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Case Report

Post-streptococcal erythema nodosum

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Abstract Erythema Nodosum (EN) is the most common panniculitis, presented as acutely eruptive painful erythematous nodules on lower extremities symmetrically, with a wide spectrum etiology from infection to malignancy. The aim of this case report is to comprehend the diagnosis and the underlying treatable origin of EN. A 24-year-old female presented with painful red bumps on both legs a week after an episode of fever and sore throath. She also noted tenderness on both ankle joints. She was diagnosed with vasculitis by the internist and was treated with Methylprednisolone (MP) 16mg/day for 2 weeks. The symptomps were resolved but re-emmerged 1 week after the MP was stopped. Physical examination revealed erythematous nodules on both legs with tenderness on palpation. ASTO test was positive. Septal panniculitis and Miescher's granuloma was identified through histopathology examination. Exclusion of inflammatory subcutaneous differential diagnosis such as EN, nodular vasculitis (NV), and cutaneous polyarteritis nodosa (CPAN) require clinical and histopathologic consideration. Etiology identification of EN was done through a relevant supporting examination based on epidemiology, history, and physical examination. Post-streptococcal EN possibly related to molecular mimicry and immune complex deposition leading to reactive inflammation. Hereby we reported one case of post-streptococcal EN that was confirmed by laboratory examination and skin biopsy. The clinical response was good towards the etiology-based treatment.

Key words
Erythema nodosum; Post-streptococcal; ASTO; Miescher's granuloma.

Introduction

Erythema nodosum (EN) is the most common type of panniculitis presented as acute eruption of painful, erythema to violaceous nodules on lower extremities symmetrically.[1] There have been no reports on the incidence of EN in Indonesia, but there were 117 cases of EN at dr. Sardjito General Hospital in between 2014 to 2019. The exact pathomechanism remains unclear, but several evidence revealed a type IV hypersensitivity reaction towards various antigens.[5] A rational approach is needed in identifying the etiology of EN considering the wide spectrum of causes, where infection is the main identified etiology (28-48%).[9] The prognosis of EN is good with administration of definitive treatment according to the underlying etiology. The aim of this case report is to comprehend the diagnosis and the underlying treatable origin of EN.

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Case report

A 24-year-old female from Yogyakarta presented with painful red bumps on both legs a week after an episode of fever and sore throath. She also had noted tenderness on both ankle joints. She was diagnosed with vasculitis by the internist and was treated with Methylprednisolone (MP) 16mg/day for 2 consecutive weeks, The symptomps were resolved but re-emmerged 1 week after the MP was stopped. She was referred to dermatology

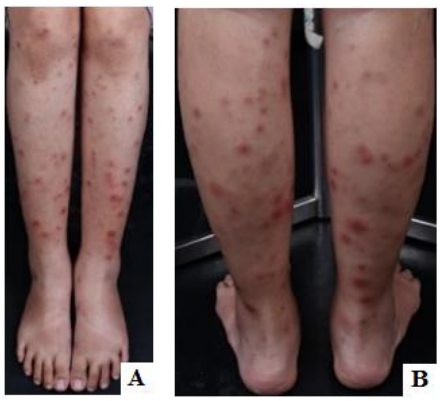

Figure 1 Erythematous nodules on both anterior and posterior legs.

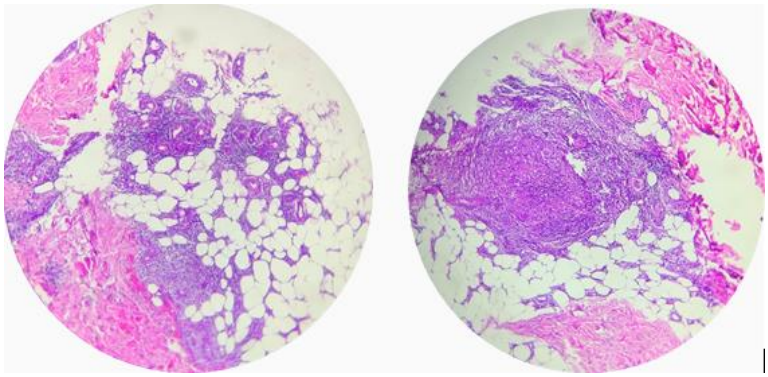

Figure 2 Septal panniculitis and Miescher's granuloma.

outpatient clinic dr. Sardjito General Hospital for skin biopsy. Any similar complaint, history of chronic cough or night sweats, consumption of certain medications and hormonal contraception were denied.

The physical examination revealed multiple erythematous nodules on both anterior and posterior legs with tenderness and warm on palpation (**Figure 1**). The history and physical examination were led to several differential diagnosis such as EN, nodular vasculitis (NV), and cutaneous polyarteritis nodosa (CPAN). Laboratory panels revealed positive Antistreptolysin-O (ASTO) test and increase of erythrocyte sedimentation rate (ESR). Chest X-Ray was normal and tuberculin test was negative. Skin biopsy revealed septal panniculitis and Miescher's granuloma (**Figure 2**). She was given azythromycin 500mg/day and sodium diclofenac 50mg twice a day for 10 days. The nodules were resolved with no appearance of new lesion, fever, and joint pain.

Discussion

There are several subcutaneous inflammatory entities with erythematous nodules on inferior extremities as the manifestation, such as EN as the most common entity, NV, and CPAN. Epidemiologically, both EN and NV was mainly found in productive age female with female to male ratio 6:1 to 9:1. The predilection and morphology is quite similar, the only difference between both entities is the NV one had a tendency to left necrotic to cycatrical lesion.[5] The initial sign of CPAN is often in the form of livedo reticularis that later followed by painful subcutaneous nodules that only identified on palpation to ulcerative nodules mostly on legs.[2] The clinical presentation in this case was non-ulcerative inflammatory nodules on lower extremities bilaterally alongside constitutional symptoms.

