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Alloimmunization against human platelet antigen 2 (HPA2) in a series of multi-transfused β -thalassemia patients

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In our study we investigated the presence of anti-human platelet antigen (HPA) alloantibodies in a series of 10 β -thalassemia major patients submitted for more than 10 years to periodic blood transfusions (every 2-3 weeks). We found that 2 out of the 10 patients developed anti-HPA2a+HPA1b and anti-HPA2b antibodies. Our results highlight that HPA alloimmunization in multitransfused patients is a real possibility.

Patients affected by β -thalassemia major are usually submitted to many transfusions of packed red blood cells during their life. Multitransfused patients are exposed to different immunogens due to the presence of leukocytes and platelets in packed red blood cells.^{1,2} Antibodies raised against the latter components are responsible for some of the febrile non-hemolytic transfusions reactions (FNHTR) and filtered packed red cells are then needed to avoid this kind of reactions. Little is known about possible alloimmunization against human platelets antigens (HPA); this is more difficult to study and to characterize than HLA alloimmunization.^{3,4} In this context we analyzed our series of β -thalassemia patients to find alloimmunization against red blood cells, leukocyte and platelets.

Ten patients affected by β -thalassemia major (clinical characteristics summarized in Table 1) were submitted to periodic tests for the presence of alloantibodies. Tests were also performed in the case of transfusion reactions.

Antibodies against red cell antigens were detected by standard indirect tests using rabbit anti-human immunoglobulin antisera. Antibodies against HLA were analyzed by a standard cytotoxicity test on HLA-typed donors.

The search for alloantibodies against HPA was performed by a standard indirect immunofluorescence test on random and HPA-typed donor platelets.⁵ The samples were also run on a monoclonal antibody-

immobilized platelet antigen (MAIPA) test⁶ to define the specificity of the recognized antigen. Patients found positive for anti-HPA antibodies were genotyped for HPA-1,-2,-3,-5 genes with SSP-PCR.

Clinical records (Table 1) showed that 6 patients had suffered from FNHTR, indicating a possible alloimmunization against platelets and/or leukocytes. Two patients showed alloimmunization against red blood cell (one anti-Kell and the other anti-Kp^a), while 5 out of 10 had HLA antibodies with a very wide specificity (>80% of positive donors). One patient (#4) had anti- HLA-B35+51 antibodies.

Concerning HPA alloantibodies, patient #1 had HPA2b alloantibodies and patient #2 HPA2a+HPA1b alloantibodies. It should be underlined that HLA antibodies with wide reactivity were found in sera from both patients, and patient #1 had also anti-Kell antibodies. HPA gene typing showed that patient n.1 (anti-HPA2b) was HPA1a/a, HPA2a/a, HPA3b/b, HPA5a/b. Patient #2 (anti-HPA2a) showed the following typing: HPA1a/a, HPA2b/b, HPA3a/a, HPA5a/a.

We analyzed sera from 10 multitransfused patients suffering from β -thalassemia major, looking for both HLA and HPA specificities. HLA antibodies were found in 6 out of the 10 patients. Our investigation also showed that HPA alloimmunization is a real possibility since two patients developed HPA antibodies (anti HPA2b and anti HPA2a+HPA1b).

In multitransfused patients alloimmunization is usually regarded as strictly related to the presence of HLA alloantibodies, since these are responsible for most of the FNHTRs. In addition HPA alloantibodies may be implicated. A retrospective analysis showed that patient #2 also suffered from FNHTR also when receiving blood from HLA-matched donors, positive for the HPA2a antigen. These results suggest that HPA may have been responsible for the FNHTRs.

Table 1. Characteristics of β -thalassemia patients.

N.	Pts.	Age/Sex	No. of transfused RBC units		Transfusion reactions
			(non-filtered U until 1990)	(filtered U beginning from 1991)	
1	C.M.	26/M	464	215	chills-hyperthermia
2	C.A.	24/F	568	160	chills-hyperthermia
3	D.F.M.	34/F	760	212	chills-hyperthermia
4	D.L.	21/F	423	202	chills-hyperthermia
5	F.L.	31/M	804	240	chills-hyperthermia
6	F.A.	23/F	420	184	none
7	F.M.	19/M	260	162	none
8	I.I.	27/F	740	187	chills-hyperthermia
9	R.A.	21/F	324	164	none
10	S.F.	26/M	580	215	none

M= male; F=female; U=units.

A few considerations should be highlighted: (i) in chronically multitransfused patients, HPA alloantibodies might be responsible for some of the FNHTRs; (ii) in our series rare HPA specificities were found, involving the HPA2 alloantigens. In this context, it could be hypothesized that the mechanisms of recognition in multitransfused patients might be different: alloantigens expressed on the CD42 protein (HPA2) might be more immunogenic in multitransfused patients than alloantigens expressed in the CD41/61 complex (HPA1 or HPA3) or in the CD49b-related antigen (HPA5), which are more frequently involved in neonatal alloimmune thrombocytopenia or in post-transfusional purpura.⁷⁻¹⁰

Key words

Alloimmunization, β -thalassemia, human platelet antigen (HPA), multitransfused patients

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Spontaneous decrease of spleen size in a patient with type 1 Gaucher's disease

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We present a patient with type 1 Gaucher's disease in whom the spleen size during 34 years of follow-up reached a maximum of 6 cm. below the costal margin, but in 1993 began to decrease spontaneously and presently can no longer be felt by abdominal palpation.

Gaucher's disease is an autosomal, recessive storage disease due to glucocerebrosidase deficiency; the spleen may increase to ten times the normal size.¹ We have treated more than 30 patients with this condition, but the patient presented here is the only one in our series in whom a spontaneous regression of the spleen size was noted.

A.M. is a 62-year-old nurse of Ashkenazi origin, a mother of two sons. In 1959, when she was 37 year-old, she was diagnosed as having Gaucher's disease following the appearance of mild purpura, petechiae and hepatosplenomegaly of 2 and 4 cm. below the costal margins. Blood examinations showed: hemoglobin 12.2 g/dL, white blood cells $4.7 \times 10^9/L$ and platelets $330 \times 10^9/L$. Serum acid phosphatase 5.5 U (normal range 0-0.8 U). Bone marrow aspiration biopsy revealed Gaucher's cells. X-ray examination was remarkable for Erlenmeyer flask deformity of the femora.

One son is a heterozygous carrier of the disease.

During the years of follow-up the size of the spleen progressively increased, reaching a maximum of 6 cm. below the costal margin. Bone biopsies performed in 1966 and 1973 showed the presence of Gaucher's cells. However, beginning in 1993, the size of the spleen progressively decreased by about one cm per year until 1996, when the spleen could be not palpated at all. Two abdominal ultrasounds and a ⁹⁹Technetium sulfur colloidal scan, showed a spleen size of 10 cm. A Doppler examination of the spleen vessels was without pathological findings. Examination of her peripheral white blood cells showed that she is a homozygote for the 1226 G variant of Gaucher's disease.

The onset of the disease, the clinical and laboratory findings and the family history of the patient are consistent with the diagnosis of adult, type 1 Gaucher's disease. The long course and almost asymptomatic presentation of the illness, exclude the possibility of myeloproliferative disorders in which pseudo-Gaucher's cells may be found. Our patient should be distinguished from those with asplenomegaly (cryp-