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Childhood tuberculosis: Erythema nodosum as the only clinical manifestation

RU Sulakshi[1], PP Jayawardana[1], G Gunathilaka[2]

[1]*Professorial Paediatric Unit,* [2]*Paediatric Pulmonology Unit, Teaching Hospital Karapitiya, Galle, Sri Lanka.*

Correspondence: Dr. Umesha Sulakshi
e-mail: *usulakshi@gmail.com*
https://orcid.org/0000-0001-7645-8411
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Introduction

Erythema nodosum (EN) is a hypersensitivity reaction that typically appears with multiple painful erythematous subcutaneous nodules of varying sizes. Lesions are oval-shaped and symmetrically distributed with the longer axis parallel to the extremity (1).

It is a type of panniculitis; the result of type IV delayed-type hypersensitivity reaction to various antigens. Up to 50% of cases are idiopathic (1). It is associated with many etiologies; infections, inflammations, malignancies and drugs (1,2). Streptococcal infections are the commonest cause identified (1). It can also be associated with infections-tuberculosis; inflammatory conditions like sarcoidosis, inflammatory bowel disease and systemic lupus erythematosus; drugs such as oral contraceptives and sulphonamides. It can rarely be associated with infections due to human immunodeficiency virus, Epstein Barr virus, hepatitis B and C viruses, parasitic infections like amoebiasis and giardiasis and malignancies like lymphomas (2).

Tuberculosis (TB) is a chronic infection caused by *Mycobacterium tuberculosis.* It mainly affects the lung but can involve extrapulmonary sites like the brain, kidney, intestines, spine, skin etc. In 'Latent TB' patients remain asymptomatic even though they are infected.

In the immune-compromised patient, it can progress to an active infection (3). Respiratory and systemic symptoms include chronic cough, chest pain, fever, night sweats, weight loss, poor appetite, generalised weakness and malaise.

Childhood TB contributes to nearly 5-10% of all TB cases (4). The disease is usually acquired from an infected adult and transmitted through air-borne droplets. It is often underdiagnosed because the majority are asymptomatic and the smears are negative. We report an 8-year-old girl presented with erythema nodosum, as the single manifestation to suggest tuberculosis.

Case presentation

An 8-year-old previously healthy girl was admitted with non-specific lower back pain for more than a month, with no other constitutional symptoms or a focus of infection. A detailed and thorough clinical examination was negative. Basic investigations were within normal limits except for the marginally raised Erythrocyte Sedimentation Rate (ESR) which was 50 in the first hour. Total white cell count was 12.0×10^9 /L with 42% lymphocytes and 54% neutrophils, platelets 450×10^9 /L, haemoglobin 11.2 g/dL and C reactive protein (CRP) <6 mg/dL. Urine analysis was normal. Abdominal ultra-sonography and radiographs of the lumbosacral spine were reported as normal. She was treated with a simple analgesic (paracetamol) and was sent home in 72 hours. It was decided to review her in the clinic in two weeks due to the raised ESR.

She was reviewed two weeks later and was "Better" with no back pain. She had 4-5 small reddish palpable, painless nodular skin lesions distributed on the medial sides of both ankles. She was admitted for further investigations. Due to the ambiguity of the lesions, a biopsy was performed. Sooner these red nodules extended up to the shin giving the typical appearance of erythema nodosum (Figures 1 & 2).

She denied a history of cough, night sweats, or recent weight loss. Her appetite was normal and did not complain of abdominal pain or vomiting. She denied a history of hair loss, joint symptoms, oral ulcers or photosensitivity rashes. The examination was totally unremarkable except for the skin nodules. She was BCG vaccinated at birth and the immunization was up to date, not been on any long-term medications.

She hailed from a family with a poor socio-economic background. This girl had close contact with her grandfather who had completed a 6-month course of treatment for pulmonary tuberculosis one year ago. He was also a drug addict.

There was no difference in the blood counts. Total white cell count was 15.6 $\times 10^{9}$ /L with 40% lymphocytes and 55% neutrophils, platelets 484×10^{9} /L and hemoglobin 11.4 g/dL. The blood picture was consistent with an infection or inflammation. Liver transaminases were normal; aspartate transaminase (AST) 18 U/L and alanine transaminase (ALT) 14 U/L. Serum albumin 41 mg/dL, Antistreptolysin O titre (ASOT) < 200 IU/mL, serum Na^{+} 138 mEq/L, serum K^{+} 4.2 mEq/L. Inflammatory markers showed rising values at 2 weeks with CRP 36 mg/dL and ESR 78 mm/1st Hr.

Three consecutive morning sputum samples for acid-fast bacilli and sputum TB-PCR were negative. The chest radiograph was normal.

The Mantoux test was performed and showed a 24mm diameter on day 3 indicating a highly positive Mantoux test (Figure 3). The result of the skin biopsy was in keeping with erythema nodosum.

With the presence of erythema nodosum, a strongly positive Mantoux test and close exposure to a patient with active tuberculosis, a diagnosis of extrapulmonary tuberculosis were suggested. The child was treated with a paediatric fixed drug combination of the anti-tuberculosis drugs. She was given 2 tablets of HRZ+E combination once daily for 2 months in the intensive phase. HRZ +E contains isoniazid (H) 50 mg, rifampicin (R) 75 mg, pyrazinamide (Z) 150 mg and ethambutol (E) 400 mg. Then one tablet of HR combination; isoniazid (H) 50 mg and rifampicin (R) 75 mg was continued daily for another 4 months.

