Hypersensitivity Pneumonitis Secondary to Klebsiella oxytoca*  
A New Cause of Humidifier Lung  
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A 30-year-old woman developed recurrent episodes of fever, dyspnea, and nonproductive cough after repeated exposure to a home humidifier. The diagnosis of hypersensitivity pneumonitis was confirmed by detection of serum-binding antibodies at a significant titer to Klebsiella oxytoca colonizing the humidifier water but not to other potential antigens. This represents a newly recognized cause of hypersensitivity pneumonitis related to exposure to K oxytoca contaminating a commercially available ultrasonic cold air home humidifier. The potential role for these frequently used home humidifier devices in unexplained pulmonary illness is emphasized. (Chest 1993; 104:627-29)

Hypersensitivity pneumonitis (HP) is an immunologically mediated lung disease resulting from repeated exposure to organic dusts or other environmental antigens. Despite the diversity of implicated antigens, the resultant clinical syndromes are strikingly similar. We report a case of HP as a result of exposure to a previously undescribed but widely prevalent environmental antigen, Klebsiella oxytoca, colonizing an ultrasonic cold air home humidifier.

CASE REPORT

A 30-year-old previously healthy woman was evaluated for recurrent episodes of dry cough, dyspnea, and fever. Approximately eight weeks prior to evaluation, the patient's 2-year-old son developed cough and coryza requiring symptomatic treatment with acetaminophen and a room humidifier. Over the next month, the patient was hospitalized on three occasions with fever, dyspnea, and nonproductive cough.

At the time of the initial hospital admission, there was radiographic evidence of bilateral infiltrates and hypoxemia (Po2, 65 mm Hg). After three days of treatment with intravenous erythromycin, her condition improved and she was discharged from the hospital. A second recurrence of symptoms led to rehospitalization and therapy with intravenous doxycycline. Again, there was rapid clinical improvement and she was discharged from the hospital after only a few days of therapy. The third recurrence of these symptoms led to more extensive evaluation. An arterial blood sample showed a pH of 7.45, Pco2 of 30 mm Hg, and Po2 of 60 mm Hg. The chest radiograph (CXR) demonstrated bilateral interstitial infiltrates and pulmonary function tests (PFT) revealed a mild restrictive ventilatory pattern (FVC, 74 percent; TLC, 77 percent; Dco, 53 percent predicted). The WBC was 23.4/L with 91 percent polymorphonuclear leukocytes and 4 percent lymphocytes (no eosinophils). The serum IgE level was 2.0 U/ml (normal level [nl], 1 to 180) and angiotensin-converting enzyme level was 31 U/ml (nl, 30 to 140). The patient underwent bronchoscopy with bronchoalveolar lavage (BAL). The lavage fluid showed 70 percent neutrophils, 20 percent lymphocytes, and 10 percent macrophages. Routine cultures grew only normal flora. Treatment included oxygen and intravenous penicillin with rapid defervescence and the patient was discharged from the hospital three days later. Following one week of empiric corticosteroid therapy, there was complete resolution of symptoms.

Two weeks later, CXR showed clearing of the infiltrates. That night the patient turned on a home humidifier in her son's room. Four hours later she noted the sudden recurrence of dyspnea, cough, and fever. She was transferred to this hospital for further evaluation.

The patient was a nonsmoker without history of atopy or asthma and no exposure to pets or travel. With detailed questioning, she recalled exposure to the home humidifier prior to each of the previous episodes of respiratory illness. The patient appeared to be in mild respiratory distress. The temperature was 38.5°C, the blood pressure was 150/90 mm Hg, the pulse was 120 (min -1), and the respirations were 35 (min -1). The lungs revealed crackles at both bases without wheezes or rhonchi. Results of the remainder of the examination were normal.

Initial CXR showed bilateral interstitial infiltrates (Fig 1A, left) as well as hilar adenopathy. An arterial blood sample taken on oxygen at 2 L/min revealed a pH of 7.49, PCO2 of 35, and Po2 of 76. The WBC was 23.4 cells per microliter with 62 percent polymorphonuclear leukocytes and 36 percent bands. The hemoglobin, serum chemistries, electrolytes, and urinalysis values were normal.

Based on the temporal relationship to the use of the home humidifier, the patient was given a presumptive diagnosis of HP and was treated with oral corticosteroids. Serum was obtained for evaluation of precipitating antibodies. Bacterial and fungal cultures of the humidifier fluid revealed Pseudomonas and Klebsiella species, and a few colonies of Aureobasidium pullulans. The patient was counseled as to the nature of her disease and the humidifier was removed from the home. Four days after hospital admission, the patient was discharged in markedly improved condition. The FPTs prior to hospital discharge showed FVC of 3.35 L (83 percent), FEV1 of 2.88 L (87 percent), TLC of 4.62 L (76 percent), and Dco of 21.13 (78 percent).

