Cutaneous Infiltrations Can Herald an Inapparent Myelodysplastic Syndrome

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Sir,

Bone marrow disorders rarely present first to a dermatologist. However, as the skin can show the initial clinical signs of such a disease, it is important for a dermatologist to know about these conditions. We present such a case, where the diagnosis had puzzled several physicians for some time.

CASE REPORT

A 68-year-old man was referred with a 2-year history of periodic, partly itchy skin changes, located mainly on his chest, which flared intermittently and then vanished after a while, leaving pigmented residual macules behind. The only known disease in this patient was an occasional arrhythmia, otherwise he was fit and healthy. On examination we noticed several erythematous papules and plaques, mainly on the right side of the chest but also scattered solitary lesions in other areas (Fig. 1). The list of differential diagnoses initially encompassed lymphoma, pseudo-lymphoma and a drug reaction.

However, clinical examination was unremarkable and the results of all investigations performed were normal. These included: histological examination of a skin biopsy, which revealed non-specific findings (i.e. a moderately dense dermal infiltrate of lymphocytes and histiocytes), erythrocyte sedimentation rate (ESR), full blood count, routine biochemistry, serology for lues and Borrelia burgdorferi, computed tomography (CT) scan of the abdomen and thorax, T-cell receptor polymerase-γ chain reaction (PCR) from skin and serum, and a bone marrow smear.

In this setting the preliminary diagnosis remained that of a pseudo-lymphoma. The patient received a 3-week course of topical steroids, which lead to a partial remission of the skin changes, but an immediate recurrence 3 weeks after discontinuation of the therapy was noted. Therefore a short course of oral prednisolone was initiated, again with partial success, but, as before, a prompt relapse of the skin eruption was seen 4 weeks later.

At this point it was decided to monitor the clinical course closely and stop further interventions until a definite diagnosis was reached. Over the next 10 months the patient was seen every 6 weeks in the outpatient clinic. A repeated full blood count 8 months after initial presentation revealed a slight anaemia with reduced platelet count, poikilocytosis, anisocytosis and some atypical cells in the blood smear. At this time the cutaneous lesions had slowly become more infiltrated and had increased in number, especially on the chest, as shown in Fig. 1.

Another skin biopsy was performed and now, one year after the initial examination, a diffuse mixed-cell dermal infiltrate with atypical myeloid cells was seen (Fig. 2A). In addition some of these infiltrating cells were lined up in a so-called "figurate pattern" in some areas (Fig. 2B). This pattern is highly suspicious for an infiltrate of bone marrow derived cells.

Further immunohistochemical characterization demonstrated positive staining for CD68, MAC-387, lysozyme and myeloperoxidase, moderately positive staining for CD15, CD43 and CD56. A lower percentage of cells were also positive for the proliferation marker MIB-1 (Fig. 3).

Taken together the clinical, histological and immunohistological data finally indicated a diagnosis of specific infiltrates of the skin by bone marrow derived cells. The patient was referred again to the haematology department and at this point, one year after the initial investigation, a repetition of the bone marrow smear showed undoubtably erythropoetic dysplasia and some dysplastic megacaryocytes, but still no sign of acute leukaemia and no cytogenetic abnormality.

The final diagnosis was thus that of a myelodysplastic syndrome (MDS). The MDS was subtyped according to the current World Health Organization (WHO) classification as refractory anaemia (RA) without ringed sideroblasts. In terms of a clinical risk stratification score, such as the International Prognostic Scoring System (IPSS) (1), our patient fell into the low-risk group. Therefore it was decided to offer best supportive care and close follow-up every 3 months, but to take no further therapeutic measures at that time. Today, 12 months after establishing the final diagnosis, his cutaneous lesions are nearly unchanged, cause only very little discomfort and the patient is otherwise not compromised by the MDS. The disease thus shows a benign clinical course with no sign of evolving into acute leukaemia.