A remarkable improvement was noted in the nodules by the 7th day of treatment and inflammatory markers declined (CRP <6 mg/dL and ESR 30 mm/hr) after 2 weeks of treatment. The family was screened but both parents and siblings were negative for tuberculosis.

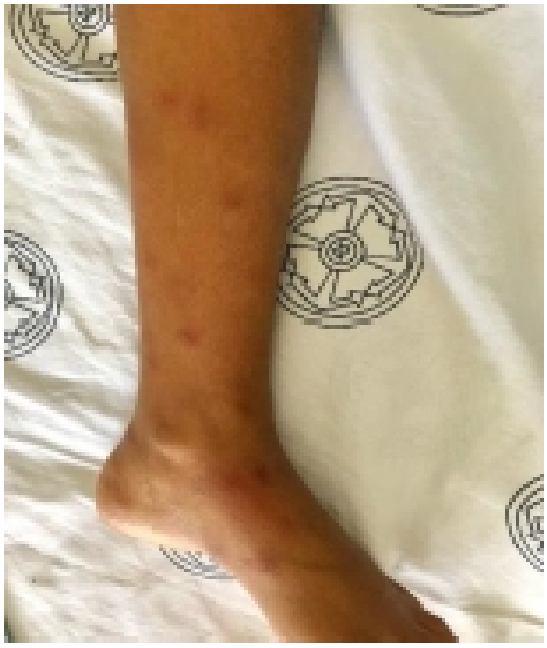

Figure 1: Early appearance of the skin lesions

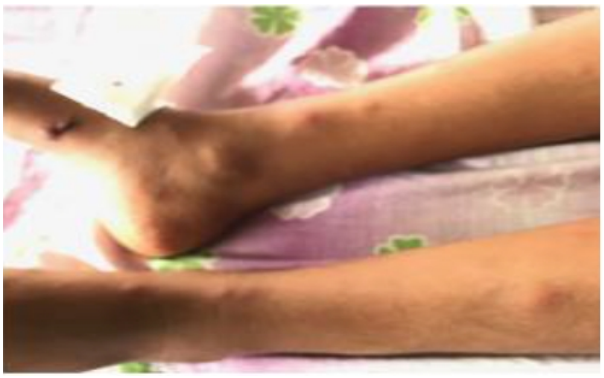

Figure 2: Typical appearance of erythema nodosum

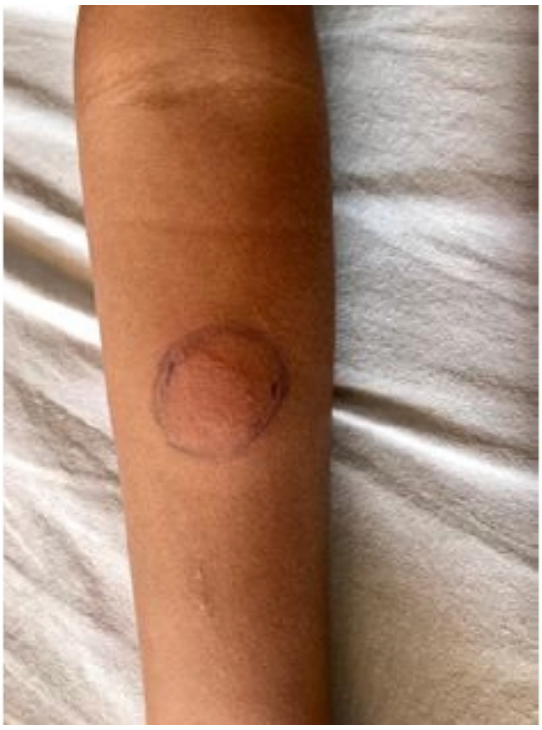

Figure 3: Strongly positive Mantoux test with induration 24 mm

Discussion

Erythema nodosum is a Type IV hypersensitivity reaction to different antigenic stimuli; infections, inflammations, autoimmune diseases, malignancy or drugs. There is a well-known association of erythema nodosum with primary tuberculosis and it may even manifest before the Mantoux skin test reaction becomes positive (4). There are reported cases of erythema nodosum following BCG vaccination with positive Mantoux skin tests (4).

Erythema nodosum has been reported in patients with strongly positive Mantoux test even in the absence of any detectable focus of TB (4).

Erythema nodosum and a strongly positive Mantoux in a patient who has had a contact history of TB or from a TB endemic region are sufficient to diagnose tuberculosis and to proceed with anti-tuberculosis treatment (5). It is suggested that patients with highly positive tuberculin skin tests may have a small focus on *Mycobacterium tuberculosis* which could not be detected by available investigations (5).

In our case report, the child presented with erythema nodosum and had a positive contact history and a strongly positive Mantoux test which prompted us to initiate anti-TB treatment. Rapid recovery from the clinical symptoms and marked decline of inflammatory parameters were witnessed.

Erythema nodosum seen in the primary care set-up should be evaluated to find out the aetiology. Most of the conditions have definite treatment. They should be investigated with full blood count, inflammatory markers, chest radiograph, sputum for acid fast bacilli and Mantoux test to rule out the possibility of tuberculosis (6). Early treatment will prevent the progression and complications of the disease (7).

Conclusions

Diagnosing childhood tuberculosis remains a challenge. Its timely diagnosis is important in patient care to prevent complications and disease transmission.

Written informed consent has been obtained to publish this case report with photographs.

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