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Corresponding Author: Ms Noemi Puig,

Corresponding Author's Institution: Hospital Universitario de Salamanca

First Author: Noemi Puig

Order of Authors: Noemi Puig; Maria D Caballero; Miguel Alcoceba; Elena Sebastian; Ana Balanzategui; Maria E Sarasquete; Ramon Garcia-Sanz

Abstract: According to the instructions, no abstract is needed in Letters to the Editor.

**Sustained Complete Remission with Single Agent Rituximab in Relapsed
Follicular Lymphoma as Transformed Disease after Unrelated Reduced Intensity
Conditioning Allogeneic Stem Cell Transplantation**

Noemí Puig¹, María D Caballero¹, Miguel Alcoceba¹, Elena Sebastián¹, Ana
Balanzategui¹, María E Sarasquete¹, Ramón García-Sanz^{1,2} and Marcos González-
Díaz^{1,2}

¹Haematology Department, University Hospital of Salamanca, Salamanca, Spain

²Centro de Investigación del Cáncer-IBMCC (USAL-CSIC), Salamanca, Spain

Corresponding author: Marcos González-Díaz, Hematology Department, University
Hospital of Salamanca, Paseo de San Vicente, 58-182, 37007, Salamanca, Spain.
Phone: +34-923-291-629. Fax: +34-923-29 46 24. E-mail: margondi@usal.es

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1 A 42 year-old female presented with a right submandibular mass and was diagnosed
2 with stage IVA grade II follicular lymphoma. After receiving multiple lines of treatment,
3 (including CHOP, FMD, autologous transplant, rituximab and yttrium-90-ibritumomab)
4 she underwent an unrelated, HLA-mismatched (9/10), non-myeloablative, allogeneic
5 peripheral blood stem cell transplantation in partial remission December 29th, 2006.
6 Conditioning regimen consisted of fludarabine and melphalan [1]. Cyclosporin and
7 mycophenolate-mofetil were used as graft-versus host disease (GVHD) prophylaxis.
8 Patient and donor had EBV IgG antibodies. Complete chimerism was documented on
9 day +28, remaining stable up to date. She developed grade II (skin III, gastrointestinal
10 I) acute GVHD managed with methyl-prednisolone (2mg/Kg) and beclometasone
11 (2mg/6h). Signs and symptoms subsided on day +54 and steroids were tapered.
12

13 On day +100, she presented with a right inguinal mass. PET/CT-scan showed right
14 iliac (1.5x2.5cm) and inguinal (3x1.5cm) lymphadenopathies, the latter FDG avid
15 (SUV10.5). Incisional biopsy of the right inguinal node showed DLBCL with a
16 proliferation index of 90%; EBV was negative; qualitative PCR showed the presence of
17 the BCL2/JH (Mbr) rearrangement; cytogenetics and FISH detected the t(14;18) with
18 no other added lesions; GeneScanning analysis and sequencing of the immunoglobulin
19 chain gene rearrangement V_K-Kde was identical to that detected at diagnosis
20 confirming the re-appearance of the malignant clone and thus the diagnosis of relapsed
21 disease transformed to diffuse large B cell lymphoma (Fig.1a) [2]. Flow cytometric
22 analysis on lymphadenopathy cell suspensions identified a B-cell malignancy
23 intermingled with a polyclonal T-cell population representing 42% of the cellularity;
24 chimerism analysis (STR&GeneScanning) detected 42% of donor cells and 58% of
25 patient cells (fig.1b). Taken together, results can be explained by the presence in the
26 sample of patient-derived clonal B-cells together with infiltrating T-cell lymphocytes
27 (TIL-T) of donor origin, findings suggestive of an active graft *versus* lymphoma effect.
28
29

Baseline immunosuppression was reduced and she received 4 doses of single agent rituximab at a standard dose. Three months later, re-evaluation with PET/CT and bone marrow biopsy showed complete remission. She developed chronic GVHD affecting the gastrointestinal tract and joints (+874) and is currently taking tacrolimus and steroids at a low-dose. Repeated follow-up imaging, including the most recent PET/CT scan (February09) showed no significant abnormalities. There is no evidence of disease in the last bone marrow assessment (March09).

In summary, our patient presented with a rapidly enlarging, PET positive, right inguinal node early post-allotransplant. A post-transplant lymphoproliferative disorder was suspected but an identical immunoglobulin chain gene rearrangement to that detected at diagnosis was identified, confirming the diagnosis of relapsed lymphoma transformed to DLBCL. The frequency of this entity is unknown since most studies do not specify/confirm histologies at relapse [3-6]. Despite the poor prognosis of transformed follicular lymphoma [7], our patient remains clinically and radiologically in complete remission on day +915 post-transplant. It is likely rituximab and a GVL effect exerted by a TIL-T population and forced by reducing the immunosuppression influenced the outcome of our patient [8,9].

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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FIGURE LEGENDS

Figure 1a. GeneScanning analysis of kappa light chain immunoglobulin rearrangement (V_K -Kde) at diagnosis and at relapse post-allogeneic stem cell transplantation. Note that PCR product size is similar in both samples and therefore highly suggestive of relapsed disease.

Figure1b. Chimerism analysis at relapse post-allogeneic transplantation showing recipient, donor and recipient's adenopathy short tandem repeat (STR) genotypes. Focused on shadowed peaks in adenopathy sample, arrows point out peaks of recipient origin.

Figure 1a

Figure 1b