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## Conditions currently associated with erythema nodosum in Swiss children

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**Abstract** A review was made of the 36 paediatric patients in whom the diagnosis of erythema nodosum had been established between 1977 and 1996 at the Department of Paediatrics, University of Bern, Switzerland. Infectious diseases were associated with erythema nodosum in 20 (including 10 streptococcal infections) and non-infectious inflammatory diseases in 8 patients. None of the 36 patients had tuberculosis or had been exposed to sulphonamides, phenytoin or hormonal contraceptives. There were eight patients in whom either the associated disease was not diagnosed, or there was no other disease.

**Conclusion** Most cases of erythema nodosum are nowadays caused by non-mycobacterial infectious diseases or by non-infectious inflammatory diseases.

**Key words** Child · Erythema nodosum · Inflammatory bowel disease · Streptococcal infections · Tuberculosis

### Introduction

In childhood erythema nodosum is the most prevalent panniculitis. It has a characteristic clinical picture and the diagnosis can be made on the basis of physical examination alone [5, 6]. Erythema nodosum has been associated with various infectious and non-infectious disorders [5, 6]. In addition, various pharmacological agents have also been considered responsible for this panniculitis [5, 6]. The relative weight of the various causes of erythema nodosum is influenced by geographical and racial factors as well by the age of the patients [1–6, 8–10, 12]. Their importance may also vary from

time to time [1–6, 8–10, 12]. Previous surveys emphasized mycobacterial and streptococcal infections as the conditions most often linked with erythema nodosum, but a better control of these diseases is now possible. There have been no general series of cases reported in recent years which might mirror these mutations. The purpose of this study was to review the conditions associated with erythema nodosum in the period 1977 to 1996 as encountered in a paediatric referral hospital in Switzerland.

### Patients and methods

A review was made of all patients aged 16 years or less in whom the diagnosis of erythema nodosum had been established between 1977 and 1996 at the Department of Paediatrics, University of Bern, Switzerland. For this purpose, the clinical and the laboratory records of the Department of Paediatrics and those of the referring family doctors were evaluated in terms of established criteria for the diagnosis of associated conditions. The use of sulphonamides, phenytoin and hormonal contraceptives was expressly inquired. Total white blood cell count, erythrocyte sedimentation rate, tuberculin skin test and chest roentgenography had been performed in all children. Additional investigations were performed in patients with a positive tuberculin test. Information on follow up was obtained directly by the patient or by the referring physicians 6 months or more after the skin lesion had resolved. The results are expressed as median and interquartile range. The  $\chi^2$ -test and the Kruskal-Wallis test were used to analyse the results obtained in the various subgroups of patients.  $P < 0.05$  was accepted to indicate statistical significance.

### Results

All 36 patients (18 girls and 18 boys, aged between 1.5 and 16 years, median 10 years) were Caucasian. The skin lesions were confined to the shins and knees in 29 cases. In 7 patients the rash was concurrently found on the forearms ( $n = 7$ ) or the face ( $n = 1$ ). Infectious diseases were diagnosed in 20 patients and non-infectious diseases in 8 (Table 1). None of the patients had tuberculosis. There were 8 patients in whom either the associated disease was not diagnosed, or there was no other disease. General information on the three different

**Table 1** Disorders associated with erythema nodosum in 28 out of the 36 patients. In the remaining 8 patients the associated disease was not diagnosed, or there was no other disease

Condition	Cases
Streptococcal infections	
– pharyngitis <sup>a</sup>	8
– impetigo <sup>b</sup>	1
– cellulitis <sup>b</sup>	1
Non-streptococcal respiratory infections	
– upper respiratory tract	2
– lower respiratory tract	2
<i>Burkholderia cepacia</i> pulmonary infection <sup>c</sup>	1
Parvovirus B19	1
Infectious mononucleosis	1
Infectious gastro-enteritis <sup>d</sup>	3
Ulcerative colitis	3
Crohn disease	3
Sarcoidosis	1
Behçet disease	1

