Healthcare-associated Legionnaires' disease: Limitations of surveillance definitions and importance of epidemiologic investigation

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Abstract

Healthcare-associated Legionnaires' disease (HCA LD) causes significant morbidity and mortality, with varying guidance on prevention. We describe the evaluation of a case of possible HCA LD and note the pitfalls of relying solely on an epidemiologic definition for association of a case with a facility. Our detailed investigation led to the identification of a new *Legionella pneumophila* serogroup 1 sequence type, confirmed a healthcare association and helped build the framework for our ongoing preventive efforts. Our experience highlights the role of routine environmental cultures in the assessment of risk for a given facility. As clinicians increasingly rely on urinary antigen testing for the detection of *L. pneumophila*, our investigation emphasises the importance of clinical cultures in an epidemiologic investigation.

Keywords

Legionella, healthcare-associated infections, epidemiology

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Background

Legionnaires' disease (LD) was first recognised in 1976 during an outbreak of pneumonia at an American Legion convention in Philadelphia, PA, USA (Fraser et al., 1977). The causative organism, *Legionella*, is a gram-negative bacillus that has the propensity to grow in building warm water systems. Of several species, *L. pneumophila* serogroup 1 (Lp1) is most commonly associated with disease in the United States. Healthcare-associated (HCA) LD is a serious disease with a mortality rate of up to 30% (European Center for Disease Prevention and Control, 2015). Despite this, there is little consensus in guidance for either primary or secondary prevention of HCA LD cases (Parr et al., 2015). In the United States, the Centers for Disease Control and Prevention (CDC) legionellosis case report form (CDC, 2014) specifically requests information on healthcare exposure of the case; the form defines a case of legionellosis as definite HCA if the patient was hospitalised continuously for ≥ 10 days before the onset of illness, and as possible HCA if the patient had exposure to a healthcare facility

(inpatient or outpatient) for a portion of the ten days prior to onset. We describe the evaluation of a case of HCA LD and note the pitfalls of relying solely on an epidemiologic definition for association of a case with a facility.

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Case presentation

In 2014, a 62-year-old male patient presented to the hospital for an acute exacerbation of severe chronic obstructive pulmonary disease. Following treatment, his clinical status improved and he was discharged to an inpatient rehabilitation facility located on the same hospital campus. Over the course of nine weeks of rehabilitation therapy, the patient made a steady improvement in his functional status. In anticipation of eventually transitioning to living independently, he went home for a weekend and returned to the same inpatient rehabilitation unit to complete his course of physical therapy.

Six days after his return to the inpatient rehabilitation facility, he was found to have fallen on the floor while getting out of bed. Nursing staff had observed that he had difficulty swallowing around the time of his fall. Two days after this event, the patient was confused, febrile, tachycardic and tachypneic. Physical examination revealed diminished breath sounds at the right lung base. Laboratory evaluation noted a leukocytosis of 15,800/cmm and a chest radiograph showed dense right middle and lower lobe infiltrates consistent with pneumonia. He was transferred back to an acute care medical ward and treated with vancomycin and piperacillin/tazobactam for presumed aspiration pneumonia. In keeping with the Veterans Health Administration's (VHA's) HCA LD prevention policy (U.S. Department of Veterans Affairs, 2014) that promotes heightened awareness for possible cases of HCA LD, the patient was tested for *Legionella* by urinary antigen test. Testing was positive for Lp1 and the patient's antibiotics were changed to levofloxacin. He received a 21-day course of levofloxacin and was ultimately discharged back to the inpatient rehabilitation facility.

Pursuant with the CDC's epidemiologic case definition, this case was classified as possible HCA LD, since the patient had spent 48 h at home during the incubation period (CDC, 2014). VHA's HCA LD prevention policy (U.S. Department of Veterans Affairs, 2014) requires that a single case of possible HCA LD triggers an environmental investigation to determine if remediation of the water distribution system is necessary. The policy also requires routine quarterly testing of environmental water samples for *Legionella*. The most recent routine environmental testing for *Legionella* had been obtained three weeks prior to this case, and the results for the building in which the patient was located showed 6/36 water samples (17%) were positive by culture for Lp1 (two cold water samples and four hot water samples). As a result, facility staff had remediated and retested the water supply, one week prior to this case of possible HCA LD being identified. In light of the recent routine environmental findings, a detailed epidemiologic investigation was pursued when this case of possible HCA LD was identified.

