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Health Care–Associated Hepatitis C Virus Infections Attributed to Narcotic Diversion

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Background: Three cases of genetically related hepatitis C virus (HCV) infection that were unattributable to infection control breaches were identified at a health care facility.

Objective: To investigate HCV transmission from an HCV-infected health care worker to patients through drug diversion.

Design: Cluster and look-back investigations.

Setting: Acute care hospital and affiliated multispecialty clinic.

Patients: Inpatients and outpatients during the period of HCV transmission.

Measurements: Employee work and narcotic dispensing records, blood testing for HCV antibody and RNA, and sequencing of the *NS5B* gene and the hypervariable region 1 of the *E2* gene.

Results: 21 employees were recorded as being at work or as retrieving a narcotic from an automated dispensing cabinet in an area where a narcotic was administered to each of the 3 case patients; all employees provided blood samples for HCV testing. One employee was infected with HCV that had more than 95% *NS5B* sequence homology with the HCV strains of the 3 case patients. Quasi-species analysis showed close genetic relatedness with variants from each of the case patients and more than 97.9% nucleotide identity. The employee acknowledged parenteral opiate diversion. An investigation identified 6132 patients at risk for exposure to HCV because of the drug diversion. Of the 3929 living patients, 3444 (87.7%) were screened for infection. Two additional cases of genetically related HCV infection attributable to the employee were identified.

Limitation: Of the living patients at risk for HCV exposure, 12.3% were not tested.

Conclusion: Five cases of HCV infection occurring over 3 to 4 years were attributed to drug diversion by an HCV-infected health care worker. Studies of drug diversion and assessments of strategies to prevent narcotics tampering in all health care settings are needed.

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Transmission of hepatitis C virus (HCV) to patients in health care settings is well-documented (1). Most health care–associated HCV infections represent patient-to-patient transmission of HCV after breaches of infection control by health care personnel (1, 2). Instances of HCV transmission from health care personnel to patients are reported infrequently. Worldwide, many of these instances involved transmission from an HCV-infected surgeon during an invasive procedure (3). However, of the 5 previously recognized instances of HCV transmission from an infected health care worker in the United States (4), 4 occurred in the setting of narcotic diversion (5–8).

Between January 2007 and December 2008, 3 cases of incident HCV infection were identified among patients at a single institution. Previous HCV infection had been ruled out by HCV RNA testing within 3 months before diagnosis of each case. The cases were identified after a liver transplant, before a liver transplant, and after an autologous hematopoietic stem cell transplant. The patients had no behavioral risk factors for HCV infection. No evidence of infection related to blood product transfusion or organ transplantation was found. The HCV isolates from the 3 case patients were found to be genetically related by sequencing of the nonstructural 5b (*NS5B*) gene. A review of all clinic visits, hospital stays, medication administration records, and diagnostic and therapeutic procedures identified no epidemiologic links that would have provided opportunities for patient-to-patient transmission of a common HCV strain to or between these patients. Opportunities for transmission of a common HCV strain from a health care worker during an exposure-prone procedure or from a common device or product were also not identified. A hypothesis of HCV transmission through drug diversion by a health care worker infected with HCV was therefore investigated.

METHODS

Electronic medical records of case patients were reviewed to identify episodes of care during which a narcotic (benzodiazepine or opiate) was administered. The location within the facility where relevant episodes of care were delivered was determined by reviewing procedure logs. The location of narcotic dispensing within the facility was determined by reviewing electronic records of when automated dispensing cabinets were accessed. Employee work records were reviewed to determine which employees were assigned to locations where a

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Context

Hepatitis C virus (HCV) infection acquired in health care settings is usually due to breaches in infection control.

Contribution

Three transplant patients were unexpectedly found to have incident HCV infection. The HCV identified in all 3 patients had close genetic relatedness to the HCV identified in a technician in an interventional radiology area where the patients had received fentanyl. The technician admitted to diverting fentanyl in a manner that could cause contamination of syringes used for patient care. Nearly 4000 potentially exposed patients were screened, and 2 additional cases of HCV were identified.

