unlike CLF
- It reduces the prednisolone requirement

S/E : Peripheral Neuropathy

Pruritus (increase in AEC)

Arrhythmia, Venous thrombo embolism

Hypotension

Teratogenicity

C/I : Women In Reproductive Age Group. Therefore It is only recommended in tertiary care hospitals after taking necessary **consent**.

Table 4: Thalidomide Data

Drugs	Indications	Dosage
C.Thalidomide	<p>1.In post menopausal Women and male with severe ENL.</p> <p>2.Steroid dependent / Clofazimine unresponsive patients</p> <p>3.Steroid and Clofazimine contraindicated patients.</p> <p>4.Steroid induced complication patients.</p>	<p>Monotherapy (not in neuritis) 400mg /day, Maximum dose should be at night time at initial presentation.</p> <p>Dose is reduced as per patients clinical response.</p> <p>C.TLD 100mg TDS X 1 Month (increased / reduced) as per response</p> <p>C.TLD 100mg BD X 1 Month (increased / reduced) as per response</p> <p>C.TLD 100mg OD X 1 Month (increased / reduced) as per response.</p> <p>Latter alternative days and thrice a week and weekly once and stopped(Tapering is based on patients satisfactions only)</p>

Side effects



Thank you