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STREPTOCOCCI RELATED CHRONIC RELAPSING ERYTHEMA NODOSUM: A RARE CASE REPORT AND A BRIEF REVIEW OF LITERATURE

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ABSTRACT

We report an 19-year-old boy who presented with multiple recurrent nodular lesions over arms and painful reddish nodular lesions over both legs and thigh region of 6 months duration. He was diagnosed to have Streptococci related chronic relapsing erythema nodosum on the basis of clinical presentation and laboratory findings. All other common & numerous causes of Erythema Nodosum were ruled out. Throat swab/culture evaluation for group A streptococci was positive and streptococcal antistreptolysin-O (ASO) titers were high. Erythema Nodosum is an acute, tender, erythematous, subcutaneous nodular eruption that is typically located symmetrically on the extensor aspects of the lower extremities. Chronic or recurrent erythema nodosum is rare but may occur, incidence being two to three cases/100,000 persond per year[27]. Female/ male ratio of 3 to 4:1 and predominant age is 25 to 40 year.

KEY WORDS: Erythema nodosum, Panniculus, Inflammatory bowel disease.

INTRODUCTION

Erythema nodosum is basically panniculitis and affects the subcutaneous fat in the skin, usually first evident as erythematous nodules that are highly sensitive to touch.[1] Most nodules are located symmetrically on the ventral aspect of the lower extremities. Although erythema nodosum usually has no specific documented cause, it is imperative to investigate

possible triggers. Drug and hormonal reactions, inflammatory bowel disease (I BD), tuberculosis, leprosy and sarcoidosis are other common causes among adults.[2] Often, erythema nodosum may be a sign of a serious disorder which may be potentially treatable; management of an underlying aetiology is the most definitive means of treating erythema nodosum. In adults, erythema nodosum is more common among women, with a male:female ratio of 1:6.[3] In children, both the genders are equally affected. Age and gender distribution vary according to the etiology and geographic location.[4]

CASE REPORT

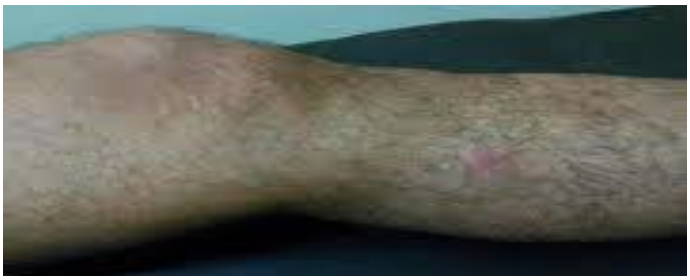
An 19-year-old boy, presented with chief complaints of febrile illness, large joint pain, multiple, nodular lesions over arms, shoulders and painful reddish nodular lesions over both legs and thigh region & knee, ankle and wrist pain of six months duration. Patient was apparently well till six months back when he noticed painful nodules over the arms. The nodules were initially red in color. Later, they became hyperpigmented over a period of one month. Similar nodular lesions were also seen on forearms, legs and thigh region. The lesions usually manifested after a febrile episode.

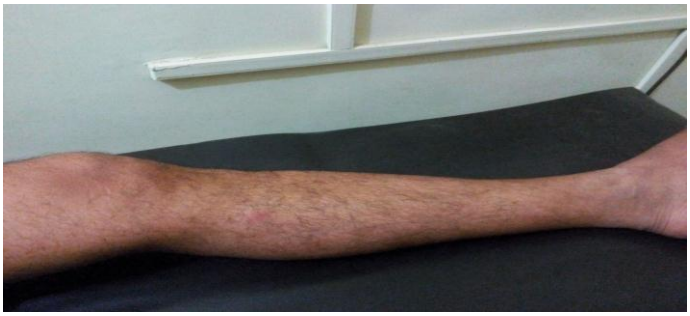
The patient also complained of loss of appetite, loss of weight associated with abdominal pain, and generalized weakness. He had experienced two episodes of similar nature prior to the present episode. The first episode occurred four years back with painful eruptions restricted to anterior tibial surface which resolved over a period of 6-8 weeks, without any sequelae. Six months aftert he first episode, he again developed painful nodules on the shin on both sides and the arms as well. For these earlier episodes, he had taken treatment from a local practitioner after which he had improved symptomatically. There was no history of diabetes meiilitus, tuberculosis, bronchial asthma or hypertension.

