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Periodic morphologic, cytogenetic and clonality evaluation after autologous peripheral blood progenitor cell transplantation in patients with lymphoproliferative malignancies

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Background and Objectives. Myelodysplastic syndrome (MDS), secondary acute myeloid leukemia (sAML) and clonal karyotypic abnormalities, have been recognized as relatively frequent and potentially serious complications of autologous peripheral blood progenitor cell transplantation (PBPCT) for Hodgkin's disease (HD), non-Hodgkin's lymphoma (NHL) or multiple myeloma (MM).

Design and Methods. We analyzed 66 patients, undergoing PBPCT for HD, NHL, MM or chronic lymphocytic leukemia (CLL). Patients reported in this study had to be in continuous complete remission after transplantation without receiving chemo-radiotherapy or other biological response modifiers, had to show absence of cytogenetic abnormalities and myelodysplastic features at transplantation and had to have at least 12 months of follow-up. We evaluated the bone marrow, peripheral blood, cytogenetics and clonality (HUMARA) 12 months after the transplant and thereafter every 12 months or every 6 months if lineage dysplasia, clonal or cytogenetic abnormalities were detected.

Results. We did not observe MDS/sAML, according to the FAB classification, in 163 assessments of 66 patients over a median follow-up of 25 months (range 12-106) after PBPCT. Twelve patients showed lineage dysplasia: six patients had dyserythropoiesis, 2 patients dysgranulopoiesis, one dysmegakaryocytopoiesis, two patients showed double lineage dysplasia (erythroid and granulocytic), and one patient showed dysgranulopoiesis at the first control acquiring dyserythropoiesis at the next follow-up. We found three cytogenetic abnormalities in the absence of concomitant dysplastic features: transient -5q, –Y, fra(10)(q25). The female patient with the cytogenetic abnormality –5q showed transient unbalanced clonality by HUMARA assay; further controls documented normalization of both clonality and cytogenetics.

Interpretation and Conclusions. The occurrence of MDS/sAML depends on a variety of risk factors such as the number and type of prior courses of chemo-radiotherapy, total body irradiation in conditioning regimen, cytogenetic and morphologic alterations prior to transplant. This may account for the difference in reporting MDS/sAML after transplantation. The lack of exposure to recognized risk factors for MDS/sAML in our patients may account for the absence of this complication in this study. We consider that the use of stringent morphologic criteria, especially during the first period after PBPCT, combined with cytogenetic, clonality and FISH analyses are necessary for a correct diagnosis of MDS and to overcome the limitations of the FAB and WHO classifications in this setting.

Key words: clonality evaluation, PBPC transplantation, lymphoproliferative malignancies.

High-dose chemotherapy followed by reinfusion of previously harvested bone marrow or peripheral blood stem cells (PBPCT) is currently being applied in the treatment of patients with various malignancies.[1] Autologous bone marrow transplantation and PBPCT have been recently used with success in the treatment of hematopoietic malignancies such as HD, NHL and MM.[2-4] The mortality from transplantation has been reduced to less than 5% as a result of careful pre-transplantation evaluation and supportive care.[5] As prolonged survival becomes a reality, assess-

ment of the long-term side effects of treatment is becoming increasingly relevant. Recently published studies suggest that the incidence of MDS/sAML observed after autologous bone marrow transplantation is 6-7% at 5 years.[6-8] Most patients in these studies received multiple courses of chemotherapy and it is, therefore, difficult to establish whether the previous chemotherapy, the transplant itself or the combination is responsible for this complication. Patients with HD treated initially and/or at first relapse with MOPP are known to have an increased risk of secondary MDS,[9] due to exposure to alkylators (especially nitrogen mustard and/or chlorambucil) and procarbazine. Another recognized risk factor is the use of total body irradiation in the conditioning regimen.[10] However, some reports disagree with the high incidence of secondary MDS/sAML after PBPCT especially if this diagnosis is made less than 12 months after the transplant when FAB or WHO criteria for the diagnosis of MDS or refractory cytopenia are questionable because lineage dysplasias and cytopenias could be related to the transplant procedure itself.[11-13] MDS/sAML are often associated with particular cytogenetic abnormalities frequently involving chromosomes 5, 7 and 11.[7] Here we report the absence of MDS/sAML in a group of 66 patients who proceeded to PBPCT for HD, NHL, MM or CLL. This represents a review of a single-institution experience over 13 years.

