117. Another Japanese A_2B_3 Blood-Group Family with the Propositus Having O-Group Father

By Hideo YAMAGUCHI,^{*)} Yasuto OKUBO,^{**)}
and Fumio HAZAMA^{**)}

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In our previous paper,¹⁾ we reported on a family having an atypical AB-group blood which gave weaker reactions with both anti-A and anti-B, and designated provisionally as A_2B_3 . This blood seemed to be of the genotype O/A_2B_3 , judging from its atypical mode of inheritance. According to Prof. Komai,¹⁾ this family presented a conclusive evidence for the hypothesis that the genes governing the ABO-blood groups are not allelic in the strict sense, rather, the genes *A* and *B* are pseudo-allelic. Crossing-over between the loci *A* and *B* may take place on very rare occasions, bringing the genes for *A* and *B* in close juxta-position on one and the same chromosome. If this view is valid, we should expect an exceptional family in which an O-group parent could have an AB-group child, or vice versa.

Recently, we came across another family having an A_2B_3 type blood very similar, if not identical, to that in our previous report. The propositus of this Sa. Family (Figure) is a 24-year-old healthy Japanese male (II-3). To our surprise, his mother's (I-2) blood was much like the propositus' and his father's (I-1) was of the normal O-group. Further family investigations revealed that both the two sisters of the propositus (II-1 and II-2) also had the A_2B_3 blood.

Serological findings. Red cells. The agglutinability of the red cells of these four atypical AB members is shown in Table I. All of them gave reactions somewhat weaker than average with both routine anti-A and anti-B, but they could easily and definitely be typed as of AB. They did react neither with human anti- A_1 (natural or absorbed) nor with *Dolichos biflorus* lectin, showing that their antigen was of the A_2 level. Almost all the fresh sera from O, A, or B unselected donors tested, except those from A_1B , agglutinated the four specimens. The anti-H *Ulex europaeus* lectin agglutinated them more strongly than the control A_1B cells. Other serological findings, such as agglutination patterns on the slide and capacity of absorbing anti-A and anti-B, were nearly the same as in

^{*)} Osaka Red Cross Hospital.

^{**)} Osaka Red Cross Blood Center.

Table I. Agglutinability of the red cells

Cells from	Agglutinin		Anti-A ₁			Anti-H <i>Ulex</i>
	Anti-A	Anti-B	Natural	Absorbed	<i>Dolichos</i>	
I-2	1:64	1:32	—	—	—	1:16
II-1	1:128	1:32	—	—	—	1:16
II-2	1:128	1:32	—	—	—	1:16
II-3*	1:64	1:32	—	—	—	1:8
Control						
A ₂ B	1:32	1:256	.	.	—	1:8
A ₁ B	1:512	1:512	.	.	1:32	1:1

* Propositus of Sa. Family.

the atypical AB members of our previous family example.

Serum. All the four atypical AB members of Sa. Family possessed anti-B antibody of varying titers (1:2-4) which was specifically inhibited by salivas from B or AB secretor donors. The auto-sensitization of the cells by their own anti-B was not demonstrated by direct Coombs' and elution tests. All cross-matching tests as available as possible among the atypical bloods of this family gave negative results, though their anti-B antibodies were active even at 37°C against randomly selected B, A₁B, or A₂B cells. Other atypical antibodies such as anti-A₁ were not detectable.

Saliva. The amounts of blood group substances in saliva were expressed as the highest dilution of saliva which completely inhibited 16 units of anti-A, anti-B, and undiluted anti-H (*Ulex europaeus*) (Table II). All the four members secreted somewhat less A-substance

Table II. A-, B-, and H-substances in saliva

Substance			
	A	B	H
Saliva from			
I-2	1:8	<1:1	1:16
II-1	1:32	1:1	1:8
II-2	1:64	1:1	1:16
II-3	1:8	<1:1	1:8
Control			
A ₂ B } Secretor	1:2	>1:512	1:2
A ₁ B }	>1:256	>1:256	1:2
A ₂ B Non-secretor	<1:2	1:2	<1:2

than did the control A₁B group person. Some of the saliva lacked in B-substance and some contained a trace of that substance, whereas all the salivas had plenty of H-substance.

From the above serological findings, we have concluded that all the four members of Sa. Family have very similar bloods, if not identical, to the blood of O. Family in our previous report, namely, an A_2B_3 phenotype blood. The only serological difference between the two families seems to be found in that, while the A_2B_3 members of O. Family secreted as much A-substance as did a normal AB person, all the salivas of the atypical AB members of Sa. Family contained that substance much less than we had expected.

Pedigree studies: As the father of the propositus (I-1) is of the normal O-group, the genotypes of all his children are to be assumed as O/A_2B_3 . The mother's (I-2) genotype may also be either O/A_2B_3 (or A_2/A_2B_3 , though the chance is very low). The genotype A_2B_3/A_2B_3 may well be ruled out, since she positively denied the consanguineous marriage of her parents. We could exclude the possibility that her husband I-1 may be of any variant of ABO, such

Figure

as "Bombay", because his red cells reacted strongly with anti-H reagent, and furthermore, his saliva contained neither A- nor B-substance but had much H-substance.

Race and Sanger²⁾ mention three possible causes of variants of

ABO blood: i) rare alleles of ABO, ii) action of other genes on normal ABO genes, iii) action of environment on normal ABO genes. Our atypical AB examples seem to fit neither of these three possibilities. The weaker antigens of both A and B in our bloods are probably not due to the exceptional property of the genes in question, but rather owing to a position effect of cis-arrangement of the normal *A* and *B* genes on one and the same chromosome. Accordingly, we feel like designating this atypical AB as "Cis-AB" to distinguish it from the ordinary AB, namely, "Trans-AB".

At any rate, as Seyfried *et al.*³⁾ stated, the abnormality in the inheritance of the ABO groups found in Sa. Family is not only of theoretical interest in human genetics but also of great significance in disputed paternity. In any case we seem to have to admit that the acknowledged general rule, that an O-group parent could never have any AB-group child, and vice versa, should allow some exceptions, even if very seldom. It is likely that such an exceptional case may be discriminated by the peculiarity of the reactions of the AB blood, as found in our two families.

More recently, at the 14th Congress of Japan Society of Blood Transfusion 1966, Yasuda *et al.*⁴⁾ presented two examples of atypical AB blood similar to our own and supported our genetic hypothesis. Kitahama⁵⁾ also discussed on this kind of blood with his own example.

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