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Hypersensitivity Pneumonitis Associated with Environmental Mycobacteria

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Case Presentation

A 57-year-old nonsmoking auto-parts machine operator presented in 1995 because of shortness of breath on exertion, cough, fatigue, and chest congestion. In his job he operated a machine that cut metal parts using a semisynthetic metalworking fluid (Figure 1) that was collected and recycled through large tanks holding > 1,000 gal fluid. A chest radiograph showed a generalized increase in interstitial markings. He was treated with empiric antibiotics on two occasions. Later, his treating physician suspected occupational asthma due to exposure to oil mist, and asked the employer to remove him from exposure to metalworking fluids. Symptoms recurred when he was later reexposed to metalworking fluids, and further permanent decrement in his lung function occurred. Investigation of his workplace showed that five of six large reservoirs of metalworking fluids (cutting oils) grew Mycobacterium chelonae (or Mycobacterium immunogenum), an organism previously associated with outbreaks of hypersensitivity pneumonitis in automaking factories. His lung function remained stable after complete removal from exposure. The employer, metalworking fluid supplier, union, and the National Institute for Occupational Safety and Health were notified of this sentinel health event. No further cases have been documented in this workplace.

Key words: atypical mycobacteria, extrinsic allergic alveolitis, hot tub, hypersensitivity pneumonitis, metalworking fluids, Mycobacterium chelonae, Mycobacterium immunogenum, nontuberculous mycobacteria, occupational lung disease. Environ Health Perspect 113:767–770 (2005). doi:10.1289/ehp.7727 available via http://dx.doi.org/[Online 10 February 2005]

A previously healthy man working as a machine operator in an automotive factory developed respiratory symptoms. Medical evaluation showed abnormal pulmonary function tests, a lung biopsy showed hypersensitivity pneumonitis, and his illness was traced to his work environment. His physician asked the employer to remove him from exposure to metalworking fluids. Symptoms recurred when he was later reexposed to metalworking fluids, and further permanent decrement in his lung function occurred. Investigation of his workplace showed that five of six large reservoirs of metalworking fluids (cutting oils) grew Mycobacterium chelonae (or Mycobacterium immunogenum), an organism previously associated with outbreaks of hypersensitivity pneumonitis in automaking factories. His lung function remained stable after complete removal from exposure. The employer, metalworking fluid supplier, union, and the National Institute for Occupational Safety and Health were notified of this sentinel health event. No further cases have been documented in this workplace.

No specific interventions were made in the workplace with regard to the metalworking fluids, although a plantwide program of reduction of fluid aerosol exposures for all workers was already in progress. Several months later the patient had an uncomplicated myocardial infarction, and after 3 months returned to work with continued exposure to metalworking fluids. Three years later, in 2000, he noted daily nasal congestion associated with work, and worsening dyspnea reaction was negative for sequences found in Mycobacterium chelonae. The patient’s treating pulmonologist suspected that the hypersensitivity pneumonitis was due to bacteria growing in the metalworking fluid. Serum-prefecting antibodies to a standard panel of nine substances, including bacteria, several fungi, and pigeon serum, were all negative. The pulmonologist gave the patient a brief note for his employer restricting exposure to metalworking fluids; the company physician misinterpreted the message as indicating that the patient had chronic obstructive pulmonary disease made worse by metalworking fluid exposures, and changed his work location but did not fully restrict him from exposure to metalworking fluids.

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on exertion. His pulmonologist repeated lung function tests, which showed a further decline in diffusing capacity to 44% predicted (Table 1), and a thin-section computed tomography (CT) scan of the chest (Figure 3) showed "ground glass" opacities indicating interstitial lung disease and mild bronchiectasis. A visit to the patient's residence by a treating physician trained in occupational and environmental medicine did not reveal any exposures suggestive of contributing to his hypersensitivity pneumonitis.

