A woman developed acute hepatitis C (HCV) infection 2 months after delivering her baby at a London Hospital. The other patients who had been on the unit at the same time all had negative HCV serology antenatally. Testing of the healthcare workers who had been involved in this patient’s care revealed that one of the midwives who only worked on the postnatal unit was chronically infected with the same viral genotype. Sequencing and phylogenetic analysis revealed close identity between the viruses from the two individuals. Although, the midwife had only performed non-exposure prone procedures including venepuncture and cannulation, our findings indicate that transmission of the virus had occurred from the healthcare worker to the patient. The potential implications of this case within the setting of national policy on blood borne viruses and healthcare workers are discussed. J. Med. Virol. © 2013 Wiley Periodicals, Inc.

KEY WORDS: nosocomial; blood borne viruses; maternity unit; phylogenetic analysis

INTRODUCTION

Transmission incidents of hepatitis C (HCV) infection from patients to either staff members (primarily via percutaneous exposure), or to other patients (where environmental contamination or indirect transmission via uninfected staff members are thought to play a role), within healthcare settings, are well described [Lanphear et al., 1994; McLaughlin et al., 1997; Mizuno et al., 1997; Irish et al., 1999; Bruguer et al., 2002; Silini et al., 2002; De Carli et al., 2003; Krause et al., 2003; Forns et al., 2005; Savey et al., 2005; Yazdanpanah et al., 2005; Pekova et al., 2007; Quer et al., 2008; Almroth et al., 2010; Marconi et al., 2010; Denes et al., 2011; Tomkins et al., 2012]. Transmission from healthcare workers to patients is a rarer event and predominantly linked to exposure prone procedures [Anon., 1995; Esteban et al., 1996; Duckworth et al., 1999; Balogun et al., 2000; Lesourd et al., 2000; Ross et al., 2002, 2008; Henderson, 2003; Cardell et al., 2008; Martinez-Bauer et al., 2008; Dawar et al., 2010]. We describe a case of apparent HCV transmission from a midwife to a patient on a postnatal ward, in the absence of any record of exposure prone procedures having been performed. Comparison of viral sequences from both the midwife and the patient revealed close identity between the two strains. While the mechanism of transmission in this case remains undetermined, this is the first time that HCV transmission from healthcare worker to patient, in the apparent absence of exposure prone procedures, has been reported in the UK. The midwife had been employed at the Hospital prior to the introduction of screening of new appointments in the NHS. The potential implications for national policy are considered.

METHODS

Screening for hepatitis C antibody was performed using the Abbott (Lake Forest, IL) Architect platform. HCV quantitative PCR was performed using the

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A 27-year-old healthy female of Middle Eastern origin delivered a baby at term by normal vaginal delivery, requiring no instrumentation, in a London hospital in June 2011. She spent 2 days on the labor ward and 1 day on the postnatal unit. While in hospital she underwent the following routine procedures: venepuncture, IV cannulation, epidural insertion, rupturing of membranes, and suturing of a second degree perineal tear. Blood cultures were collected during labor due to a temperature spike. Her routine antenatal viral serology screen performed in December 2010 had been unremarkable with negative hepatitis C serology, and an HCV PCR performed retrospectively also proved negative. HCV serology is performed routinely as part of the antenatal screen at that particular hospital as this represents an opportunity for cost-effective screening in a well defined population.

Eight weeks later, in August 2011, she developed acute hepatitis with an ALT reaching 1,000 IU/L and bilirubin of 40 μmol/L. Her hepatitis C serology was positive at that time, and her HCV viral load was \( 5 \times 10^4 \) IU/ml in plasma from the 1st of September. The HCV genotype was 1b. The patient denied all possibility of any of the usual risk factors for HCV infection including intravenous drug use, family contacts of the case all tested HCV antibody-negative, and there was no relevant travel history. STR DNA profiling was performed on her antenatal sample from December 2010, and on serum from August 2011, in order to exclude the possibility that her booking blood might have represented a mismatched sample obtained from a different patient. This showed concordance between the two samples at all of the 11 loci examined, giving a combined identity index of \( 1.33 \times 10^{13} \), hence confirming with a high degree of confidence that both specimens had been obtained from the same individual.