Caution

Not all potentially exposed patients were tested.

Implication

Drug diversion can lead to HCV infection in the health care setting and may be difficult to detect.

—The Editors

narcotic was administered and who was at work on the day of narcotic administration. By necessity, the cluster and look-back investigations were conducted for patient safety, not for research. Review by the institutional review board was not required and was waived.

The case patients received care at an outpatient, integrated, multispecialty clinic affiliated with a single hospital. The affiliated hospital incorporated 289 beds and was located 8 miles from the clinic until April 2008, when a 214-bed hospital was opened immediately adjacent to the outpatient clinic. The hospital and clinic provide a full range of adult medical and surgical care, including active solid organ and hematopoietic stem cell transplantation programs.

Hepatitis C virus antibody was identified by using the Vitros anti-HCV IgG chemiluminescent immunoassay (Ortho Clinical Diagnostics, High Wycombe, Buckinghamshire, United Kingdom) and confirmed with recombinant immunoblot assay (Chiron RIBA HCV 3.0 strip immunoblot assay; Novartis Vaccines and Diagnostics, Emeryville, California). Detection of HCV RNA was performed with a laboratory-developed method using TaqMan HCV analyte-specific reagents (Roche Molecular Systems, Branchburg, New Jersey). Genotyping was completed with the Trugene HCV 5'NC genotyping assay (Siemens Healthcare Diagnostics, Tarrytown, New York). Sequencing of the HCV *NS5B* gene for phylogenetic relatedness and sequencing of hypervariable region 1 (HVR1) of the *E2* gene for quasi-species analysis were done at the Molecular Epidemiology Laboratory, Division of Viral Hepatitis, Centers for Disease Control and Prevention, by using methods described elsewhere (9, 10).

Statistical Analysis

The pairwise genetic distances of nucleotide quasi-species sequences were estimated with the DNADIST program in the PHYLIP package, version 3.6 (Joseph Felsenstein and the University of Washington, Seattle, Washington). Differences in the distributions of the HVR1 genetic distances among 6 randomly selected participants with HCV genotype 1a from NHANES III (Third National Health and Nutrition Examination Survey) and the case patient clusters were compared using the analysis-of-variance program in SAS for Windows, version 9.2 (SAS Institute, Cary, North Carolina). A P value of less than 0.05 was considered significant.

Role of the Funding Source

Our study received no external funding.

RESULTS

The HCV infections of the 3 case patients were identified in January 2007, January 2008, and December 2008. The HCV genotype in all 3 cases was 1a, the most common genotype of HCV identified in the United States (11). The *NS5B* sequence of specimens from the 3 patients had greater than 97.9% homology.

The potential exposure period for each patient's HCV infection was considered to be from 6 weeks before the last negative HCV RNA test result to 1 week before the first positive HCV RNA result. The only area in the facility where all 3 case patients received a narcotic during their respective HCV exposure periods was in the interventional radiology unit of the hospital. Twenty-one employees assigned to the interventional radiology area were recorded as being at work when each case patient received a benzodiazepine or opiate in the interventional radiology unit. The only benzodiazepine or opiate that all 3 case patients received was fentanyl.

All 21 employees submitted blood specimens for testing. Hepatitis C virus was identified in a specimen from 1 employee, a licensed radiology technician, and classified as genotype 1a. In June 2010, the *NS5B* sequence showed more than 96% homology with the variants identified from the 3 case patients. In July 2010, phylogenetic analysis of the HVR1 quasi-species confirmed close genetic relatedness among HCV variants from the 3 case patients and the technician. The HVR1 quasi-species obtained from the 4 HCV-infected persons formed a single distinct cluster in a phylogenetic tree (**Figure**) that was significantly different from other genotype-1a quasi-species clusters identified from 6 NHANES III participants ($P < 0.010$). The maximum nucleotide identity among 73 *E1*-HVR1 quasi-species sequences obtained from the 4 persons ranged from 97.9% to 100%, whereas it ranged from 80.5% to 88.4% when these sequences were compared with those obtained from NHANES III participants.

