A Case of Modified A antigen in Acute Leukaemia

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Introduction

MODIFICATION OF a blood group antigen by disease was first recognized in 1957, when van Loghem et al. reported a case in which the red cells of a patient suffering from myeloblastic leukaemia were found to possess an exceedingly weak A antigen, though his cells had been typed a year previously and reported without comment as A. Similar changes in acute leukaemia have since been reported independently by a number of workers and the phenomenon has also been observed in a case of Hodgkin's Disease (Scott and Rasbridge, 1972).

The present report concerns a case of myeloblastic leukaemia in which fewer than 20% of the patient's red cells were agglutinable by anti-A and by anti-A,B and in which the patient's typing was initially misinterpreted as O. Details of the serological findings are presented with the object of illustrating the ease with which atypical and often significant features may be overlooked and an incorrect interpretation of agglutination tests may be made.

Materials and Methods

Case Report

Mrs. R. F., a 44-year-old Indian patient, was admitted to the General Hospital at Kuala Lumpur on 22 September 1973 with a diagnosis of incomplete abortion. Besides her vaginal bleeding, she was also suffering from purpura and other clinical manifestations suggestive of a haemorrhagic diathesis, and a total of two units of blood was requested from the Blood Transfusion Service.

The patient's group was interpreted by the technician on call as O Rh(D) positive and two units of group O Blood were crossmatched without difficulty. These were not administered, but a further request for blood was made on 25 September, when a fresh sample of the patient's blood was submitted to the laboratory.

Testing was carried out in the manner customary to the laboratory, on a white plastic tile ruled to provide separation of individual tests, the patient's cells being tested against anti-A, anti-B, anti-A,B and Anti-D, the patient's serum against A, B and O cells. Saline and albumin auto controls were also run in accordance with the routine practice.

Results

A distinct "mixed-field" agglutination reaction was observed with both anti-A and anti-A,B typing reagents. The majority of the cells in each case were unagglutinated, but a number estimated at 20% of the cells were seen to have formed into coarse agglutinates, readily visible to the naked eye in the anti-A,B test but somewhat less easily perceptible in the anti-A test due to the presence of a blue dye in the reagent. The reaction with anti-D was a normal positive one, whilst that with anti-B was unequivocally negative.

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The patient's serum agglutinated B cells strongly, but neither group O nor (significantly) group A_1 cells showed any reaction. Saline and albumin auto controls were also negative.

The possibilities considered initially were that:–

(a) the patient was of the sub-type A_3

or (b) this was a group A patient who had been transfused recently (perhaps elsewhere) with group O blood.

Either event could give rise to a "mixed field" agglutination reaction with antisera containing anti-A, but the appearances were not typically those seen with A_3 blood and the patient's history did not include a previous transfusion. It was then learned that a bone marrow examination performed on the day prior to the second transfusion request had established a diagnosis of myeloblastic leukaemia, and it was realised that the reactions observed may represent an example of A antigen modification, as is occasionally encountered in association with this disease.

The initial sample was retested and was found to give reactions identical with those of the later sample.

Further tests

The patient's cells were tested with anti-A_1 and anti-H reagents, both obtained from a commercial source. The anti-A_1 was prepared from an extract of *Dolichos biflorus* seeds and the anti-H from seeds of *Ulex europaeus*. Both tests could be interpreted as weakly positive, that with anti-H being distinctly the weaker of the two. In both cases "mixed-field" agglutination was seen, but the agglutinates were smaller and fewer than had been seen in tests with anti-A and anti-A,B.

A sample of the patient's saliva was also tested in the hope of being able to demonstrate that she secreted both A and H substance, but this information was not obtainable as she turned out to be a non-secretor (genotype *sese*).

Discussion

There are several schools of thought regarding the cause of blood group antigen modification in acute leukaemia, and the subject is reviewed by Race and Sanger (1968). The proportion of cells remaining agglutinable seems to be variable in different patients – and may even be variable in the same patient on different occasions. One case reported by Gold et al. (1958) showed only 2% of the cells agglutinable by anti-A, but during a remission the number rose to 35% and fell again before death to 8%. Reports suggest that the changes may occur not only to the A antigen but that they may also affect the H, B, I and D antigens, and Cooper et al. (1968) have reported decreased I antigenicity accompanied by increased i antigenicity in sideroblastic and megaloblastic anaemia.

In the present case the Rh antigen D was not perceptibly abnormal and the estimated proportion of cells reactive with anti-A and anti-A,B was in the region of 20%. The "mixed-field" agglutination reaction with anti-A_1 suggested that the true group of Mrs. R. F. was A_1. There was no clue as to the manner in which the disease process interferes with red cell antigen synthesis, but the fact that the patient's cells reacted only very feebly with anti-H indicates that the loss of A was not accompanied by a reversion to H.

The initial misinterpretation of the patient's group as O was not a serious matter, as the error was on the side of safety and group O blood proved to be perfectly compatible. The typing results on the earlier sample are interesting, however, because they indicate the manner in which an inexperienced laboratory worker may miss weak agglutination and may tend to enter the results he expects to observe rather than those actually obtained. The first protocol showed a negative reaction with both anti-A and anti-A,B reagents, as well as with anti-B, and this was perhaps excusable because the minor population of agglutinable cells formed into plaques of agglutination that looked not unlike the fibrin strands sometimes seen when cells from imperfectly clotted samples are typed, whilst the majority of cells remained unagglutinated. However, conscious bias came into play when the reverse grouping results were recorded, because a positive reaction was erroneously recorded for the test between the patient's serum and group A cells, leading to an apparent confirmation that the patient's group was O. Subsequent testing of the original sample of patient's serum showed that A cells were not in fact agglutinated, and group A donor blood was matched satisfactorily and administered without event.

Summary

Details of the blood grouping reactions obtained on the blood of a patient suffering from myeloblastic leukaemia are presented and it is concluded that these signify the modification of a normal A antigen associated with the disease process. Though without serious implications in this case, conscious bias in the recording of agglutination reactions caused a misinterpretation of the patient's grouping in the first instance, and there could be some situations in which such erroneous recording could invite adverse consequences.

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