Outbreak of Nontuberculous Mycobacterial Subcutaneous Infections Related to Multiple Mesotherapy Injections

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We describe an outbreak of severe subcutaneous infections due to nontuberculous mycobacteria following mesotherapy. Epidemiological studies and molecular comparisons of Mycobacterium chelonae strains from different patients and the environment suggested that contamination may be associated with inappropriate cleaning of the multiple-injection device with tap water.

CASE REPORT

In January 2007, a general practitioner notified the health authorities and the regional center for nosocomial infection control of a cluster of subcutaneous infections due to nontuberculosis mycobacteria (NTM) following mesotherapy.

A complete screening for all potentially exposed patients who underwent mesotherapy with the practitioner from 1 October 2006 (the date of the first mesotherapy in the medical room suspected of contamination) to 15 January 2007 (the date of disruption of the mesotherapy practice) was designed. Each patient was contacted both by phone and by mail and urged to be examined by a specialist in the department of infectious diseases at a tertiary-care reference hospital in Paris. A retrospective cohort study of all exposed patients was performed to describe the temporal and spatial distribution of cases and identify risk factors. A case was defined as certain if the exposed patient had clinical subcutaneous lesions at the site of mesotherapy injections in association with cultures positive for NTM. A case was defined as probable if the exposed patient had clinical subcutaneous lesions but smear and culture results negative for NTM. An assessment study of hygiene practices was performed by an infection control practitioner at the outpatient clinic to determine potential risk factors to be tested in a comparative epidemiological study. Risk factors included the day of an outpatient visit, a patient’s place in a series of patients receiving therapy on the same day, and the site of and reason for injections. For each case, the incubation period was estimated as the time between the last mesotherapy session before the onset of symptoms and the date of the first symptoms of NTM infection. Comparisons of means and proportions were calculated with standard statistics. As the clinic was closed on Wednesdays, Saturdays, and Sundays, visits on the days after closure, i.e., Mondays and Thursdays, were considered as a potential risk factor, expressed as the number of such visits per 100 patient visits. Multivariate analysis was performed using stepwise logistic regression with P-to-enter and P-to-remove values at 0.20. The Hosmer-Lemeshow statistic was used to test the goodness of fit of the model. All calculations were performed using SAS software release 8.02 (SAS Institute, Cary, NC) and considered significant at $P < 0.05$.

Samples from tap water in the medical examination room, as well as from the injection device and topical creams, were examined to search for mycobacteria. Products used for mesotherapy injections were recovered from the office and analyzed by the laboratory of the French Agency for Sanitary Safety in Health Products. The initial flow of cold water (between 18 and 20°C) from the tap in the practitioner’s clinic was sampled on 1 February 2007. The detection of rapidly growing mycobacteria was performed after membrane filtration (5) and decontamination by lauryl sulfate-NaOH. Typing of Mycobacterium chelonae strains was performed using pulsed-field gel electrophoresis (PFGE) with XbaI as the restriction enzyme at the National Reference Centre laboratory, as described previously (6, 8, 9). Gel images were analyzed by GelCompar version 3.0 (Applied Maths). The band-based Dice-unweighted-pair group method with arithmetic means was used to prepare a dendrogram based on PFGE patterns and to calculate similarity indexes for M. chelonae isolates. To evaluate the clonality of strains from patients and the environment, nine epidemiologically unrelated strains received at the national reference center for mycobacteria between 2004 and 2007 were tested as controls.

Among 105 exposed patients, 48 responded to the mailing and were examined by the infectious-disease specialist. Overall, 16 cases were identified during an 8-month period (attack rate, 15.2%), including 12 certain cases (10 in which the patients were positive for M. chelonae, 1 in which the patient was positive for Mycobacterium frederiksesbergense, and 1 in which the patient was positive for both mycobacteria) and 4 probable cases in which the abscess cultures were negative for NTM. A...
search for other pathogens in clinical samples was systematically performed. The results were not concordant with clinical findings. The patients with identified cases of NTM infection, certain or probable, were on average 33 years old (range, 24 to 58 years), most (15 of 16) were female, and they presented with 1 to 120 skin lesions, predominantly on the hip area, upper legs, and abdomen (Fig. 1). Between October 2006 and January 2007, the number of developing cases varied from 1 to 3 per week. Two later cases were detected in April and May 2007. The median incubation period was 9 days (range, 7 to 152 days). The median number of mesotherapy courses per infected patient before the diagnosis of infection was approximately 5 (range, 1 to 8) and did not differ significantly from the median number of mesotherapy courses per noninfected patient (4.8 versus 5.17, respectively; \( P = 0.76 \)). In the univariate analysis (Table 1), patients having Monday or Thursday visits, being the second in a series of patients receiving the injections on the same day, having cosmetic weight loss as a purpose, or having injections on the abdomen, upper leg, or hip had a higher incidence of NTM infection than patients without these risk factors. In the multivariate analysis, being the second patient of the day and having a higher rate of visits on Monday or Thursday than other patients remained the only independent risk factors for NTM infection.

The assessment of hygiene practices showed inappropriate cleaning of the automatic repetitive injector with nonsterile tap water. Indeed, the injector was often soiled with injection products leaking out of the syringe, which may encourage cleaning of the material with tap water and soap. No clear recommendation for the cleaning of this injector was given by the manufacturer. No other breach in hygiene practices, such as those for skin disinfection or hand hygiene, was observed.