Design and Methods

Between January 1, 1988 and January 1, 2001, 225 patients were submitted to autologous PBPCT in our Division of Hematology. All patients fulfilling the following criteria were included in the study: absence of cytogenetic abnormalities and myelodysplastic figures at transplantation, at least 12 months of follow-up in continuous complete remission without receiving chemotherapy or other biological response modifiers. We arbitrarily excluded all patients affected by acute myelogenous leukemia (AML) because of the possible association of lineage dysplasia at the time of diagnosis. Sixty-six patients fulfilled the above mentioned criteria and are reported here. Some of these patients have been reported elsewhere.[12] Thirty-eight patients were male and 28 were female; their median age was 43.5 years (range 17-62). Thirty-one patients were affected by NHL, 19 patients were affected by MM, 14 patients by HD, and 2 patients by CLL. All patients received standard chemotherapy at diagnosis, 47 patients underwent second line chemotherapy, and eleven patients received radiotherapy after second-line chemotherapy. Disease status at PBPCT was first complete remission (CR) in 24 patients, second CR (2nd CR) in 8 patients, third CR (3rd CR) in 2 patients, and partial remission (PR) in 32 patients. Ten patients who underwent double transplant for multiple myeloma entered the study after completion of the second transplant. The characteristics of the patients are shown in Table 1.

Table 1. Characteristics of patients.

	Values
No. of patients	66
Median age (range)	43.5 (17-62)
Gender (M/F)	38/28
Diagnosis	
NHL	31
MM	19
HD	14
CLL	2
Type of treatment	
Standard chemotherapy	8
Second line chemotherapy	47
Second line & radiotherapy	11
Status at transplant	
CR	24
2nd CR	8
3rd CR	2
PR	32
Conditioning regimen	
BuMel	26
BuCy2	22
BEAM	11
HDMel	5
MitMel	2
Type of transplantation	
Unselected	44
CD34+ selected	22

Forty-three patients were submitted to mobilizing chemotherapy consisting of mitoxantrone (10 mg/m^2/day on day 1), aracytin (2 g/m^2/day on day 5) carboplatinum (100 mg/m^2/day on days 1-4) and methylprednisolone (500 mg/m^2/day on days 1-5) (MiCMA), 18 patients underwent high-dose cyclophosphamide (7 g/m^2/day on day 1) and 5 patients high-dose etoposide (2 g/m^2/day on day 1), followed by granulocyte colony-stimulating factor (G-CSF) and leukapheresis collection of peripherral blood progenitor cells (PBSCs). The pretransplant conditioning regimen included busulphan (4 mg/kg on

days -7 to -4), and cyclophosphamide (60 mg/kg on days -3 to -2) (BuCy2) in 22 patients, busulphan (4 mg/kg on days -6 to -3) and melphalan (90 mg/m^2 on day -2) (BuMel) in 26 patients, BCNU (300 mg/m^2 on day -7), etoposide and aracytin (200 mg/m^2 on days -6 to -3), and melphalan (140 mg/m^2 on day -2) (BEAM) in 11 patients, high-dose melphalan (100 mg/m^2 on days -3 to -2) (HDMel) in 5 patients, mitoxantrone (60 mg/m^2 on day –5) and melphalan (180 mg/m^2 on day –2) in 2 patients (Mit-Mel).

The conditioning regimen was followed by unselected PBPC (44 patients) or CD34$^+$ selected PBPC infusion obtained with Ceprate®SC (18 patients) or CliniMACS® (4 patients) on day 0. Sixteen patients received subcutaneous G-CSF (5 μg/kg/die) starting on day 1 or day 7 from CD34$^+$ selected infusion and in 2 patients with CLL until a stable absolute neutrophil count (ANC) > 0.5×10^9/L, as part of a randomized trial aimed at evaluating the optimal timing of G-CSF administration after transplantation of autologous CD34$^+$ cells.[14] Informed consent was obtained from each patient or from guardians. We repeated annual follow-ups for each of these patients, with the exception of those in whom follow-up showed cytogenetic, clonal or morphologic changes; these patients were evaluated every 6 months. All patients relapsing after PBPCT and requiring further treatment were excluded from further follow-up.

