POST TRANSFUSION HEPATITIS C TRANSMISSION FROM SCREENED BLOOD

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INTRODUCTION

Blood transfusion has remained a major risk for hepatitis in the past, with more than 10 percent of transfusion recipients acquiring infection in some studies [1]. The screening of blood donors for historical risk factors, serologic evidence of hepatitis B infection (HBsAg and anti-HBc), and elevated serum ALT caused a striking reduction of post-transfusion hepatitis (PTH), even before HCV was identified. The subsequent initiation of donor screening for anti-HCV antibodies in 1990 has nearly eliminated the risk of post transfusion acute HCV infection. The estimated risk is now 1:100,000, with the remaining small risk probably being due to recent acquisition of HCV infection by the donor prior to the appearance of anti-HCV antibodies [2].

We describe here case history of a patient who during her prolonged hospital admission was transfused four units of properly screened blood and contracted HCV. We will also discuss the evolution of safe transfusion practices, where we stand now and what more can be done to eliminate the residual risk.

CASE REPORT

A 60 years old lady was admitted in CMH Rawalpindi with diabetic foot on 23 Sep 20006. She had diabetes for last 25 years and had complicated disease with ischemic heart disease, nephropathy, neuropathy and maculopathy. At the time of admission her Hb was 8.0 g/dl, liver function tests were normal, urea 25.7 mmol/l and creatinine 371 micromol/l. Her HBsAg and anti HCV were negative. She was managed with protein restricted diet, daily dressings for foot ulcer and injection erythropoeitin. Her diabetes was controlled with insulin and she started to improve gradually. During her stay in hospital received four units of blood, two units within first week of admission and two units in last week of Nov. In last week of Nov she complained of persistent nausea despite improvement in her renal functions (urea 8.4 mmol/l, creatinine 96 micromol/l). Her liver functions were repeated which revealed raised ALT 492 u/l. Anti HCV was repeated and was found positive. Later on hepatitis C PCR was also found strongly positive. Her bilirubin increased to 160 micromol/l and ALT 1124 u/l over next couple of weeks but has started to settle now.

DISCUSSION

The risk of hepatitis virus transmission from transfusions has declined dramatically from that of the 1940s when post transfusion hepatitis (PTH) was first appreciated [3]. Introduction of hepatitis B surface antigen screening and conversion to volunteer donors for whole-blood donations in the late 1960s and early 1970s led to substantial reduction in PTH cases [4]. However, up to 10% of the recipients continued to develop PTH, most cases of which were attributed to an unknown non-A, non-B viral agent [5]. Implementation of surrogate marker testing i.e., alanine aminotransferase and anti-hepatitis B virus core antigen) for residual non-A, non-B hepatitis in the late 1980s reduced the per unit risk of PTH from 1 in 200 to about 1 in 400. Hepatitis C virus was discovered in 1989 and quickly was established as the causative agent of >90% of non-A, non-B PTH. Introduction of progressively improved antibody assays in the early 1990s reduced the risk of PTH due to hepatitis C virus to about in 100,000 [6].

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PTH was first reported in the US by Beeson in 1943 [3]. Seven cases of PTH occurring 1–4 months after transfusion of blood or plasma were reported. In 1964 Grady [7] and Chalmers reported the results of a retrospective study of PTH in nine Boston teaching hospitals, 1952–1962. In one of the hospitals 29% of the blood transfused was from commercial sources, while in the other eight hospitals blood only from volunteer blood donors was transfused. The incidence of PTH in recipients of blood products from volunteer blood donors was 0.6 cases/1000 units compared with 2.8 cases/ 1000 units in recipients of blood products from a mixture of volunteer and commercial blood donors.

A viral etiology for PTH was long suspected. In 1965, Blumberg et al. [8] first described the Australia antigen and stated that this antigen could be identified in the sera of many hemophiliacs who had received multiple transfusions. In 1970, Gocke et al. [4], using retrospective studies, indicated that the presence of the Australia antigen in donor blood seemed to be clearly associated with the occurrence of PTH and estimated that the exclusion of HBsAg-positive blood donors through either first- or second-generation assays would decrease the rate of PTH by 25%. On the basis of these studies, screening of blood donations for HBsAg began in 1971.

