MAJOR ARTICLE

Pedicure-Associated Rapidly Growing Mycobacterial Infection: An Endemic Disease

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Background. Pedicure-associated nontuberculous mycobacterial furunculosis has been reported in the setting of either outbreaks or sporadic case reports. The epidemiology of these infections is not well understood.

Methods. Systematic surveillance for pedicure-associated nontuberculous mycobacterial furunculosis was conducted in 2 North Carolina counties from 1 January 2005 through 31 December 2008. A subset of implicated nail salons and control salons was inspected and sampled for nontuberculous mycobacteria.

Results. Forty cases of suspected or confirmed pedicure-associated nontuberculous mycobacterial furunculosis were reported during the 4-year study period. Furunculosis incidence in the surveillance region was 1.00, 0.96, 0.83, and 0.89 cases per 100,000 population in 2005, 2006, 2007, and 2008, respectively. The responsible organisms primarily belonged to the Mycobacterium chelonae/abscessus group (30 [91%] of 33 isolates). Thirteen implicated salons and 11 control salons were visited and environmentally sampled. An assortment of nontuberculous mycobacteria was cultured from footbaths, but there was no association between the species distribution of the environmental isolates and implication of the salon in human infection. Evidence of suboptimal cleaning (visible debris or surface biofilms) was observed in at least 1 footbath for 11 of 13 implicated salons and 4 of 11 control salons (P = .032).

Conclusions. Pedicure-associated mycobacterial furunculosis was endemic in these 2 North Carolina counties during 2005–2008. Suboptimal footbath cleaning may have contributed to these infections, which suggests straightforward means of potential prevention. The relative rarity of this type of infection in the setting of nearly ubiquitous exposure to these pathogens suggests that as yet undefined host-specific or procedure-related factors may be involved in susceptibility to these infections.

Nontuberculous mycobacteria frequently colonize water distribution systems, and human exposure to these organisms is therefore common. In most cases, exposure does not result in significant clinical consequences. However, under certain conditions, exposure may result in human disease. Disease caused by nontuberculous mycobacteria is relatively uncommon, so health care providers frequently fail to consider these organisms when patients present with nontuberculous mycobacterial infection. This failure may result in delayed diagnosis, increased morbidity, and a lack of recognition of a potential public health threat.

Rapidly growing mycobacteria (RGM), a subgroup of nontuberculous mycobacteria, have been implicated in outbreaks of skin and soft tissue infections in a number of settings [1–5]. In particular, pedicure-associated furunculosis caused by RGM is an emerging syndrome. A large outbreak of 110 cases of pedicure-associated furunculosis caused by RGM (specifically Mycobacterium fortuitum) occurred in California in 2000 [6]. This outbreak was associated with suboptimal cleaning practices at a single nail salon, resulting in accumulation of organic debris in pedicure footbaths. This organic debris
provided an environment in which the mycobacteria could multiply and presumably achieve very high concentrations in the recirculated footbath water. Although sporadic cases of pedicure-associated RGM furunculosis have been reported [7–9], no other outbreaks have been reported. Subsequent work demonstrated that RGM were commonly present in pedicure footbaths; in one study, 29 of 30 footbaths from 18 different salons grew RGM [10]. This study suggested that exposure to RGM in footbaths is common, but whether this common exposure results in disease outside an epidemic setting was unclear.

In 2005, 2 cultures growing RGM isolated from skin biopsy specimens of women’s legs were reported in Wake County, North Carolina. Initial communication with these patients’ physicians confirmed that the infections were pedicure-associated. The North Carolina Division of Public Health authorized an official public health investigation to better understand the nature and extent of the problem.

METHODS

Case Definitions
A case of pedicure-associated furunculosis caused by RGM was defined as follows.