Morphologic studies

Bone marrow aspirate smears were air-dried and stained with a May-Grünwald-Giemsa stain. Iron staining was performed on marrow aspirates to identify ring sideroblasts. The bone marrow smears were examined independently by three experienced morphologists. MDS/sAML was diagnosed if both the presence of cytopenia in the absence of an identified cause and dysplastic features were detected in erythroid, granulocytic, and megakaryocytic lineages in the bone marrow, according to the FAB classifications.[15] We also investigated any morphologic change in the bone marrow smears even in the absence of MDS/sAML. According to Kahl *et al.*,[16] we used this score with some modifications. Dyserythropoietic features were defined as more than 10% dysplastic features in at least 100 erythroblasts, i.e. megaloblastic changes, multinuclearity, abnormal nuclear shape, nuclear and cytoplasmic bridging, nuclear fragments or karyorrhexis, Jolly bodies, nuclear/cytoplasm asynchronism. Dysgranulopoietic features were defined as three or more hyposegmented nuclei (pseudo-Pelger-Huet nuclear anomaly) or as more neutrophils being agranular or hypogranular. Dysmegakaryocytic features were defined as three or more megakaryocytes being micronuclear (mono or binuclear), multi-separated nuclear, or large mononuclear forms. According to Amigo *et al.*,[11] for the definition of cytopenias, we considered the following values: Hb < 10 g/dL, leukocyte count < 4×10^9/L and platelet count < 100×10^9/L in the absence of an identified cause.

Cytogenetic analysis

The cytogenetic analyses performed on bone marrow cells karyotypes were analyzed using Q- and G- banding methods and required the presence of at least 20 metaphases in each bone marrow sample.

HUMARA assay

DNA. High molecular genomic DNA was extracted and purified from bone marrow cells of female patients. Samples were screened for heterozygosity of the HUMARA genes, then clonal analysis was performed as described previously.[17] After extraction DNA was resuspended in 40 μL of dH_2O: one half of the sample was digested for 6h at 37°C with 20U *Rsa*I and 20U *Hpa* (New England Biolabs), the other half was incubated for 6h at 37°C under the same reaction conditions but except for the presence of *Hpa*II. Five microliters of digested DNA were added to a reaction mix containing 1 × *Taq* polymerase buffer (50 mmol/L KCl, 10 mmol/L Tris-HCl, pH 9.0, 0.1% Triton X-100), 0.5 U *Taq* polymerase, 0.2 mmol/L of each dNTP (all from Amersham-Pharmacia), and 10 pmol of each primer, in a total volume of 50 μL. The primer sequences were: T1 5'-TCCAGAATCTGTTCCAGAGCGTGC-3' and T2 5'-GCTGTGAAGGTTGCTGTTCCTCAT-3. T2 primer was labeled with γ[^{32}P]ATP kinase. The mix was heated to 95°C for 5 minutes, and then 35 cycles at 95°C for 30 seconds, 65°C for 30 seconds, and 72°C for 30 seconds were performed, followed by a final extension at 72°C for 5 minutes. After DNA amplification 5 μL of stop solution ((95% formamide and 0.025% bromophenol blue) were added to 4 μL of PCR product and 4 μL of the mixture were loaded on a 6% polyacrylamide denaturing gel. The gel was dried and exposed to Hyperfilm-MP (Amersham Life Science, Little Chalfont, UK). Autoradiographic signals were quantified by scanning densitometry and reported as the percentage of expression of the lower allele.

Results

Morphologic evaluation of the bone marrow was performed on samples obtained from 66 patients

Table 2. Characteristics and prior treatment of patients with morphologic, cytogenetic and clonal abnormalities.

UPN	Sex/Age	Dx	N° of CT lines	RT	Status at TX	Conditioning regimen	Stem cell support
26	F/36	NHL	2	N	CR	BuCy2	PBPC
31	M/36	NHL	1	N	CR	BuCy2	PBPC
97	F/37	HD	2	N	3rd CR	BuMel	PBPC
107	M/59	NHL	2	N	PR	BuCy2	PBPC
117	M/26	HD	2	Y	CR	BEAM	PBPC
119	M/48	NHL	2	N	PR	BuMel	CD34+
121	F/34	HD	2	N	3rd CR	BEAM	PBPC
125	M/21	HD	2	Y	2nd CR	BuCy2	PBPC
144	M/46	NHL	1	N	CR	BuMel	PBPC
153	F/52	MM	1	N	CR	BuMel	CD34+
163	M/60	MM	2	N	PR	HDMel	PBPC
167	M/47	NHL	1	N	CR	BuMel	CD34+
189	F/40	NHL	1	N	PR	BuMel	PBPC
228	M/33	NHL	1	N	PR	BuMel	CD34+
239	F/56	NHL	2	N	PR	BuCy2	CD34+

