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An Uncommon Cause of Erythema Nodosum

Instructive Case

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Learning Points

- Erythema Nodosum is an uncommon cause of rash in children which is most commonly caused by an infectious agent.
- Atypical features should prompt further investigation and consideration of other diagnoses or underlying causes.
- Most EN can be diagnosed clinically and will resolve with supportive treatment.

Case

A 14 year old girl was referred to the skin clinic with a 2 year history of painful lumps on her lower legs and occasional associated knee pain. In clinic, active lesions were not evident, but some areas of dark pigmentation were noted on the shins that were similar to bruising. Further history revealed that the lesions were red, raised and tender. They appeared almost exclusively on the lower legs, and slowly involuted over a period of about a month. They were occasionally associated with knee pain, but no swelling. There were no triggers noted. The patient had seen several doctors but no diagnosis had been made. The patient's mother had taken a picture of the active lesions and based on these and the history, a presumptive diagnosis of erythema nodosum was made. Figures 1 and 2 show the lesions after they re-appeared during her workup.

Erythema nodosum, common causes, natural history

Erythema nodosum (EN) is a reactive panniculitis (inflammation of the subcutaneous fat) that usually presents with inflammatory nodules and plaques on the extensor aspects of the lower limbs.⁽¹⁾ Lesions typically present as sudden onset, painful, warm erythematous nodules and plaques which are bilateral and symmetrical, and become "bruise like", then resolve without scarring over a two to eight week period.⁽¹⁾ A prodromal syndrome of fatigue and malaise (67%) with low grade fevers (60%) arthralgia (64%) and arthritis (31%) can precede the lesions by one to three weeks.⁽¹⁾ Lesions can recur in a minority of paediatric patients.^(2, 3)

EN reaches peak incidence in early adulthood, and is relatively rare in prepubertal children, where it shows an even gender distribution, rather than the female predominance seen in adult patients.^(1, 3) Common EN triggers are listed in the table 1 below.

The relative contribution of causes for EN will vary by region as well as ethnicity and age.⁽²⁾ Recent case series in Switzerland and Greece have found paediatric EN to be most commonly triggered by an infectious agent (55-77%), most commonly group A streptococci (GAS) (27-48%), less commonly by a systemic illness such as ulcerative colitis or Crohn Disease, and idiopathic in 22% of cases.^(2, 3) In neither of these studies had any of the patients taken any medications such as sulphonamides, phenytoin or oral contraceptives, which have been associated with EN in adults.

Case Continued

On further history, the patient had had a sore throat prior to the appearance of the first lesions. She had also experienced some vague abdominal pain or bloating over the past six months, with episodic diarrhoea but no blood or mucous.

She was not on any medications.

The patient had emigrated from the Philippines at 6 years of age. Her mother had recently completed treatment for tuberculous adenitis, and her uncle and grandfather had been treated for tuberculosis (TB) in the past. She had occasional cough, which was generally non-productive. She was unsure if she had lost weight recently, but was actively trying to gain weight. She had no loss of appetite, fever, or night sweats.

She had no mouth ulcers, although she had been seen 4 months earlier with a vulval ulcer which was thought to be viral in origin. It had resolved prior to review.

Investigations included full blood count (FBE) and C-reactive protein, which were within normal limits, and erythrocyte sedimentation rate (ESR) which was 56mm/hr 5 months prior to referral and 57mm/hr at the time of referral.

Erythema nodosum investigation, when and what

Erythema nodosum can usually be diagnosed on clinical history alone. Biopsies should be considered for patients with a prolonged or atypical course or atypical distribution (eg ulceration or affected area other than leg).(1, 3, 4) Given the high incidence of GAS infections, anti-streptolysin O titres (ASOT) and throat culture may help to confirm the diagnosis, as well as prompting treatment for eradication of GAS.(1, 4). Elevation of ESR is common in both idiopathic and secondary erythema nodosum, and was not discriminatory in children.(2, 3) A thorough history examining possible causes should direct investigations beyond this.