Culture-Confirmed Case
A culture-confirmed case met the following criteria: papules, plaques, pustules, or nodules on one or both legs persisting for >1 month, below the knee; growth of RGM from 1 or more biopsy specimens from the leg; history of pedicure within the 3 months prior to onset of the initial lesion or lesions; and no alternative diagnosis for the lesion or lesions after a dermatologist’s evaluation.

Clinical Case
A clinical case met the following criteria: papules, plaques, pustules, or nodules on one or both legs persisting for >1 month, below the knee; no alternative pathogens grown from culture of a lesion, if a culture was obtained; history of pedicure within the 3 months prior to onset of the initial lesion or lesions; and no alternative diagnosis for the lesion or lesions after a dermatologist’s evaluation.

Surveillance Methods
The surveillance area included all of Wake and Durham counties in North Carolina. All cultures of skin and/or soft tissue specimens collected from 1 January 2005 through 31 December 2008 that grew RGM were reviewed. We obtained all positive culture reports from the North Carolina Laboratory of Public Health, which serves as a reference laboratory for mycobacterial species identification. All reports from the 2 academic medical centers in the area (Duke University Medical Center and the University of North Carolina at Chapel Hill) were also obtained. In addition, certain private laboratories (eg, LabCorp) send all positive mycobacterial culture reports to the state tuberculosis control program, and these were also reviewed. The physician whose name was on the laboratory requisition (generally the ordering physician) was contacted to determine whether the patient might have pedicure-associated furunculosis. In addition to laboratory-based surveillance, dermatologists practicing in Wake and Durham counties were made aware of the syndrome and requested to notify the surveillance team of any suspected cases of pedicure-associated furunculosis. Furthermore, in May 2006, local television media presented a story on the problem, which raised public awareness. Incidence was calculated using US Census midyear population estimates for the combined populations of Wake and Durham counties, North Carolina (estimated 2005 population, 997,123) [11].

We estimated the date of onset of furunculosis to the nearest month, based on information in medical records. When possible, we also estimated the incubation period as the time from the most recent pedicure to the onset of leg lesions. Diagnostic delay was defined as the time between the onset of the lesions and either empiric use of antibiotics with activity against RGM (in the setting of clinical suspicion of RGM furunculosis) or growth of RGM from a leg biopsy specimen.

At the end of the investigation, a de-identified data set was provided to the investigators for research purposes. Use of this de-identified data set was given an exemption from oversight by the Duke University Medical Center institutional review board.

Environmental Sampling
A list of all licensed nail salons operating in Durham and Wake counties (n = 202) was obtained from the North Carolina State Board of Cosmetic Examiners. A subset of potentially implicated salons was visited for environmental sampling from October 2006 through June 2007. This subset included every salon visited by a case patient prior to June 2007, excluding out-of-area salons and 1 salon that had closed. For each potentially implicated salon chosen for sampling, a control salon in the same zip code and with roughly the same number of footbaths was selected at random for inspection and sampling. For each salon examined, a tap water sample and a sample of water from each footbath (obtained after running the whirlpool function of the footbath for 2 minutes) was obtained. Water samples were obtained by filling a sterile bottle with ~500 mL of the water, then adding 10 mL of 0.1% sodium thiosulfate. After water samples were obtained from the footbaths, the footbaths were drained and the grate was removed from the intake. The intake pipe was inspected and the presence of any debris or visible biofilm was recorded. A cotton swab was used to obtain biofilm samples and was placed into a sterile vial for transport. If any debris was present in the intake pipe, the debris was placed into the same sterile vial and processed with the swab.
Laboratory Methods

Processing and culture was performed using a modification of methods employed by Falkinham et al. [12]. Sixty milliliters of each water specimen was filtered through each of two 0.45-μm membrane filters. One filter was plated directly onto Lowenstein-Jensen medium, and the other onto 7H10 medium supplemented with an additional 5 μg/mL malachite green.