<sup>a</sup> *β-haemolytic streptococcus* cultured ( $n = 4$ ), strongly increased antistreptolysin titre ( $n = 2$ ) or both ( $n = 2$ )

<sup>b</sup> *β-haemolytic streptococcus* cultured

<sup>c</sup> Patient with cystic fibrosis

<sup>d</sup> *Yersinia enterocolitica* and *Salmonella enteritidis* each on one occasion

groups of patients appears in Table 2. The patients without associated diagnosis tended to be younger by approximately 5 years than those with associated infectious or non-infectious disease. Duration of the rash was longer by approximately 10 days in patients with an underlying non-infectious disease. In three patients with a non-infectious underlying disease the final diagnosis (each one patient with Crohn disease, Behçet disease or sarcoidosis) was made 2, 3 and 4 months after resolution of the skin lesions. None of the 36 patients had been exposed to sulphonamides, phenytoin or hormonal contraceptives.

Erythema nodosum tended to recur in the patient with sarcoidosis, in one patient with Crohn disease and

in one patient with erythema nodosum associated with upper respiratory infection.

## Discussion

The present report indicates that most cases of childhood erythema nodosum are nowadays caused either by non-mycobacterial infectious diseases or by non-infectious inflammatory diseases. The most common infectious precipitating agents are streptococcal infections, non-streptococcal respiratory infections likely caused by unidentified viral agents and other viral or bacterial infections. The most common non-infectious causes are inflammatory bowel diseases, sarcoidosis, Behçet disease or collagen vascular diseases [5–7]. The tendency for erythema nodosum to occasionally antedate other manifestations of non-infectious systemic diseases noted in this survey corroborates the data of the literature [7]. In spite of information on follow up for at least 6 months there was a large minority of patients in whom the associated disease was not diagnosed, or there was no other disease [1–6, 8–10, 12].

Sulphonamides, phenytoin and hormonal contraceptives have also been considered responsible for erythema nodosum in adulthood [5, 6] but none of our paediatric patients had been exposed to these agents.

In the past, tuberculosis was the foremost cause of erythema nodosum but in this survey tuberculosis failed to account for erythema nodosum [1–6, 8–10, 12]. After decades of decline in the incidence, the number of tuberculosis cases has tended to increase over the last years in Switzerland as a consequence of the immigration from high prevalence countries and the outbreak of human immunodeficiency virus [11, 13]. It is therefore assumed that tuberculosis still deserves consideration in children with erythema nodosum [5, 6].

**Table 2** Conditions associated with erythema nodosum in 36 paediatric patients. Results are given as median [interquartile range between brackets]

	Infectious diseases	Non-infectious diseases	No associated diagnosis	All
Cases	20	8	8	36
Female:male	10:10	5:3	3:5	18:18
Age, years	10 [18.8–13]	11 [10–14]	4.8 <sup>a</sup> [3.4–8.4]	9.6 [5.3–13]
Clinical findings				
Fever <sup>b</sup>	13	4	3	20
Arthralgia without synovitis	6	2	2	10
Synovitis	3	2	0	5
Rash duration, days	12 [11–15]	21 <sup>a</sup> [16–30]	10 [9–11]	12 [10–16]
Laboratory findings				
Elevated white cell count <sup>c</sup> ( $n$ )	9	5	2	16
Left shift <sup>d</sup> ( $n$ )	4	3	0	7
Elevated sedimentation rate <sup>e</sup> ( $n$ )	15	8	3	26

<sup>a</sup> Versus the remaining groups

<sup>b</sup>  $> 38.0^{\circ}\text{C}$

<sup>c</sup> Leucocytes  $> 15 \times 10^9/l$

<sup>d</sup> Nonsegmented polymorphonuclear leucocytes  $> 15\%$

<sup>e</sup>  $> 30 \text{ mm/h}$

It is concluded that in Switzerland most cases of childhood erythema nodosum are nowadays caused either by non-mycobacterial infectious diseases or by non-infectious inflammatory diseases.

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