OBSTRUCTIVE JAUNDICE IN HAEMOLYTIC DISEASE OF THE NEWBORN TREATED WITH MAGNESIUM SULPHATE

BY

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Obstructive jaundice seldom follows haemolytic disease of the newborn. It may occur at the height of the haemolytic process or not until some weeks later. In the latter instance, an evanescent phase of haemolytic jaundice may occur after birth with a recurrence of icterus after a few weeks, and then biliary obstruction. The degree of biliary obstruction is usually only partial but it may be complete. Jaundice may continue for any period between 3 weeks and 6 months of age, with an average duration of seven to eight weeks (Hsia, Patterson, Allen, Diamond and Gellis, 1952).

Still (1927) was the first to describe this type of obstructive jaundice and he thought that the bile arising from excessive haemolysis had become too viscous to pass freely along the ducts. Ladd (1935) also considered that some of these cases of obstructive jaundice were due to ‘inspissated bile’, with stenosis or narrowing of the common duct though without definite evidence of atresia. Skelton and Tovey (1945) accepted the inspissated bile theory but also suggested that, in some cases, the bile ducts might be converted into a fibrous cord following organization of a plug of inspissated bile. Lightwood and Bodian (1946) thought that the inspissated bile theory did not adequately explain the facts and pointed out that a markedly obstructive phase did not necessarily go with the greatest haemolysis nor with the deepest preceding jaundice. They suggested that biliary obstruction was due to swelling of damaged liver cells. Gilmour (1944) and Craig (1950) have described the post-mortem appearances in the liver consisting of erythropoiesis, distortion of hepatic cords, pigmentation and necrosis of liver cells and bile thrombi in the canaliculi. Craig also noted giant multinucleated cells and suggested that they might accompany regeneration of liver cells in young infants.

Hsia et al. (1952), discussing both theories, thought that it was not clear whether inspissation occurred as the result of damage to the liver parenchyma or whether the excessive load of bilirubin presented to the liver caused blockage of the ducts during excretion. Assuming the latter to be true, it was probable that the biliary system was gradually cleared of inspissated bile as the haemolytic process ceased and as the bile ducts became larger. The fact that obstructive jaundice occurs in some patients and not in others might, they thought, be due to variation in functional maturity of the liver and size of the bile ducts in infants. Harris, Andersen and Day (1954) agreed with Bodian and Lightwood that the major abnormality was in the liver cells and that plugs of inspissated bile in the biliary canaliculi were present as a secondary phenomenon. This also occurs in infective hepatitis where stagnation of bile may be seen in canaliculi just outside the areas of maximal necrosis.

Two cases of obstructive jaundice associated with haemolytic disease of the newborn will now be reported and their treatment described.

Case Reports

Case 1. This girl was born in hospital and weighed 6 lb. 11 oz. at birth. The mother was Rh negative and her one previous baby had not been affected by haemolytic disease. This second baby was jaundiced at birth, the direct Coombs test on the cord blood was positive, and an exchange transfusion (350 ml.) was given soon after birth. All jaundice had disappeared at the age of 2 weeks and the baby's stools were then normal in colour. A further blood transfusion (100 ml.) was given at that time as she was anaemic. At the age of 26 days the baby suddenly became jaundiced once more and her stools were noticed to be very pale. She was admitted to hospital at the age of 28 days and was then deeply jaundiced; the liver and spleen were enlarged, the urine was dark and the stools were very pale.
Investigations gave the following results:

Haemoglobin, 50% (7.4 g. %); white cell count, 6,000 per c.mm. (2 late normoblasts per 100 nucleated cells); reticulocyte count, 2.8%; red cell fragility test, normal; blood Wassermann reaction, negative; blood group, O Rh positive. The urine contained bile pigments; otherwise it was normal. Fouchet's test for faecal bilirubin was negative.

Liver function tests gave serum bilirubin, 8.0 mg. %, serum alkaline phosphatase, 13 units % (King-Armstrong); thymol flocculation, negative; thymol turbidity, 0-8 units.

