

# Erythema nodosum associated with *Yersinia enterocolitica* infection – case report

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**Abstract:** A 48-year-old female patient was admitted to the Department of Internal Medicine for diagnostic evaluation of recurrent erythema nodosum. The examination findings excluded sarcoidosis, tuberculosis, non-specific enteritis or collagenoses, but demonstrated the presence of yersiniosis. Antibiotic therapy was applied and the skin nodular lesions resolved.

**Key words:** erythema nodosum, yersiniosis

## INTRODUCTION

Erythema nodosum is an inflammation of the subcutaneous tissue, most commonly located on the anterior surface of shins. It mainly affects young females 30-40 years of age – about 90%; males are sporadically affected [1]. The pathogenesis of erythema nodosum is unknown although the involvement of immune complexes is implicated. The disease manifests in the development of inflammatory, sharply delimited and painful nodules. The affected skin is reddened and excessively warm, although without necrotic changes. In the clinical picture, skin lesions are accompanied by general symptoms (fever, painful joints, malaise), and symptoms of underlying disease related mainly to the respiratory and gastrointestinal systems. The etiological factors which are likely to induce erythema nodosum include: infections (*Mycobacterium tuberculosis*, *Chlamydia*, *Salmonella*, *Streptococcus*, *Yersinia*, HBV, HCV, EBV), sarcoidosis, non-specific enteritis, Crohn's disease, or less commonly ulcerative colitis, drugs (penicillin derivatives, sulfonamides, NSAID, oral contraceptives), and connective tissue diseases (lupus erythematosus, systemic sclerosis). In cases of diagnostic doubts, a biopsy of the subcutaneous tissue is recommended – histopathological findings disclose inflammatory infiltrations of the connective tissue septa between fatty lobules [3]. Differential diagnosis should consider superficial thrombophlebitis, bacterial infections of the subcutaneous tissue, adipose tissue inflammation, erysipelas and vasculitis [1, 2]. Yersiniosis is an infectious disease, which may be complicated by erythema nodosum. It is acute, sub-acute or chronic (less commonly) antropozoonosis caused by Gram-negative *Yersinia enterocolitica*, belonging to the family *Enterobacteriaceae*. In most cases, infections develop due to ingestion of undercooked pork contaminated with faeces during slaughter, unboiled milk, and water contaminated with animal or human faeces [4, 6]. The clinical picture of the infection is diverse – the bacterium can cause food poisoning, enteritis (particularly in small children), inflammation of

the mesenteric lymph nodes and the terminal portion of the ileum (mainly in adults), as well as bacteraemia, sepsis and purulent infections of various locations [4]. Involvement of lymph nodes and ileum may imitate acute appendicitis. Faecal cultures and serological tests are essential for the diagnosis. Other yersiniosis complications, including those of immune origin, are reactive arthritis, Reiter's syndrome and erythema multiforme.

## CASE REPORT

A 48-year-old female patient was admitted to the Department of Internal Diseases for diagnostic procedures of recurrent erythema of the internal surface of hands and feet over a period of 3 months, and painful inflammatory nodules on the anterior surface of both shins. Local lesions were accompanied by osteoarticular pain, periodic febrile temperature (38°C) and weakness (Fig. 1).

The patient had been hospitalized 3 times in the Department of Dermatology due to the above-mentioned symptoms. One week before the occurrence of the first skin lesions, the patient had an episode of angina which was treated with non-steroidal anti-inflammatory drugs and amoxicillin with clavulanic acid. The laboratory tests performed during her first stay in the Department of Dermatology showed features of systemic inflammation: leucocytosis – 13.100 K/ $\mu$ l, neutrocytosis – 11.090 K/ $\mu$ l (84.4% of leucocytes), CRP – 62.6 mg/l (norm <5 mg/l), SR (sedimentation rate) – 42 mm/h. After therapy of doxycycline, clemastine 3 mg/day, local anti-inflammatory drugs and dexamethasone – 4mg/day for 5 days, the inflammatory lesions quickly resolved leaving slight discolorations on the skin of the shin. The patient was discharged home in good general condition with the diagnosis of erythema nodosum of probable post-medication etiology. During the next 4 weeks, 2 recurrences of erythema were observed and treated in the Department of Dermatology and Internal Diseases. The widened diagnostic procedures were carried out for:

- Tuberculosis (positive TB test – 25mm verified with the QuantiFeron test – negative; chest X-ray – no abnormalities)

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Received: 11 December 2009; accepted: 28 December 2009



Figure 1 Erythema nodosum – acute stage.

