Leukemia Research Reports 8 (2017) 7–10

Contents lists available at ScienceDirect

Leukemia Research Reports

journal homepage: www.elsevier.com/locate/lrr

An unusual type of myeloid sarcoma localization following myelofibrosis: A case report and literature review

Nicola Orofino[a], Daniele Cattaneo[a], Cristina Bucelli[a], Loredana Pettine[a], Sonia Fabris[a], Umberto Gianelli[b], Nicola Stefano Fracchiolla[a], Agostino Cortelezzi[a], Alessandra Iurlo[a,*]

[a] Hematology Division, IRCCS Ca' Granda – Maggiore Policlinico Hospital Foundation, Milan, Italy
[b] Division of Pathology, Department of Pathophysiology and Transplantation, University of Milan, and IRCCS Ca' Granda - Maggiore Policlinico Hospital Foundation, Milan, Italy

ARTICLE INFO

Keywords:
Myeloid sarcoma
Primary myelofibrosis
Calreticulin

ABSTRACT

Myeloid Sarcoma (MS) is a rare malignancy that can present as an isolated disease or more frequently in association with or following acute myeloid leukemia or other myeloid neoplasms and rarely following myelofibrosis.

Since molecular pathogenesis and prognostic factors of MS are not well understood, its prognosis remains poor even in the era of novel agents and target therapies.

We report the case of a patient with MS following myelofibrosis with multiple subcutaneous, cutaneous and muscle localizations; the latter has been reported in the literature as anecdotal. In this way we aimed to enhance the understanding of this disease.

1. Introduction

Myeloid Sarcoma (MS) is a rare entity characterized by the proliferation of immature myeloid cells in extramedullary sites. The 2008 WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues and its updated 2016 version clarified the diagnosis of MS as "a tumor mass consisting of myeloid blasts with or without maturation occurring at an anatomic site other than the bone marrow" [1,2]. A predilection for males (male: female ratio = 1.2:1) is reported, with a median age at diagnosis of 56 years [3].

Myeloid sarcoma can be observed as a de novo malignancy (without leukemic presentation in peripheral blood and bone marrow), during the course of acute myeloid leukemia (AML), affecting 2.5–9% of all AML patients, myelodysplastic syndromes (MDS) or myeloproliferative neoplasms (MPNs, both chronic myeloid leukemia and *BCR-ABL1*-negative MPNs) or MDS/MPNs such as chronic myelomonocytic leukemia (CMML); it has also been described as a relapse in a previous AML [1,4,5].

Myeloid sarcoma most commonly involve lymph nodes, skin, soft tissues and testes. In less than 10% of cases the presentation may be at multiple anatomical sites.

Since MS can present at multiple sites that can be often clinically silent, Positron Emission Tomography (FDG-PET) has been demonstrated as a useful tool in detecting extramedullary AML and, as previously revealed, it should be used both in diagnosis and after treatment, in order to evaluate response to therapy [6]

Differential diagnosis should be made with other hematological malignancies involving lymph nodes, skin and other extra-hematological sites, such as B-cell lymphomas, cutaneous or peripheral T-cell lymphomas [3].

As far as genetic/molecular lesions are concerned, MS does not differ from AML. In fact, chromosomal aberrations are detected by Fluoresce in Situ Hybridization (FISH) and/or conventional cytogenetics in about half of cases and include: −7, +8, MLL-rearrangement, inv(16), +4, −16/16q-, 5q-, 20q- and +11. About 16% of patients carries nucleophosmin (NPM1) mutations, as shown by aberrant cytoplasmic NPM1 expression [1]. Furthermore, about 20–30% of MS, especially those evolving from AML, harbor mutations of FMS-like tyrosine kinase 3 (FLT3) gene, commonly Internal Tandem Duplications (ITD) [7].

Here we report an unusual case of MS presenting with multiple skin, subcutaneous and muscular lesions in a patient affected by primary myelofibrosis (PMF) which was diagnosed approximately 16 years before.

2. Case report

A 53-years-old man was diagnosed with pre-fibrotic PMF in 2000 in

* Correspondence to: Hematology Division, IRCCS Ca' Granda – Maggiore Policlinico Hospital Foundation, Via Francesco Sforza 35, 20122 Milan, Italy.
E-mail address: aiurlo@policlinico.mi.it (A. Iurlo).

http://dx.doi.org/10.1016/j.lrr.2017.07.002
Received 10 May 2017; Received in revised form 20 July 2017; Accepted 25 July 2017
Available online 27 July 2017

