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CLINICAL REPORT

Myeloid Sarcoma Developing in Pre-existing Pyoderma Gangrenosum

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We report here a case of pyoderma gangrenosum in a patient with myelodysplastic syndrome developing into myeloid sarcoma as a sign of transformation to acute leukaemia. The patient was treated successfully with intensive chemotherapy and achieved complete remission, and her otherwise expanding ulcers started to heal. This is the first reported case of secondary blastic infiltration in pyoderma gangrenosum, and it underlines the importance of performing re-biopsy of non-healing ulcers, especially in patients with an underlying haematological disease. ***Key words: myeloid sarcoma; leukaemia; pyoderma gangrenosum; myelodysplastic syndrome; blastic transformation.***

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Myeloid sarcoma (MS) is an extramedullary tumour consisting of myeloblasts or immature myeloid cells located in an extramedullary site. Clinically it presents either as single or multiple tumours in lymphoid organs, bone, skin, mucosa and other organs. It is most common in young adults and children and most frequent in men (1).

We describe here a patient with pyoderma gangrenosum (PG) transforming to MS at the time of blastic transformation of myelodysplastic syndrome (MDS) into acute myeloid leukaemia (AML).

CASE REPORT

A 61-year-old woman with a history of rheumatoid arthritis, recently treated with methotrexate, was referred to the department of dermatology due to several crural ulcers up to 7 cm in diameter (Fig. 1). The ulcers had increased in size during the previous 6 months, and PG was suspected clinically. A biopsy showed subepidermal oedema, with a mostly diffuse mixed inflammatory infiltrate predominated by lymphocytes, but also including plasma cells and eosinophils, with no signs of vasculitis (Fig. 2). These histopathological findings were compatible with the diagnosis of PG. The wounds were treated with compression and topical steroids. Because of concomitant anaemia a bone marrow biopsy was performed, and the patient was diagnosed with MDS with 10–15% blasts (refractory anaemia with excess blasts, RAEB-2) positive for CD117 and negative for CD34.

Due to progression of the ulcers after an initial response, she was transferred to the plastic surgery department 3 months later. The ulcers were described as crater-like, deep ulcerations with a border overhanging the ulcer bed, which was covered by a thick layer of yellowish fibrin (Fig. 3). The ulcers were very painful and revision under general anaesthesia was necessary. Renewed biopsies showed granulocytic sarcoma with myeloblasts CD117, CD45, vimentin and myeloperoxidase positivity, but CD34, CD61, CD235a, CD30, CD7 and CD56 negativity (Fig. 4). A second bone marrow biopsy showed transformation into AML with 36% myeloblasts with a normal karyotype, but positivity of Wilms Tumour Antigen 1 (WT1) found by polymerase chain reaction indicating an adverse prognosis (2).

The patient underwent an intensive chemotherapeutic regimen (fludarabine-etoposide-mitoxanthrone-cytarabine together with granulocyte colony stimulating factor), and 4 weeks later a new bone marrow aspirate showed complete morphological and molecular remission. Two weeks after chemotherapy was initiated the ulcers showed signs of healing, and biopsies 6 weeks after chemotherapy no longer showed leukaemic infiltration (Fig. 5). The patient received consolidation chemotherapy, initially with mitoxanthrone/high-dose cytarabine, and later a single course of high-dose cytarabine, after 6 weeks and 4 months, respectively.

DISCUSSION

Four clinical presentations of MS have been proposed (1, 3):

- In patients with known active AML – approximately 3–8% develop MS.
- As a sign of blastic transformation in patients known with either chronic myeloproliferative disease or MDS. It is estimated that 50% of this group, which develop MS, will transform to AML.
- As a sign of relapse in patients previously treated for AML or after bone marrow transplantation for chronic myeloid leukaemia.