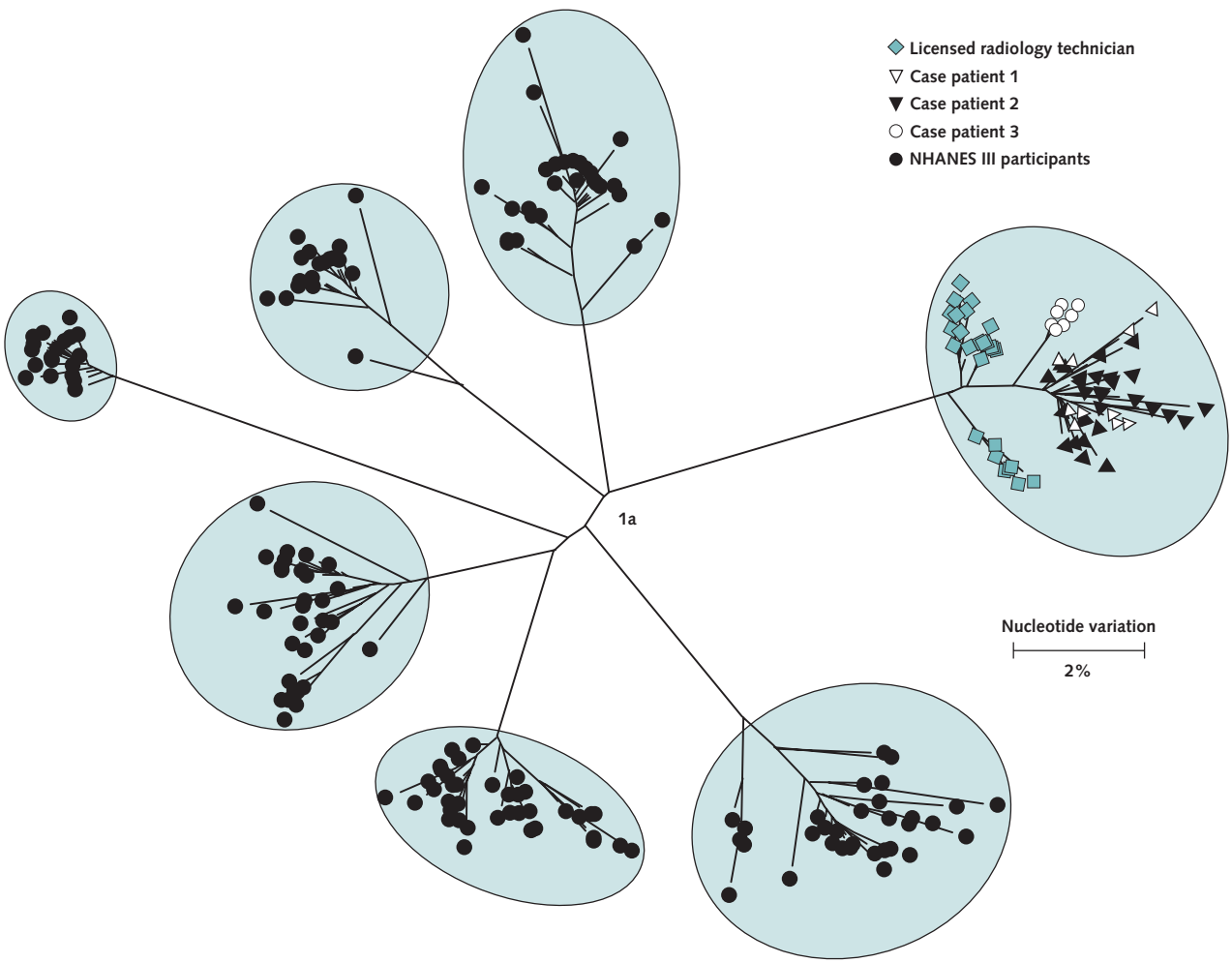
After several interviews in August 2010, the radiology technician acknowledged diversion of fentanyl intended for patients in the interventional radiology area; the diversion began sometime after hire in 2004. The technician described 2