Investigation

A sputum sample was obtained from the patient and cultured for *Legionella*, yielding a single colony of Lp1. An

investigation of the patient's activities in the days preceding his illness revealed contact with the hospital's potable water system in the patient's room and bathroom. Accordingly, five water samples were obtained from the tap and shower in the patient's room and bathroom.

Lp1 was cultured from three water samples (cold or mixed hot/cold water) from the patient's bathroom sink, shower and an electronic tap in the patient's room (Table 1). Hot water samples from the sink and shower in the patient's bathroom were positive for *Legionella* by polymerase chain reaction screening, but no *Legionella* was detected by culture. The Lp1 isolates from the patient's room, as well as 8/9 isolates that were available from the routine environmental testing of the medical campus three weeks prior, were further analysed at the VHA Public Health Reference Laboratory (Palo Alto, CA, USA). Molecular analysis was conducted by sequence-based typing (SBT) using the European Working Group for *Legionella* Infections (EWGLI) typing protocol version 5.0 (EWGLI, 2015). Results of these tests are summarised in Table 1.

The patient-derived isolate as well as three of 11 environmental isolates were closely related to EWGLI sequence type (ST) 1, but possessed a previously undescribed polymorphism in the *proA* gene (T→G at position 38), resulting in an overall new sequence type designation (ST 2485). Two of these environmental isolates were from the patient's bathroom collected during the investigation. The third environmental isolate was from a different unit on the same floor as the patient and was obtained during routine environmental testing three weeks prior. Both of these units shared the same water loop. This led to the conclusion that this patient had acquired his LD from the hospital water system, resulting in the reclassification of the case from possible HCA LD to definite HCA LD.

A review of the water supply in the building revealed variable levels of *Legionella* control parameters. Free chlorine levels at taps in the building, measured at the time of routine environmental sampling three weeks prior to the case, were in the range of 0.03–0.20 ppm (median = 0.1 ppm) at 18 hot water taps and 0.06–0.79 ppm (median = 0.74 ppm) at 18 cold water taps. Hot water was generated by instantaneous water heaters that released heated water at 140°F; water from all 18 hot water taps tested was at or above a temperature of 124°F. Cold water temperatures at the taps were in the range of 71–77°F.

Discussion

Since 2008, the VHA has had a comprehensive policy directed at assessing and reducing the risk of HCA LD in VHA medical facilities, which included testing for LD among patients with healthcare-associated pneumonia (U.S. Department of Veterans Affairs, 2008). Historically, this hospital had not identified any cases of definite HCA LD prior to this patient. In August 2014, VHA policy was

Table 1. Results of the molecular analysis of *L. pneumophila* serogroup 1 isolates.

Sample source	Sample location and/or type	<i>Legionella</i> concentration* (CFU/mL)	Sequence type†
Patient	Sputum	N/A	2485
Case investigation	Patient bathroom sink – cold water	10	2485
	Patient bathroom shower – cold water	10	2485
	Electronic tap in patient room - mixed hot/cold water	10*	I
Routine	Same building but different unit from patient (same floor and water loop) sink – cold water	I	2485
Sampling (three weeks prior to case)	Same building but different unit from patient, sink – hot water	2	I‡
	Same building but different unit from patient, sink – cold water	I	I
	Same building but different unit from patient, sink – hot water	I	I
	Same building but different unit from patient, sink – hot water	I	I
	Same building but different unit from patient, sink – hot water	I	I
	Different building on campus, sink – cold water	2	I
	Different building on campus, sink – cold water	I	I

**Legionella* concentrations in water samples detected by ISO 11731 spread plate protocol except for the sink in the patient room (mixed sample), which was detected by the Phigenics Validation Test® protocol.

†Sequence-based typing was performed in accordance with the European Working Group for *Legionella* Infections (EWGLI) protocol.