As part of an investigation into the possibility of acquisition of infection on the maternity unit (e.g., through environmental transmission), the antenatal HCV serology status of the 32 other women who had been on the unit at the same time was checked from the records. In addition, both HCV serology and PCR were carried out on samples obtained from seven healthcare workers involved in the care of the index case. All the patients proved seronegative for hepatitis C, and all the staff members proved seronegative and PCR-negative with the exception of one midwife who had provided care only on the postnatal ward, and who was shown to have a high viral load of \( 3.9 \times 10^4 \) IU/ml, also with HCV genotype 1b.

In order to determine the likelihood that the viruses from the two individuals were related, plasma samples from the index case and the midwife were sent to the Virus Reference Division (Colindale), and to the Roslin Institute (University of Edinburgh), for sequencing and phylogenetic analysis:

The Virus Reference Division sequenced a 328 nucleotide fragment of the NS5B sub-genomic region which revealed a single nucleotide difference between the two virus strains, giving a homology of 99.7%. A dendrogram compiled using HCV genotype 1 sequences generated locally by the Virus Reference Division, showed that the sequences from the two viral strains of interest were closely related to each other and distinct from all the other sequences.

Similar findings were obtained at the University of Edinburgh. For the core, E2 hypervariable and NS5B regions, the sequences from the two subjects clustered closely together and were distinct from all other HCV variants included in the analysis (see Fig. 1). These groupings were supported by a bootstrap test
with values of 98% for core, 99% for the E2 hypervariable region, and 100% for NS5B. The core gene is generally a well conserved area, but nonetheless sequences from the two subjects were identical to each other in that region, and the two sequences were 99.7% similar in the NS5B region with a single nucleotide difference.

The close identity of the viruses obtained from the two individuals also indicates that the transmission event had occurred within the recent past, so that viral diversification had not had time to occur.

The finding by both centers of close relatedness of the two HCV strains infecting the index case and the midwife, respectively, is consistent with either a transmission event having occurred between the two individuals, or with both individuals having contracted the infection during the same time period from a common source. As no past history of HCV infection in the member of staff had been forthcoming at the time, HCV antibody avidity testing and RIBA analysis were performed on serum samples obtained from the midwife in order to determine whether her
infection was recent or established. The RIBA assay showed no evidence of a recent infection, with strong (4+) reactions to all HCV proteins. HCV antibody avidity testing was performed on two specimens collected 6 weeks apart (in October and November 2011). Both the HCV antibody titers and avidity remained constant at a very high level in both samples. Although this assay was still under development at the time, and firm conclusions cannot therefore be drawn, these results are at least theoretically suggestive of an established HCV infection of 6 months’ duration or more.

DISCUSSION

Hepatitis C infection in a midwife was identified as a result of an investigation brought about by the occurrence of acute hepatitis C in one of her patients. The former is known to have performed only non-exposure prone procedures including venepuncture and cannulation during which she states she had worn gloves, her skin had been intact and non-eczematous and there was no evidence that an inoculation incident had occurred. Despite these facts, our findings provide convincing evidence of a close genetic link between the respective viruses from the two individuals. Serological test results were consistent with an established (rather than a recent) infection in the midwife, and further past history obtained from the midwife’s general practitioner (GP) subsequently confirmed this. Taken together, the epidemiological and virological evidence indicates that transmission from the midwife to the patient had occurred.

The local Health Protection Unit and the Health Protection Agency were part of the investigative team from the start, and advice from the Advisory Panel for Healthcare Workers Infected with Blood-borne Viruses (UKAP) was also subsequently sought. A two-phased lookback exercise was triggered by this incident whereby a HCV serology screen was offered to the other women who had been in the hospital unit at the same time as the index case in the first phase, and after reviewing over 4,000 sets of patient records, testing was offered to patients on whom the member of staff had performed category 2 exposure prone procedures (repairs following episiotomies and following second degree lacerations, and assisting Caesarean sections) [Anon., 2007b] since starting work with the Hospital. No further cases were identified, with an uptake for testing of 56% (18 out of 32 patients) in the first phase, and 42% (15 out of 36 patients) in the second. Some problems were encountered in contacting the patients, many of whom had changed address (and GP) or moved abroad. Our experience from the first phase was used to guide our subsequent strategy, balancing what was expected to be a low yield, against the potential for causing undue anxiety combined with the anticipated operational difficulties in contacting a large number of individuals as described above. We accordingly followed UKAP’s advice and limited the scope of the phase 2 lookback to patients on whom the midwife had performed category 2 exposure prone procedures.

