Centro Comunitario de Sangre y Tejidos de Asturias

IN ASTURIAS, SPAIN ASYMPTOMATIC DONOR TRANSMITS HEV BY TRANSFUSION OF RBCC BUT NOT PC DUE TO RIBOFLAVIN/UV PRT TREATMENT

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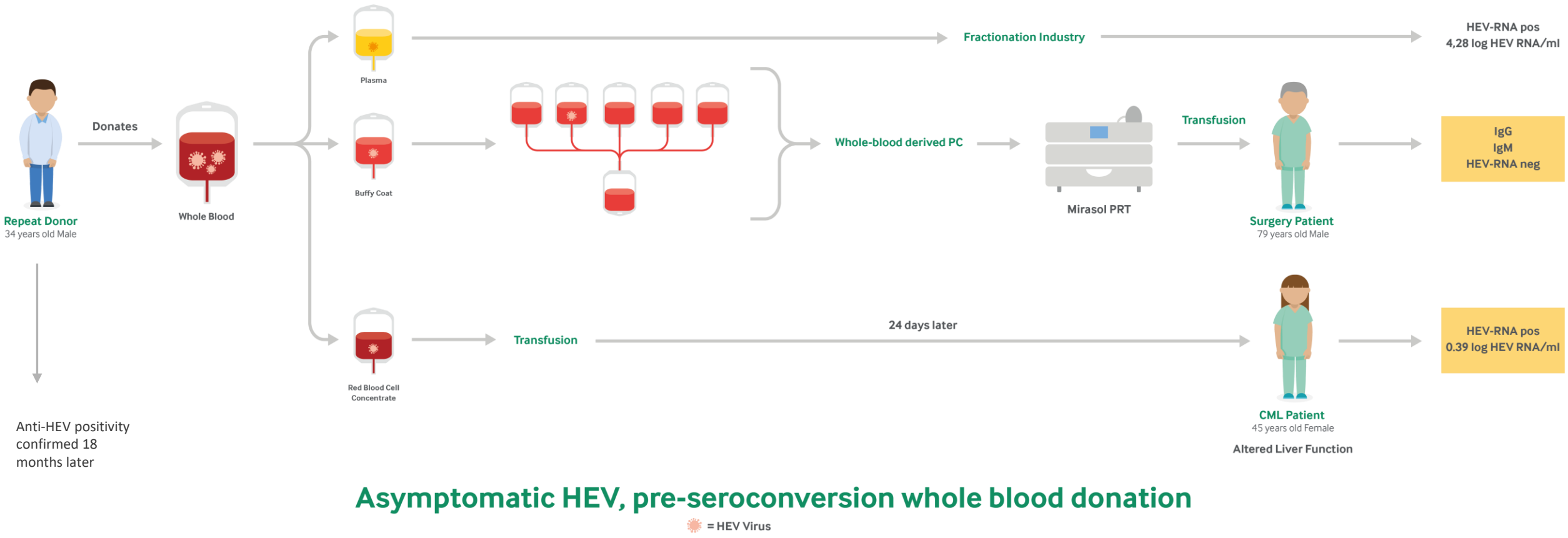
Conflict of Interest

A. Ojea, C. Seco, P. Mata, C. Muñoz, M. Rodriguez have no conflict of interest to declare.

S. Keil & M. Cardoso are employees of Terumo Blood & Cell Technologies

ILLUSTRATION (CASE REPORT)



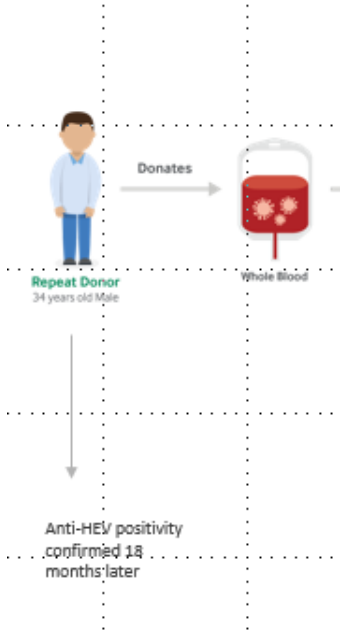
Asymptomatic HEV, pre-seroconversion whole blood donation