Evaluation of the patient's serum by enzyme immunoassay demonstrated significant antibody binding to concentrated humidifier fluid. The patient's serum was also tested against a panel of standard HP antigens (a Penicillium species, two Aspergillus species [As fumigatus and As niger], and three thermophilic actinomycetes species [Thermoactinomyces vulgarus, T candidus, and T sacchari], and Microsporidia fueni) without evidence of primary binding. Finally, specific cultures for each organism grown from the humidifier fluid were tested against the patient's serum. Significant antibody binding to K oxytoca was demonstrated at a titer of 1:640 but to no other organism, including Au pullulans. Increased binding to K oxytoca was not demonstrated in three laboratory controls. A diagnosis of HP secondary to exposure to K oxytoca colonizing a home humidifier was established. After six months, the patient remains well. Repeated CXRs have shown clearing of infiltrates and the hilar adenopathy (Fig 1B, right).

DISCUSSION

This case represents the first documented report of HP potentially occurring from a common water-borne organism, K oxytoca, that had contaminated a home humidifier. The diagnosis, we believe, is confirmed by the classic history and rapid clinical and radiologic improvement following removal from the antigen, and the detection of serum-binding antibodies at significant titer to this organism isolated from the humidifier fluid. Although reproduction of
symptoms by inhalation challenge would be confirmatory, we were concerned that future antigen exposure could result in chronic lung injury and we elected to forego such a challenge. While the possibility exists that an organism which failed to grow in culture could be potentially implicated, we believe that the high titer of binding to K oxytoca in this patient's serum and lack of serum binding to a standard panel of HP antigens (and other antigens from the humidifier fluid) provide compelling evidence that K oxytoca was indeed the cause of HP in this case.

Laboratory evaluations in this patient yielded results characteristic of HP with the exception of two features. The PFT abnormalities detected, mild restriction, and a reduced Dco during the acute presentation have been well described. The leukocytosis with leftward shift is also seen frequently in acute HP usually without eosinophilia as in this patient. A normal serum IgE level is also the rule; however, concentrations of IgG, IgM, and IgA immunoglobulins are often elevated.

Two laboratory features of this case were atypical, however. First, hilar adenopathy has rarely been documented together with the acute interstitial infiltrates in these patients, although a "hilar haze" pattern has been described previously. Hilar adenopathy has been described in mushroom worker's lung and other isolated reports of patients with well-documented HP in the literature. Despite the rarity of hilar adenopathy, the remainder of this patient's radiographic findings, including patchy diffuse parenchymal densities (primarily in the lower lobes) without pleural effusion, were consistent with acute HP. The second atypical feature of this case was the BAL finding reported from the referring institution. Although this patient did demonstrate an elevation in lung lymphocyte values, this increase was not as high as previous studies have suggested. A contributing factor may have been the timing of the procedure in relation to the onset of symptoms. Unfortunately, details of this BAL such as lavage volume and method of processing were not available. These factors have been demonstrated to alter the BAL cell count results.

Finally, the atypical laboratory features could be related to this bacterial antigen, which may only be a rare cause of HP. While the implication of a bacterial antigen in HP may be unusual, it certainly is plausible, requiring only initial exposure and sensitization and subsequent inhalation of sufficient concentration of aerosolized antigen.

Several authors have examined patients with HP whose disease is related to the exposure to contaminated forced air systems, including home humidifiers, air conditioners, and cool mist vaporizers. It is not surprising that these systems are frequent causes of HP because they often provide pools of stagnant water that are prone to microbial colonization and the aerosol systems effectively disperse the offending antigens in droplets of appropriate size (0.5 μm to 3 μm) to reach the distal lung. These illnesses are commonly referred to as humidifier lung or humidifier fever. The most frequently implicated organisms include the following: thermophilic actinomycetes (T vulgaris, T candidus); fungi such as Penicillium species, Cephalosporium species, As fumigatus and As niger; and Am pullulens; and certain amebas such as Naegleria gruberi. The implication of K oxytoca in this case of humidifier lung may represent a new aspect of the spectrum of HP.

