



Erythema Nodosum in Israeli children

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Abstract

Background: Erythema nodosum, although uncommon in children, is the most frequent form of panniculitis in pediatrics. EN has been associated with various infections and chronic inflammations, and its course varies with age, gender, and racial and geographic factors. There is no information on EN in Israeli children.

Objectives: To examine the clinical course of EN and the conditions with which it is associated in Israeli children.

Methods: We conducted a retrospective study of 24 children with a diagnosis of EN who presented at our Center over a 10 year period (1989–98).

Results: EN was more frequent in females than males (ratio 2:1) due to a cluster of adolescent girls. The mean duration of the skin manifestation was 18 days. The course was benign in all patients. Streptococcal infection was the most common cause (25%), followed by Epstein-Barr virus infection (18%) and inflammatory bowel disease (13%). In one-third of cases, no specific cause could be identified. Tuberculosis, an important cause of EN in the past, was not found in our patients.

Conclusions: Most cases of EN in Israeli children are related to streptococcal and EBV infections or to chronic inflammatory conditions. Despite the increase in tuberculosis morbidity in Israel during recent years, we found no association of EN and tuberculosis in our study.

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Erythema nodosum is the most frequent panniculitis in children [1]. It is, however, a relatively uncommon entity in the pediatric population. EN has characteristic clinical features, and the diagnosis is made on a clinical basis [2,3]. It has been associated with a variety of disorders, especially mycobacterial and streptococcal infections [1–3], followed by other types of infections, chronic inflammations, malignancies, and exposure to certain medications [4]. Its course is influenced by gender, age, race, and geographic location [5–8]. In view of the lack of information to date on EN in the pediatric population in Israel, the aim of

the present study was to examine the clinical features of EN and the conditions with which it is associated in Israeli children.

Patients and Methods

We reviewed the medical files of all children with a diagnosis of EN who presented at the Department of Pediatrics at the Beilinson Medical Center and Schneider Children's Medical Center over a 10 year period (1989–98). The diagnosis was based on the clinical finding of the characteristic rash, namely tender, erythematous nodules with a bruise-like evolution on the lower extremities that lasts for several days without suppuration or ulceration. All affected children underwent the following investigations: complete blood count, erythrocyte sedimentation rate, blood chemistry (SMA-18), throat culture, tuberculin test, antistreptolysin O titer, antinuclear antibody, viral serologies, and chest X-ray. Clinical features including systemic manifestations, duration of the rash, use of drugs, and associated disorders were noted. Specific investigations were performed in individual cases.

Results

Of the 28 children in whom EN was diagnosed over the 10 year period, 24 were found eligible for the study. (In the other four cases the clinical data were insufficient.) There were 16 girls and 8 boys (ratio 2:1), all of Jewish origin. Mean age was 9.9 years (range 4–18 years): 8.6 in the boys and 11.8 in the girls. The skewed age distribution was due to a cluster of adolescent girls (>12 years old), comprising 9 of the 24 patients.

The skin lesions were confined to the shins and knees in all patients. One child also had lesions on the upper limbs. The mean duration of the rash was 18 days (range 5–35 days). The rash recurred in one patient who had ulcerative colitis.

Most of the laboratory tests were nonspecific. Erythrocyte sedimentation rate was moderately elevated in eight patients (40–60 mmHg/h) and markedly elevated in seven (60–120 mmHg/h). Chest X-ray was not informative except in one patient with interstitial pneumonitis. Purified protein derivative was either negative or <5 mm in all patients.

EN = erythema nodosum
EBV = Epstein-Barr virus

The most frequent clinical disease associated with EN was streptococcal infection, found in six patients. It was confirmed by throat culture in five and ASO titer (>400 units/ml) in three (two patients had both). Recent Epstein-Barr virus infection was found in four children and confirmed by high IgM titers. Inflammatory bowel disease was present in three patients. None of the patients had tuberculosis or *Yersinia* infection. In eight children (33%), no specific associated condition or etiologic factor could be identified, although several had a nonspecific condition, such as pharyngitis or lymphadenopathy [Table 1].

Arthralgia was noted in six children, and arthritis was found in one child who also had ulcerative colitis and recurrent EN. One of the girls had Crohn disease and hypothyroidism. Interstitial pneumonitis (diagnosed by chest X-ray) without prominent respiratory symptoms was found in one child.

Paracetamol was used by most patients before the appearance of the eruption. Eleven children reported taking at least one additional medication, including penicillin (5 patients), cephalosporins (3 patients), non-steroidal anti-inflammatory drugs (3 patients), systemic corticosteroids (2 patients), cyclophosphamide (1 patient) and thyroxine (1 patient). Hormonal contraceptives were not used by the adolescent girls in our study.

Most of the patients received treatment with paracetamol during the skin eruption; five with more severe pain were treated with aspirin. The eruption disappeared within a few weeks in all patients. In six patients antibiotic treatment was also initially prescribed because cellulitis was suspected.

Discussion

Erythema nodosum affects mainly women between the ages of 25 and 40 [4,6]. In children, it is unusual before the age of 2 years; indeed, our youngest patients were 4 years old. Though there is a female predominance of 5:1 in adults [4], the sex ratio is approximately equal before puberty [4,6]. In our sample, the female:male ratio was 7:7 until the age of 12 years, and 9:1 thereafter, indicating a peak in adolescent girls.

The diagnosis of EN is usually easily made following history taking and physical examination. Biopsy study is rarely required and typically shows a classic septal panniculitis. The differential diagnosis of EN in childhood includes battered child syndrome, cellulitis, Henoch-Schönlein purpura, cold-induced panniculitis, and the cutaneous form of periarteritis nodosa.

EN is frequently associated with other clinical conditions. The most common in our study were streptococcal infections, EBV infections and inflammatory bowel disease. Tuberculosis, once considered to be the leading cause of EN [1-3,5], and which has shown a rising incidence in Israel in recent years as a result of the mass immigration from Ethiopia and Eastern Europe [9], was not

Table 1. Underlying or associated clinical conditions in 24 children with erythema nodosum

Diagnosis	No.	%
Streptococcal infection	6	25
Epstein-Barr infections	4	17
Inflammatory bowel disease	3	13
Behcet disease	2	8
Cat scratch disease	1	4
Undetermined*	8	33

* 2 children with tonsillitis/pharyngitis, 1 child with interstitial pneumonia, 1 child with cervical lymphadenitis, 1 child with insect bites

noted in any of our patients. This finding is in accordance with two recent studies of EN in Swiss and French children [1,4].

In one-third of our patients, no specific cause of the EN could be identified, although in some of these cases a viral or bacterial infection was probable. Almost half the patients used medications before the appearance of EN, mainly paracetamol, penicillin and cephalosporins. However, none used sulfonamides, phenantoin or hormonal contraceptives, all of which have been considered to be associated with EN [1,3,5].

The treatment of EN is symptomatic and consists mainly of analgesic drugs to alleviate the pain. The disorder is usually self-limited, but the question of a possible underlying cause warrants laboratory investigations.

In conclusion, most cases of EN in children in Israel are associated with non-mycobacterial infections, mainly streptococcal and EBV, or non-infectious inflammatory conditions, especially inflammatory bowel disease. The course of the disease is benign and self-limited.

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ASO = antistreptolysin O