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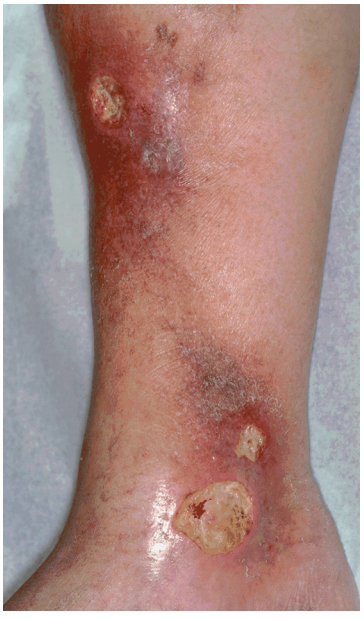

Fig. 1. Initial ulcers diagnosed as pyoderma gangrenosum.

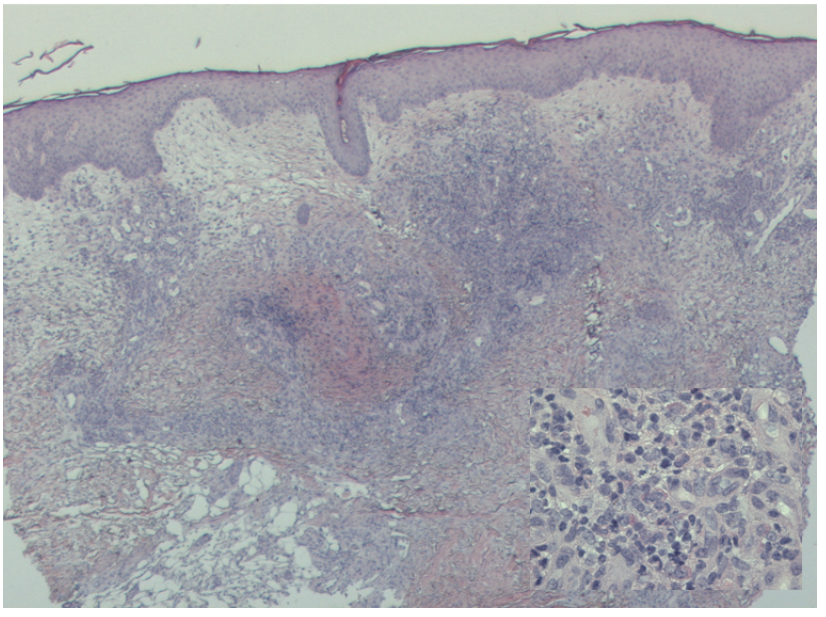

Fig. 2. Initial biopsy compatible with pyoderma gangrenosum, (H&E ×25, insert ×400).

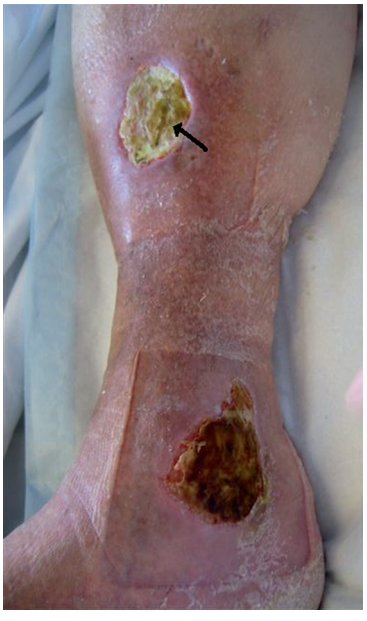

Fig. 3. Myeloid sarcoma (arrow) before surgical revision.