With the assistance of the county health department, samples of metalworking fluid were obtained for culture from the large reservoir supplying metalworking fluids to the patient's work area. Standard bacterial and fungal counts were below the level of detection of 10 organisms/mL, unusually low for industrial metalworking fluids, which are usually contaminated by microorganisms. Stain of the centrifuged fluid pellet for acid-fast bacilli was qualitatively "very high," and culture grew 1.6 × 10^7 mycobacteria/mL, which were identified as M. chelonae. This mycobacterium, although similar to the M. chelonae-abscessus group, has been proposed as a new species, Mycobacterium immunogenum (Brown-Elliott and Wallace 2002). Additional, separate fluid specimens were sent to another laboratory, which cultured and identified the same organism. Samples of fluid from five reservoirs, a blank of "virgin" metalworking fluid, and a tap water control were for a third time tested and showed >2,500 mycobacteria/mL, with single-stranded conformational polymorphism analysis showing M. immunogenum in the used fluid samples, and none in the virgin fluid or tap water. Endotoxin, the active agent in the walls of gram-negative bacteria, was measured in the five samples from the five reservoirs at from 2.4 × 10^2 to 2.5 × 10^4 endotoxin units per milliliter of fluid by the Limulus assay. Based on these findings, the patient was removed completely from exposure to metalworking fluids.

The treating occupational physician scheduled a meeting with the plant occupational physician, industrial hygienists, and the contracting supplier of the metalworking fluids to recommend a) a survey of symptoms and chest X-rays of workers exposed to metalworking fluids to identify any additional cases and b) testing of all metalworking fluid reservoirs in the facility for mycobacteria. In addition, the disease occurrence was reported to the Division of Respiratory Disease Studies of the National Institute for Occupational Safety and Health (NIOSH) and the New York State Department Occupational Lung Disease registry.

**Discussion**

Metalworking fluids may be pure petroleum oils ("straight oils"), emulsions of petroleum in a water base (semisynthetic fluids), or emulsions of synthetic oils in water (synthetic fluids). Because they contain biologically available carbon (in the form of lipids) and water, metalworking fluids routinely sustain microbial growth, but excess growth degrades the fluids and leads to loss of usefulness. Thus, standard use of these metalworking fluids in industry often includes routine testing for bacteria counts (without identification of all organisms) and the use of microbicides with the objective of suppressing, although not necessarily sterilizing, microbial growth.

A variety of respiratory illnesses have been reported to be associated with occupational inhalation of metalworking fluids, including bronchitis, asthma, and lipoid pneumonia (Cullen et al. 1981; Kennedy et al. 1989; Leigh and Hargrave 1999), and their toxicology has recently been reviewed (Gordon 2004). Currently there is no specific Occupational Safety and Health Administration (OSHA) standard for metalworking fluids, although guidance in prevention of health hazards is provided in an NIOSH criteria document.

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Table 1. Patient’s pulmonary function laboratory data.

<table>
<thead>
<tr>
<th>Date</th>
<th>FEV1 (%)</th>
<th>FVC (%)</th>
<th>DLCO (%)</th>
<th>Rest O₂ saturation (%)</th>
<th>Exercise O₂ saturation (%)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 1985</td>
<td>2.70 (88)</td>
<td>3.0 (70)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Preplacement work exam before onset of symptoms</td>
</tr>
<tr>
<td>January 1996</td>
<td>2.77 (94)</td>
<td>3.47 (95)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>After onset of symptoms; spirometry before the work week</td>
</tr>
<tr>
<td>January 1996</td>
<td>2.98 (101)</td>
<td>3.40 (93)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>After shift at end of work week</td>
</tr>
<tr>
<td>September 1997</td>
<td>—</td>
<td>— (67)</td>
<td>96</td>
<td>96</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>January 1998</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>April 2000</td>
<td>2.52 (89)</td>
<td>3.14 (89)</td>
<td>9.8 (44)</td>
<td>92</td>
<td>89</td>
<td>More symptomatic</td>
</tr>
<tr>
<td>June 2000</td>
<td>1.88 (60)</td>
<td>2.55 (65)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Symptoms stable</td>
</tr>
<tr>
<td>April 2004</td>
<td>2.42 (83)</td>
<td>3.15 (92)</td>
<td>11.5 (45)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: —, not measured; DLCO, diffusing capacity for carbon monoxide (percent predicted); FEV1, forced expiratory volume in 1 sec in liters (percent predicted); FVC, forced vital capacity in liters (percent predicted).
Gaenser 1997), most frequently working fluids containing nontuberculous bacteria have been found in workplaces with metalworking fluids. However, at present, this recommendation has not been the subject of rule making. Hypersensitivity pneumonitis associated with metalworking fluids was first described in 1995 (Bernstein et al. 1995). Since then, numerous outbreaks have been described, associated with inhalation of aerosols of water-containing metalworking fluids (reviewed in Kreiss and Cox-Gaenser 1997). Prevention efforts have focused on reduction of inhalation exposures by workplace modifications that reduce generation of aerosols or improve dilution and ventilation of workplace air, and one follow-up study has documented successful remediation (Bracker et al. 2003).

