

医薬品
医薬部外品 研究報告 調査報告書
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識別番号・報告回数		報告日	第一報入手日	新医薬品等の区分	機構処理欄
一般的名称	解冻人赤血球濃厚液	研究報告の公表状況	2005.1.28	該当なし	公表国 英国
販売名(企業名)	解冻赤血球濃厚液「日赤」(日本赤十字社) 照射解冻赤血球濃厚液「日赤」(日本赤十字社)		J Med Virol 2005 Mar; 75(3): 399-401.		
研究報告の概要	44歳の女性が子宮摘出8週間後に急性C型肝炎ウイルス(HCV)感染と診断された。同患者の手術時にHCV抗体陽性である麻酔科医が立ち会っていた。核酸配列解析および系統比較から、麻酔科医から患者にHCVが伝播したことが証明された。患者は気管内挿管および末梢静脈内カニューレ挿入時に全身麻酔を受けていた。麻酔時にHCV曝露のおそれがあるような行為は行われなかった。今回の症例は英国において、麻酔の手順上、感染のおそれがない状況下で麻酔科医から患者に感染が伝播した最初の報告である。また、手術前に麻酔科医がHCV抗体陽性であることが判明していた初めての事例である。				使用上の注意記載状況・ その他参考事項等
	<p style="text-align: center;">報告企業の意見</p> 英国において、麻酔の手順上、感染のおそれがない状況下で麻酔科医から患者にHCVが伝播した最初の報告である。このことから、輸血後HCV感染症の調査には、院内感染など輸血以外の伝播ルートについて考慮する必要がある。				解冻赤血球濃厚液「日赤」 照射解冻赤血球濃厚液「日赤」 血液を介するウイルス、細菌、原虫等の感染 vCJD等の伝播のリスク
		<p style="text-align: center;">今後の対応</p> HCV感染の新たな伝播ルート等について、今後とも情報の収集に努める。			

Case Report

Anesthetist to Patient Transmission of Hepatitis C Virus Associated With Non Exposure-Prone Procedures

J. Mawdsley,^{1*} C.G. Teo,² M. Kyi,³ and M. Anderson⁴

¹Barts and Royal London Hospital, Queen Mary College of Medicine and Dentistry, London, United Kingdom

²Sexually Transmitted and Blood Borne Virus Laboratory, Health Protection Agency, London, United Kingdom

³West Middlesex University Hospital, London, United Kingdom

⁴Chelsea and Westminster Hospital, London, United Kingdom

A 44-year-old lady was diagnosed with acute hepatitis C virus (HCV) infection 8 weeks after hysterectomy at which the attending anesthetist was known to be hepatitis C seropositive. Comparative nucleotide sequence analysis and phylogenetic comparison proved that transmission had occurred from the anesthetist to the patient. The patient had received general anesthesia with endotracheal intubation and peripheral intravenous cannulation. No exposure-prone anesthetic procedures had been performed. This is the first case described in UK involving transmission from an anesthetist to a patient during anesthesia where no exposure prone procedures were carried out. It is the first example in which the anesthetist was known to be seropositive for hepatitis C prior to the operation. *J. Med. Virol.* 75:399–401, 2005. © 2005 Wiley-Liss, Inc.

KEY WORDS: hepatitis C virus; transmission; anesthetist

CASE DESCRIPTION

A 44-year-old lady presented to her general physician with a 3-day febrile illness associated with painless jaundice. She was referred to the hepatology clinic at her local hospital. By the time she attended the clinic a month later her symptoms had resolved.

Eight weeks prior to becoming jaundiced, a hysterectomy with bilateral salpingoophrectomy had been carried out for menorrhagia attributed to adenomyosis and uterine leiomyomatosis. Hormone replacement therapy was started after the operation, but was stopped due to the development of jaundice. It was restarted 2 weeks prior to the attendance at the hepatology clinic with no recurrence of the jaundice. She had taken no other medications or herbal remedies.

The patient drank approximately 10 U of alcohol per week. She had never injected drugs and had not been sexually active for the last 5 years. There was no relevant travel history. She had never received a blood transfusion but had donated blood in 1995.