Swab and biofilm specimens were processed by vortexing for 5 minutes in 10 mL of 0.005% cetylpyridium chloride in sterile water. The resulting suspension was then filtered through each of two 0.45-μm membrane filters (5 mL each), and the filters were plated onto Lowenstein-Jensen and supplemented 7H10 medium as noted above. All plates were incubated for up to 6 weeks at 30°C. Colonies with acid-fast staining by the modified Kinyoun method were subcultured and sent to the North Carolina Laboratory of Public Health for species identification by use of high-performance liquid chromatography.

Statistical Methods

SAS software (version 9.2; SAS Institute) was used for statistical analyses. The Fisher exact test was used to compare categorical variables. A P value of <.05 was considered to be statistically significant.

RESULTS

Between 1 January 2005 and 31 December 2008, 40 cases of suspected or confirmed pedicure-associated RGM furunculosis were detected (Table 1). Two patients were pregnant at the time of lesion onset, and 1 patient had diabetes mellitus; no other immunocompromising conditions were noted. Figure 1 presents the onset dates for the lesions. A suggestion of seasonality was noted, with more cases reported in summer and winter. The estimated incidences of RGM furunculosis in Wake and Durham counties combined were 1.00, 0.96, 0.83, and 0.89 cases per 100 000 population in 2005, 2006, 2007, and 2008, respectively. A broad spectrum of disease was observed, ranging from a single plaque (Figure 2) to multiple, nodular, and excoriated lesions (Figure 2). Diagnosis was usually delayed, with a median time from onset of lesions to biopsy (when biopsied) of 2.5 months (range, 0–8 months). An incubation period could be estimated for 21 cases, with a median time of 28 days between the salon visit and appearance of lesions (range, 7–90 days). Among the 33 patients with positive cultures, the responsible organisms were primarily in the *M. chelonae/abscessus* group, with only 2 (6.3%) identified as *Mycobacterium fortuitum*. Interestingly,
5 (12.5%) of 40 case patients reported having similar lesions in the past associated with pedicures. However, only 1 case patient had a prior culture-proven diagnosis of RGM furunculosis, which had resolved 2 years before the current episode. Initial treatment with antibiotics directed against *Staphylococcus aureus* was common (26 of 32 cases). In no case was there evidence of systemic dissemination of the RGM infection.

The 40 case patients had visited 19 distinct nail salons prior to onset of lesions (some case patients had visited >1 salon during the potential incubation period). Additionally, 4 case patients either had visited an out-of-state nail salon or could not provide the name of the salon visited. Potentially implicated salons were associated with a median of 1 case (range, 1–7 cases). Environmental sampling of 126 footbaths located in 13 potentially implicated salons (case salons) and 11 control salons was performed. Because of diagnostic, reporting, and logistical delays, case salons were sampled a median of 9 months after the onset of symptoms in the most recent case (range, 0–23 months). At the time of sampling, documentation that footbaths had been cleaned in the previous 24 hours was absent from 8 of 13 case salons and 7 of 11 control salons. Organic debris or visible biofilm was noted behind the intake screen of 64 of 126 footbaths; 11 of 13 case salons and 4 of 11 control salons had at least 1 footbath with debris or biofilm (P = .032) (Figure 3). RGM were grown from tap water in all salons. Microbiological contamination by other environmental organisms, resulting in inability to isolate RGM, only allowed precise isolation and speciation from 7 of 13 case salons and 8 of 11 control salons.

We were able to isolate RGM from footbath water in 7 of 13 case salons and 6 of 11 control salons (Table 2). Biofilm specimens grew RGM in 10 of 13 case salons and 9 of 11 control salons. The proportion of salons growing each RGM species group (*M. chelonae/abscessus*, *M. fortuitum*, *Mycobacterium mucogenicum*, or other) from tap water, footbath water, and biofilms did not significantly differ by case or control status (P > .05 for comparisons of species distributions within specimen types). RGM in the same species group as an isolate from a case patient who received a pedicure at that salon were isolated from 6 of 13 case salons. These 6 salons had been attended by 12 of the patients. For 2 of the case salons, same-species group RGM were isolated from both footbath water and pipe biofilms, 3 had same-species group RGM isolated from pipe biofilms only, and 1 had same-species group RGM isolated from water only.