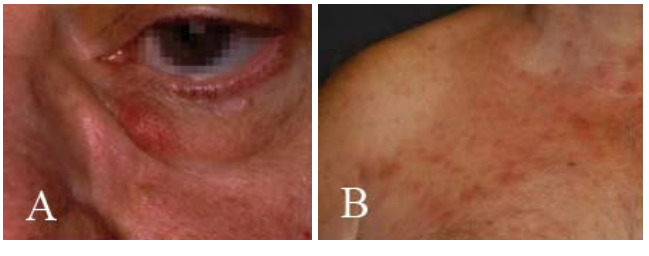

Fig. 1. Initial clinical presentation. (A) Solitary infiltrated patch on the left side of the nose. (B) Disseminated erythematous smooth nodules on the chest 5 months after initial presentation.

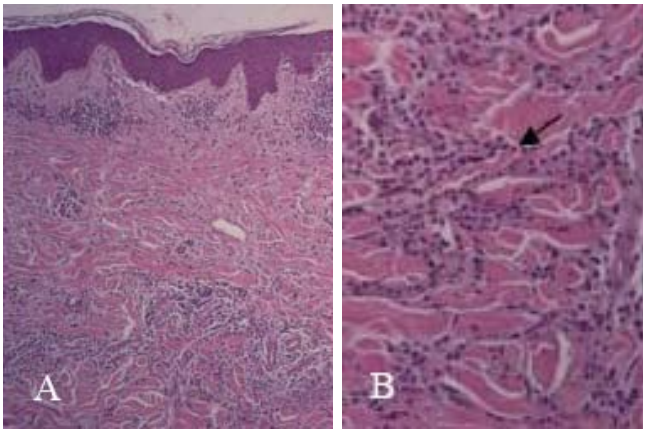

Fig. 2. Haematoxylin and eosin (H&E) stain showing (A) a mixed-cell dermal infiltrate in uneven distribution of variable density. (B) Classical "figurate pattern" of infiltrating cells (arrow) lined up between the collagen bundles.

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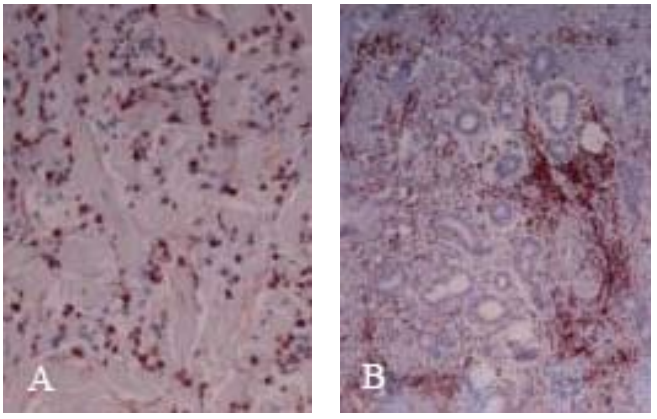

Fig. 3. (A) Immunohistology demonstrates anti-lysozyme reactivity of numerous atypical myeloid cells. (B) Anti-CD43 reactivity of dermal cell infiltrate and "figurate pattern" adjacent to some sweat gland tubuli.

DISCUSSION

MDS is a heterogeneous group of bone marrow disorders, which are rare and carry an approximate 25% overall risk of progression towards an acute myeloid leukaemia (2). MDS is caused by a stem cell defect, which comprises abnormalities of red blood cells, platelets and granulocytes (3). Until now there has been no clearly established concept of pathogenesis for this group of complex bone marrow disorders. The transformation into myeloid leukaemia is reported in 10–35% of cases, depending on the study, and median survival varies between 6 and 66 months (4, 5).

The former French-American-British (FAB) classification of 1982 was replaced by the current WHO classification, which differentiates four main types (6). Our patient fell into the group of MDS with a low blast percentage in the bone marrow smear, sub-typed as refractory anaemia (RA) without ringed sideroblasts. However, based on this pathological classification, only a limited prognostic outlook can be given. Patients with this RA-subtype of MDS have a reported 4-year survival rate of about 66% (6). To come to a more precise prognosis assessment in the individual case, several clinical scores have been developed, of which the IPSS (1, 2) is the most accepted one. In terms of such a score our patient fell into the low-risk group. Hence aggressive clinical management is not justified and best supportive care is the treatment option of choice until definite indicators for disease progression are seen. At this point several treatment options exist, including chemotherapy protocols, stem cell transplantation, thalidomide and all-*trans*-retinoic acid, the latter representing a new approach that is currently being tested in clinical studies.

