Report

I-int phenotype among three individuals of a Parsi community from Mumbai, India

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The red blood cells (RBCs) of most adult individuals display an I+i– phenotype, whereas those of newborns and some rare adult individuals are typed as I–i+. The phenotype in the latter category, designated as adult i, is under genetic influence as the RBCs of I+i+ individuals display strengths of I and i antigen expression intermediate to that of ordinary adults and ii-adults. As there was no information on the occurrence of adult i phenotype in the Indian population, the present study was undertaken. The RBCs of randomly selected subjects were screened with anti-I and anti-i reagents by a saline tube technique at 22°C. Individuals with unusual I and i antigen reactivity patterns were further tested by a semi-quantitative method with a battery of anti-I and anti-i reagents, followed by family studies. Three of the 5864 donors tested showed an elevated strength of i antigen. Further study revealed an intermediate strength of both I and i antigens compared with those on RBCs from adult and cord blood samples. All three probands came from an ethnic Parsi community. The phenotype (referred to as I-int) was shown to be inherited, being passed through two generations, but none of the members of the families had displayed an adult i phenotype. The I-int phenotype detected showed an ethnic association because all three subjects belonged to an endogamous Parsi community that has migrated to India some centuries ago from Persia, the present-day Iran. ***Immunohematology* 2014;30:11–13.**

Key Words: I-int phenotype, Parsi community, India

I and i blood group antigens are considered developmental antigens. Antigenic strength gradually alters during the first 18 months of life. The I antigen, weakly expressed at birth, becomes stronger, whereas the i antigen, strongly expressed at birth, becomes weaker to undetectable through this period.[1] Almost all adult red blood cells (RBCs) are observed as I+i–. The rare adult I–i+ RBC phenotype is comparable to that of newborns, is under genetic influence, and is designated as the adult i phenotype. The I+i+ phenotype with levels of I and i antigen strength intermediate between ordinary adults and ii-adults or newborns is referred to as the I-int phenotype.[1] I-int phenotype is often detected in the parents or the offspring of ii-adults. Earlier, Joshi and Bhatia[2] described a unique phenotype in adults with traces of I antigen comparable to that on RBCs of newborn infants but without any reciprocal i antigen. This phenotype was designated as I–i–.[2] The present report describes the I-int phenotype in three individuals, and their families, encountered while screening donors for I and i. It is interesting to note that all three subjects belonged to the Parsi community, an ethnic population group that migrated centuries ago from Persia, i.e., present-day Iran.

Materials and Methods

Blood samples used in screening for I and i were obtained from the local blood center in Mumbai. The RBCs of 5864 randomly selected donors were screened with anti-I and anti-i reagents by a saline tube technique at 22°C. Individuals with unusual I and i antigen reactivity patterns were further tested by a semiquantitative method with a battery of anti-I and anti-i reagents, followed by family studies. The control rare ii-adult RBC specimen was made available through the Serum, Cells, and Rare Fluids Exchange (SCARF; Houston, TX). Reagent antisera used including anti-I (Ste) and anti-i (Mac) were a gift from the late M.C. Crookston, Toronto, Ontario, Canada; anti-i (Ziag) was from Peter Issitt, Cincinnati, OH; and anti-i (Mort) was from Carolyn Giles, Chelsea, London, U.K. The other two anti-I sera, Gov and Gan, were from locally diagnosed patients with cold agglutinin disease. The methods used were standard serologic techniques recommended by Bhatia.[3] Antigen strength on RBCs was obtained by titration of antisera and expressed as score values calculated as per Marsh.[4]

Results

Three (RD, RV, and ND) of the 5864 donors tested showed an elevated strength of i antigen. The RBC I and i antigen strengths were expressed as score values obtained by titration of different antisera using RBCs from the three donors alongside appropriate control samples. All three anti-I sera gave a lower antigen score on these donors as compared with the control RBCs from adults. Anti-I (Ste) showed score values of 20, 22, and 23 for RD, RV, and ND, respectively, as compared with the control value of 36; anti-I (Gov) showed respective score values of 14, 17, and 20 in contrast to a control value of 44; similarly, anti-I (Gan) showed respective scores of 39, 31, and 21 versus a control adult RBC score of 55 (see Table 1).

Table 1. Comparison of the I and i antigen scores of the proband and their family members having I-int phenotype with control RBCs

Red blood cells		ABO groups	Anti-I			Anti-i		
			Ste	Gov	Gan	Ziag	McD	Mort
RD Family	RD (Proband)	O	20	14	39	22	56	21
	Father	O	23	18	34	26	56	25
ND Family	ND (Proband)	B	23	20	21	26	61	12
	Father	B	21	25	25	26	64	19
	Sister	B	22	16	19	23	53	19
	Niece	B	23	25	25	18	59	21
RV Family	RV (Proband)	A1B	22	17	31	23	50	10
Controls	Adults	B; O	36	44	55	0	26	2
	Cord	B; O	4	0	3	34	64	36
	ii-Adult	O	2	0	1	38	70	NT

NT = not tested.