principal methods of fentanyl diversion. First, the technician reported frequent retrieval of syringes containing residual fentanyl from used sharps containers that were removed from the work site at the end of work shifts. After self-administration of the fentanyl, the syringes were discarded. Although this method of diversion created obvious risk for transmission of infection to the technician, it did not introduce risk for transmission of HCV to patients. Second, the technician reported rare self-administration of fentanyl from a syringe that had been filled with fentanyl in preparation for patient care. The technician would replace the removable needle of the prefilled syringe with a smaller-gauge needle, self-administer the fentanyl, replace the smaller-gauge needle with the original needle, replace the administered fentanyl with saline, and return the filled syringe to patient care. Consistent with other descriptions of syringe reuse (2), this method of fentanyl diversion would allow the syringe to be contaminated with HCV from the technician before it was used to administer fentanyl to a patient.

The technician denied diverting benzodiazepines or hydromorphone, the only other opiate used in the interventional radiology area. Testing the technician's blood excluded infection with hepatitis B or HIV. The technician had a documented history of hepatitis B vaccination and the presence of hepatitis B surface antibody from before hire and did not recall an illness consistent with acute hepatitis.

A look-back investigation was done to identify additional patients who may have acquired HCV infection from the radiology technician and whose infections had not been identified by infection surveillance at the facility. Patients were considered to be at risk for exposure to HCV from the employee if they had an episode of care that fulfilled the following 3 criteria: procedure performed in interventional radiology, fentanyl or hydromorphone re-

Figure. **Phylogenetic tree of 291 nucleotide sequences derived from the *E1*-HRV1 genomic region of hepatitis C virus intrahost variants obtained from 3 case patients, 1 licensed radiology technician, and 6 randomly selected NHANES III participants.**



NHANES III = Third National Health and Nutrition Examination Survey.

trieved from an automated dispensing cabinet affiliated with interventional radiology on the day of the procedure, and radiology technician was recorded as being at work. Beginning in September 2010, patients with episodes that fulfilled these criteria were notified by mail of possible exposure to HCV and were asked to undergo blood testing for HCV antibody and HCV RNA.

A review of the 6-year period that the technician worked in the interventional radiology unit, from being hired in 2004 until being removed from work in the summer of 2010, identified 6132 patients as being at risk for exposure to HCV. Of these, 2203 (35.9%) had died. As of 9 March 2011, 3444 of the 3929 living patients (87.7%) had submitted blood specimens for HCV screening. Two patients were found to have HCV infection genotype 1a that was attributable to the technician by *NS5B* sequencing and quasi-species analysis. One patient had a single procedure performed in the interventional radiology unit in January 2007, and the other had multiple procedures between January 2005 and July 2009. These patients had received fentanyl, not hydromorphone, in interventional radiology.

DISCUSSION

Five cases of hepatitis C were attributed to diversion of fentanyl by an HCV-infected health care worker. The diversion of fentanyl resulted in contamination of syringes with HCV, and other health care workers subsequently used these syringes to administer fentanyl to patients. The evidence in support of this conclusion is 4-fold. First, the health care worker was epidemiologically linked with the 3 case patients during the administration of fentanyl. Second, the samples of HCV recovered from the worker and the 3 case patients were related genetically. Third, the worker acknowledged diverting fentanyl in a manner that created risk for transmission to patients. Finally, 2 additional cases of health care–associated HCV infection attributable to the worker were identified by prediction of risk related to administration of fentanyl in the vicinity of this employee.

Our report describes a novel approach to investigating cases of HCV infection of unknown origin. Association of the 3 initial cases with health care, exclusion of community-based risk factors for infection, demonstration of genetic relatedness, and exclusion of opportunities for transmission through breaches of infection control led to the hypothesis of transmission from an HCV-infected health care worker through narcotic tampering. Twenty-one health care workers were thereby epidemiologically linked with all 3 of the initial case patients. One worker with a previously unrecognized HCV infection was identified as the source through genetic relatedness of HCV samples and acknowledgment of narcotic diversion.

