NHSBT Board

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Patient Story: Focus on antibody investigations to support antenatal care of pregnant women

This patient story is about a pregnant 29-year-old woman whose sample was referred to Liverpool RCI. It highlights the crucial role of antibody investigations provided by NHSBT to improve the outcome of pregnancy for mothers who have antibodies to red cells. This case also shows how we contribute to scientific knowledge within Pathology whilst we improve investigation and patient management not just nationally but also internationally. It also illustrates the value of the National Frozen Blood Bank (NFBB) now working under the management of IBGRL to align operations to clinical need, and the importance of ensuring our continued ability to develop and share diagnostic products as the regulatory environment changes. Though this is a complex case which led to a development in our knowledge of blood groups, it is illustrative of the sort of clinical issues that RCI and IBGRL deal with daily.

The central clinical and scientific problem is that a mother can make antibodies during pregnancy to red cells of the developing fetus and these can cross the placenta into the fetal circulation. These antibodies can subsequently cause serious, even life-threatening anaemia in the fetus and newborn, and require careful selection of blood for the mother and baby if a transfusion is needed.

In the UK, everyone is screened twice in pregnancy to detect antibodies which might cross the placenta and cause destruction of fetal red cells resulting in Haemolytic Disease of the Fetus and Newborn. This routine screening is part of the standard antenatal care; approximately 600,000 pregnancies are screened annually in England and Wales.

During pregnancy, the need for a transfusion is more likely at delivery when transfusion can be very urgent and sometimes demanding large transfusions. Red cell usage in maternity/obstetrics is about 3.5% of total red cell usage. This woman had previously required transfusion at delivery, therefore increasing the likelihood of the need for further transfusions.

In many cases, the same antibodies that can harm a baby can also cause adverse reactions to transfusion so the information gained from the screen to detect antibodies and subsequent investigations can be invaluable in supporting women who need transfusion during pregnancy or at the time of delivery.

The diagnostics challenge

In this case, the lady was known to have a red cell antibody, anti-Jk^{a}. While this antibody is known to cause fetal anaemia occasionally, the concentration, and hence the risk to the baby, was low in the sample sent to RCI Liverpool.

On investigation, it became apparent that there was an additional antibody in this woman's plasma, which reacted with all the reagent cells available in RCI, but not with the individual's own cells. This pointed to the presence of an antibody to a high frequency antigen, that's to say, an antibody which makes the blood of more than 99% of the population incompatible with the patient, making transfusion for the mother or the baby very difficult.

To support a potential transfusion for this mother, we needed to identify the antibody. Liverpool RCI laboratory had exhausted their options to identify the antibody so referred the sample to the Red Cell reference Laboratory at IBGRL in Filton for further investigations.

There are over 377 known blood group antigens arranged into 43 systems and some collections, so IBGRL's task was to start to narrow the search. It was soon clear this was an unusual antibody. Several advanced serological techniques were employed including testing the patient's antibody with red cells treated with a range of enzymes. Other testing included the use of recombinant soluble blood group proteins. These proteins are produced by the Protein Development and Production Unit (PDPU) of IBGRL and neutralise specific antibodies. In this case, the antibody was localised to the Yt blood group system, but a panel of cells which collectively lacked all the known Yt system antigens continued to be incompatible with the patient's plasma, suggesting that this antibody was new to science. The next stage of investigation was to extract DNA from the sample, then perform sequencing of the Yt blood group *ACHE* gene. This revealed a novel mutation and strongly suggests that none of the world's stock of rare blood contain any compatible blood.

The challenge to provide matched red cells for this mother

With this knowledge, regular meetings to manage the case were established between NHSBT (RCI and haematologists) and the obstetric Team at Manchester Royal Infirmary. This group considered options to manage the delivery, including a planned induction on the expected date of delivery which was 2nd January. This group also arranged for the immediate family of the prospective mother to be tested to assess whether any of them might be compatible. This testing was undertaken by IBGRL, and a sibling was found to be suitable as a donor. They donated one unit ahead of the planned induction date. The unit was crossmatched at Liverpool RCI, found to be compatible, and was transferred to Manchester Hospital Services to be stored overnight.

Transfusion between siblings is usually contra-indicated as the similarities between HLA types means that transfusion related graft versus host disease is a hazard which can be fatal. The risk can be managed by irradiating the product before transfusion. If the unit wasn't required for the delivery, we wanted to freeze it at NFBB for future use, but as units cannot be frozen after irradiation the unit was held at Hospital Services in Manchester for urgent processing and irradiation if required.

The induction went ahead without incident on 2nd January. Tests on the baby's sample showed evidence that the maternal antibody had crossed the placenta and was detected on the baby's red cells, but no evidence that this had caused a clinical problem. Thus, the unit was sent to NFBB for freezing for potential use for this patient or any other who are found to have this antibody.

The scientific discovery and looking into the future

The blood group is one of several from NHSBT that has been ratified as a novel antigen by the International Society for Blood Transfusion and has been named anti-YtLi (Li for Liverpool).

This is an example of several NHSBT departments working together to provide care for under very challenging circumstances. It included RCI, IBGRL Red Cell Reference Laboratory, the IBGRL Protein Development Unit, Blood Donation, Manufacturing and Logistics and the National Frozen Blood Bank. It's also an example of NHSBT's contribution to scientific knowledge. Discoveries of this nature inform advancing technologies such as mass genotyping to enable identification of donors and patients with rare blood groups. Furthermore, it underscores the value of the reagents (e.g., the soluble blood group proteins) developed and produced within NHSBT and the expertise of the scientists and clinicians employed across Pathology and the wider organisation.

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