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Erythema Nodosum Associated with Myelodysplastic Syndrome: A Case Report

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Keywords

Myelodysplastic syndrome (MDS) · Erythema nodosum · Immunosuppressive treatment

Introduction

The myelodysplastic syndrome (MDS) is caused by a heterogeneous group of malignant stem cell disorders. It is characterised by dysplastic and ineffective blood cell production with possible progression to acute myeloid leukaemia. Different types of skin lesions have been described in patients with MDS, ranging from specific lesions defined by the presence of malignant haematopoietic cells in the skin to non-specific lesions such as infections, vasculitis and neutrophilic dermatoses [1]. Furthermore, multiple autoimmune manifestations are associated with MDS. They are thought to be caused by abnormal T cell responses to antigen presentation and abnormal B cell and T cell interactions [2, 3]. However, erythema nodosum in patients with MDS is a rare condition [4].

Case Report

In March 2010, a 74-year-old woman was admitted with fatigue, painful swelling of the right ankle, and multiple erythematous, edematous subcutaneous nodular skin lesions at the extensor sides of the lower legs and forearms (fig. 1). Dermatologic examination involving skin biopsy revealed erythema nodosum (fig. 2). X-ray of the right ankle joint showed soft-tissue swelling, but no sign of chronic inflammation (fig. 3). Arthralgia with or without arthritis is a frequently seen symptom accompanying erythema nodosum [5]. Duplex sonography revealed epifascial oedema at the lower legs. The symptoms persisted for 3 months before presentation in our clinic.

The patient had been diagnosed with transfusion-dependent World Health Organisation (WHO) MDS with del (5q) syndrome in September 2005. Other aberrations or mutations (JAK2, FLT3, or NPM1 mutation) were not detected. The patient had initially received lenalidomide therapy, which was terminated due to insufficient effectivity after several months. Apart from intermittent transfusions of erythrocyte and thrombocyte concentrates, the patient received no further treatment.

When presenting, the haemoglobin level was 8.1 g/dl, reticulocytes 0.4%, white blood cell count 17.6 × 10^9 cells/l with 4% blast cells, 2% myelocytes, 77% polymorphonuclear leukocytes, 5% band cells, 6% monocytes and 7% lymphocytes. The platelet count was 30 × 10^9/l. Further laboratory tests revealed a lactate dehydrogenase (LDH) level of 251 U/l (normal < 250 U/l), a serum ferritin level of 4720 µg/l (normal 15–160 µg/l) and a C-reactive protein (CRP) level of 13 mg/dl (< 0.5 mg/dl).

No other reason for the erythema nodosum was found. Rheumatoid factor and anti-neutrophil cytoplasmic antibodies (ANCA) were not detectable; complement factors C3 and C4 were normal. The anti-streptolysine level was 26 IU/ml (normal < 360 IU/ml); the Mantoux tuberculin skin test, Lyme serology, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and trachomatis serology were negative. Chest X-ray and chest computed tomography (CT) scan revealed no sign of pneumonia or sarcoidosis. Colonoscopy demonstrated bland diverticulosis, but no signs of inflammation. The histological examination of mucosa biopsies displayed no inflammatory bowel disease. The bacteriological stool examination was inconspicuous. No malignancy was found in the chest CT scan, the colonoscopy and the abdominal sonography. The lenalidomide therapy was terminated about 4 years before the onset of the erythema nodosum, making a causal link unlikely.

The bone marrow biopsy from January 2010, which was taken after the onset of the erythema nodosum, showed no disease progression in comparison to the bone marrow biopsy from September 2009. The International Prognostic Scoring System (IPSS) indicated an intermediate risk II. After immunosuppressive treatment with prednisone 40 mg daily, the skin lesions and the ankle pain as well as the laboratory inflammatory signs improved within days. The total white blood cell count dropped to a normal value of 9.2 × 10^9 cells/l with 2% blast cells, 1% myelocytes, 70% polymorphonuclear leucocytes, 3% band cells, 5% monocytes and 15% lymphocytes.

Discussion

MDS can be associated with a variety of skin disorders. In general, an early recognition of cutaneous lesions in MDS is important because they can precede blood or bone marrow acute transformation, thus predicting a poor prognosis. This is especially true for specific skin lesions, whereas the impact of unspecific lesions, such as erythema nodosum, is not yet entirely clear. Erythema nodosum represents an inflammation

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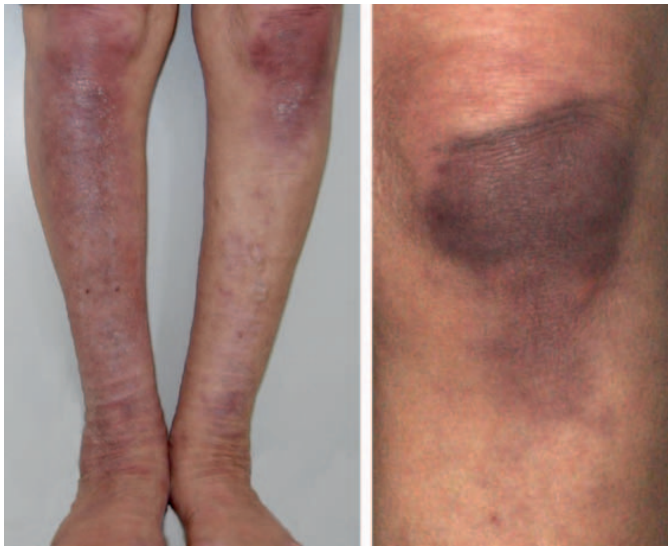

Fig. 1. Left: Multiple erythematous nodules on the knees and shins. Individual nodules coalesce and form large areas of hardened skin. Right: Close-up of an erythematous nodule on the left knee.