= HEV Virus

Index Case

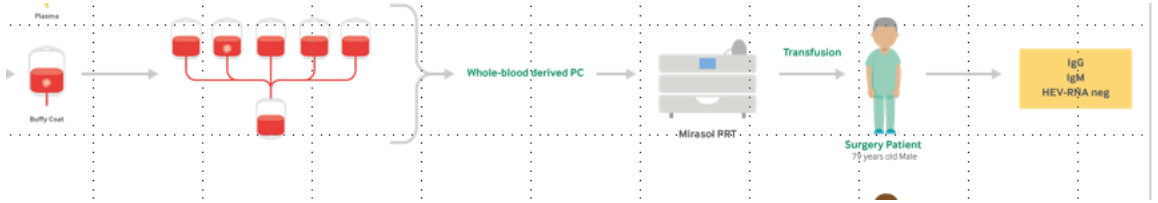
- A female patient diagnosed with chronic myeloid leukemia underwent an allogeneic bone marrow transplant in March 2019 showing alterations of liver function shortly afterwards, with alanine transaminase values of 2138 U/L and aspartate aminotransferase levels of 1557 U/L.
- Thirty blood components from 30 distinct donors had been transfused to this patient during the 3 months prior to the transplant. These donations were investigated for presence of HEV-RNA.
- The lookback investigation revealed that the patient had received a contaminated red cell concentrate and converted to HEV RNA-positive 24 days after the transfusion and had a viral titer of 0.39 log HEV RNA/mL.
- The patient had a HEV anti-IgM positive result with immunoblot confirmation at day +47 post-transplant.

Blood Donor



- A 34-year-old male, frequent donor, who resided in a rural area and consumed freshly slaughtered food derived from pork was identified as HEV RNA-positive at the time of donation. He was asymptomatic before and after donation.
- The donor's anti-HEV positive status was confirmed 18 months after the index donation.
- The investigation of the blood components processed out of the index whole blood donation revealed that the plasma unit was HEV NAT-positive, with a titer of 4.28 log HEV RNA/mL.
- A bootstrap, phylogenetic tree investigation was performed with isolates from donor and RCC recipient and revealed only 2 mutations. Isolates from both the donor and the recipient were of subtype 3f.
- Previous donation in July 2017 HEV-NAT was retrospectively investigated. Plasma was sent to fractionation industry, pooled BC-PC and RBC units were transfused. Complete hemovigilance study performed for those patients transfused: all results negative.

Platelet Concentrate & Recipient



- The PC was prepared by pooling 5 buffy-coat units, each buffy-coat unit contributing approximately 25-30 ml of donor plasma.
- The total HEV load in the final PC was estimated to be 5.7-5.8 log HEV RNA, which is similar to the levels estimated in the RCC (25-30 ml of residual plasma) that led to the infection of the index patient.
- The pooled leukoreduced PC was subsequently treated with PRT, in accordance to manufacturer's instructions (Mirasol, Terumo BCT). Mirasol PRT is a technology based on riboflavin and UV light that inactivates pathogens and leukocytes potentially found in donated blood components.
- Two samples from the PC recipient, one obtained prior and another after the transfusion (in the current investigation), were screened for HEV IgM and IgG (ELISA kits, DiaPro). The results from both samples were negative for HEV IgM and IgG. Moreover, HEV RNA tests were also negative in both samples.

Methods I

- Whole blood donations are screened routinely at the Community Blood and Tissue Center of Asturias (CBTCA) serologically for HCV, HBV, HIV and *Treponema pallidum* with Elecsys® anti-HCV/HBsAg II/HIV Duo/Syphilis and with COBAS TaqScreen MPX Test for HIV/HBV/HCV nucleic acid. Frozen samples from the suspected 30 donations were sent to the Department of Microbiology at the Hospital Vall d'Hebron and were tested with the Cobas HEV NAT in 6800/8800 Systems. Donor virus load in the index donation, as well as patient virus load was determined by an in-house quantitative PCR performed at the Hospital Universitario Central de Asturias (HUCA).

Methods II

- Bootstrap phylogentic tree investigation was performed with isolates from donor and recipient.
- Anti-HEV status of blood donor and patients was determined using HEV IgM/HEV IgG ELISA kits from DiaPro. Mirasol® PRT system was used to treat PC in accordance to manufacturer's instructions (Figure 1).

Figure: The Mirasol® PRT System

Conclusion

- This case study shows the value of a proactive safety measure like PRT. The technology based on riboflavin and UV light possibly prevented further transmission of HEV to the PC recipient.
- This real-life case supports previous experimental data showing reduction of HEV by the Riboflavin/UV-light technology to the limit of detection. CBTCA is committed to transfusion security and implemented in January 2020 HEV-NAT mini-pool screening, while continuing to apply pathogen reduction technologies in 100% of the produced PC.