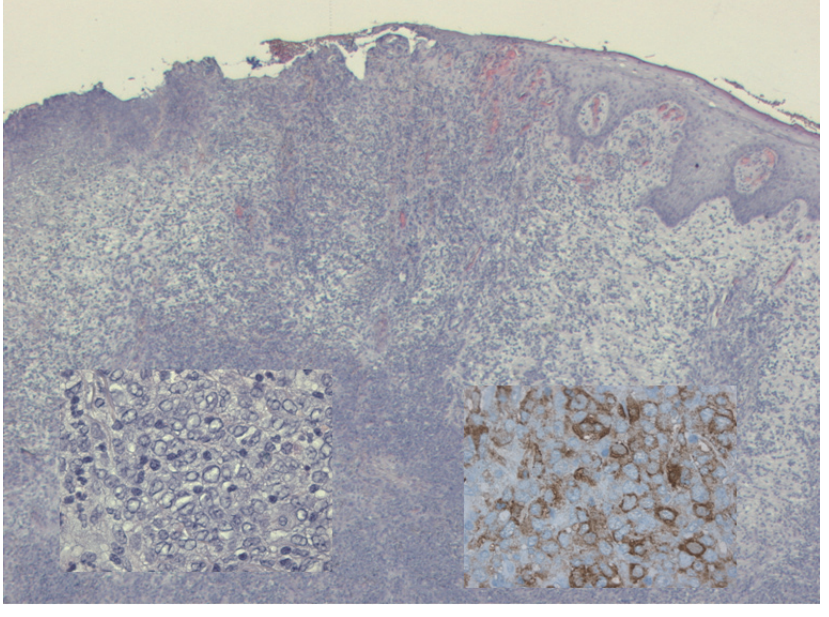

Fig. 4. Biopsy with ulceration and myeloid sarcoma (H&E ×25, left insert with blast ×400, right insert with myeloperoxidase-positive blasts ×400).

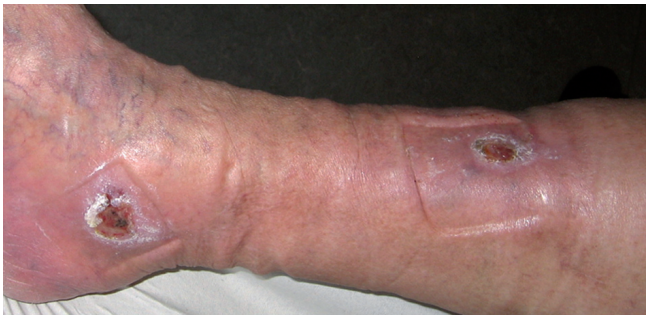

Fig. 5. Ulcers 3.5 months after initial chemotherapy.

Table I. *Antigen panel for immunohistochemical identification of myeloid sarcoma*

Antigen	Reactivity
CD3	T cells
CD7	T cells
CD20	B cells
CD30	Activated T and B cells
CD34	Haematopoietic progenitor cells
CD45	Leucocytes
CD56	NK cells
CD61	Megakaryocytes
CD68	Monocytes, macrophages
CD117	Haematopoietic progenitor cells
CD235a	Erythroid cells
Myeloperoxidase (MPO)	Granulocytes and myeloid progenitor cells
Vimentin	Mesenchymal cells

NK: natural killer.

- As primary MS in an aleukaemic form, approximately two-thirds transform to AML over an average period of 9 months (4).

MS might be misdiagnosed as non-Hodgkin's lymphoma, small round cell tumours (e.g. Ewing's sarcoma, neuroblastoma, rhabdomyosarcoma), undifferentiated sarcoma or melanoma, or as extramedullary chronic myeloproliferative disease without blast crisis (1). Immunohistochemistry plays a central role in the diagnosis of MS. It has recently been suggested that a panel including myeloperoxidase (MPO), CD 117, CD 43, CD 3, CD 20, CD 68 (or CD 163) can identify most of the variants of MS (for specification of the panel see Table I) (5).

Our patient was diagnosed with PG and MDS at the same time. PG is the most common neutrophilic dermatosis in patients with MDS (6). PG is well-known to be associated with systemic disorders, and the haemorrhagic bullous variant is known to be associated with acute leukaemia and other haematological disorders. For this reason an extensive search should be made for an underlying haematological disease (7).

Revision of the initial skin biopsy was done after the diagnosis of MS, confirming the absence of myeloblasts consistent with the diagnosis of PG. The infiltration of blasts in the ulcers developed later.

A MS developing in an already existing PG as the first sign of an AML in a patient with MDS has not been described before. The development in an area with neutrophilic infiltrates might be a sign of retained ability of chemotaxis of the malignant cells. This has also been described in deeply neutropaenic patients with AML developing Sweet's syndrome (8). Our case underlines the importance of re-biopsy in the case of non-healing ulcers, especially in patients with underlying haematological disease.

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