Based on the patient's known exposure to TB and history of abdominal pain and diarrhoea, longstanding erythema nodosum and persistently elevated ESR, further investigations were ordered. CRP was mildly elevated at 13mg/L and the ESR was markedly elevated at 81mm/hr. Faecal calprotectin was negative at 21 (<50), while QuantiFERON-TB gold was strongly positive at 9.05 IU.mL (>0.35). Chest x-ray revealed increased linear interstitial markings in the right upper lobe. She was referred to the infectious diseases team for further workup. CT chest revealed two tiny (<5mm) nodules in the right upper lobe of the lungs, and several calcified mediastinal lymph nodes of up to 9mm in short axis diameter. Ultrasound of the abdomen revealed multiple enlarged lymph nodes around the porta hepatis and pancreatic head with scattered central calcification, largest measuring 24x15x21 mm. Stool microscopy and culture was negative as was coeliac serology. Consideration was given to lymph node biopsy for definitive diagnosis, but the location was not amenable to biopsy. Given her good general health, the patient was monitored clinically

for several months before a recrudescence of the ESR (75mm/hr) and persistently elevated ferritin (254 (9-136) ug/L as well as unchanged sonographic findings forced a commencement of anti-TB therapy. One month after commencing Isoniazid, Rifampicin and Pyrazinamide, the ESR had dropped to 36mm/hr, the ferritin to 77 ug/L and the lymph nodes were starting to shrink on repeat ultrasound. No further erythema nodosum lesions have appeared since the start of anti-TB treatment.

Treatment

Erythema nodosum is a self limiting condition, and usually resolves, even without treatment for the underlying cause.(1) If there is a treatable cause, this should be addressed. Treatment is otherwise supportive; non steroidal anti-inflammatory drugs (NSAIDs) can help to relieve pain(1) and bed rest may decrease the duration of the rash in patients with an infectious cause.(3)

Conclusion

Erythema Nodosum is an uncommon cause of rash in children which can be diagnosed on history and examination. Identification of EN should prompt a search for potential underlying causes. Tuberculosis remains a major cause of paediatric mortality worldwide and remains relevant to paediatricians in Australia due to increased international travel, immigration and refugee resettlement.(5)

Conflicts

None of the authors have any conflicts of interest to declare.

Questions.

1: What is the commonest cause of erythema nodosum in children?

- A Idiopathic
- B Inflammatory Bowel Disease
- C Group A Streptococcal infection *
- D Tuberculosis
- E Medication reactions

A common in adults but less so in children

B An important differential, but not the most common

C Infectious causes, particularly GAS infection are the most common causes of EN in children

D Uncommon in high income settings due to low background incidence of TB, but an important differential, particularly in patient subgroups with higher incidence.

E Not seen commonly in children

2: What features of suspected erythema nodosum should prompt consideration of a biopsy

- A Elevated inflammatory markers
- B Distribution on the anterior shins
- C Associated joint pain
- D Prolonged course
- E No clear precipitant

A: Elevated inflammatory markers are common in EN and are not associated with specific aetiologies.

B: This is the typical distribution of EN and does not, on its own warrant consideration of biopsy.

C: Joint pain, in particular knee pain is commonly associated with EN

D: EN is usually short in duration, and a prolonged course should prompt consideration of a biopsy to rule out other, less common, panniculitides.

E: While less common in children than in adults, 22% of EN in children is idiopathic in origin

3: Which of the following may represent a reasonable treatment option for a child with an episode of EN secondary to a viral URTI.

- A: Exercises to encourage blood flow to the affected limb
- B: Excision of lesions
- C: Topical corticosteroids
- D: Expectant waiting
- E: Penicillin for eradication of Group A Streptococci

A: While we wouldn't necessarily advocate for strict bed rest, this may decrease the duration of the rash

B: Not indicated as the lesions resolve spontaneously without scarring

C: While case reports exist for the use of oral corticosteroids in particularly severe cases, steroids are not indicated in the first instance

D: As this is likely to resolve of its own accord, if the child is not in too much pain, expectant waiting may be a reasonable treatment option, or supportive treatment with NSAIDS

E: Not indicated without proof of carriage.

Bibliography

1. Blake T, Manahan M, Rodins K. Erythema nodosum - a review of an uncommon panniculitis. Dermatol Online J. 2014;20(4):22376.

2. Hassink RI, Pasquinelli-Egli CE, Jacomella V, Laux-End R, Bianchetti MG. Conditions currently associated with erythema nodosum in Swiss children. *Eur J Pediatr*. 1997;156(11):851-3.
3. Kakourou T, Drosatou P, Psychou F, Aroni K, Nicolaidou P. Erythema nodosum in children: a prospective study. *J Am Acad Dermatol*. 2001;44(1):17-21.
4. Pink A, Barker J. Erythema nodosum. *Br J Hosp Med (Lond)*. 2012;73(4):C50-2.
5. Marais BJ. Tuberculosis in children. *J Paediatr Child Health*. 2014;50(10):759-67.