Dx: diagnosis; RT: radiotherapy; CT: chemotherapy; TX: transplant.

for a total of 163 evaluations over a median follow-up of 25 months (range 12-106). Twenty out of 66 patients had a follow-up of at least 4 years (48-106). Sixteen patients relapsing after PBPCT, with a median of 2 evaluations (range 1-4), were excluded from further follow-up.

No abnormalities of peripheral blood values, as above mentioned, were observed and all patients achieved stable and complete hematopoietic reconstitution after transplantation.[18] We did not find cytopenia, according to criteria described above, in the 163 peripheral blood controls evaluated at the same times as bone marrow specimens. No patients showed ring sideroblasts at iron staining. The morphologic examination of bone marrow revealed no consistent features of MDS or sAML according to the FAB classifications.[15] Twelve patients showed morphologic signs of dysplasia. They were affected by NHL (8 pts), HD (2 pts) and MM (2 pts); 5 of patients had been submitted to standard chemotherapy, 5 had undergone second line chemotherapy and 2 had received second line chemotherapy plus radiotherapy before transplantation. The disease status of patients at transplantation was: 6 in PR, 5 in CR, 1 in 2nd CR (Table 2).

Six patients showed dyserythropoiesis in the absence of morphologic abnormalities of the other lineages. Two patients showed dysgranulopoiesis and one dysmegakaryocytopoiesis. Only one patient showed dysgranulopoiesis acquiring dyserythropoiesis at the next follow-up. No patients lost lineage dysplasia at their subsequent evaluations. Four patients (UPN 117, 119, 125, 163), 3 with dyserythropoiesis and 1 with dysgranulopoiesis, relapsed: they had all received chemotherapy and 1 had also received involved field radiotherapy. Three patients died from their disease and 1 patient is currently alive and well (UPN 117) with no signs of MDS. Two patients showed double lineage dysplasia (dysgranulo-dyserythropoiesis) starting from the first evaluation after transplantation. Comparing patients with or without dysplastic features, there was no statistical difference in the extent of prior chemotherapy and/or radiotherapy (Fisher's exact test, p=ns). We performed 129 cytogenetic analyses; 6 of them (4.66%) were not evaluable because of insufficient number of metaphases. In the remaining analyses, no cytogenetic abnormalities were detected in patients with lineage dysplasia. Indeed three patients showed cytogenetic abnormalities in the absence of lineage dysplasia (Table 3). The first patient, affected by HD, was treated with standard and second line chemotherapy in association with radiotherapy. Thirty-two months after transplantation (second follow-up) she showed a transient deletion of the long arm of chromosome 5 (-5q). The second patient, affected by NHL, treated with standard and second line chemotherapy, showed transient deletion of chromosome Y (-Y). The third patient, affected by HD who received standard and second line chemotherapy, acquired an abnormal karyotype 46,XXfra(10)(q25) from the second to the fourth follow-up, with normalization in the next control.

HUMARA analysis, performed in 23 female patients (47 analyses), documented the absence of clonal hematopoiesis except a transient unbalanced pattern of clonality concomitant to the detection of –5q; both abnormalities were not confirmed during the two following evaluations (Table 3).

Discussion

MDS/sAML are a very rare late complications after allogeneic transplant, suggesting that they develop from accumulating mutations in the recipient cells as a result of prior exposure to subablative chemotherapy.[19] In contrast, a growing number of reports over the last few years describe the incidence of MDS/sAML after ABMT/PBPCT for HD, NHL, and MM. Several reports[6-8,20] suggest that the