Two days after admission the serum bilirubin had risen to 14.4 mg. % and the haemoglobin had fallen to 46% (6.8 g. %). Duodenal intubation was carried out on the seventh hospital day and 10 grains of magnesium sulphate (2.6 ml. of a 25% solution) were given into the duodenum. On the same evening the baby passed a bile-stained stool and a similar stool was passed on the following day. Duodenal intubation was repeated on the ninth hospital day and the same dose of magnesium sulphate was administered. Two days later the stools contained the normal amount of bile pigment and the serum bilirubin had fallen to 4 mg. %. By this time the baby's jaundice was fading rapidly and she had begun to gain weight for the first time since admission. Duodenal intubation was repeated on the twelfth hospital day and a further dose of magnesium sulphate was given. A blood transfusion was then given to correct the anaemia and she was discharged after 15 days in hospital. She was seen as an out-patient three weeks later, when her general condition was satisfactory. She had gained weight, the stools were normal in colour, and the liver and spleen were just palpable. Haemoglobin was 87% (12.8 g. %) serum bilirubin was 0.5 % and serum alkaline phosphatase was 16 K.-A. units %. Her subsequent progress was uneventful.

Case 2. This girl was born in hospital at term and weighed 6 lb. 13 oz. at birth. The mother, who was Rh-negative, had had 13 pregnancies. Four of her babies had been stillborn but there was no record of their having been affected by haemolytic disease. Only one previous child, the eldest in birth rank, had been jaundiced at birth. He received a blood transfusion in the neonatal period and his subsequent growth and development were normal. The mother had not had any miscarriages, blood transfusions or injections of blood or plasma, and she had never suffered from jaundice herself. Her serum had been examined for Rh antibodies in the fifth month of the present pregnancy but none were found.

At birth, the child was covered with golden yellow vernix but there was no jaundice and the liver and spleen were not enlarged. The cord blood haemoglobin was 97% (14.4 g. %) and the direct Coombs test on the cord blood was negative. A tinge of jaundice was noted on the second day of life; the peripheral blood haemoglobin was then 97% (14.4 g. %). All trace of jaundice had disappeared by the fourth day, when the direct Coombs test was repeated and was still negative. The baby was removed from hospital against medical advice on that day.

She remained well until the age of 6 weeks, when jaundice reappeared. The baby was still jaundiced when seen in hospital at the age of 9 weeks and dark urine and pale stools had been noted by the mother during the preceding week. She weighed 8 lb. 8 oz. and the liver and spleen were enlarged, the liver edge being felt 3 cm. below the right costal margin in the nipple line.

Investigations gave the following results:

Haemoglobin, 70% (10.4 g. %); white cell count, 10,000 per c.mm. (2 late normoblasts per 100 nucleated cells); reticulocyte count, 2.8%; blood Wassermann reaction, negative; blood group, O Rh-positive.

The urine contained bile pigments, otherwise it was normal. The faeces were grey in colour, and Fouchet's test for bilirubin was negative.

Liver function tests gave serum bilirubin, 5.2 mg. %; serum alkaline phosphatase, 29 (King-Armstrong) units%; thymol flocculation negative; and thymol turbidity, 0-6 units.

Rhesus antibodies were demonstrated in the mother's serum in albumin and saline, and the indirect Coombs test, using the baby's red cells and the mother's serum, was strongly positive. The direct Coombs test was negative.

