organ dysfunction, autoimmunity). Genotyping of the globin loci revealed that the fetus had inherited the mother's (ε,γ,δ,β)° thal and an anti -3.7 α-triplication from the father (Figure 1). Two intrauterine RBC transfusions were performed at weeks 22 and 29. Hydrops did not recur and growth was satisfactory. The baby was born by caesarean section at 35 weeks and was well without hepatosplenomegaly; his Hb was 9.3 g/dL, reticulocyte count 356 10^6/L, bilirubin 40 mg/L. RBC transfusions have been necessary every three weeks to maintain Hb value above 9 g/dL, the baby now being four months old.

The severe hydrops foetalis was due in this case to inheritance of an (εγδβ)°-thalassemia and an anti -3.7 α-globin gene triplication. Typically, patients heterozygous for an (εγδβ)°-thalassemia deletion alone exhibit at birth a hypochromic anemia with various degrees of hemolysis. Blood transfusion in the neonatal period is sometimes necessary in (εγδβ)°-thalassemia like in the probant's mother's case II.2.[2,3] However contrasting phenotypes have been reported in one family.[1,9] The occurrence of early manifestations in this case is explained by the increasing imbalance between the α and non α-globin chains ratio during fetal life. In our case III.2, the association with the triplicated α-genes increased the imbalanced α/non α-globin ratio which explains the "fetal thalassemia intermedia" requiring blood transfusions during the intra-uterine period. *Thalassemia intermedia* is characterized by an unstable thalassemic erythropoiesis needing transfusion when an erytroid stress occurs. In our case, it is very likely that the transition from embryonic to fetal erythropoiesis was the "erythroid stress" causing a greater sensitivity to the effect of globin imbalance and the hydrops foetalis. Intra uterine transfusion in (εγδβ)°-thalassemia related to the presence of such a deletion has been previously cited twice; it could be hypothesized that triplication alpha might also be involved in these cases (α-triplication not evaluated).[2,3] The frequency of α-triplication varies according to population origin[10] and cannot be identified with routine parameters, as attested by the father's normal phenotype (II.3).[4] However the impact of such an association is extremely important and could threaten the fetus's life.

Our observation emphasizes the absolute necessity of systematically looking at α-gene status in partners of (εγδβ)°-thalassemia carriers before conception considering the severity of such an association. Careful follow-up of both the fetus and the mother, if carrier of the (εγδβ)°-thalassemia deletion, is mandatory.

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Successful unrelated donor stem cell transplantation for advanced myelofibrosis in an adult patient with history of orthotopic liver transplantation

Patriarca *et al.*[1] recently reported a significant improvement in outcome of patients with myelofibrosis (MF) after allogeneic stem cell transplantation (SCT). Some MF patients present to the transplant center with severe complications after a long disease history and their treatment may be very challenging.

In 1987, a 33-year old woman was diagnosed with polycythemia vera (PV) associated with portal and splenic vein thrombosis. A year later she developed acute Budd-Chiari syndrome and required orthotopic liver transplantation. In 2002, 15 years since diagnosis, PV progressed to MF. Molecular genetics revealed heterozygous V617F mutation in the Janus Kinase 2 (*JAK 2*) gene. In 2006, blood count showed: leukocytes 1.5×10^9/L, hemoglobin 8.1 g/dL, platelets 124×10^9/L and 13% circulating blasts. Blood transfusions were required every eight weeks. According to the Lille Scoring System the patient was at high risk of progression to acute leukemia. Since she had no siblings, we decided to start an unrelated donor search, although very few reports exist on allogeneic SCT in patients after preceding solid organ, respectively liver, transplantation. A compatible donor with a single human leukocyte antigen (HLA) Cw mismatch was identified. Patient and donor were mismatched for blood group and cytomegalovirus serology. In April 2007 allogeneic SCT following treosulfan (30