Specific involvement of the skin at such an early stage, as in our case has, to our knowledge, very rarely been described in a patient suffering from MDS with low clinical risk for acute progression into frank leukaemia. Conversely, specific skin infiltrates in patients with intermediate- or high-risk MDS have been reported several times as a herald sign of transformation into myeloid leukaemia (7–10).

Therefore skin involvement is generally regarded as a sign of disseminated disease or as a manifestation of recurrence in previously treated patients (11). The case described here therefore demonstrates that it can indeed be different, as once so far reported (12). It took approximately one year to establish the correct diagnosis in our patient and meanwhile another year has passed without clinical signs of disease progression. Skin lesions may thus already provide an important diagnostic clue at early stages of MDS, and every haematological patient referred with skin changes needs early skin biopsies as the diagnosis might well be established on the basis of the dermato-histopathological findings. Otherwise a chance of making an early diagnosis of rarer conditions, such as MDS, will be missed.

REFERENCES

1. Germing U, Gattermann N, Strupp C, Aivado M, Hossfeld PK, Haas R, et al. Myelodysplastische syndrome. Deutsches Aerzteblatt 2001; JG98: A2272–A2278.
2. Howe RB, Porwit-MacDonald A, Wanat R, Tehranchi R, Hellstrom-Lindberg E. The WHO classification of MDS does make a difference. Blood 2004; 103: 3265–3270.
3. Foucar K, Langdon RM, 2nd, Armitage JO, Olson DB, Carroll TJ, Jr. Myelodysplastic syndromes. A clinical and pathologic analysis of 109 cases. Cancer 1985; 56: 553–561.
4. Mufti GJ, Stevens JR, Oscier DG, Hamblin TJ, Machin D. Myelodysplastic syndromes: a scoring system with prognostic significance. Br J Haematol 1985; 59: 425–433.
5. Kerkhofs H, Hermans J, Haak HL, Leeksma CH. Utility of the FAB classification for myelodysplastic syndromes: investigation of prognostic factors in 237 cases. Br J Haematol 1987; 65: 73–81.
6. Schilling C, Günther C, Haferlach T, Ruelfs C, Lipp T. Myelodysplastische syndrome (MDS). In: Manual Leukämien, myelodysplastische und myeloproliferative Syndrome. München: Zuckschwerdt Verlag, 2003: 97–114.
7. Mestre F, Pinazo I, Betlloch I, Mas JM, Galmes A, Buades J. [Cutaneous leukemia in refractory anemia with an excess of blasts in transformation]. Ann Dermatol Venereol 1988; 115: 1265–1269.
8. Namba Y, Koizumi H, Nakamura H, Tarumi T, Sawada K, Ohkawara A. Specific cutaneous lesions of the scalp in myelodysplastic syndrome with deletion of 20q. J Dermatol 1999; 26: 220–224.
9. O'Connell DM, Fagan WA, Skinner SM, Pulitzer DR, Devillez RL. Cutaneous involvement in chronic myelomonocytic leukemia. Int J Dermatol 1994; 33: 628–631.
10. Pont V, Miquel FJ, Grau TC, Hernandez F, Sanchez-Carazo JL, Aliaga A. Skin involvement in chronic myelomonocytic leukaemia as a predictor of transformation into acute myeloid leukaemia. J Eur Acad Dermatol Venereol 2001; 15: 260–262.
11. Su WP. Clinical, histopathologic, and immunohistochemical correlations in leukemia cutis. Semin Dermatol 1994; 13: 223–230.
12. Avivi I, Rosenbaum H, Levy Y, Rowe J. Myelodysplastic syndrome and associated skin lesions: a review of the literature. Leuk Res 1999; 23: 323–330.