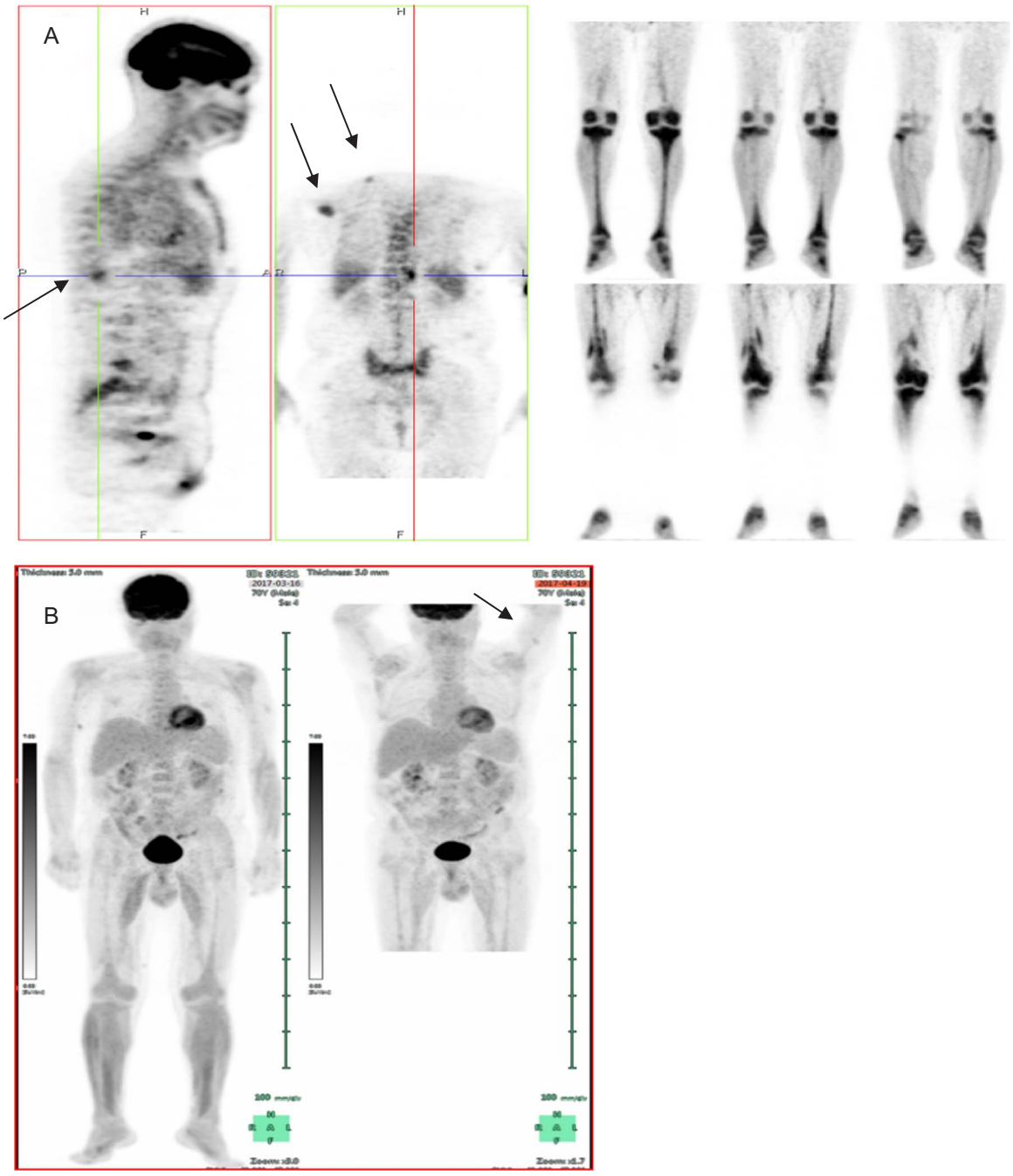

Fig. 1. (A). FDG-PET detection of multiple metabolically active lesions on soft tissues on right and left shoulder, chest wall, back, epigastric region and legs (arrows). (B). FGD post induction and consolidation chemotherapy showing persistence of one metabolic active subcutaneous lesion on left arm (arrow).

another Hospital, because of persistent, severe thrombocytosis. Conventional cytogenetic analysis showed a normal male karyotype. Consequently, he was initially treated with low-dose acetylsalicylic acid and hydroxyurea. Ten years later, he was admitted to our Institution and molecular evaluations were done, demonstrating the absence of *JAK2*V617F and *MPL* mutations, as well as *BCR-ABL1* fusion gene.

After one year of follow-up, hematological investigations revealed severe anemia (hemoglobin level of 7.6 g/dL). Since the negativity of further diagnostic evaluations, a new bone marrow biopsy was performed, revealing an increase in bone marrow fibrosis (MF-2, according to the EUMNET consensus) [7]. Consequently, the patient stopped assuming hydroxyurea and was started on corticosteroids and transfusional supportive therapy. Further molecular tests showed a type-2 mutation of the CALR gene (ins5-bp). At that point, MySEC score [8] was retrospectively evaluated and it resulted Intermediate − 1.

In September 2016 the patient presented with asymptomatic subcutaneous nodules on the chest wall, neck and left arm, with a maximum diameter of 2 cm; at ultrasound examination they were hypoechogenic irregular nodules that invaded the surrounding muscle tissue. Furthermore, a FDG-PET detected multiple metabolically active lesions in soft tissues (SUV max 4.5) on right and left shoulder, chest wall, back, epigastric region and legs (Fig. 1).

Finally, a biopsy of a sub-cutaneous lesion was performed and the histopathologic examination revealed the presence of a granulocytic sarcoma. Immunohistochemistry showed that the majority of proliferating cells expressed CD34, CD43, CD117(+/-), CD45/LCA(+/-) antigens, but were negative for CD20, CD3, CD30, CD68/kp1, CD68R antigens and for myeloperoxidase. Immunohistochemical positivity of