g/m^2), fludarabine (150 mg/m^2) and anti-thymocyte globuline (ATG 30 mg/kg, Fresenius Biotech, Germany) conditioning was performed. Graft versus host disease (GvHD) prophylaxis consisted of cyclosporine A and mycophenolate mofetil. Engraftment was achieved rapidly. The first 100 days after SCT were complicated by an asymptomatic CMV reactivation and probable viral encephalitis with lymphocytic pleocytosis in spinal fluid and meningeal MRI enhancement but without positive virology findings. Both episodes were successfully treated with foscarnet. As a further complication, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) occurred. Acute GVHD or veno-occlusive disease (VOD) did not occur and liver function remained stable. From day 100 onwards, polymerase chain reactions (PCR) of peripheral blood samples were negative for the *JAK2* gene mutation consistent with complete molecular remission of MF. Also sustained complete donor chimerism was confirmed by molecular studies. Bone marrow biopsy at day 100 showed a normal hematopoiesis without signs of fibrosis. Imunosuppression was reduced but the patient remained on low-dose cyclosporine A and prednisone as prior to SCT. A biopsy proven chronic scleroderma GvHD of the skin developed eight months after SCT and mycophenolate mofetil was re-started. Sicca symptoms, persistant cachexy and senso-motoric polyneuropathy developed in the following few months. Eighteen months after SCT the blood count showed: leukocytes 4.0/nL, hemoglobin 13.7 g/dL, platelets 112×10^9/L.

In MF allogeneic SCT is the only treatment modality with the potential to provide prolonged disease control or even cure, whereas conventional treatment results are usually disappointing. Recent reports showed hematologic response in up to 100% and complete histopathological remission in 75% of patients with MF who underwent allogeneic SCT.[2,3] High rates of molecular remission are achievable in JAK2-positive patients.[4] The feasibility of allogeneic bone marrow transplantation (BMT) from a sibling donor following cadaveric liver transplantation has been demonstrated in a pediatric patient with severe aplastic anemia (SAA) following non-A, non-B, non-C (NANBNC) hepatitis.[5] Also long-term follow-up after sibling donor BMT for SAA following orthotopic liver transplantation for hepatitis was reported in another pediatric patient.[6] Combined cord blood and haplo-identical BMT for SAA after living-related liver transplantation from the same donor was proposed as an option for children with liver failure due to diseases that can be cured by allogeneic SCT.[7] A single case of an adult 29-year old patient with SAA, who received myeloablative conditioning for sibling allogeneic BMT four months after orthotopic liver transplantation for NANBNC hepatitis, has been reported.[8,9] Severe acute GvHD of the liver was not observed in any of these cases.[5-8] It has been suggested by studies in mice and humans that the liver is the most capable of inducing tolerance after solid organ transplantation due to high leukocyte content, particularly due to the antigen-presenting dendritic cells and their progenitors that migrate from the liver into peripheral blood and tissues, modulate immune responsiveness and induce immunological tolerance.[10] In this case we could not detect liver-donor derived leukocyte microchimerism for technical reasons after cadaveric liver transplantation. We postulate that microchimerism after solid organ transplantation might facilitate engraftment and prevent GvHD, but further studies are necessary in this field. To our knowledge this is the first report of a successful reduced intensity conditioning allogeneic SCT from an unrelated donor in an adult patient with a history of liver transplantation. This case might encourage physicians to propose allogeneic SCT to patients with hematologic diseases, who had previous liver or other solid organ transplantations.

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CIITA or RFX coding region loss of function mutations occur rarely in diffuse large B-cell lymphoma cases and cell lines with low levels of major histocompatibility complex class II expression

Loss of major histocompatibility complex class II (MHCII) gene expression was associated with poor outcome in diffuse large B-cell lymphoma (DLBCL) in several studies.[1-3] The mechanism for lost expression is unknown. MHCII gene expression is controlled by several transcription factors, including RFX (composed of *RFXB, RFX5*, and *RFXAP*), CREB, and NF-Y. These transcription factors interact with a master transactivator protein class II transactivator (CIITA) to form an enhanceosome complex.[4] In the Bare Lymphocyte Syndrome (BLS), MHCII gene expression is absent due to small deletions or point mutations in the coding or splicing regions of either CIITA or an RFX subunit.[5] This study investigated whether DLBCL with low MHCII expression had mutations similar to BLS.