After implementation of specific screening tests it became clear that a substantial proportion of PTH cases continued to occur. Termed non-A, non-B hepatitis (NANBH), this entity represented 90% of residual PTH cases in the US. Extensive research was conducted in the 1970s and 1980s to identify the etiological agent(s) of NANBH. Then, in 1988, the hepatitis C virus (HCV) was identified with molecular biology techniques by M. Houghton and associates. Early studies established that HCV was the etiological agent of at least 80–90% of residual NANBH [6]. Blood donor screening was implemented immediately with the first-generation anti-HCV enzyme immunoassay (HCV 1.0 EIA) in 1990. Even though this assay facilitated the screening of blood donors for anti-HCV antibodies, it did not detect all infectious blood donations [10] and had a protracted window of infectivity ranging from 12 weeks to .26 weeks post infection [11]. Nevertheless, the risk of transfusion-associated HCV infection per unit dropped from 0.36% (1 in 274) before anti-HCV screening to 0.07% (1 in 3300) for donations screened with both ALT and first generation anti-HCV tests [12]. A second-generation anti-HCV EIA (HCV 2.0 EIA) was licensed and implemented in 1992. This test incorporated two additional proteins. This test was substantially more sensitive than HCV 1.0 EIA in detecting acute and chronic HCV infections. Antibodies to these proteins generally appear much earlier so the seroconversion window period could be shortened by 10–20 days. In 1996, a third-generation screening test (HCV 3.0 EIA) was licensed that detected antibodies to an even greater number of HCV-encoded epitopes. HCV 3.0 EIA has consequently narrowed the seroconversion window by about 10 days relative to the HCV 2.0 EIA. This window period reduction is projected to detect 1–2 additional seroconverting donors per million units screened [13].

In USA 1999, another blood donor HCV testing technology, nucleic acid testing (NAT), was introduced [2] which detects HCV genetic material by amplification rather than later-appearing antibodies, to identify donations made during window period before seroconversion. The test was performed on "minipools" (pool of 16-24 donations). The results till Jan 2002 were analyzed. A total of 170 or 1 in every 230,000 antibody non reactive donations was found positive. Follow-up of 67 donors demonstrated that seroconversion occurred a median of 35 days after donation. It is estimated that adoption of this new technique will prevent 56 HCV infections annually with a residual risk of 1 in 2 million blood units [13]. The test however is expensive and is unlikely to be adopted in near future in countries with limited health budget. Till that time there will be a small but definite risk of

HCV transmission with transfusion of blood products.

REFERENCES

1. Alter, HJ, Purcell, RH, Shih, JW, Melpolder JC, Houghton M, Choo QL, et al. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. N Engl J Med. 1989; 321: 1494.
2. Schreiber, GB, Busch, MP, Kleinman, SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. N Engl J Med. 1996; 334: 1685-90.
3. Beeson PB. Jaundice occurring one to four months after transfusion of blood or plasma. Report of seven cases. JAMA 1943; 121: 1332–4.
4. Gocke DJ, Greenberg HB, Kavey NB. Correlation of Australia antigen with posttransfusion hepatitis. JAMA. 1970; 77: 877–9.
5. Infectious disease testing for blood transfusions. NIH Consensus Statement. 1995 Jan 9–11; 13: 1–27.
6. Alter HJ. To C or not to C: these are the questions. Blood. 1995; 85: 1681–95.
7. Grady GF, Chalmers TC. Risk of post-transfusion viral hepatitis N Engl J Med. 1964; 271: 337–42.
8. Blumberg BS, Alter HJ, Visnich S. A "new" antigen in leukemia sera. JAMA 1965; 191: 541–6.
9. Gocke DJ, Greenberg HB, Kavey NB. Hepatitis antigen. Detection of infectious blood donors. Lancet. 1969 Aug 2; 2(7612): 248–9.
10. Ezzell C. Candidate cause identified of non-A, non-B hepatitis [News]. Nature. 1988; 333: 195.
11. Alter H. Transfusion-transmitted non-A, non-B and hepatitis C virus infections. In: Rossi EC, Simon TL, Moss GS, Gould SA, editors. Principles of transfusion medicine. 2nd ed. Baltimore: Williams & Wilkins; 1996: 687–98.
12. Donahue JG, Munoz A, Ness PM, Brown DE, Yawn DH, McAllister HA, et al. The declining risk of post- transfusion hepatitis C virus infection. N Engl J Med. 1992; 327: 369–73.
13. Stramer LS, Glynn SA, Kleinman SH, Strong M, Caglioti S, Wright DJ. Detection of HIV-1 and HCV infections among antibody negative blood donors by nucleic acid amplification testing. N Eng J Med. 2004; 351: 760–68.