A CASE HISTORY OF HAEMOLYTIC DISEASE OF THE NEWBORN DUE TO ANTI-DUFFY (ANTI-Fy^a)*

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The purpose of this paper is to present a case history of haemolytic disease of the newborn due to anti-Duffy (anti-Fy^a), and also to mention two further cases in which antibodies were found during routine antenatal testing of maternal blood, but in whom the anti-Duffy (anti-Fy^a) was of no clinical significance.

The blood-group system called Duffy was first reported by Cutbush *et al.*[1] early in 1950. The antibody which enabled the new blood-group antigen to be recognized was found in the serum of a man suffering from haemophilia who had received several blood transfusions, and the system was subsequently named after the donor in whom the antigen was found.

It is now believed that in 22% of all matings there is a possibility of iso-immunization against the Fy^a antigen. The first case of haemolytic disease of the newborn due to anti-Duffy (anti-Fy^a) was published by Baker *et al.*[2] in 1956. This was followed by a report by Chown *et al.*[3] in 1957. In 1959 Bevan[4] published a case. Greenwalt *et al.*,[5] in 1959, published a case of their own and 7 from other laboratories. Geezy,[6] in 1960, reported a further case which brings the total number of cases mentioned in the literature to 12. Of these 12 cases, details of the degree of haemolytic disease and treatment are provided in 7. No case was induced prematurely and 3 required exchange transfusion. The highest postpartum antibody titre was 1 : 512 with the indirect Coombs test.[5]

According to Greenwalt *et al.*[5] there appears to be no correlation between the maternal titre, the strength of the direct Coombs tests and the severity of involvement. However, they mentioned the hazards of such comparisons because the immunological studies depend on whether the antibody being studied is a gammaglobulin or not and also on the spectrum of activity of the antiglobulin serum employed.

CASE REPORTS

Case 1

A 31-year-old White patient was 24 weeks pregnant when she was referred to Karl Bremer Hospital in July 1967. An antibody anti-Duffy (Fy^a) had been found in her serum to a titre of 1 : 4 in the Coombs test on routine laboratory investigation of the blood sent by her general practitioner to the Provincial Blood Grouping Laboratory. Her blood group was rhesus negative (cde.cde) (rh.rh) Fy(a-). In 1959 she had had a normal full-term pregnancy. There was no history of previous blood transfusions.

The anti-Fy^a titre rose to a level of 1 : 32 by the indirect Coombs test at 32 weeks' pregnancy and by the time amniocentesis could be arranged the patient had already reached approximately 34 weeks' pregnancy. Spectrophotometric assays of the amniotic fluid gave the following readings: Optical density difference at 450 mμ = 0·056 and the bilirubin level was 0·23 mg./100 ml. These values fall into Liley's group b for rhesus incompatibility.[7] It was thus felt that an induction should be attempted beween 37 and 38 weeks.

A medical induction was done which was then followed by high and low amniotomy. The patient delivered a normal male child of 7 lb. 10 oz. (3·66 kg.) on 5 October. The amniotomy delivery interval was 12 hours and the child was born with an Apgar score of 10.

Laboratory examination of the cord blood showed the blood group to be rhesus negative (cde.cde) (rh.rh) Fy(a-); the direct Coombs test was positive, the haemoglobin was 11·6 G/100 ml. and the total serum bilirubin was 2·2 mg./100 ml. Anti-Fy^a was identified in the eluate of the baby's red blood cells.

The infant became visibly jaundiced soon after birth. The total serum bilirubin value rose to 9·9 mg./100 ml. on the second day and then fell to 7·9 mg./100 ml. on the third day. Haematocrit value fell from 66% to 52% on the second day and to 49% on the third day.

On 7 October 1967 (3rd day after delivery) the infant's condition deteriorated very rapidly. The abdomen was hard and slightly distended, response to stimuli was weak and the extremities were cyanosed. Electrolytes done at this stage showed the infant's blood to have a pH of 7·26; PCO_2 41 mm.Hg; base excess -8; blood ureum 78 mg./100 ml.; potassium 7·2 mEq./litre; sodium 133 mEq./litre; chloride 102 mEq./litre; balance 12 mEq./litre; and the CO_2 content 18·7 mmol./litre. Respiratory arrest followed and in spite of resuscitation the baby died.

A postmortem examination was done, with the following macroscopic findings: The baby was visibly jaundiced and there was a serous exudate present in the abdominal cavity with gross dilatation of the caecum and the transverse colon. No obstruction or perforation could be demonstrated. An effusion was present on the surface of both lungs. The basal ganglion was macroscopically very yellow and appeared to be similar to that of kernicterus. Culture of the peritoneal exudate taken at the time of the postmortem examination gave a positive culture of *E. coli.*

Microscopic examination. The lungs showed partial atelectasis and oedema and hyperaemia. The liver was severely hyperaemic and there were multiple centres of extramedullary haemopoiesis. The spleen showed extensive haemopoietic reaction and the kidneys were hyperaemic with hyaline degeneration and casts. There were exudate on the peritoneum and peritonitis. *E. coli* was cultured.