DNA from 46 patient tumors, for which gene expression profiling was available, was obtained from the

Table 1. Mutations found in CIITA and RFX, organized 5' to 3' down the lengths of the genes. Bolded mutations indicate those which were interpreted as likely to affect expression or function of the mutated protein.

Gene	Site	Mutation	Mutation Type	SNP?	Alleles	Sample ID number	Sample type
CIITA	pIII	-136bpA->G	Non-coding	SNP	Excl.	38, 91, 255, 273, 322, 397, S7, LN2, 1030, 1043, Raji, RJ2.2.5 lines	MHCII-, MHCII+, PTCL, benign, MHCII+ & - cell
CIITA	pIII	-136bpA->G	Non-coding	SNP	Poly	12, 19, 80, 122, 123, 129, 132, 134, 139, 166, 169, 249, 263, 277, 285, 298, 315, 435, S5, S6, LN1, 1112, 1113, 1114	MHCII-, MHCII+, Benign
**CIITA*	1	deletion 5' UTR-130	Non-coding		Poly	172	MHCII+
**CIITA*	1	deletion 5' UTR-41	Non-coding		Poly	435	MHCII+
CIITA	1	aa 11	Silent		Poly	38	MHCII-
CIITA	2	aa L45V	Mis-sense		Excl.	LN2	benign
CIITA	2	aa L45V	Mis-sense		Poly	12,397,1030,1112	MHCII-, MHCII+, benign
**CIITA*	6+	intron 6+8G->T	Intronic		Poly	41,91,134,315	MHCII-, MHCII+
CIITA	7	aa 197	Silent		Poly	58	MHCII-
**CIITA*	9	aa P292S	Mis-sense		Poly	SUDHL4	MHCII+ cell line
***CIITA**	**11 & 12**	**deletion 11 & 12**	**deletion**		**Excl.**	**RJ2.2.5**	**MHCII- cell line**
CIITA	11	aa G500A	Mis-sense	SNP	Excl.	67,91,132,142,269,OCILy3,OCILy19,Raji	MHCII-, MHCII+, MHCII+cell lines
CIITA	11	aa G500A	Mis-sense	SNP	Poly	38, 58, 80, 123, 129, 152, 213, 255, 263, 273, 277, 285, 298, 406, tonsil, 1030, 1039, 1112, 1114, OCILy10, SUDHL6	MHCII-, MHCII+, benign, MHCII+ & - cell lines
**CIITA*	11	aa A691D	Mis-sense		Poly	315, 397	MHCII+
CIITA	11	aa 777	Silent		Excl.	8, 273	MHCII-
CIITA	11	aa 777	Silent		Poly	15, 64, 80, 101, 119, 134, 166, 179, 203, 322, 397, 423, 1028, 1113	MHCII-, MCHII+, benign
CIITA	11	aa S781L	Mis-sense		Excl.	213	MHCII+
CIITA	11	aa S781L	Mis-sense		Poly	38, 41, 67, 80, 132, 142, 152, 255, 273, 1030, 1112, OCILy10, OCILy19	MHCII-, MHCII+, benign, MHCII+ & - cell lines
CIITA	11	aa V782A	Mis-sense		Excl.	213	MHCII+
CIITA	11	aa V782A	Mis-sense		Poly	38, 41, 67, 80, 132, 225, 273, 1030, 1112, OCILy10, OCILy19	MHCII-, MHCII+, benign, MHCII+ & - cell lines
CITA	11	aa 798	Silent	SNP	Excl.	25, 139, 140, 435, S5, S6	MHCII-, MHCII+
CIITA	11	aa 798	Silent	SNP	Poly	19, 38, 58, 65, 249, 255, 285, 322, S7, S8, 1030, 1112, DB, OCILy7	MHCII-, MHCII+, PTCL MHCII-, benign, MHCII+ & - cell lines
CIITA	11	aa 807	Silent		Excl.	269, LN2, OCILy3, Raji	MHCII-, benign, MHCII+ cell lines
CIITA	11	aa 807	Silent		Poly	41, 58, 67, 91, 123, 129, 142, 263, 277, 285, 298, 406, tonsil, 1039, 1114, OCILy19, SUDHL6	MHCII-, PMBL, MHCII+, MHCII+ cell lines

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