When tested, RGM isolates were noted to be resistant in vitro to multiple oral antibiotics. Empiric staphylococcal treatment usually consisted of a tetracycline or trimethoprim-sulfamethoxazole. Of 13 RGM isolates for which susceptibility testing was performed, only 1 was susceptible to trimethoprim-sulfamethoxazole, and 1 had intermediate susceptibility to doxycycline. The remaining isolates were resistant to both of these antibiotics, and patients did not demonstrate clinical improvement after empiric staphylococcal treatment. Clarithromycin susceptibility was noted for 12 of 13 isolates (1 of the *M. fortuitum* isolates was resistant), but only 2 of 12 tested isolates were susceptible to ciprofloxacin. Linezolid susceptibility was performed for 3 isolates; 1 was susceptible and 2 had intermediate susceptibility to this agent. Intravenous antibiotics such as cefoxitin (11 of 12 tested isolates susceptible, 1 intermediate) and amikacin (12 of 12 tested isolates susceptible) generally were active.

Antibiotics with activity against the RGM (ie, macrolides) were used for treatment in 28 of 40 cases. Among these cases, antibiotics were initiated a median of 3 months after initial onset of the lesions (range, 0–10 months). Treatment regimens were heterogeneous, often consisting of a macrolide (azithromycin or clarithromycin) plus a fluoroquinolone (which usually had questionable in vitro activity). This heterogeneity and small

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**Figure 3.** Example of visible biofilm in the intake pipe of a pedicure footbath. The photograph is of the proximal portion of the inlet pipe after the external mesh screen was removed. The white circle is the pipe, and the gray/brown material covering parts of the pipe is the biofilm.

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**Table 2. Distribution of Rapidly Growing Mycobacterium in Water and Biofilms From Case and Control Salons**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Case salons (n = 13)</th>
<th>Control salons (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. chelonae/abscessus</em></td>
<td>24 3 4</td>
<td>13 4 3</td>
</tr>
<tr>
<td><em>M. fortuitum</em></td>
<td>1 6 8</td>
<td>0 4 4</td>
</tr>
<tr>
<td><em>M. mucogenicum</em></td>
<td>4 2 4</td>
<td>4 3 2</td>
</tr>
<tr>
<td>Unidentified or other RGM</td>
<td>1 1 4</td>
<td>1 2 1</td>
</tr>
</tbody>
</table>

Data represent the no. of salons that grew a given species of rapidly growing mycobacteria (RGM) from each environmental specimen.
sample size precluded associating any particular treatment regimen with outcome. Among 16 cases with follow-up treatment data, a median of 105 days of antibiotic therapy was received (range, 14–180 days), and in all of these cases the lesions resolved with varying degrees of residual scarring. Five patients did not receive any antibiotic regimen with predicted activity against the RGM, and 3 of these were known to have resolution of the lesions with some residual scarring.

DISCUSSION

The temporal and spatial distribution of cases strongly suggests that pedicure-associated RGM furunculosis is an endemic disease in Wake and Durham counties. Unlike the previously described outbreak, pedicure-associated RGM furunculosis in these counties was associated with a number of different salons. Underreporting of cases is very likely to have occurred in this investigation, and incidence estimates are probably significantly lower than the true disease incidence. Spontaneous resolution of these infections, similar to what has been observed with nontuberculous mycobacterial lymphadenitis in children [13], likely contributes to underdiagnosis and underreporting. As has been described in previous reports [9, 14], delayed diagnosis and inappropriate treatment were common in patients presenting with RGM furunculosis.