General physical examination revealed that he was in distress and was looking ill. His body weight was 54 kg. He was febrile (101°F), blood pressure was 120/70 mm Hg, pulse 90/min, respirations 18/min. Pallor was present; there was no icterus or lymphadenopathy. Oedema was evident over left foot.

Systemic examination was unremarkable. Dermatological examination revealed poorly defined, erythematous, painful nodules over the extensor aspects of the legs and the arms, bilaterally(picture). The lesions were firm and tender. The lesions were warm and very tender

to touch. Fresh nodules continued to appear on the legs & arms over a period of 3 weeks interspersed with febrile episodes.





Laboratory investigations revealed haemoglob 9.5 g/dL; total leucocyte count 22400/ mm^3; with a differential count of neutrophils 70%, lymphocytes 30% ; platelet count 160,000/ mm^3; red blood cell (RBC) 2.79 count/mm^3; mean corpuscular volume 89. 9 fL; mean corpuscular volume 25%; mean corpuscular haemoglobin 30.6 pg; erythrocyte sedimentation rate 45 mm at the end of first hour; blood urea 16 mg/dL serum creatinine 0.72 mg/dL;; serum sodium 119 mEq/L; serum potassium 3 mEq/L; ionic calcium 1.03 mmol/L; serum calcium 8 mg/ dL; total serum proteins 6. 5 g/ dL; serum albumin 2.6 g/dL; serum bilirubin 0.39 mg/ dL, alanine aminotransferase 20 IU/L, aspartate aminotransferase 30 IU/L, serum alkaline phosphatase 150 IU/L; serum T 3 0.982 ng/mL. T 4 24 mg/dL, serum thyroid stimulating hormone 1.31 IU/mL; C-reactive protein tested positive; antinuclear antibody negative; rheumatoid factor negative; hepatitis B surface antigen negative. Serological testing for hepatitis C virus and human immunodeficiency virus were negative. Urinalysis was normal. Throat swab/culture evaluation for group A streptococci was positive and streptococcal antistreptolysin-O (ASO) titers was too high.

He was put on short steroid therapy (methyl-prednisolone 1 gm i.v.) for 3 days and salycilates for his arthritis. He also received Penidura prophylaxis for five years. Till 5 years he did not have any relapse. He was then started on oral prednisolone 10 mg once daily for 15 days and

hydroxychloroquine 200 mg twice daily for 2 months along with haematinics to which patient has responded satisfactorily.

The patient has been under follow up and after 1 month of treatment, his lesions were decreased and he did not have any complaint. This case has been presented with a view to highlight the entity of Streptococci related chronic relapsing erythema nodosum.

DISCUSSION

Erythema Nodosum is a nodular painful syndrome which results from a hypersensitivity reaction to various possible antigenic stimulus, and forms immune complexes that deposits in dermi's venules. It appears in the course of various diseases as well as during therapeutics.[3] Erythema nodosum may be the first sign of a systemic disease such as tuberculosis, bacterial or deep fungal infection, sarcoidosis, leprosy, inflammatory bowel disease, or cancer. Certain drugs, including oral contraceptives and some antibiotics, also may be etiologic.[4] The hallmark of erythema nodosum is tender, erythematous, subcutaneous nodules that typically are located symmetrically on the anterior surface of the lower extremities. Erythema nodosum does not ulcerate and usually resolves without atrophy or scarring**.** Most direct and indirect evidence supports the involvement of a type IV delayed hypersensitivity response to numerous antigens.[4]

Basic Features of Erythema Nodosum[5]

Painful, symmetric, red nodules
Anterior legs most common location
Involutes in weeks with bruise-like appearance
Does not ulcerate; tends to heal completely.