Only 4 other instances of HCV transmission to patients due to narcotic diversion by a health care worker have been reported in the United States (5–8). One small and 3 large incidents of this type have been recognized and reported outside the United States (12–15). In the previous U.S. incidents, health care–associated HCV infection related to narcotic diversion was suspected after unexplained cases of symptomatic acute hepatitis C were identified in patients and linked to infected health care workers. In these cases, the workers did not perform invasive procedures but were suspected of tampering with narcotics or had recent evidence of acute hepatitis. The number of cases of HCV transmission ranged from 1 to 45. Two of the incidents involved infected anesthesia staff, and the other 2 involved infected surgical technicians (5–8).

Our investigation differs from the previous reports. None of the infected patients in our initial cluster had symptomatic acute hepatitis. Instead, all were asymptomatic and were identified by HCV screening of 2 organ transplant patients or by evaluation of an unexplained increase in hepatocellular enzyme levels in 1 patient. Moreover, no evidence of HCV infection or narcotic tampering was available at the outset of our investigation to implicate this employee. In the absence of diagnoses of acute hepatitis C infection and without recognition of HCV transmission through narcotic diversion as a potential cause of health care–associated HCV infection, transmission as a consequence of narcotic tampering will probably go unnoticed.

Recognition of health care–associated HCV infection is hindered by barriers to surveillance and investigation (16, 17). For example, newly acquired HCV infection is often asymptomatic and not readily identified or diagnosed. At the facility reporting this investigation, surveillance for health care–associated HCV infection was enhanced after detection of a case of patient-to-patient transmission of HCV (18). Enhancements included regular HCV RNA testing of recipients of and candidates for solid organ transplants and episodic reviews of the clinical laboratory database to identify results of HCV diagnostic testing over time that are consistent with acute HCV infection, specifically HCV seroconversion or detection of HCV RNA after lack of detection. These enhancements allowed recognition of the initial 3 case patients. However, surveillance of the population at risk for exposure to HCV because of drug diversion was incomplete—2 additional cases of health care–associated HCV infection were identified only after discovery of the diversion necessitated a large patient-notification and look-back investigation.

This investigation had several challenges and limitations. The 3 case patients in the initial cluster had been treated at the facility multiple times over an extended period. Identification and testing of health care workers for HCV infection, molecular testing of HCV isolates, patient notification, and the look-back investigation required extensive resources for planning and execution. Despite our comprehensive approach to the investigation, of the 6132 patients identified as being at risk for exposure to HCV because of the drug diversion, approximately 36% had died before patients were notified and 12.3% of the living patients were not tested.

Offers to evaluate and treat HCV infection and its complications and to compensate for expenses related to the care and complications of HCV infection were extended to all patients whose infections were attributable to narcotic diversion by the licensed radiology technician. Testing of patients possibly exposed to HCV by the narcotic diversion was completed without expense to patients or their insurers. The natural history and complications of HCV infection and the challenges and consequences of large-scale adverse events in health care settings (19) are well-known. Many issues related to the narcotic diversion reported here, including legal actions, have not been reviewed because they exceed the scope of the epidemiologic investigation and are not determined or resolved.

Preventing health care–associated HCV infection related to drug diversion will require implementing strategies to control narcotics in health care settings that cannot be circumvented. More than 4% of health care workers have acknowledged illicit drug use (20), and prevalence of abuse has been reported to be higher in subsections of the health care workforce directly involved in administering controlled substances to patients, such as anesthesiologists (21) and nurses (22). However, narcotic diversion and security in the operating room have been investigated (23–25), and important lessons have been learned from those investigations (26), whereas relatively little is known about the epidemiology of drug diversion and the effectiveness of strategies to prevent it outside of the operating room environment. Among the instances of reported drug diversion that have led to transmission of infection in health care settings, fentanyl is overrepresented as the implicated narcotic (5, 27, 28). Studies of drug diversion and assessments of strategies to prevent narcotic theft in all health care settings are needed.

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