Given clear evidence that exposure to RGM in salon water is nearly universal, RGM furunculosis is surprisingly uncommon. Although no case patient was obviously immunocompromised, the relatively small number of cases suggests that there is a significant component of host susceptibility in the pathogenesis of RGM furunculosis. Interestingly, 5 of the 40 case patients reported a prior episode of similar lesions after pedicures, 1 of which was culture-proven RGM furunculosis. Patients with localized (as opposed to systemic, or disseminated) RGM skin infections in other case series have also generally been described as immunocompetent [5, 9, 15–20]. Recent skin trauma with visible or microscopic skin damage probably serves as a predisposing factor, as evidenced by the link between recent leg shaving and pedicure-associated RGM infection [6]. Leg shaving prior to a pedicure is a very common behavior, and small nicks in the skin are likely to be present on many women’s legs during pedicures. We did not observe any practices in the salons that might have led to trauma to the legs, but salon-specific practices such as leg massage cannot be ruled out as contributing factors. We noted a disproportionate incidence of the syndrome in white women: 95% of case patients were white women, but the underlying population is only 52% white. This may be related to differential use of nail salons and leg shaving behavior, but additional host genetic or behavioral factors must be considered, including differential health care utilization.

Many pedicure baths had visible biofilms present in the water intake pipes, and the presence of organic debris or biofilm at a salon was significantly associated with a patient with an RGM infection who attended that salon. Cultures of these biofilms usually grew RGM, providing a possible source of the pathogenic RGM that caused the furunculosis syndrome. The organisms that grew from the biofilms did not always correspond to the organisms isolated from the pedicure bathwater. This may be a function of inadequate sensitivity of the techniques used for culture and isolation, differential prevalence of organisms in biofilms compared with water, or dynamic environmental microorganisms with delayed environmental culturing. Other investigators have demonstrated that organisms residing in such biofilms are more resistant to disinfectants [21] and may persist for long periods [22].

Our study had a number of limitations. Data for patients who did not personally see one of the investigators were obtained indirectly via medical records and interviews with the treating physicians, which may have reduced the accuracy of some of the reports. Only patients presenting for medical care and for whom the provider had either a suspicion of pedicure-associated RGM furunculosis or a culture specimen that grew RGM were detected by the surveillance protocol. Given the spectrum of disease, patients with milder disease were likely to have remained undetected. Environmental assessment was usually performed several months after the initial exposure, and quantitative cultures of the environmental specimens were not obtained. Therefore, it was not possible to directly correlate the extent of exposure with the probability of infection. Furthermore, the true at-risk population consists only of persons who obtain pedicures (the numbers of whom were unobtainable), so the true incidence in the at-risk population is higher than the numbers reported here for the general population. Species groups for environmental organisms were determined solely by high-performance liquid chromatography, and no higher-resolution molecular testing was performed that would permit matching of environmental isolates to patient isolates. We therefore cannot definitively conclude that all of these infections were acquired by pedicures at the nail salons, although the timing and distribution of lesions were highly suggestive. Similarly, several patients visited multiple salons, making attribution of infection to a single salon difficult. There were a small number of patients with other cutaneous RGM identified during this investigation, but they were relatively easy to differentiate from pedicure-associated infections (site of infection not on the legs, postoperative infection, etc).

Regardless of these limitations, our data demonstrate that pedicure-associated RGM was endemic in our community during the study period. Health care providers likely to encounter patients with RGM furunculosis should be educated about this entity, including clinical features and diagnostic
procedures (ie, skin biopsy and mycobacterial culture). The involvement of the community of dermatologists in this investigation was important both in recognizing cases of RGM furunculosis present in the community and in increasing awareness of the syndrome and its management. The North Carolina Cosmetology Board worked closely with public health authorities during this outbreak and developed a multifaceted intervention strategy including inspection for debris and biofilms behind pedicure bath intake grates, advising use of a 10% bleach solution (which is mycobactericidal [23]) to run through the pedicure bath pipes on a daily basis, and education of pedicure providers about appropriate cleaning practices. Continued surveillance will be necessary to determine whether this intervention is effective in reducing RGM furunculosis.

Notes

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