CASE REPORT

Erythema nodosum associated with Salmonella enteritidis

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Abstract

Background: Erythema nodosum (EN) is the most frequent type of panniculitis in childhood. Although frequently idiopathic, it may be associated with a wide variety of conditions ranging from infections, to sarcoidosis, to collagen vascular diseases to drugs.

Case report: We present an 8-year-old boy who developed EN during the course of febrile gastroenteritis due to salmonella enteritidis. He received intravenous ampicillin 150 mg/kg/day divided in equal doses every six hours for 10 days. The skin lesions gradually disappeared, and he recovered fully without sequelae.

Conclusions: Salmonellosis should be considered in the differential diagnosis of EN in children with gastrointestinal symptoms, and stool cultures should be performed when indicated. Hippokratia 2010; 14 (1): 51-53

Key words: erythema nodosum, children, differential diagnosis, salmonellosis

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Erythema nodosum (EN) is the most frequent type of panniculitis in childhood with a prevalence of 2.4 per 10,000 population. It occurs more rarely in children than in adults[1,2]. EN represents a hypersensitivity reaction seated in the subcutaneous fat. It is associated with numerous insults. The cutaneous lesions evolve into a spectrum of colours resembling bruises. The inflammation is focused primarily in the subcutaneous septa with common peripheral lobular involvement[3]. Importantly, the lesions of EN neither ulcerate nor scar. In children, there is no sex predilection, while in adolescence and adults there is a clear female predominance[1].

A case of EN in a child that occurred during an episode of gastroenteritis due to Salmonella enteritidis is described. A brief review of the relevant literature is also carried out.

Case presentation

An 8-year-old boy presented in the emergency room with vomiting and abdominal pain during the last two days. On admission the child was afebrile, normotensive with signs of mild dehydration. Physical examination revealed mild abdominal pain on deep palpation, without rebound tenderness or hepatosplenomegaly. Moreover, he had four well-demarcated, painless, warm, palpable erythematous nodules in both shins. He was not receiving any medications. His previous medical history and the family history were non-contributory. A throat culture showed normal oropharyngeal flora, while a complete blood count demonstrated leukocytes 11,420/μl (77% neutrophils, 15% lymphocytes, 5% monocytes), hemoglobin 12.5 g/dl, hematocrit 36.1% and platelets 406,000/μl. Liver function tests, serum electrolytes creatinine and urea were normal. Immunological work-up showed IgG 1,470 mg/dl, IgA 286 mg/dl, IgM 157 mg/dl, IgE 660U/ml, normal C3 and C4, CRP 8.4mg/dl, while no antinuclear antibodies were detected. Erythrocyte sedimentation rate was 60mm/ hour. Epstein Barr virus and Mycoplasma pneumoniae serologies were consistent with past infections, while serologies for Chlamydia pneumoniae were negative. A chest radiograph showed normal findings. A purified protein derivative skin test for tuberculosis was negative. Due to high fever up to 39°C and persistent diarrhea with 2 to 3 watery bowel movements per day, stool cultures were sent and grew Salmonella enteritidis. The isolated pathogen was sensitive to co-amoxiclav, ampicillin, piperacillin/tazobactam, ticarcillin/clavulanic acid, cefotaxime, ceftazidime, imipenem, ciprofloxacin, and trimethoprim/sulfamethoxazole. The strain was resistant to cephalothin, cefaclor, nalidixic acid, netilmicin, tobramycin, amikacin, and nitrofurantoin. He received intravenous ampicillin 150 mg/kg/day divided in equal doses four times/day for 10 days. Prior to ampicillin, a second blood culture was obtained and was also sterile. The second day of ampicillin treatment his clinical condition improved and he defervesced. The skin lesions gradually resolved and completely disappeared over the next 10 days. At the same time his stools normalized. A repeat stool culture after the end of the 10-day ampicillin therapy was negative for S. enteritidis. At the 3-month follow-up, he remained in excellent health.