**TABLE 1. Epidemiological analysis of risk factors for NTM infections**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate analysis</th>
<th>Multivariate analysis$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk factor present</td>
<td>No. of exposed patients</td>
</tr>
<tr>
<td>At least one visit on Monday or Thursday</td>
<td>Yes</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>26</td>
</tr>
<tr>
<td>At least one visit as the second patient of the day</td>
<td>Yes</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>73</td>
</tr>
<tr>
<td>Treatment for weight loss purpose</td>
<td>Yes</td>
<td>68</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>37</td>
</tr>
<tr>
<td>Injections on abdomen, upper leg, or hip</td>
<td>Yes</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>39</td>
</tr>
<tr>
<td>Rate of risk visits greater than ( P_{50} ) value$^a$</td>
<td>Yes</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>52</td>
</tr>
</tbody>
</table>

$^a$ The rate of risk visits was calculated as follows: \( \frac{\text{number of visits on Monday or Thursday}}{\text{total number of visits}} \times \frac{\text{number of patients}}{100} \). These rates are categorized into two classes of less and more than the median \( P_{50} \) value of 33.3%.

$^b$ Shown are the multivariate logistic regression estimates for the adjusted odds ratios (OR) and 95% confidence intervals (CI). Hosmer-Lemeshow statistic, 0.48.
The injected products were sterile, and disposable injection material was for single use. The tap water sample from the room where mesotherapy had been practiced since October 2006 showed 2,400 CFU/liter of \textit{M. chelonae}. Products used for mesotherapy treatment recovered from the clinic were negative for NTM. The PFGE patterns of \textit{M. chelonae} isolates from 11 mesotherapy patients and from tap water in the medical examination room showed 100% similarity indexes by Dice analyses and were considered indistinguishable (Fig. 2), while nonepidemiologically related control strains showed indexes of 60 to 89% similarity to the \textit{M. chelonae} outbreak isolate (Fig. 1A). No further cases occurred after the implementation of control measures.

Mesotherapy is a nonacademic health care-related practice involving subcutaneous injections of minute quantities of various medical drugs. First indicated for medical trauma treatment purposes, the practice was extended to accomplish various cosmetic and noncosmetic objectives, including fat reduction, body contouring, and treatment of rheumatism pain or psychoneurological disorders. This procedure is performed worldwide, mostly by physicians, and has gained wider popularity while being used mainly for esthetic fat reduction.

Although outbreaks of mesotherapy-associated skin complications have already been reported (2), this is the first time that a cluster of NTM infections is clearly related to a device prone to transmission during mesotherapy. Our study based on epidemiological and microbiological data demonstrated a relationship between infection and the incorrect use of injecting material. Although the practitioner concerned in the present outbreak respected standard precautions for hygiene and used only sterile products, evidence identified the automatic repetitive injector as the vehicle of transmission. Such an injection device is nonsterile material which is commonly shared among patients and re-used consecutively by the practitioner for different patients. The NTM contamination was likely to occur between two patient therapy sessions when the device was soiled during rinsing with contaminated nonsterile tap water. As the device was insufficiently dried before reuse, residual water on the surface could suffuse along the needle and then contaminate further injections. This hypothesis is supported by the findings in other studies describing a similar mechanism of NTM transmission related to the use of nonsterile water to disinfect devices used for discovertebral or plastic surgery (1, 3).

Data from epidemiological combined with microbiological molecular analyses provide strong evidence for contaminated tap water as a source of NTM infection. First, the risk factors of being treated as the second patient of the day, after the first tap water flow used to clean the injector, and having visits the day after clinic closure may be related to prolonged water stagnation in the pipe, favoring NTM multiplication. Second, the presence of similar NTM profiles, with \textit{M. chelonae} as the predominant NTM species, for samples from tap water and from subcutaneous abscesses of the patients confirms this environmental source. In addition, comparison with control strains demonstrated the highly discriminative power of the PFGE method to identify clonal origin. Other reports have suggested the potential role of tap water in NTM infection during nonmedical practices such pedicures or other cosmetic care (7, 10). Recently, an outbreak of \textit{Mycobacterium abscessus} wound infection among “lipotourists” from the United States who underwent abdominoplasty was reported, suggesting a link with tap water used to irrigate the wound (4).

Despite some flaws, such as the possible omission of infected patients (less than 50% of potentially exposed patients responded to our mailing), the few cases with undocumented microbiological data, and the temporal discrepancy between the occurrence of cases and the finding of NTM in the environment, this outbreak investigation highlights that a failure in the disinfection of injecting material may generate severe infections with NTM related to nonregular medical care. Efforts should focus on informing practitioners of hygiene practices.

![A] A dendrogram based on the PFGE patterns of 20 \textit{M. chelonae} isolates (11 from mesotherapy patients, 1 from tap water in the medical examination room, and 9 control strains), prepared using the Dice-unweighted-pair group method with arithmetic means. The letters of the corresponding lanes in panel B are indicated to the right. (B) PFGE patterns of \textit{M. chelonae} genomic DNA digested with XbaI. Lanes: A, \textit{M. chelonae} control strain 4; B to L, \textit{M. chelonae} isolates from mesotherapy patients; M, \textit{M. chelonae} isolate from tap water in the medical examination room; N, lambda ladder gel marker. Molecular sizes (in kilobases) of the DNA standards are given to the right of the gel.
based on appropriate guideline recommendations, especially for invasive procedures in nonhospital settings. In addition, guidelines for the use and disinfection of the automatic repetitive injectors are warranted.

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REFERENCES