Examination in the clinic was normal with no evidence of jaundice or stigmata of chronic liver disease. A blood sample, taken at the time of her acute illness, showed a marked hepatitic picture: bilirubin 138 $\mu\text{mol/L}$ (normal range (NR): 0–17 $\mu\text{mol/L}$), aspartate transaminase 724 IU/L (NR: 11–55 IU/L), gamma-glutamyl transpeptidase 372 IU/L (NR: 6–51 IU/L), and alkaline phosphatase 937 IU/L (NR: 110–300 IU/L). At this time serum anti-hepatitis C virus (HCV) IgG, hepatitis B surface antigen and anti-hepatitis A IgM and IgG tests were negative.

A second sample taken 4 weeks later at the time of her attendance at the hepatology clinic showed that liver function tests had become normal, but serum anti-HCV IgG was now detectable, as determined by enzyme immunoassay (EIA) (Ortho Diagnostic Systems, Raritan, NJ). On repeat serological testing 6 months later, anti-HCV IgG was now also detectable by a second EIA (Sanofi Diagnostics, Marnes-la-Coquette, France) and a radioimmunosorbant assay (Ortho Diagnostic systems). It was concluded that the patient's illness was due to acute hepatitis C.

Abbreviations: HCV, hepatitis C virus; NR, normal range; UK, United Kingdom; 5'NCR, 5' non coding region; NS5, non structural protein 5; CDC, Center for Disease Control and Prevention, USA.

*Correspondence to: J. Mawdsley, Department of Adult and Paediatric Gastroenterology, Digestive Disease Research Centre, Royal London Hospital, Turner Street, London E1 2AD.
E-mail: J.E.D.Mawdsley@qmul.ac.uk

Accepted 14 October 2004

DOI 10.1002/jmv.20282

Published online in Wiley InterScience
(www.interscience.wiley.com)

The anesthetist, attending the total abdominal hysterectomy 3 months earlier, was known to be seropositive for anti-HCV IgG and was HCV RNA positive. He had emigrated to the UK from Egypt 20 years earlier. His hepatitis C seropositivity had been diagnosed several years earlier, during investigations for abnormal liver function tests which were found ultimately to be due to biliary colic. It was thought most likely that he had acquired the infection in Egypt, as he had no other risk factors for infection. He had been allowed to continue to practice according to the UK Department of Health guidelines. Hepatitis C RNA levels are not available from the time of the transmission incident, but were 11 million copies per ml when tested several years later.

The other members of the operating team were also screened but were all anti-HCV seronegative. The operation itself had been uncomplicated with no high-risk anesthetic procedures undertaken and no blood transfusions given. The anesthetist had inserted a cuffed oral endotracheal tube, to give intermittent positive pressure ventilation, and had also sited a peripheral cannula. He had no open wounds prior to the operation, had not sustained any injuries during the procedure and, as was his normal practice, had washed his hands before the operation and had worn gloves throughout.

To investigate the possibility of transmission from the anesthetist to the patient, a comparative nucleotide sequence analysis was undertaken of cDNA amplified by reverse-transcriptase PCR from the HCV genome carried in serum samples from both individuals. Two blood samples were taken at separate times from the patient and the anesthetist to minimize the chance of confounding due to PCR contamination. Sequences in the 5' non-coding region (5'NCR) and the region coding for the highly variable non structural protein 5 (NS5) were examined. The sequence of the 5'NCR fragment (139 base-pairs in length) was identical in both subjects, and permitted assignment of HCV to genotype 4. Type 4 sequences are identified infrequently among Caucasians in the UK, but are prevalent in people originating from the Middle East (Harris et al., 1999).

Pair-wise analysis of the more variable 185 base pair segment in the NS5 region showed the two sequences to be greater than 99.9% homologous. Phylogenetic comparisons revealed the two sequences to be clustered together, segregated from other genotype 4 sequences archived in the United Kingdom Health Protection Agency sequence database. The molecular findings indicate that the HCV carried by the anesthetist and by the patient are very closely related, consistent with transmission from the anesthetist to the patient.

The most recent blood tests, taken 2 years after the acute infection, have shown the patient to be seropositive for anti-HCV IgG but negative for HCV RNA. Her biochemical tests of liver function have remained in the normal range.