Discussion

EN is a painful disorder of subcutaneous fat characterized by the sudden appearance of symmetrical erythematous, warm, tender, and hard nodules, usually located on

the anterior surface of the lower extremities, especially the tibias. Less common sites of involvement are the trunk, the face, the neck and the arms. EN is uncommon in children, especially those under the age of two years. Despite that, it remains the most frequent type of panniculitis in pediatrics[1]. Most direct and indirect evidence support the involvement of a type IV delayed hypersensitivity reaction to antigens derived from infections, sarcoidosis, collagen vascular diseases or drugs, such as penicillin, phenytoin, sulfonamides, other antibiotics, or hormonal contraceptives[4]. The most common identifiable cause is streptococcal pharyngitis[5], but it may be also the first sign of a systemic disease, such as tuberculosis, sarcoidosis, rheumatologic diseases, autoimmune disorders, inflammatory bowel diseases and cancer[1]. Rarely, EN has been linked to bacterial or deep fungal infections, such as cat-scratch disease[6], leptospirosis[7], or sporotrichosis[8] and with viral infections (hepatitis B, C, EBV) and vaccinations[9-11]. Fever, malaise and arthralgias may develop before or during the course of EN. Initially, the nodules show a bright red colour. After a few days they become purplish, and, finally exhibit a yellow or greenish appearance. The lesions exist for a period of 2 to 6 weeks; they never ulcerate, and usually resolve without atrophy or scarring[4]. The main treatment of EN is that of the underlying conditions, if known. Aspirin and other non-steroidal anti-inflammatory agents in full doses are frequently prescribed and often are adequate treatment, although we did not use them in our case[12].

In a retrospective study of 45 children, the most frequent etiology was tuberculosis (10 patients), followed by S. enteritidis (7 patients), group A β-hemolytic Streptococcus (3 patients), Salmonella typhimurium, Campylobacter jejuni (2 patients each), and Yersinia enterocolitica, EBV-related infectious mononucleosis, cat scratch disease, BCG vaccination, chronic hepatitis B infection, and amoxicillin treatment (1 patient each).

Etiology remained unknown in 15 cases. Interestingly, the last case of EN that was associated with tuberculosis in this series dated back to 1991, after which the most frequent etiologic factors were gastrointestinal pathogens[13]. In another study from Spain, where 22 children were diagnosed with EN, the etiologic factors were determined in 77% of the patients. Tuberculosis was the most frequent cause (36%); in 22% of the cases, no reason was identified[14]. In a series of 35 children with EN from Switzerland dating back to 1977, infections other than tuberculosis were implicated in 20 cases, including 10 streptococcal infections and 3 cases of infectious gastroenteritis due to S. enteritidis and Y. enterocolitica. Interestingly, non-infectious inflammatory diseases, such as ulcerative colitis, Crohn's disease, Behcet's disease and sarcoidosis were responsible for another 8 cases[15]. In a series of 24 children from Israel, streptococcal infections were implicated in one quarter of the cases, followed by EBV infections and inflammatory bowel diseases, while in one-third of the cases, no specific cause could be identified[16]. Finally, in a recent series from Turkey of 10 children with a mean age of 8.8 years, the etiology of EN was established in 5 cases. Three had streptococcal infection, while 2 were diagnosed with primary tuberculosis[17]. In a recent adult series (mean age: 37 years old) from the same country, the leading etiology was also streptococcal infections and responsible for 11% of the cases. In that series, sore throat, diarrhea, arthritis, and pulmonary pathology were predictors of secondary EN[18].

Regarding Greece, to the best of our knowledge, there is only one relevant publication. Thirty-five children with EN (17 boys and 18 girls, with a mean age of 8.8 years) were prospectively studied. In 27 of them (77%), the etiology of EN was confirmed by laboratory investigations. In 25 children the causative factor was infectious, including β-hemolytic Streptococcus in 17 cases, and Mycobacterium tuberculosis in two, whereas in two patients EN was associated with Crohn's disease and Hodgkin's disease, respectively[19]. In this series, no case of EN was linked to gastroenteritis due to Salmonella spp. Apparently, the frequency with which Salmonella spp. are linked to EN is a matter of both the prevalence of salmonellosis and the genetic composition of the population involved.

Diagnostic evaluation after comprehensive history and physical examination should include complete blood count with differential; erythrocyte sedimentation rate, serum C-reactive protein, or both; and testing for streptococcal infection. In atypical or chronic cases, when the lesions persist for many weeks or in recurrences, a biopsy is also indicated[20].

Conclusions

The list of possible etiologic factors in EN is extensive. A symptom and clinical sign-based cost-effective diagnostic approach is essential. Salmonellosis should be considered in the differential diagnosis of EN in children with gastrointestinal symptoms, while stool cultures should be performed when indicated.

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