The clinical picture is always that of a non-specific systemic diseases with malaise (67%), arthralgia (64%), low fever (60%), and arthritis (31%). However, it may be over come by the presentation of an associated disease.[5] A prodrome commonly occurs as early as one to three weeks before the onset of erythema nodosum, regardless of the etiology. Arthralgias have been known to persist for up to two years after the resolution of erythema nodosum. They are seronegative for rheumatoid factor and cause nonspecific destructive joint changes. Abnormal laboratory findings may include leukocytosis in excess of 10,000 per mm and elevated erythrocyte sedimentation rate and C-reactive protein levels.[6]

Causes of Erythema Nodosum[7]

Common

Idiopathic (up to 55 percent)

Infections: streptococcal pharyngitis (28 to 48 percent), *Yersinia* spp. (in Europe), mycoplasma, chlamydia, histoplasmosis, coccidioidomycosis, mycobacteria

Sarcoidosis (11 to 25 percent) with bilateral hilar adenopathy

Drugs (3 to 10 percent): antibiotics (e.g., sulfonamides, amoxicillin), oral contraceptives

Pregnancy (2 to 5 percent)

Enteropathies (1 to 4 percent): regional enteritis, ulcerative colitis

Rare (less than 1 percent)

Infections

Viral: herpes simplex virus, Epstein-Barr virus, hepatitis B and C viruses, human immunodeficiency virus

Bacterial: *Campylobacter* spp., rickettsiae, *Salmonella* spp., psittacosis, *Bartonella* spp., syphilis

Parasitic: amoebiasis, giardiasis

Miscellaneous: lymphoma, other malignancies.

Beta-hemolytic streptococcal infections are the most common identifiable cause of erythema nodosum. Streptococcal infections account for up to 44 percent of cases in adults and 48 percent of cases in children. Erythema nodosum eruptions may appear two to three weeks after an episode of streptococcal pharyngitis 2; therefore, patients with erythema nodosum should have throat culture evaluation for group A streptococci, as well as streptococcal antistreptolysin-O (ASO) titers or polymerase chain reaction (PCR) assays, or both.

Streptococcal infection was the most frequent cause in the serious of MONREAL et al.[8] (23.2%), LARIO et al.[9] (22.3%) and FOLCH et al.[10](30%).

In VESEY and WILKINSON'S report[11], sarcoidosis and streptococcal infection appear in equal proportions (45.6%).

Tuberculosis has long been linked with erythema nodosum.[12] Erythema nodosum may occur with primary tuberculosis and may even manifest before the development of a skin-test reaction to tuberculin. The bacilli Calmette-Guérin vaccination and the tuberculin skin test have been asociated with the development of erythema nodosum. Furthermore, erythema nodosum may be found in patients with highly positive reactions to the Mantoux skin test but no detectable focus of tubercular infection.[13]

The patient's geographic location and travel history should be considered. *Histoplasma capsulatum, Blastomyces dermatitidis, Paracoccidioides brasiliensis,* and *Coccidioides immitis* have been implicated in the development of erythema nodosum. In western and southwestern areas of the United States, erythema nodosum commonly is caused by coccidioidomycosis, also known as San Joaquin Valley fever. The incidence of erythema nodosum in patients with symptomatic coccidioidomycosis is approximately 5 percent.[14]

Infectious causes of erythema nodosum occasionally involve the gastrointestinal tract, and reports indicate that the incidence of gastrointestinal infections may be increasing.[15] Therefore, a thorough patient evaluation, including stool cultures, should be considered in patients with erythema nodosum and diarrhea.[16]