The anesthetist retired shortly afterwards on the grounds of ill health. The Hospital involved considered performing a look back procedure and consulted the UK

Health Protection Agency. However, this was ultimately felt to be impractical as it would have involved contacting all the patients he had attended during his 20 year career.

DISCUSSION

Transmission of HCV is described from an anesthetist to a patient. The patient had no exposure risks for contracting the virus other than her recent surgery. The timing of the acute illness, 2 months after the operation, is consistent with infection acquired during surgery. She was infected by HCV belonging to a genotype that is uncommon in the UK, and the very close evolutionary distances of the 5'NCR and NS5 sequences amplified from the HCV genome in the blood of the anesthetist and the patient indicate transmission from one to the other.

Transmission of hepatitis C from infected healthcare workers to patients during surgery has been described previously (Esteban et al., 1996; Duckworth et al., 1999). HCV-infected surgeons are usually the source. The principal route is thought to be via abrasions and cuts sustained by the surgeon during surgery. Infection of patients in the course of anesthesia is more rarely reported. Patient-to-patient infection due to repeated use of contaminated anesthetic ampoules has been observed (Tallis et al., 2003). The reusable part of the breathing apparatus was implicated as the vehicle of transmission in another series of patient-to-patient transmissions of HCV (Chant et al., 1994). It was suggested that once the apparatus had been contaminated with HCV, the virus was transmitted to other patients via abrasions sustained in the upper airway during laryngeal mask insertion.

Reports of transmission from infected anesthetists or anesthetic assistants to patients are even rarer than reports of transmission involving infected surgeons. Stefan-Ross et al. [2000] described transmission from a chronically infected patient to an anesthetic assistant, and from him to five other patients. In this series an open wound on the assistant's hand was considered to be the most likely route of transmission, particularly as he had not worn gloves. Cody et al. [2002] described transmission of HCV from an anesthetist to a patient during an operation in which the only anesthetic procedures performed were endotracheal intubation and peripheral intravenous cannulation. The anesthetist was incubating HCV after having been exposed to an HCV-infected patient 9 weeks earlier. In both of these incidents the anesthetist and assistant were not known to be infected with HCV. In contrast, in the case described above, the anesthetist was known to be hepatitis C positive prior to the operation and hence adhered to all existing infection protocols formulated to minimize the risk of transmission.

No other cases of HCV transmission unassociated with performance of exposure-prone procedures have yet been described. As HCV can be transmitted via wound secretions or through minute skin abrasions (Chouela et al., 1996), it is plausible that transmission

may have occurred by HCV shed from abrasions and then inoculated to the patient during intravenous cannulation, or via microabrasions sustained during endotracheal intubation. The US Centre for Disease Control and Prevention (CDC) has recommended that, in all cases involving transmission from medical personnel with no obvious route, the possibility that the member of staff might be injecting residual opiates and then reusing the vial should be considered. However, in this case the anesthetist had no history of intravenous drug use and strongly denied this possibility.

Our findings have implications for the control of HCV transmission from the health professional to the patient. Current UK Department of Health guidelines relating to known HCV-seropositive healthcare workers state that they should not perform exposure-prone procedures [UK Health Departments, 2002] including procedures in which "the workers gloved hands may be in contact with sharp instruments, needle tips or sharp tissues inside a patient's open body cavity, wound or confined anatomical space where the hands or fingertips may not be completely visible at all times" [UK Health Departments, 1994]. In 1996, the Association of Anaesthetists of Great Britain and Ireland published this advice regarding transmission of blood borne viruses: "anesthetists necessarily put their fingers into patients' mouths in order to perform a number of procedures. However, the group can find no evidence either in the literature or from experience of its members and their colleagues that anesthetists sustain soft tissue injuries during these procedures" [Association of Anaesthetists of Great Britain and Ireland, 1996]. It was therefore recommended that the insertion of the anesthetist's fingers into patients' mouths during intubation should not be regarded as an exposure-prone procedure. Furthermore, with regard to intravenous cannulation, the UK Department of Health guidelines state that "setting up and maintaining iv lines" is not an exposure-prone procedure [UK Health Departments, 1994]. This led the Association of Anaesthetists of Great Britain and Ireland to conclude that, provided exposure-prone procedures were avoided, "a hepatitis infected anesthetist may continue in clinical practice" [Association of Anaesthetists of Great Britain and Ireland, 1992]. Similarly, the CDC state that "no recommendations exist to restrict professional activities of health-care workers with HCV infection. As recommended for all health-care workers, those who are HCV-positive should follow strict aseptic technique and standard precautions, including appropriate use of hand washing,

protective barriers, and care in the use and disposal of needles and other sharp instruments" [Centers for Disease Control and Prevention, 1998].