crude incidence of MDS/sAML observed after ABMT reaches 5-7% while Taylor *et al.*[21] in 1995 reported a low frequency of MDS after ABMT, describing only one case of MDS in a group of 149 patients submitted to ABMT and in 1996 recorded the absence of MDS after 152 ABMT procedures.[22] The occurrence of MDS/sAML is probably due to multifactorial pathogenesis including individual predisposition, pretransplantation chemotherapy, prior radiotherapy, TBI-including regimen and the interval between first chemotherapy and transplantation.[23] In particular, HD patients treated initially and/or at first relapse with MOPP are known to be at a significant risk of secondary MDS,[9] due to exposure to alkylators (especially nitrogen mustard and/or chlorambucil) and procarbazine although no significant differences have been reported in the incidence of post-transplantation MDS/sAML for HD. Radiotherapy prior to transplantation and the use of total body irradiation in the conditioning regimen have been related to the development of MDS/sAML in the autologous setting.[10] Time between the beginning of chemotherapy and transplantation was directly correlated with the development of MDS/sAML as a result of prolonged use of alkylating agents, exposure to radiation therapy and a prior relapse before transplantation.[24-26] More recently the use of etoposide as priming for stem cell collection has been significantly associated with the development of MDS/sAML.[27]

MDS/sAML have often been associated with particular cytogenetic abnormalities, predominantly involving chromosome 5 and 7, in relation to the use of alkylating agents especially when administered in association with radiotherapy,[7] or involving chromosome 11 typically after the use of epipodophyllotoxins.[28] Chromosome abnormalities were assessed by cytogenetic analysis by standard G-banding or more recently by retrospective FISH analysis on pretransplant bone marrow samples.[29,30] The development of abnormal cytogenetics in patients treated with ABMT/PBPCT may be the result of exposure to toxic agents prior to transplantation so that any abnormal cytogenetic findings detected before PBPCT were suggested to be considered as a exclusion criterion for ABMT/PBPCT, at least for HD patients.[31,32] In fact the presence of prior chromosome abnormalities resulted as a striking predictive factor for the subsequent development of MDS/sAML.[29,30]

Our report shows the absence of MDS/sAML after PBPCT in 163 analyses over a median follow-up of 25 months (range 12-106), obtained in 66 out of 225 patients affected by lymphoproliferative malignancies. Major reasons for exclusion were:

Table 3. Morphologic, cytogenetic and clonal abnormalities.

UPN	*Morph1/ Months*	*Morph2/ Months*	*Morph3/ Months*	*Morph4/ Months*	*Morph5/ Months*	*CY1/ Months*	*CY2/ Months*	*CY3/ Months*	*CY4/ Months*	*CY5/ Months*	*Clonality (n° of controls)*
26	N/58	N/76	Dysgr/90	Dysgr/106		N	N	N	nd		nd
31	N/60	Dysgr/76	Dysgr-Dyser/90			N	N	N			na
97	N/21	N/32	N/43	N/48	N/67	N	- 5q	N	N	N	N 1st , C 2nd, N 3rd, N 4th (4)
107	N/17	N/28	Dyser/57	Dyser/63		N	ne	N	N		na
117	N/12	N/25	Dysgr/38			N	N	N			na
119	N/11	Dyser/24				N	N				na
121	N/12	N/16	N/27	N/34	N/49	N	fra10(q25)	fra10(q25)	fra10(q25)	N	N (3)
125	Dyser/12					N					na
144	N/12	Dysmeg/24				N	N				na
153	Dyser/12	Dyser/ 21	Dyser/34			N	N	N			N (3)
163	Dyser/13					ne					na
167	N/12	N/18	N/33			-Y	N	N			na
189	N/12	Dyser/28				N	N				N (2)
228	N/17	Dysgr-Dyser/17				N					na
239	N/15	Dysgr-Dyser/15				N					Sk (1)

Morph = morphology; CY = cytogenetic; Dyser = dyserythropoiesis; Dysgr = dysgranulopoiesis; Dysmeg = dysmegakariocytopoiesis; nd = not done; ne = not evaluable; N = normal; C = clonal; na = not applicable; Sk = skewed.

relapse and/or further treatment after PBPCT, a follow-up of less than 12 months, refusal or failure to contact patients. Although this number is quite small, the follow-up was at least 4 years in about one third of the cohort. Twelve patients showed lineage dysplasia without cytopenia or evidence of clonal or cytogenetic abnormalities. All patients who acquired lineage dysplasia had these same abnormalities confirmed in the subsequent follow-up indicating that these abnormalities were constantly expressed.