Finally, this case underscores the potential hazards of home ultrasound cool mist vaporizers that are not generally appreciated. Appropriate cleaning procedures and periodic drainage of these devices are required to prevent the
microbial colonization that occurred in this patient. When not maintained properly, they can become colonized by multiple organisms with potentially pathogenetic antigens that are readily aerosolized when the device is activated.

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REFERENCES

Sleep-related Eating Disorder as a Cause of Obstructive Sleep Apnea*

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A patient with obesity resulting from sleep-related eating disorder demonstrated signs and symptoms of obstructive sleep apnea (OSA). Incarceration restricted access to food during the night, leading to weight loss and clinical improvement. Release from prison allowed recurrence of unrestricted sleep-eating, recurrent obesity, and documented OSA. Successful treatment of sleep-related eating disorder can result in improvement in coexisting OSA.

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OSA = obstructive sleep apnea

Sleep-related eating disorder is best defined as the nocturnal occurrence of involuntary, often disinhibited eating during sleep; the subject is either totally unaware of the behavior or behaves in an involuntary, automatic manner despite awareness of the nocturnal eating behavior. In most reports of the syndrome, the majority of subjects are overweight based on body mass index (BMI).1,2 Despite the well-known relationship between obesity and obstructive sleep apnea (OSA), to our knowledge, there has been no previous documentation of a relationship between nocturnal sleep-related eating disorder, consequent obesity, and development of OSA. We therefore report a patient with significant obesity on the basis of nocturnal sleep-related eating, who developed OSA. Clinical improvement of sleep apnea correlated with cessation of nocturnal eating, achieved through a drastic yet effective form of behavior modification.

CASE REPORT

The patient is a 34-year-old white man without significant medical problems or preexisting sleep disorders. There was no history of childhood sleepwalking or night terrors, nor was there a family history of parasomnias. He was involved in a motorcycle accident in 1979, suffering nasal and mandibular injury. After recuperation, the patient was noted to snore more heavily than before the accident, and would intermittently awaken with a snort. Witnessed apneas were not observed. Many of these awakenings were associated with the patient walking into the kitchen and gorging himself on food. Specifically, he would usually drink ½ to 1 gallon of milk at a time, with copious quantities of cookies, breads, or leftovers. He would then return to bed and fall asleep. This behavior was initially repeated two to three times per night. He reported no recollection of any nocturnal binging, and became aware of the nocturnal activity by finding bits of food in his bed or crumbs in his beard or by being observed by his wife. The sleep-eating behavior did not exist prior to the motorcycle accident.

Over the subsequent year, the patient gained 40.5 to 45 kg, which was attributed to nocturnal eating. His daytime caloric intake actually decreased in an attempt to lose weight. During this time, his wife noted progressively heavy snoring, now accompanied by episodes of struggling to breathe during sleep, lasting approximately 30 s and terminated by gasping or choking. These episodes would frequently be associated with awakenings and sleep-eating.

In 1981, the patient was incarcerated for 1.5 years, during which time he lost 36 kg. The weight loss was believed to be the direct result of the inaccessibility to food during nocturnal awakenings while the patient was in his prison cell. On release from prison, the patient's wife noted decreased snoring and a significant reduction in witnessed apneas. The nocturnal sleep-eating persisted, however, still associated with nocturnal binging, sleep-onset behavior while eating, and no recollection by the patient. He gradually gained approximately 40 kg, and demonstrated resumption of severe snoring and witnessed apneas.

In 1991, the patient presented to the Rhode Island Hospital Sleep Disorders Center for evaluation of the sleep-eating, snoring, and witnessed apneas. He had been diagnosed as having hypertension during the previous five years. He denied nocturnal alcohol use or illegal drug abuse. He also denied significant daytime hypersomnolence, but noted an eight- to nine-month history of impotence. The BMI at the time of evaluation was 37.5 kg/m.2

The patient underwent full polysomnography to better evaluate his sleep disorder. Monitoring was conducted using 2-channel EEG, electro-oculogram (EOG), and submental, intercostal, and anterior tibialis electromyogram (EMG) by surface electrodes. Airflow was detected using nasal and oral thermistors. Arterial oxygen saturation was recorded with a pulse oximeter, and respiratory effort was detected by impedance bands around the chest and abdomen. The sleep study demonstrated OSA. The apnea-hypopnea index was 25 episodes per hour, associated with oxygen desaturation to 81 percent. There was no evidence of seizure activity by the two-channel EEG, nor was significant nocturnal myoclonus or REM-associated behavior observed. No abnormal nocturnal behavior was noted during the study.

The patient refused nasal continuous positive airway pressure (CPAP), and instead underwent correction of nasal septal deviation.