The midwife had also worked in other Hospital Trusts as an agency midwife, and these were duly notified, and similar lookback exercises were carried out. Of five patients notified, one was abroad and four were tested and were HCV antibody negative. In addition to caring for women on the maternity and postnatal units, the midwife in question had also performed a limited range of procedures on neonates. These included BCG vaccination, vitamin K injection, heel pricks for blood sampling, and intravenous antibiotics administration. A risk assessment was carried out in conjunction with the Pediatrics team, and the risk was deemed insufficient to justify including these babies in the lookback exercise.

The midwife involved in this case was restricted from performing exposure prone procedures and any percutaneous procedure as soon as she tested positive for hepatitis C. Both patient and midwife were offered specialist Hepatology review, counseling, and psychiatric support.

The risk of transmission of hepatitis C in a healthcare setting is small, and transmission of hepatitis C from healthcare workers to patients has previously been reported only in association with exposure prone procedures, for which reported transmission rates are within the range 0% to >3% (depending on the type and frequency of exposure prone procedures performed), and with the administration of intravenous preparations (including multi-vial drugs and heparin) [Anon., 1995; Esteban et al., 1996; Duckworth et al., 1999; Balogun et al., 2000; Lesourd et al., 2000; Ross et al., 2002, 2008; Henderson, 2003; Cardell et al., 2008; Martinez-Bauer et al., 2008; Dawar et al., 2010]. The mechanism whereby transmission occurred in the case presented here remains unclear. Cannulation and venepuncture could have provided a route of entry for the virus, particularly if there had been an (unidentified) failure to adhere to infection control procedures such as aseptic technique, and the midwife’s high blood viral load would in theory be associated with an increased level of infectivity [Dore et al., 1997]. To our knowledge there is no data to suggest an increased risk of nosocomial transmission with HCV subtype 1b relative to other subtypes. A risk assessment of the maternity unit, in relation to risks for HCV transmission, revealed that space was constrained in the preparation room of the labor ward, but this would not have been relevant to patient care on the postnatal unit.

Specific concerns remain over the failure of both the midwife’s GP and Hepatologists to notify the Public Health authorities of her infection, which is a UK statutory requirement, as well as the lack of communication with the hospital’s Occupational Health service. Occupational health services are
responsible for advising about fitness for work of healthcare workers and play a central role in coordinating the workplace response to illnesses that might affect patient care. This case has highlighted an apparent blind spot amongst the treating clinicians.

Routine screening of new healthcare workers expected to undertake exposure prone procedures had been introduced at the Hospital in 2002 in accordance with national guidelines [Anon., 2002], but this was too late to identify the midwife as a carrier as she had been recruited to the Hospital prior to that date. The staff member in question was from an area of high endemicity for hepatitis C with overall seroprevalence rates of >5%.

Current UK guidance introduced in 2002 recommends that all new healthcare workers be offered testing for hepatitis C, and that for those who will be performing exposure prone procedures additional health clearance, including a requirement to be negative for hepatitis C RNA in order to be eligible for an exposure prone procedure post, should be enforced prior to confirmation of an appointment [Anon., 2007a]. As there was no requirement for routine hepatitis C screening of NHS staff before 2002 (even of those performing exposure prone procedures), it can be argued that there may be a case for doing so retrospectively for healthcare workers appointed prior to that date and involved in high risk procedures, and also for introducing regular surveillance, considering the significant implications of a transmission incident (including anxiety and potential morbidity for the patient, anxiety for the staff who are investigated, and cost, disruption and reputational damage to the Hospitals involved), and also particularly in light of the availability now of more effective and patient-friendly antiviral treatment regimens. The exceptional nature of this incident however, together with the fact that the transmission event described here appears to have occurred outside of an exposure prone procedure setting, limits the impact it is likely to have on national policy relating to blood-borne viral infections in healthcare workers, and the Hospital Trust’s internal guidelines remain unchanged after careful deliberation. The Department of Health national guidance was carefully devised and represents a pragmatic approach which has been vindicated by the lack of reports of healthcare worker to patient transmission of hepatitis C through exposure prone procedures since its introduction in 2002.

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REFERENCES


