

Pet-imaging as a useful tool for early detection of the relapse site in the management of primary myeloid sarcoma

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Myeloid sarcoma (MS), also called chloroma, is an extramedullary tumor composed of immature myeloid cells, which develops in about three percent of patients with acute non-lymphocytic leukemia. Rare cases can occur in a very wide variety of organs without bone marrow involvement, defining primary MS. Moreover, extramedullary MS are associated with a high incidence of particular cytogenetic abnormalities, especially with (8;21) translocation and inversion of chromosome 16.¹ We report here a new case of primary MS involving the small intestine, associated with CBF β /MYH11 fusion gene, as a striking example of useful contribution of MRD combined with positron emission tomography (PET) imaging for early detection of extramedullary relapse.

A 44-year-old man was admitted to hospital for progressive occlusive syndrome. Physical examination was unremarkable, with no tumor syndrome. Tomodensitometry revealed a major intestinal distension. Laparoscopic exploration found a 5 centimeter tumor in the small intestine causing the occlusive syndrome, which was removed. Histological examination established the diagnosis of MS with immature myeloid cells positive for myeloperoxidase, CD34 and CD68 antigens. Cytological analyses from peripheral blood, bone marrow aspirate, and cerebrospinal fluid were normal, as well as cytogenetic marrow analysis. However, the CBF β /MYH11 fusion transcript was detected by real-time quantitative RT-PCR from bone marrow aspirate. Specific initial treatment included an intensive chemotherapy similar to that used in acute myeloid leukemia, followed by 4 high-dose cytarabine consolidation sequences. The molecular signal became negative at the end of consolidation chemotherapy but began to increase gradually a few months later, as illustrated in Figure 1A. However, neither clinical evaluation nor computed tomography were suggestive of relapse, and bone marrow aspirate remained cytologically normal. Therefore, PET imaging with [¹⁸F]fluorodeoxyglucose (¹⁸FDG) was performed and showed a significant uptake at the junction between the first and second segments of duodenum (Figure 1B). Given these results, echoendoscopy with biopsies permitted to obtain the histological confirmation of localized relapse at the corresponding site. A second clinical, radiological (including computed tomography and PET-imaging) and molecular remission was obtained after high-dose cytarabine sequences. He further had an isolated neuromeningeal relapse of the malignancy that could be controlled with intrathecal chemotherapy alone. Because of the poor prognosis of the disease, allogeneic bone marrow transplantation with an unrelated HLA-identical donor and using total body irradiation as conditioning was performed, leading to a prolonged clinical and molecular remission.

In a retrospective study of 74 cases of non-leukemic myeloid sarcoma, *Yamauchi et al.* showed that patients who received an intensive chemotherapy similar to that used to treat acute myeloid leukemia had a prolonged non-leukemic course compared to patients who only had surgical resection or local irradiation of the tumor.² This finding supports the use of systemic chemotherapy in all cases of non-leukemic myeloid sarcoma, as was done in our case, even though, to our knowledge, no controlled

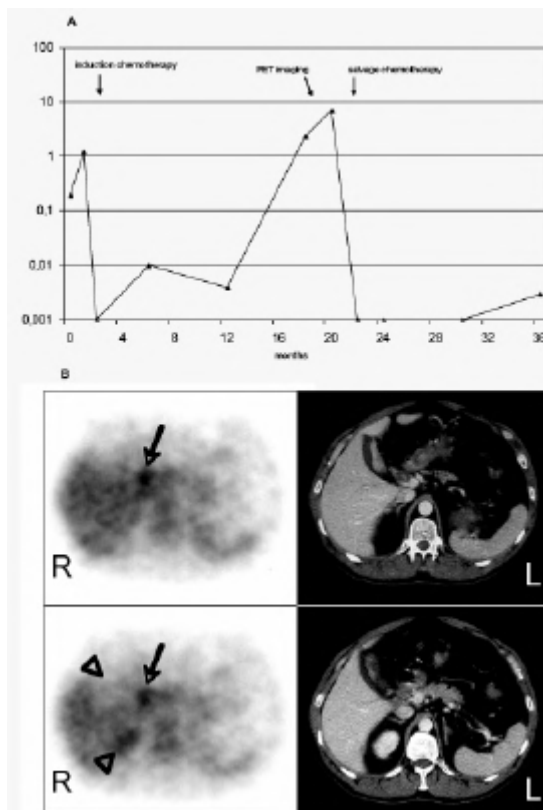


Figure 1. (A) Molecular analysis of minimal residual disease and correlation with relapse of MS. The curve indicates the evolution of minimal residual disease as determined by real-time quantitative RT-PCR as a function of time after diagnosis. Results are expressed as a ratio (%) of copy number of CBF β /MYH11 mRNA on reference beta-glucuronidase (GUS) mRNA sequence. (B) ¹⁸FDG-PET (left column) aspect of MS relapse at the junction between first and second segments of duodenum. Computed tomography (right column) does not show any abnormality. Arrow: abnormal focus of uptake at the level of the second duodenum. Arrowheads: locations of the gall bladder and the upper pole of the right kidney. R = right, L = left.

study has been reported to date. Several cases of primary digestive MS associated with the detection of the CBF β /MYH11 fusion gene from peripheral blood have already been reported, often localized to the small intestine as in our case.³ Given the possibility of extramedullary relapse at different organs and sites, as illustrated in our case, regular monitoring of MRD represents an essential tool for early detection of eventual relapses in the course of such disease. Although the initial presentation was clinically evident, the first relapse, which was suspected on the basis of MRD ascension, was asymptomatic in our case. Only PET imaging allowed the early diagnosis of the relapse site, while computed tomography remained normal. PET with the ¹⁸FDG radiopharmaceutical is routinely employed in a wide variety of tumors with detection sensitivity and specificity usually greater than 90%, particularly in cancers of the lung, colon, head and neck, melanoma and lymphoma,⁴ and for the assessment of therapy.⁵ The interest of PET imaging in the management of leukemic patients has been reported in single cases only for documentation of focal bone localizations that were already clinically suspected.⁶⁻⁸ Our case underlies the interest of such a sensitive imaging procedure for early detection of extramedullary localizations, even when (i) they are not clinically suspected and (ii) conventional computed tomography is not contributive. In the situation of pri-

mary MS associated with a specific molecular marker, the systematic combination of MRD monitoring with PET-imaging when relapse is suspected can allow a rapid and appropriate medical care while, in contrast, it may be difficult to decide a chemotherapy salvage course on the only basis of MRD remaining positive without cytological or radiological evidence of relapse. When no molecular marker is available, PET-imaging systematically performed after induction and/or at the end of the chemotherapy program could permit to identify patients with remaining ^{18}F FDG uptake, at risk for further relapse, and who may thus need intensification. The prognosis value of PET-imaging in such patients needs to be evaluated in collaborative studies in order to enroll a sufficient number of patients.

Lionel Karlin,¹ Emmanuel Itti,² Cécile Pautas,¹ Mohamed Rachid,¹
Dominique Bories,¹ Catherine Cordonnier,¹ Sébastien Maury¹
Departments of ¹Hematology and ²Nuclear Medicine, Hôpital Henri
Mondor, Créteil, France

Correspondence: Dr Sébastien Maury, Service d'Hématologie Clinique,
CHU Henri Mondor, 51 av. du Mal de Lattre de Tassigny, France.
Tel: 00 33 1 49 81 20 57 Fax : 00 33 1 49 81 20 67
E-mail: sebastien.maury@hmn.aphp.fr

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