Hypersensitivity reactions to medications have been recognized as a cause of 3 to 10 percent of erythema nodosum cases. Oral contraceptives and numerous antibiotics, including amoxicillin and especially sulfonamides, have been associated with erythema nodosum.[17]

Sarcoidosis causes up to one fourth of erythema nodosum cases. Radiographic imaging often reveals bilateral hilar adenopathy, with one study reporting chest radiography or computed tomography findings of bilateral hilar adenopathy or mediastinal lymphadenopathy in all patients with erythema nodosum caused by sarcoidosis.[18]

Erythema nodosum occurs in up to 4.6 percent of women who are pregnant, possibly as a result of estrogen production or relative levels of estrogen and progesterone.[19]

Erythema nodosum may be a cutaneous marker of malignancy, most often lymphoma or leukemia.[20] Rarely, other malignancies may be associated with erythema nodosum, including carcinoid and colorectal and pancreatic Cancers.[21]

Diagnosis of Erythema Nodosum[22]

Complete blood count with differential; erythrocyte sedimentation rate and C-reactive protein levels.

Evaluation for streptoccocal infection (i.e., throat culture for group A streptococci, rapid antigen test, antistreptolysinO titer, and polymerase chain reaction assay).

Excisional biopsy (when clinical diagnosis is in doubt); key histologic findings are septal panniculitis, lymphocytic infiltrate with neutrophils, actinic (Miescher's) radial granulomas, absence of vasculitis, and no organisms.

Clinical suspicion of chronic disease (e.g., sarcoidosis, tuberculosis); purified protein derivative test, chest radiography.

Stool culture and evaluation for ova and parasites in patients with diarrhea or gastrointestinal symptoms; consider evaluation for inflammatory bowel disease.

Differential Diagnosis of Erythema Nodosum[22]

Most common

Cytophagic histiocytic panniculitis (a lymphoma)

Lupus erythematosus profundus (lupus panniculitis)

Nodular fat necrosis

Occasional

Necrobiosis lipoidica

Necrobiotic xanthogranuloma

Scleroderma

Subcutaneous granuloma

Rare

Cold panniculitis

Infectious panniculitis

Leukemic fat infiltrates

Lipodystrophies

Poststeroid panniculitis

Povidone panniculitis

Scleroderma neonatorum

Sclerosing panniculitis

Subcutaneous fat necrosis of the newborn.

Although erythema nodosum can be exquisitely tender, it tends to be self limited. The most common approach is treatment of any underlying disorders and supportive therapy, including bed rest and avoidance of contact irritation Of affected areas. Pain can be managed conservatively with nonsteroidal anti-inflammatory drugs (NSAIDs). More aggressive pain management is reserved for clinical situations that become recurrent or unusually prolonged.[23]

Systemic steroids have been advocated as a relatively safe therapeutic option if underlying infection, risk of bacterial dissemination or sepsis, and malignancy have been excluded by a thorough evaluation. Oral prednisone 1-2 mg per kg body weight per day.[24] Treatment also may be tailored to disease-specific regimens: steroids used in combination with hydroxychloroquine (Plaquenil), cyclosporin A (Sandimmune), or thalidomide (Thalomid) have been used to treat inflammatory bowel disease–associated erythema nodosum.[25] NSAIDs should be avoided in treating erythema nodosum secondary to Crohn's disease because they may trigger a flare-up or worsen an ongoing acute bout. Colchicine has been used in patients with erythema nodosum and coexisting Behçet's syndrome, with varying results.[26]

CONCLUSION

The occurrence of streptococci related Erythema Nodosum is uncommon in adults, the incidence being two to three cases/100,000 person per year[27], Still uncommon is the report of causes of streptococci related Erythema Nodosum. The treatment of streptococci related Erythema Nodosum is at times difficult & the illness recurs often. The guidlines of Penidura prophylaxis are not clear in case of streptocci related Erythema Nodosum which makes the treatment worse is cause of recurrent cases.

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