The findings from our case, and those reported by Cody et al. [2002] suggest that anesthetist-patient transmission can occur through anesthetic techniques, even when there are no exposure-prone procedures involved and when all infection protocols are observed. However, given the high number of operative procedures performed per year and the fact that this is the first case reported in the UK and the third worldwide, the risk of transmission should be considered to be very low. Nonetheless, in the light of these findings, guidelines for the operating room conduct of HCV-seropositive anesthetic staff may need to be revised. The definition of what constitutes an exposure prone procedure may need to be reviewed, and procedures such as intravenous cannulation and endotracheal intubation, which were previously thought to carry no risk, may need to be re-evaluated.

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識別番号・報告回数		報告日	第一報入手日 2005.3.9	新医薬品等の区分 該当なし	機構処理欄
一般的名称	解凍人赤血球濃厚液	研究報告の公表状況	IASR. 情報源: 共同通信 2004 Dec 3.	公表国 日本	
販売名(企業名)	解凍赤血球濃厚液「日赤」(日本赤十字社) 照射解凍赤血球濃厚液「日赤」(日本赤十字社)				
研究報告の概要	<p>日本に定住しているアフリカ系外国人の 30 代男性で、現在は発症していないが、医療機関における HIV スクリーニング検査（抗原抗体検出 EIA 法、イムノクロマト法）で陽性を示したために、大阪府立公衆衛生研究所において確認検査を実施した。PA 法では HIV-1 にて抗体陰性であったが、HIV-2 では強い陽性を示した。ウエスタンブロット法でも、HIV-1 では HIV-1 陽性基準を満たさなかったが、HIV-2 では陽性基準を満たした。さらにイムノブロット法においては HIV-2 のみに反応を示した。以上により当検体の HIV-2 感染が確かめられた。HIV-2 の感染の拡大にも注意を払う必要がある。</p>				<p>使用上の注意記載状況・ その他参考事項等</p> <p>解凍赤血球濃厚液「日赤」 照射解凍赤血球濃厚液「日赤」</p> <p>血液を介するウイルス、 細菌、原虫等の感染 vCJD 等の伝播のリスク</p>
	報告企業の意見	今後の対応			
<p>在日外国人に HIV-2 型感染が見つかったとの報告である。日本国内での HIV-2 型感染例はこれで 3 例目、遺伝子学的に確認されたのは 2 例目であり、感染者はいずれも外国籍である。</p>		<p>国内の HIV 感染、AIDS 発生の動向について、引き続き情報の収集に努める。</p>			



<速報> 在日外国人にHIV2型感染が見つかる

患者は日本に定住しているアフリカ系外国人の30代男性であり、現在無症候の状態である。医療機関におけるスクリーニング検査(抗原抗体検出EIA法、イムノクロマト法)で陽性を示したために、大阪府立公衆衛生研究所において確認検査を実施した。

PA法(セロディアHIV-1/2)ではHIV-1にて抗体陰性であったが、HIV-2では強い陽性(抗体価 2^{19} 倍)を示した。HIV-1のウエスタンブロット(WB)法(ラブプロット1)ではgp160、p68、p55、p52、p40、p34、p25に反応しHIV-1陽性基準を満たさなかったが、HIV-2のWB法(ラブプロット2)ではgp140、gp105、p68、p56、p34、p26に反応しHIV-2の陽性基準を満たした。さらにイムノブロット法(ペプチラブ1.2)においてはHIV-2のみに反応を示した。以上により当検体のHIV-2感染が確かめられた。


HIV-2の感染の拡大にも注意を払う必要があると思われる。


大阪府立公衆衛生研究所 ウイルス課

川畑拓也 小島洋子 森 治代 大竹 徹

大阪市立大学大学院医学研究科 血液病態診断学

〒 起良 日野 雅之

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