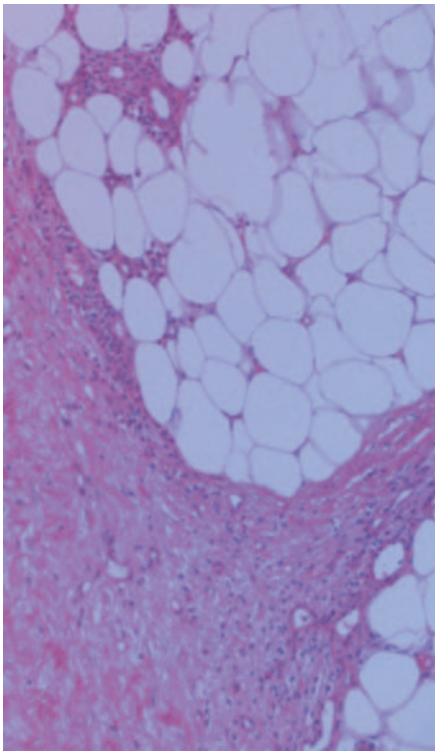

Fig. 2. Histological examination showed lymphocytic infiltration in the periphery and the septa of the subcutaneous fat lobules (haematoxylin & eosin stain).

of the septa of the subcutaneous fat tissue [6] and is thought to be determined by type IV delayed hypersensitivity response to numerous antigens [7]. Then again, the bone marrow failure characterising MDS, though generally assumed to be an intrinsic stem cell maturation defect, may be associated with T cell-mediated myelosuppression [3, 8]. In MDS, increased percentages of cytotoxic effector T cells and decreased numbers of regulatory T cells can be found [9]. Regulatory T cell numbers and function seem to correlate inversely with bone marrow apoptosis, but also with low-risk disease [10–12]. Approximately 20% of MDS patients achieve sustained red cell transfusion independence after anti-thymocyte globulin (ATG) infusion therapy [13]. However, the expansion of the now unrestrained dysplastic clone may facilitate leukaemic progression after the loss of MDS-specific cytotoxic T cells. This concern, however, was not verified in a 10-year follow-up [14]. In fact, patients responding to immunosuppressive treatment had a decreased rate of leukaemic progression [15].

Thus, although in general the onset of erythema nodosum can be an indicator for disease progression in malignancies, in MDS it might also herald the possibility of an effective immunosuppressive treatment. Disease progression has been described in 2 cases of erythema nodosum associated with MDS [4, 16]. However, immunosuppressive treatment was not only able to improve the skin lesions but also to detain the progression of dysplastic changes and to improve thrombocytopenia in 1 case [4]. The 74-year-old woman in the presented case showed no signs of disease progression 1 month after the

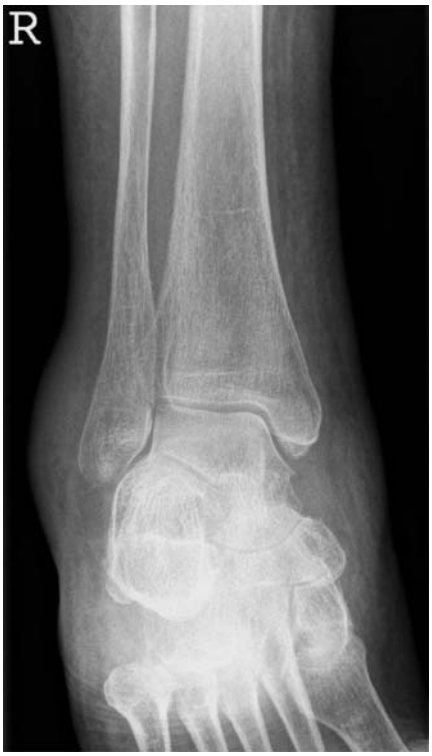

Fig. 3. X-ray of the right ankle joint shows soft-tissue swelling, but no sign of chronic inflammation.

onset of the skin lesions, as determined by bone marrow biopsy. Within 7 months after the onset of the erythema nodosum, there were no changes in haemoglobin levels and blast cell, white blood cell and platelet cell counts. The skin lesions and ankle joint inflammation responded to immunosuppressive treatment with prednisone, suggesting that these symptoms might be an immune-mediated complication of MDS. In summary, the onset of erythema nodosum in patients with MDS may be a sign of autoimmune dysfunction and is not necessarily associated with disease progression.

Disclosure Statement

The authors have no conflict of interest/competing interests.

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