More recently, outbreaks of this condition have been found in workplaces with metalworking fluids containing nontuberculous mycobacteria (CDC 2002; Kreiss and Cox-Gaenser 1997), most frequently M. immunogenum. Detection of these mycobacteria requires special laboratory culture and identification techniques that are not included in routine microbiologic testing of industrial metalworking fluids, such that their identification requires knowledge of their potential for growth and the ability to perform special testing.

During recent years, association of hypersensitivity pneumonitis disease with a different species, Mycobacterium avium complex (MAC), from hot tubs, whirlpool baths, and spas has also been identified, sometimes referred to as “hot tub lung” (Capelluti et al. 2003; Grimes et al. 2001; Rickman et al. 2002; Scully et al. 1997). In these hot water bathing tubs, water may be agitated by powerful jets of air or water that produce bubbles and hence aerosols of water droplets. MAC grows well in the high water temperature of the indoor hot tub. The combination of MAC organisms’ growth and jet aerosolization and subsequent inhalation of large amounts of MAC presumably leads to the development of this disease. Hot tub lung appears to be hypersensitivity pneumonitis to MAC aerosol rather than a direct infection of the lung, although this subject is still a matter of debate (Aksamit 2003; Embil et al. 1997). Interestingly, there have been no documented cases of hot tub lung with outdoor hot tubs.

In hot tub lung, pulmonary function tests were mainly restrictive with occasional obstruction (Anonymous 2000; Kahana and Kay 1997; Khoor et al. 2001; Mangione et al. 2001; Mery and Horan 2002; Rihawi et al. 2004). Chest radiography shows diffuse infiltrates, and high-resolution CT of the chest shows ground glass opacities and micronodules (Pham et al. 2003). Sputum culture was positive for MAC in about 70% of the patients; transbronchial biopsy and bronchoalveolar lavage cultures increased the yield further (Anonymous 2000; Kahana and Kay 1997; Khoor et al. 2001; Mangione et al. 2001; Mery and Horan 2002). Hot tub water usually grows MAC. The histopathologic findings reveal discrete nonnecrotizing granulomas with centrilobular and bronchiolocentric distribution. The granulomas described in hot tub lung were more exuberant and well formed than those seen in typical cases of hypersensitivity pneumonitis from other causes.

There is no standard approach to treatment of hot tub lung. Case reports describe significant improvement with removal from exposure to the hot tubs. Oral corticosteroids, antimycobacterial therapy, or both have also been used. The expected course of this disease after the above measures is recovery without relapse. Measures proposed as being helpful in prevention include better ventilation of the hot tub room, frequent cleaning of the hot tub, frequent change of hot tub water, and use of disinfectants such as chloramines, bromine, and ultraviolet light. These measures are similar to those usually proposed for prevention of hypersensitivity due to exposure to mycobacteria in metalworking fluids.

**Conclusions**

Environmental mycobacteria have been associated with a serious lung condition, hypersensitivity pneumonitis, when inhaled as part of liquid droplet aerosols generated from large volumes of liquids serving as a culture medium. These organisms are found commonly in nature and are able to grow in sufficient quantities to cause disease. The case reported here involved an occupational source of such an exposure (aerosolized metalworking fluid in a machining environment), although aerosols containing mycobacteria have been described in other settings as well (aerosolized water from hot tubs). For this reason, specific investigation of sources of aerosols in the work or home environment of patients with this condition should consider the growth of mycobacteria as one of the potential sources of disease. As with other causes of hypersensitivity pneumonitis, removal from exposure and remediation of exposure are the first approaches to treatment.

**REFERENCES**