Histopathologically, there is a classification that divides panniculitis into "septal" and "lobular" based on the presence of vasculitis and inflammatory cell infiltrate.[8] Septal panniculitis without vasculitis pattern mostly identified in EN cases, but mixed type panniculitis with minimal vasculitis is still possible.[10] Edema to septal fibrosis with a dominant neutrophil infiltrate, multinucleated giant cells to granulomas, and a characteristic collection of arranged radially histiocytes around a stellate slit called Miescher's granuloma. On the other hand, NV is a diffuse lobular panniculitis with granulomatous, vasculitis, focal necrosis, lymphoid and plasma cell infiltrates. Histopathologically, CPAN characterized by leukocytoclastic vasculitis of small to moderate arteries, with localized lobular or mixed panniculitis around the involved vasa.[7] The

features of septal panniculitis with dominant neutrophil infiltrate and Miescher's granuloma found in the case confirmed the EN diagnosis.

Based on the etiology, EN may classified into primary or idiopathic (37%-60%) and secondary. None of the possible causes can be proven in the primary one, which is alleged to have a correlation with estrogen such as in the early trimester of pregnancy and oral contraceptive users. The etiology of secondary EN includes infection (28–48%), sarcoidosis (11–25%), drugs such as anti-epileptics and sulfonamide and penicillin antibiotics (3–10%), to malignancies such as lymphoma and leukemia have also been reported although quite rare.[4] Streptococcal infection of the upper respiratory tract is the most common etiology of EN worldwide, both in developed and developing countries.[9] In patients with EN, a history of infection 1 to 4 weeks prior to the onset of skin lesion should be obtained which further confirmed by laboratory tests or culture. The sensitivity and specificity of antistreptolysin-O (ASTO) in the post-streptococcal condition is quite high, varies from 70.5-72.7% to 86.4-93.2%.[3]

On the other hand, Indonesia known as a country with the second highest tuberculosis (TB) incidence in the world. According to the latest World Health Organization (WHO) data, there are 1,020,000 new cases per year or 391 per 100,000 population, indicating that *M. tuberculosis* infection is one of the atiology that must be excluded.[4] Screening through history taking and physical examination, supported by tuberculin test, chest X-ray, even sputum test becomes relevant for EN cases in our setting. Prior study shown that EN is associated with a strong immunological reaction in immunocompetent individuals which proven on tuberculin test, and EN might be a strong predictor and even early symptom of TB infection in a setting with a high incidence of TB.[6] In this case, an episode of fever and sore throath was precedes the appearance of nodules on the legs and pain and swelling in the joints, with a positive ASTO test. There wasn't any history of prolonged cough, night sweats, history of contact with TB patients, or significant weight loss. The results of the tuberculin test were negative and there were no TB foci or bilateral hilar lymphadenopathy on chest X-Ray. Based on these data, it can be concluded that this is a post-streptococcal EN case.

Erythema nodosum is a non-specific cutaneous reaction related to several endogenous and exogenous factors. Molecular mimicry possibly had a role in post-streptococcal EN. The bacteria expressed a similar structure peptide that induced cell T response towards the pathogen and the auto-antigenforming antibody-antigen complex that further deposited within and around the venules on the adipose tissue septum resulting in a reactive inflammation.[1] The prognosis is relatively good, especially with a proper etiology-based treatment. In this case, due to the history of penicillin allergy, macrolide antibiotic that also had broad spectrum activity against streptococcus species was given. A non-steroidal anti-inflammatory drugs (NSAID) was also given as the first line inflammation control regimen in infection related etiology instead of corticosteroid.[8] On the evaluation, most of the nodules had resolved and there were no new lesions, fever, and joint pain.

Conclusion

Hereby we reported one case of post-streptococcal EN that was confirmed by laboratory examination and skin biopsy. The clinical response was good towards the etiology-based treatment.

References

1. Oldstone MBA. Molecular mimicry and immune-mediated diseases. *FASEB J*. 1998;**12**:1255-65.
2. Morgan AJ, Schwartz RA. Cutaneous polyarteritis nodosa: a comprehensive review. *Int J Dermatol*. 2010;**49**:750-6.
3. C. C. Blyth and P. W. Robertson. Anti-streptococcal antibodies in the diagnosis of acute and post-streptococcal disease: streptokinase versus streptolysin O and deoxyribonuclease B. *Pathology*. 2006;**38(2)**:152-6.
4. Gonzalez-gay MA, Garcia-porrua c, Pujol rm, Salvarani c: Erythema nodosum:a clinical approach. *Clin Exp Rheumatol*. 2001;**19**:365-8.
5. Schwartz RA, Nervi SJ. Erythema nodosum: a sign of systemic disease. *Am Fam Physician*. 2007;**75**:695-700.
6. Aydin-Teke T, Tanir G, Bayhan GI, *et al*. Erythema nodosum in children: evaluation of 39 patients. *Turk J Pediatr*. 2014;**56**:144-9.
7. Cho KH. Inflammatory nodules of the leg. *Ann Dermatol*. 2012;**24(4)**:383–92.
8. Lake E.P, Worobec S.M., Aronson I.Panniculitis. Fitzpatrick's Dermatology 9th edition. 2019:**73**:1251-94.
9. Garcia-porrua c, *et al*.: Erythema nodosum: etiologic and predictive factors in a defined population. *Arthritis Rheum*. 2000;**43**:584-92.
10. Segura, S., Requena, L. Anatomy and Histology of Normal Subcutaneous Fat, Necrosis of Adipocytes, and Classification of Panniculitides. *Dermatologic Clinics.* 2008;**26(4)**;419.