Acta Derm Venereol (Stockh) 1998; 78: 1–2

Non-purulent Furunculoid Cutaneous Nodules as an Indicator for Agranulocytosis

Sir,

The skin has a well-established indicator function for a variety of internal diseases, particularly in immunocompromised patients (1). The growing list of immunodeficiency diseases encompasses disturbances of different major components of the immune system, including granulocytes, lymphocytes, mononuclear phagocytes and complement proteins. We present a patient suffering from disseminated non-purulent, furunculoid nodules caused by follicular Escherichia (E.) coli infection. Of unusual clinical presentation, these cutaneous nodules provided the first hint of the underlying methimazole-induced agranulocytosis.

CASE REPORT

A 48-year-old woman presented with disseminated, non-fluctuating, non-purulent, tender nodules up to 7 cm in diameter of a dark red-purple colour, mostly on her back and thighs. Several nodules were ulcerated with a necrotic core (Fig. 1). The nodules developed one month before admission and steadily increased in number and diameter. Five months prior to admission, therapy with methimazole (15 mg/d) was initiated for hyperthyreosis. On admission, the patient's temperature was 38.4°C rising to 40.2°C one hour later. Blood analysis showed a strongly increased BSR (70/85 mm) and CRP (96.1). However, peripheral blood leukocyte number was decreased to 1.5/nl with less than 5% neutrophils and 92% lymphocytes. No yeasts or bacteria could be grown from three blood cultures at two different intervals. Histopathological analysis of an excised cutaneous nodule showed deep follicular fibrosing inflammation and abscess formation with central colliquation and necrosis from the ulcerated epidermis to the upper subcutis. However, there was only a slight neutrophile inflammatory infiltrate. E. coli was cultured from smears of three different ulcerated nodules. Bone marrow biopsy revealed agranulocytosis with strongly reduced granulocytopoiesis and only few eosinophils and basophils, whereas the number of lymphocytes and plasma cells was increased and erythropoiesis and megakaryopoiesis were unaffected. Non-purulent, furunculoid nodule due to follicular E. coli infection in a patient with impaired host defence due to methimazole-induced agranulocytosis was diagnosed. Other causes of agranulocytosis had been excluded either clinically or serologically. Methimazole as the causative drug for agranulocytosis was withdrawn and intravenous chemotherapy according to a standard regime with teicoplanin (400 mg/d), ceftriaxon (2 g/d) and fluconazole (100 mg/d) was initiated, leading to normothermia within the following 24 h. Treatment with granulocyte-colony stimulating factor (G-CSF, 48 million I.U./d) for 14 days was undertaken, but granulocytopoiesis was not restored. More aggressive approaches, such as immunosuppression or bone marrow transplantation, were postponed to a later date. Sixteen days after admission, intravenous chemotherapy was stopped and oral application of ciprofloxacin (1 g/d), cotrimoxazole (2 g/d) and fluconazole (100 mg/d) was initiated. The patient was then dismissed from hospital. Five months later, granulocytopoiesis was evident and normal counts of neutrophils could be made in the peripheral blood. All cutaneous nodules had disappeared and long-term antimicrobial chemotherapy had been discontinued.

DISCUSSION

Clinically, agranulocytosis commonly presents with a severe sore throat and necrotizing tonsils, followed by fever, chills, prostration and eventually death (2). On admission, our patient showed disseminated, non-purulent, furunculoid cutaneous nodules followed by the rapid development of septic temperature. This suggested a systemic spread of infectious agents from the skin lesions. E. coli was cultured from smears of the ulcerated skin eruptions (3). The E. coli were found to be responsible for the vellus hair follicle bound, non-purulent, furunculoid nodules. The non-purulent, necrotic aspect of the furunculoid cutaneous nodules in our patient may best be explained by the absence of granulocytes. Alternatively, a haematogenic spread and arrest in extravascular tissue of infectious emboli or antigens known as ecthyma gangrenosum in pseudomas aeruginosa sepsis or as disseminated nodules and papules in candida sepsis was discussed. However, the latter two diagnoses were excluded by blood culture analysis and histology.

Evaluation of the skin eruptions was crucial for the diagnosis of agranulocytosis. This finally resulted in causal therapy including discontinuation of methimazole as the drug responsible for agranulocytosis (4), antimicrobial chemotherapy and stimulation of granulocytopoiesis (2). Clinicians should be aware of this clinical appearance to enable an early recognition and therapy of an acquired immunodeficiency due to drug-induced agranulocytosis.

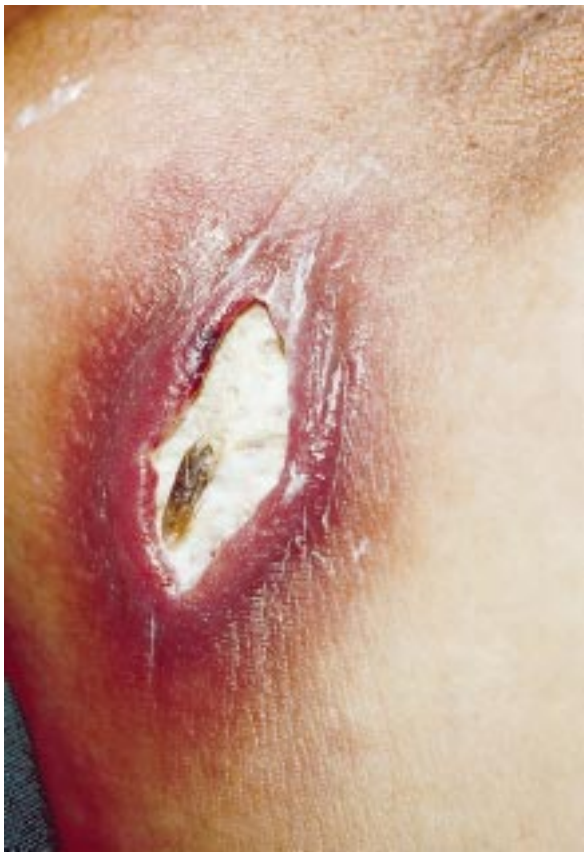

Fig. 1. Tender, non-purulent, deep red-purple furunculoid nodule with central necrotic ulceration on the inner thigh.

 ISSN 0001-5555

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Accepted May 2, 1998.

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