‡This isolate had a unique polymorphism in the *proA* gene that was unrelated to the *proA* polymorphism in sequence type 2485. The isolate was not associated with the patient and was not further evaluated.

updated and expanded to require routine testing of hospital water systems for *Legionella* (U.S. Department of Veterans Affairs, 2014). Prior to this update in policy, environmental testing for *Legionella* at the facility was done only when water lines were affected by construction at the facility. This change in policy fortuitously enabled us to compare strains from the patient and his immediate environment to strains that were present elsewhere on the campus.

This report adds to the growing body of literature on *Legionella* in healthcare facilities in several ways. Although *Legionella* pneumonia is typically acquired by inhalation, aspiration is also a risk factor for the development of LD (Blatt et al., 1993) and has been noted as a risk in patients with swallowing disorders (Bencini et al., 2005). This case study makes us question whether aspiration of colonised potable water contributed to the development of LD in this patient, who had difficulty swallowing and was initially diagnosed with aspiration pneumonia. Clinically, *Legionella* as the causative agent for aspiration pneumonia is often not considered in the initial work-up. This case indicates the value of such consideration, and diagnosis of LD allowed for optimisation of antibiotic therapy. Based on the epidemiological investigation, the patient had potential exposure to *Legionella* via both the potable water in his room as well as aerosols from the shower head in his bathroom; it is impossible to definitively conclude which of the two specific exposures might have led to disease.

This report also supports the value of routine environmental surveillance for *Legionella* in the potable water

systems of healthcare facilities as an indication of clinical risk. LD diagnostic testing of this patient with presumed aspiration pneumonia was predicated on a state of heightened awareness for LD since *Legionella* had been detected recently in the potable water distribution system after routine testing. Prior to the implementation of routine environmental surveillance for *Legionella*, sampling of the water system was done only in the setting of construction activity. The hospital campus had no known prior cases of definite HCA LD since at least 2008 when a formal policy to assess for *Legionella* was adopted. The last time environmental testing had been performed at completion of construction activity was in 2013. While there were some positive water samples, the entire building's water supply had been remediated and subsequent follow-up testing in January 2014 showed no evidence of *Legionella*.

Perhaps most significantly, while *Legionella* urinary antigen testing is most commonly used for diagnosis of LD and can guide timely clinical management for disease caused by Lp1, this case demonstrates the importance of obtaining clinical isolates to facilitate the epidemiologic investigation of HCA LD. The investigation also led to the discovery of a unique isolate of *L. pneumophila* serogroup 1 (ST 2485) that has now been added to the EWGLI database. Furthermore, in contrast to guidance (Sehulster et al., 2003) and general practice, this case study demonstrates the value of investigating even a single case of possible HCA LD as we were able to link an environmental isolate to the patient's isolate and re-classify the case as definite HCA LD. The change in classification provided a better understanding of the risk of HCA LD in the facility and has

informed subsequent routine preventive actions. Point of use filters were installed as an interim solution and the facility now routinely hyperchlorinates the water system in response to any positive environmental cultures, with subsequent testing to ensure *Legionella* is reduced to undetectable levels. Engineering staff have made significant progress in eliminating dead legs throughout the facility and have now completed installing a chlorine dioxide system as a long-term solution. Since the completion of this investigation and resultant remediation, no cases of definite or possible HCA LD from an inpatient stay have occurred at this hospital.

This case also highlights that, while proactively testing healthcare facility water for *Legionella* is informative for potential risk, the interpretation of results, the setting of any action thresholds and the response to detection of *Legionella* needs to be determined by each facility using their local clinical and environmental data. For example, testing performed three weeks prior to the identification of this case found less than 30% of water outlets positive for *Legionella*, a recognised action threshold in the literature (Squier et al., 2005) and in previous VHA policy (U.S. Department of Veterans Affairs, 2008).

This report reinforces the need for clinicians to maintain a high index of suspicion for HCA LD in the appropriate context. While an epidemiological definition can be an invaluable starting point for possible HCA LD, clinical cultures with subsequent molecular typing can greatly facilitate the work-up and guide an appropriate response towards prevention of other cases.

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