There was kernicterus, but during the preparation of the tissue the pigment was dissolved, and none of the other histological abnormalities could be demonstrated to confirm the macroscopic diagnosis.[8,9]

*Date received: 29 August 1968.

The family's blood groups are shown in Table I, as well as the titre of the antibody found in the maternal serum.

TABLE I. BLOOD GROUPS OF FAMILY

Mother:	cde.cde	(rh.rh)	A Rh-negative	Fy(a−)
Father:	CDe.cde	(Rh.′rh)	O Rh-positive	Fy(a+)
1st child:	cde.cde	(rh.rh)	A Rh-negative	Fy(a+)
2nd child:	cde.cde	(rh.rh)	A Rh-negative	Fy(a+)

Titration of anti-Duffy antibody (anti-Fy^a)

	Saline	*Albumin*	*Bromelin*	*Coombs*
One month antepartum	1 : 1	1 : 1	Nil	1 : 32
Three weeks postpartum	1 : 1	1 : 2	1 : 1	1 : 32

Case 2

The second case was a Coloured female of 42 years, para 3, gravida 13 with 10 miscarriages. Her blood group was O rhesus-negative (Cde.cde) Fy(a-). She had a stillbirth in 1942 and a normal full-term delivery in 1944. After this she had several miscarriages and in 1954 she delivered a premature baby at 30 weeks. During this last delivery she received an incompatible group O Rh-positive blood transfusion. After 1954 she never had a full-term pregnancy but again had several miscarriages.

The family's blood groups are shown in Table II, as well as titres of the antibodies found in the maternal serum.

TABLE II. BLOOD GROUPS OF FAMILY (CASE 2)

Mother:	Cde.cde	(rh.′rh)	O Rh-negative	Fy(a−)
Father:	Cde.cde	(Rh.rh)	O Rh-positive	Fy(a−)
1st child (1944):	cDe.cde	(Rh_o.rh)	B Rh-positive	Fy(a−)
2nd child (1954):	CDe.cde	(Rh.rh)	O Rh-positive	Fy(a−)

Titration of Rh antibody anti-D (anti-Rh_o) and anti-Duffy (anti-Fy^a)

	Date	*Saline*	*Albumin*	*Bromelin*	*Coombs*
Rh antibody	21/11/65	Nil	1 : 2	1 : 6	1 : 32
Anti-D (anti-Rh_o)	25/11/67	1 : 1	1 : 8	1 : 8	1 : 32
	21/11/65	Nil	Nil	Nil	1 : 8
Anti-Fy^a	25/11/67	Nil	Nil	Nil	1 : 8

Case 3

The third case was also a Coloured female, 40 years old, para 7, gravida 8 and group O Rh-positive, Duffy negative Fy(a-). She had had a blood transfusion with the delivery of her sixth child in 1963. At 38 weeks the patient's serum contained the antibody anti-Fy^a to a titre of 1 : 8 by the indirect Coombs test. The same results were found at term.

Her husband's blood group is O Rh-positive and Fy(a-). On 22 November 1967 she had a normal delivery of a female child weighing 5 lb. 4 oz. The child's blood group is O Rh-positive and Duffy negative Fy(a-). The direct Coombs test was negative, and it can therefore be assumed that the anti-Fy^a could be related to the blood transfusion.

DISCUSSION

The first case has some special features. The patient never had a blood transfusion and the antibody anti-Fy^a developed during her second pregnancy, 8 years later. This is unusual, as there is usually a history of previous transfusions.[2,3,5]

It is also interesting to note that with a relatively low titre of maternal Fy^a antibody and relatively low total serum bilirubin levels the baby nevertheless developed kernicterus which was a contributory cause of neonatal death.[8,9]

It is also the first recorded case with spectrophotometric studies of the amniotic fluid.

In the second case mentioned, the anti-Fy^a is presumably related to the blood transfusion, as the Fy(a+) genotype is absent in the children's blood.

In the third case, the anti-Fy^a could be related either to the pregnancies or the blood transfusion. The baby was not affected as the blood group was Fy(a-).

SUMMARY

A case report of the second pregnancy of a woman with the blood group A Rh-negative, genotype (cde.cde) (rh.rh) Fy(a-), whose husband is O Rh-positive with a genotype of (CDe.cde) (Rh.′rh) Fy(a+) is given. The mother's serum contained anti-Duffy (anti-Fy^a) antibodies to a titre of 1 : 32 in the Coombs test. Amniotic fluid spectrophotometric analysis showed immunization results comparable with Liley's group b for rhesus incompatibility. An induction was successful at 38 weeks. The infant died on the 3rd day from *E. coli* peritonitis and kernicterus. The serum bilirubin of the infant never rose above 9·9 mg./100 ml.

Two further cases with anti-Duffy antibodies are also mentioned.

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