On the other hand, the three anti-i reagents showed higher antigen scores on RBCs from these donors as compared with the control RBCs from adults. Anti-i (Ziag) showed score values of 22, 23, and 26 for RD, RV, and ND, respectively, whereas control RBCs from adults showed a score value of 0; anti-i (McD) gave respective score values of 56, 50, and 61 as compared with control RBCs from adults showing score values of 26; and anti-i (Mort) showed respective scores of 21, 10, and 12 as compared with control adult RBCs showing a score value of 2. The i antigen strengths on these donors' RBCs were lower than those found on control RBCs of the newborns or ii-adults. The results are displayed in Table 1.

In the family of donor ND, the I-int phenotype was found in three generations in the father (II-1), sister (III-4), and niece (IV-2) of the proband (III-1; Fig. 1), whereas in the family of donor RD, the phenotype was detected through two generations in the father (I-1) and the proband (II-1; Fig. 2).

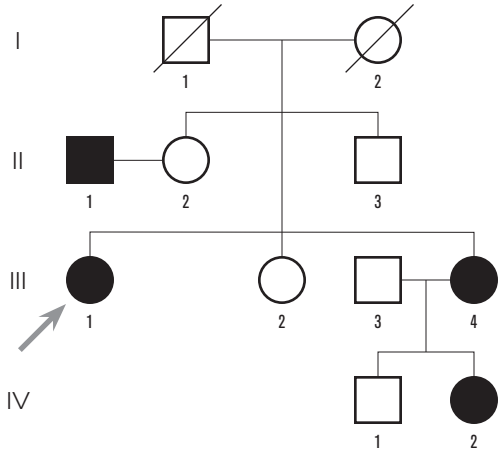

Fig. 1 I-int phenotype in members of the ND family.

Although the phenotype showed vertical inheritance, none of the members in these families have the ii-adult phenotype.

Discussion

I and i antigens are considered to be developmental antigens as they show a remarkable reciprocal relationship of expression on RBCs of individuals in early childhood and subsequent adult life.[1] Most adult RBCs are characterized by a strong expression of I antigen and a weak expression of i antigen, whereas the RBCs of newborns have weak I and strong i antigens. The rare individuals defined as ii-adult have an I/i antigen profile similar to that found in newborn infants. Additionally, these individuals have naturally occurring alloanti-I.

Joshi and Bhatia[2] earlier found weak expression of I antigen without concurrent increase in i antigen on RBCs of certain individuals and defined the phenotype as I–i–. Family study showed that this I–i– phenotype demonstrated vertical inheritance with some members showing an apparently partial expression of the I–i– character. However, the phenotype appeared to be passing through generations without showing any pattern of Mendelian inheritance.[5] Joshi and Bhatia[5] reported an association with group A1 or A1B phenotype that was characterized by a remarkable increase in A1 antigen expression on RBCs, thereby suggesting an influence of A1 blood group on expression of I in this phenotype. In the present cases, the I-int phenotype showed no bearing on the

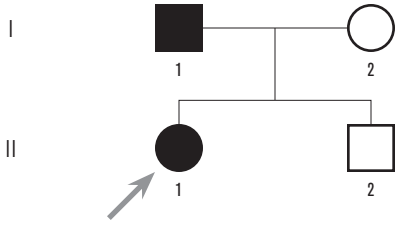

Fig. 2 I-int phenotype in members of the RD family.

A1 blood group, as two of the three probands were group B and O. The reduced I antigen in the present I-int phenotype appeared with an increase in i as is seen among the obligate heterozygotes (e.g., parents or offspring) in the families of the ii-adult probands.[6] Although there was no ii-adult phenotype found in the present families studied, such a rare phenotype was investigated by Joshi et al.[7] in a blood donor from Iran with depressed RBC ABH antigen expression. However, the three donors in the present study had normal features of ABH antigens. The Parsi community has its ancestral origin in Iran, so it is conceivable that the I-int phenotype in the present cases bears some ethnic relation to the ii-adult phenotype detected in the Irani donor. However, the level of I and i antigen strength found among those donors with an I-int phenotype as well as those reported among the family members of the ii-adult probands may potentially reflect a dosage effect shown by the I and i antibodies, a concept that, as per the author's knowledge, has not been proposed to date.

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