

Erythema Nodosum

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KEYWORDS

- Septal panniculitis • Erythema nodosum
- Miescher radial granuloma

Erythema nodosum is the most frequent clinico-pathologic variant of panniculitis. The disorder usually exhibits an acute onset and is clinically characterized by the sudden eruption of erythematous tender nodules and plaques located predominantly over the extensor aspects of the lower extremities. The lesions show spontaneous regression, without ulceration, scarring, or atrophy, and recurrent episodes are not uncommon. Erythema nodosum is a cutaneous reactive process that may be triggered by a wide variety of possible stimuli; infections, sarcoidosis, rheumatologic diseases, inflammatory bowel diseases, medications, autoimmune disorders, pregnancy, and malignancies are the most common associated conditions.

ETIOLOGY

Erythema nodosum may be associated with a wide variety of disease processes and its observation must always be followed by a search for underlying etiology. A review of the literature reveals that the list of etiologic factors that can lead to erythema nodosum is long and varied, including infections, drugs, malignant diseases, and a wide group of miscellaneous conditions (**Box 1**).^{1–104} Although there are considerable geographic variations related to endemic infections, in Spain streptococcal infections are the most frequent etiologic factor for erythema nodosum in children, whereas other infectious processes, drugs, sarcoidosis, autoimmune disorders, and inflammatory diseases of the bowel are the most commonly associated disorders in adults.

The relationship between a previous episode of upper respiratory infection by group A β -hemolytic

streptococcus and erythema nodosum is well-known, especially in children and young adults. Usually, the cutaneous lesions appear 2 or 3 weeks after the throat infection and they are accompanied by an elevation of the antistreptolysin O titer. An intradermal positive test to streptococcal antigens is often seen in patients with erythema nodosum secondary to streptococcal infections, although when the cutaneous nodules develop the cultures of routine throat swabs usually do not detect microorganisms.^{22,104}

Tuberculosis is now an uncommon etiologic factor for erythema nodosum in Spain¹⁰⁴ and other areas of southern Europe.^{105,106} These cases are seen mostly in children and the cutaneous lesions usually indicate a primary pulmonary infection, being concomitant with the conversion of the tuberculin test.²⁴

Drugs are frequently implicated as the cause of erythema nodosum. Sulphonamides, bromides, and oral contraceptive pills have been long recognized as the most common medications responsible for acute bouts of erythema nodosum, but the list of possibilities is very large (see **Box 1**). In recent years, the amount of hormones in contraceptive pills has been lowered markedly, and erythema nodosum secondary to this medication is now rare. In those cases in which the patient develops erythema nodosum when an antibiotic is taken for an infectious disease it is difficult to discern whether the cutaneous reaction is caused by the antibiotic or the infectious agent.

Sarcoidosis constitutes one of the most common etiologic factors in adult patients with secondary erythema nodosum in Spain.¹⁰⁴ In some countries, especially in northern Europe,

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Box 1**Etiologic factors in erythema nodosum***Infections***Bacterial infections**

- Atypical mycobacterial infections²
- Borrelia burgdorferi* infections³
- Boutonneuse fever⁴
- Brucellosis⁵
- Campylobacter* infections⁶
- Cat-scratch disease⁷
- Chancroid²
- Chlamydia psittaci* infections⁸
- Corynebacterium diphtheriae* infections²
- Escherichia coli* infections¹⁰⁴
- Gonorrhea⁹
- Klebsiella pneumoniae* infections¹⁰
- Leptospirosis¹¹
- Lymphogranuloma venereum¹²
- Meningococcemia¹³
- Moraxella catarrhalis* infections¹⁴
- Mycoplasma pneumoniae* infections¹⁵
- Pasteurella pseudotuberculosis* infections¹⁶
- Propionibacterium acnes*¹⁷
- Pseudomona aeruginosa* infections¹⁸
- Q fever¹⁹
- Salmonella* infections²⁰
- Shigella* infections²¹
- Streptococcal infections²²
- Syphilis²³
- Tuberculosis²⁴
- Tularemia²⁵
- Yersinia* infections²⁶

Viral infections

- Cytomegalovirus infections²⁷
- Hepatitis B²⁸
- Hepatitis C²⁹
- Herpes simplex²
- HIV infection³⁰
- Infectious mononucleosis³¹
- Measles³²
- Milker's nodules³³
- Parvovirus B19 infections³⁴
- Varicella³⁵

Fungal infections

- Aspergillosis³⁶
- Blastomycosis³⁷

Coccidioidomycosis³⁸Dermatophytes³⁹Histoplasmosis⁴⁰**Protozoal infections**

- Amebiasis⁴¹
- Ascariasis⁴²
- Giardiasis⁴¹
- Hydatidosis⁴³
- Hookworm infestation²
- Sparganum larva*⁴⁴
- Toxoplasmosis⁴⁵
- Trichomoniasis⁴⁶

Drugs

- Acetaminophen⁴⁷
- Actinomycin-D⁴⁸
- All-*trans* retinoic acid⁴⁸
- Aminopyrine²
- Amiodarone⁴⁷
- Amoxicillin¹⁰⁴
- Ampicillin¹⁰⁴
- Antimony²
- Arsphenamine⁹
- Azathioprine⁴⁷
- Bromides⁴⁹
- Busulfan⁴⁷
- Carbamazepine⁴⁷
- Carbenicillin⁵⁰
- Carbimazole⁴⁷
- Cefdinir⁴⁷
- Chlordiazepoxide⁴⁷
- Chlorotrianisene⁴⁷
- Chlorpropamide⁴⁷
- Ciprofloxacin⁴⁷
- Clomiphene⁴⁷
- Codeine⁴⁷
- Cotrimoxazole⁴⁷
- D-penicillamine⁵¹
- Dapsone⁴⁷
- Diclofenac⁴⁷
- Dicloxacillin⁴⁷
- Diethylstilbestrol⁵²
- Disopyramide⁴⁷
- Echinacea herbal therapy⁵²
- Enoxacin⁴⁷
- Erythromycin¹⁰⁴
- Estrogens⁴⁷
- Fluoxetine⁴⁷

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