Dysplastic changes are useful predictors of future myelodysplasia, especially if associated with cytogenetic and clonality abnormalities, but each of them alone is not sufficient to allow a diagnosis of post-transplantation MDS.[10, 33] Mild hematopoietic cell atypia is common after chemotherapy and PBPCT, being evident in erythroid precursors. Amigo *et al.* observed cytopenias in 51% and 44% of patients undergoing PBPCT at 6 and 12 months after transplantation, respectively. Moreover, concomitant presence of cytopenia and myelodysplasia was observed in 37.7% and 25% of patients, respectively, at 6 and 12 months after transplantation and could, therefore, be misdiagnosed with MDS. According to Amigo[11] FAB criteria are not applicable in the first period after transplantation, this being particularly true for refractory anemia (RA), because of the difficulty in distinguishing, on the basis of cytopenia and dysplasia, between PBPCT toxicity and a real MDS. Recently the WHO classification of myeloid neoplasms has included a new entity of MDS, refractory cytopenia, which is characterized by less than 5% of blasts but with significant dysplasia involving granulocytic and megakaryocytic lineages; [13] as for RA, so too for this entity, the WHO classification cannot be applied early after transplant for the above mentioned reason. FISH analysis may be extremely helpful in these situations.[29,30]

Despite a very strict follow-up in our study only 3 patients showed cytogenetic abnormalities without morphologic dysplasia. All abnormalities were transient with normalization, in 2 cases (-Y, -5q) in the successive controls and in one (fra10q25) after 3 positive controls. The HUMARA assay, which was unfortunately restricted to the female sex only, showed transient unbalanced clonality in one patient at the same time as the occurrence of the cytogenetic abnormality (-5q). Clonal hematopoiesis detected by the HUMARA assay was capable of confirming the diagnosis of MDS/sAML in female patients in a series from Mach-Pascual *et al.* in a group of 104 patients, identyifing clonal hematopoiesis at the time of ABMT in 3% of female patients. Clonality rose to 13.5% after transplantation, and 4 of 10 patients with clonal hematopoiesis developed MDS/sAML.[34] Thus a significant proportion of patients have clonal hematopoiesis at the time of ABMT and clonal hematopoiesis, as detected by HUMARA assay, could predict the development of MDS/sAML.

Although the series reported here is small and the follow-up is still limited, the absence of MDS/sAML in our series could be explained in several ways: 1) the conditioning regimen was based only on chemotherapy, while radiotherapy was performed if indicated only on an involved field before or after transplantation; 2) patients were included only if responsive to chemotherapy prior to transplantation; 3) a careful pre-transplant evaluation was performed including cytogenetic and HUMARA analysis; 4) high dose etoposide was limited to myeloma patients only; 5) MOPP was not routinely used in our HD patients. Despite the above mentioned limitations, this study was prospectively designed to evaluate patients during follow-up after transplantation and to detect the initial features of myelodysplasia combining different approaches including morphology, cytogenetic and HUMARA analysis when applicable. The adoption of pre-transplant evaluation of bone marrow function and the appropriate application of a transplant procedure early in the course of the disease would probably reduce the incidence of MDS. This complication should not be regarded as ineluctable but attention should be paid to reducing at least the recognized risk factors. Informed consent should include awareness of the possibility of MDS/sAML after autologous transplantation but we should also remember that these complications have already been renamed as *the price of progress*.[33] The inherited susceptibility to cancer development and pharmacogenomics should be included in the work-up of patients, as recently promoted by the EBMT group.

Contributions and Acknowledgments

LL designed the study with PC and SS; PC was responsible for clonality assays on female patients; MGG was involved in morphologic evaluation of peripheral blood and bone marrow with LL and GZ; FS, NP and PP collected the data on patients and provided follow-up data; MZ was responsible for cytogenetic analyses of bone marrow samples; GL reviewed the manuscript and gave final approval.

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Disclosures

Conflict of interest: none.

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Peer Review Outcomes

What is already known on this topic

Myelodysplastic syndromes have been described as possible complications of autologous hematopoietic transplantation. The role of chemotherapy administered before transplant and the impact conditioning regimen are controversial.

What this study adds

First prospective study on morphologic, genetic and clonality analyses, before and after transplantation, to assess the incidence of myelodysplatic syndrome after autologous transplantation.

Manuscript processing

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Potential implications for clinical practice

The incidence of myelodysplatic syndromes after autologous transplantation may be minimized if potential risk factors are avoided. Transient acquisition of cytogenetic and clonal abnormalities may be observed, without these developing into overt myelodysplatic syndrome.

Jordi Sierra Gil, Deputy Editor