

ERYTHEMA NODOSUM

Introduction

Erythema nodosum is an acute, nodular, erythematous eruption that is usually limited to the extensor aspects of the lower legs.

Chronic or recurrent erythema nodosum is rare but may occur.

It is presumed to be a hypersensitivity type reaction and may occur in association with several systemic diseases or drug therapies, or it may be idiopathic.

Pathophysiology

Erythema nodosum is currently thought to be a delayed hypersensitivity type reaction to a variety of antigens.

Circulating immune complexes have not been found in idiopathic or uncomplicated cases but have been demonstrated in patients with inflammatory bowel disease

Causes

1. Primary or Idiopathic.
2. Infections:

Associations have included:

- Streptococcal infections, (most common bacterial association)
- Tuberculosis
- Gastrointestinal bacterial infections, including, Yersinia enterocolitica, Campylobacter and Salmonella
- Mycoplasma pneumoniae

2. Autoimmune disease:

There are associations with:

- Sarcoidosis

♥ The most common cutaneous manifestation of sarcoidosis is erythema nodosum

- Inflammatory Bowel Disease

♥ Ulcerative colitis.

♥ Crohn's disease.

- SLE

- Behcet's Disease

3. Drugs:

Associations have included:

- Sulphonamides.
- Oral contraceptive.
- Sulfonylureas.

4. Pregnancy

6. Malignancies:

- Lymphomas.
- Leukaemia

Clinical Features

Peak age incidence is 18-35 years, but this will also depend on the etiology. It may be seen in children and the elderly.

Points on history:

1. This should be directed around the known associations of erythema nodosum, as above.
2. With respect to the lesions themselves:
 - The eruptive phase of erythema nodosum often begins with flulike symptoms of fever and generalized aching.

- Arthralgias may occur and precede the eruption or may appear during the eruptive phase.
- Most lesions in infection-induced erythema nodosum heal within 7 weeks, but active disease may last up to 18 weeks.
- In contrast, 30% of idiopathic erythema nodosum cases may last more than 6 months.
- Febrile illness with dermatologic findings includes abrupt onset of illness with initial fever, followed by a painful rash within 1-2 days.

Points on examination:

Most physical findings will relate to the skin lesions themselves and the joints.

1. Primary skin lesions:

- Lesions begin as red tender nodules.
- Lesion borders are poorly defined, and lesions vary from 2-6 cm.
- During the first week, lesions become tense, hard, and painful; during the second week, they may become fluctuant, as in an abscess, but do not suppurate or ulcerate.
- Individual lesions may last approximately 2 weeks, but occasionally, new lesions continue to appear for 3-6 weeks.
- Aching legs and swelling ankles may persist for weeks.

2. Distribution of skin lesions:

- Characteristically, lesions appear on the anterior leg; however, they may less commonly appear on any surface.

3. Color of skin lesions:

- Lesions change color in the second week from bright red to bluish or livid.
- As absorption progresses, the color gradually fades to a yellowish hue, resembling a bruise.
- This disappears in 1 or 2 weeks as the overlying skin desquamates.

4. Joints:

- Arthralgia occurs in more than 50% of patients and begins during the eruptive phase or precedes the eruption by 2-4 weeks.
- Erythema, swelling, and tenderness occur over the joint, sometimes with effusions. Joint tenderness and morning stiffness may occur.
- Any joint may be involved, but the ankles, knees, and wrist are affected most commonly.
- Synovitis resolves within a few weeks, but joint pain and stiffness may last up to 6 months. No destructive joint changes occur.
- Synovial fluid is acellular, and the rheumatoid factor is negative.

Differential Diagnosis

These include:

1. Cellulitis, (most commonly)
2. Burns
3. Trauma, (recent bruising)
4. Urticaria
5. Insect bites.



Typical Erythema Nodosum lesions.

Investigations

These will be guided by the index of suspicion for any of the known associations, but the following will need to be *considered*:

1. Throat swab for micro and culture to exclude group A beta-hemolytic streptococcal infection.
2. ESR, (is often high)
3. Antistreptolysin titer is elevated in some patients with streptococcal disease.
4. Faecal micro and culture, if an infectious gastroenteritis is suspected.
5. Intradermal skin tests can be used to exclude tuberculosis if there is clinical suspicion for this.
6. CXR
 - Look for hilar lymph nodes. Hilar adenopathy may develop as part of the hypersensitivity reaction of erythema nodosum.
 - Bilateral hilar lymphadenopathy is associated with sarcoidosis, while unilateral changes are more commonly associated with infections and malignancy and TB.
7. Biopsy
 - Erythema nodosum is most commonly a clinical diagnosis.

Biopsy may be done when the diagnosis is unclear. Punch biopsies usually are not adequate. Deep skin incisional biopsies are required to sample the subcutaneous tissue adequately as diagnostic findings are localized to the subcutaneous tissue.

Miescher granulomas are a hallmark feature of erythema nodosum.

Management

1. Referrals
 - To dermatologist may be necessary.
 - To a general medical or rheumatology unit may be necessary to further investigate an underlying cause.
2. Treat any underlying causative pathology.

3. Cease any causative drug treatment.
4. Erythema nodosum in most cases is a benign and self-limited disease and will require only symptomatic treatment.

- NSAIDs:¹

Ibuprofen 400 mg orally, twice daily.

- Corticosteroids:

If symptoms are severe and there are no contraindications (eg related to the cause), steroids can be used and are effective.

Prednisolone 37.5 to 50 mg (0.75 mg/kg) orally, once daily for 2 weeks with stepwise reduction according to response thereafter.¹

References

1. Dermatology Therapeutic Guidelines 3rd ed 2009

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