The first duodenal intubation was performed on the tenth hospital day and 10 grains of magnesium sulphate (2-6 ml. of a 25% solution) were given into the duodenum. No change in the colour of the stools occurred and, two days later, the serum bilirubin was 5.4 mg. % and the serum alkaline phosphatase was 47 units %. Duodenal intubation was repeated on the thirteenth hospital day and 20 grains of magnesium sulphate (5-2 ml. of a 25% solution) were given. After this, the baby's stools were faintly coloured and Fouchet's test became positive for the first time. The stools continued to be green-stained over the next few days and the serum bilirubin fell to 3.35 mg. %. Duodenal intubation was repeated on the twentieth hospital day and 40 grains of magnesium sulphate (5-2 ml. of a 50% solution) were given. Following this, she had severe diarrhoea for 24 hours. Over the next week she continued to pass faintly bile-stained stools and her serum bilirubin fell to 2.8 mg. %. Nine days after the last duodenal intubation, she began to pass dark, bile-stained stools and the jaundice disappeared over the next 48 hours; the serum bilirubin level fell sharply to 0.9 mg. % at this time. Following the disappearance of jaundice, she began to gain weight for the first time since admission, and the liver, which had been enlarged to a point 4·5 cm. below the right costal margin, returned to its normal size over the next two weeks. She was discharged in a satisfactory condition after eight weeks in hospital, and when she was seen as an out-patient five weeks later she had gained 4 lb. in weight, the stools were normal in colour and the liver and spleen were just palpable. Haemoglobin was 68% (10.1 g. %), serum bilirubin was less than 0.5 mg. % and serum alkaline phosphatase was 20 units %. Her subsequent progress was uneventful.

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Discussion

In general, authors agree that the prognosis of obstructive jaundice following haemolytic disease of the newborn is good but when the jaundice is prolonged cirrhosis may follow (Lightwood and Bodian, 1946). It is not clear whether this cirrhosis develops as a result of prolonged biliary obstruction or whether it should be ascribed to a severe degree of hepatitis. If it is due to obstruction of the biliary passages there would seem to be a case for promoting the flow of bile if possible. This may be attempted by medical or surgical means but the risks of surgical intervention in infants under the age of 3 months with liver damage are well known (Janeway, 1951; Hsia et al., 1952; Harris et al., 1954). Patterson (1952) used 20% sodium dehydrocholate intravenously and bile salts orally in 10 infants with this condition, and he reported an increased flow of bile following the use of these cholagogues: biliary flow was resumed in three cases immediately; five cases had a normal biliary flow after seven days, and flow was resumed in the remaining two cases after 14 and 21 days respectively.

In the two cases described in this paper, magnesium sulphate in a concentrated solution was chosen as the chologogue. When magnesium sulphate is introduced into the duodenum it causes evacuation of the gall-bladder and relaxation of the sphincter of Oddi. Lyon (1929) demonstrated this action by cholecystography and recommended the use of intraduodenal magnesium sulphate in various disorders of the liver and blood.

In the first of the two cases described, the association between the administration of intraduodenal magnesium sulphate and the relief of the jaundice seemed to be very striking. Within six hours of the first duodenal intubation the baby began to pass bile-stained stools and, following the second intubation, the stools became heavily bile-stained and the jaundice rapidly disappeared. In the second case, the association between the administration of the drug and the relief of the jaundice was not so clear cut. However, following the second intubation, the baby's stools became bile-stained and the serum bilirubin fell by 2 mg. % over the next few days. Further slight improvement followed the third intubation but the jaundice did not finally clear until nine days after the last intubation. In this case, relief of the jaundice might have taken place at this time without any treatment but it seems reasonable to suppose that the administration of intraduodenal magnesium sulphate may have helped to dislodge some of the 'inspissated' bile and so have led to the disappearance of the jaundice.

Finally, it should be mentioned that duodenal intubation is sometimes a rather time-consuming procedure in young infants. However, the results of the administration of magnesium sulphate by this method in these two cases would seem to justify a further trial.

Summary

Theories relating to the pathogenesis of obstructive jaundice following haemolytic disease of the newborn are discussed. The clinical features of two infants with this condition and their treatment with intraduodenal magnesium sulphate are described.

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References

Gilmour, J. R. (1944). Archives of Disease in Childhood, 19, 1.
Skelton, M. O. and Tovey, G. H. (1945). Brit. med. J., 2, 914.
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