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Table 1: Common Causes of Erythema Nodosum (1,4)

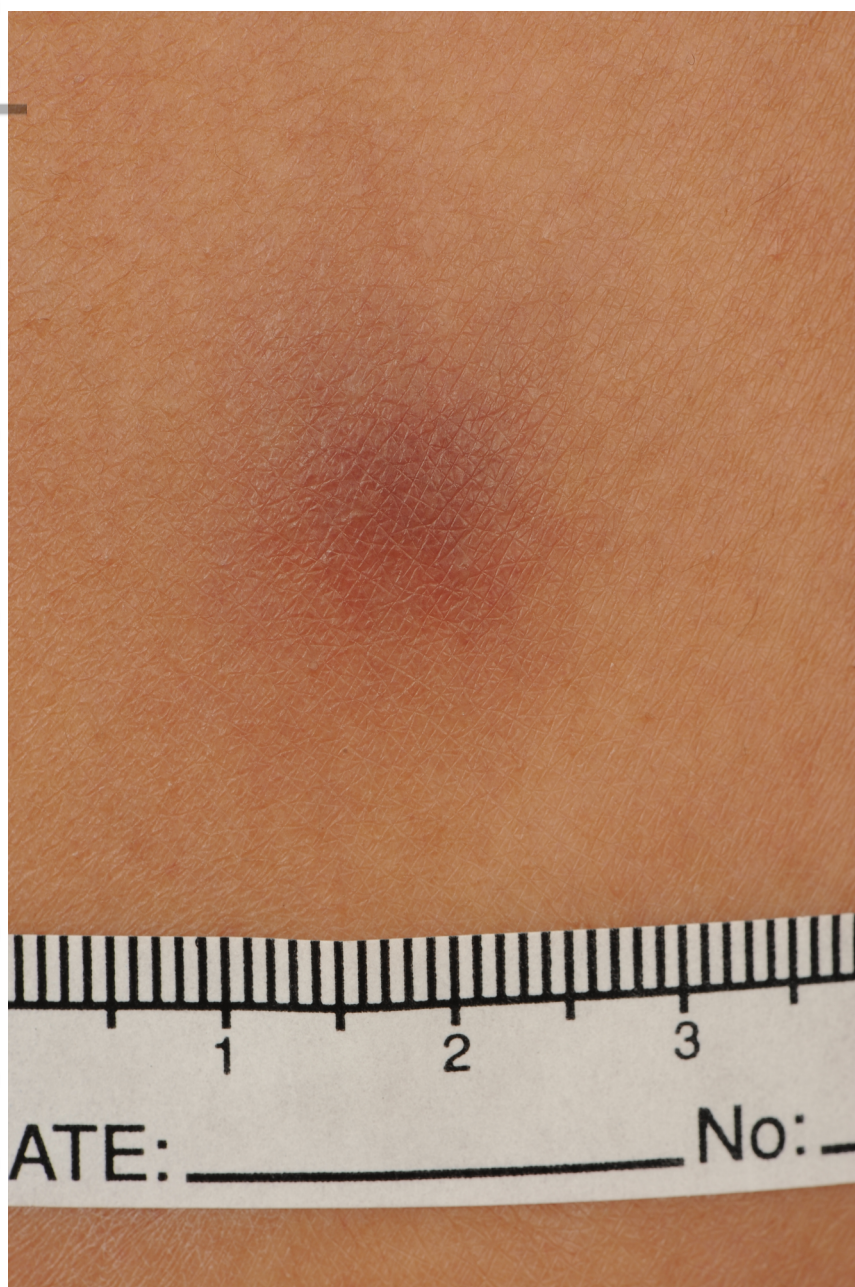
Idiopathic	Infections	Drugs	Pregnancy	Systemic Illnesses
	Streptococci	Oral Contraceptive Pill		Inflammatory Bowel Disease
	Viral URTI	Sulphonamides		Sarcoidosis
	Mycoplasma	Phenytoin		Hodgkin's Lymphoma
	Yersinia	Penicillins		Behcet's Disease
	Campylobacter			Lupus
	Salmonella			Sjogren's Syndrome
	Tuberculosis			

Figures 1 and 2 the patient's legs after a re-emergence of the lesions.

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