- Collagenoses (antinuclear antibodies – negative; electrophoresis of plasma proteins – no significant changes)
- Parasitic diseases ( parasitological exam of faeces – negative)
- Lambliosis (ELISA *Giardia lamblia* – negative)
- Löfgren syndrome (lack of chest X-ray nodal and/or parenchymal lesions characteristic of sarcoidosis)
- Non-specific enteritis (gastroscopy and rectal enema findings – normal).

The patient denied taking oral contraceptives. The renal, hepatic and thyroidal parameters were normal. Neoplastic markers (CA-125, CEA, CA19-9, CA15-3) were negative. During further recurrences of erythema nodosum, the parameters of inflammation rapidly increased - CRP – 94.2 mg/dl; SR 100 mm/hour, leucocytosis – 10.300 K/ $\mu$ l. The patient underwent orthopaedic, rheumatological and angiological consultations. Ultrasound examinations of veins did not reveal pathologic changes. Additionally, the serological test for *Yersinia enterocolitica* was performed, the result of which confirmed yersiniosis (IgM and IgG antibodies – positive) – the etiological factor of erythema nodosum. The abdominal ultrasound findings did not demonstrate enlargement of the liver, spleen and lymph nodes. After the antibiotic therapy – ciprofloxacin 500 mg 2 $\times$  a day, the erythema skin lesions resolved and inflammation markers normalized (leucocytosis to 5.100 K/ $\mu$ l, SR 20 mm/hour and CRP 9.3 mg/l).



Figure 2 Erythema nodosum during resolution of inflammatory lesions.

The patient was discharged from hospital, continuation of ciprofloxacin and follow-ups in the Infectious Diseases Outpatient Clinic were recommended.

## DISCUSSION

Erythema nodosum is an interdisciplinary medical issue in which specialists in infectious diseases, rheumatologists, gastrologists and primary health care physicians are interested. The diagnosis of this dermatosis requires comprehensive diagnostic procedures to determine the underlying disease. Causal treatment is the most effective management, both to resolve the skin eruptions and to reduce the risk of erythema recurrences. Literature data demonstrate that despite advances in diagnostic methods, in half of the cases, the underlying cause is not found. In our patient, erythema nodosum was associated with *Yersinia enterocolitica* infection. The likely route of infection was ingestion of uncooked pork meat during preparation of meatballs. The infection was asymptomatic – the patient denied vomiting, abdominal pain or diarrhoea. The cause-effect relationship between yersiniosis and erythema was evidenced by marked improvement of the local status of the shins (Fig. 2), and no recurrences after antibiotic therapy. Erythema nodosum is the commonest complication of yersiniosis. It is estimated that 20% of all cases of erythema nodosum is caused by *Yersinia enterocolitica*.

Faeces are the material most commonly collected for microbiological tests. The serological diagnosis is based on detection of antibodies occurring in serum in response to *Yersinia* infection. IgM antibodies appear first, followed by IgG and IgA antibodies. The concentration of antibodies depends on the severity of infection. In mild intestinal forms, the humoral response is often undetectable, while higher levels of antibodies are detected in more severe infections, particularly of extra-intestinal location.

The main symptoms include: diarrhoea lasting for even several days, epigastric pain, sometimes vomiting and fever – from subfebrile to 39°C. In the majority of cases, the complaints subside spontaneously.

Food poisoning, enteritis, inflammation of the mesenteric lymph nodes and the terminal portion of the small intestine generally require symptomatic treatment.

Since *Y. enterocolitica* is resistant to penicillin and first generation cephalosporins, third generation cephalosporins are recommended, preferably combinations of third generation cephalosporin, aminoglycoside, third generation cephalosporin, fluorochinolone, aminoglycoside, and fluorochinolone [4-6].

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