Symptomatic Coccidioidomycosis following a Severe Natural Dust Storm*

An Outbreak at the Naval Air Station, Lemoore, Calif.

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Eighteen newly diagnosed cases of symptomatic coccidioidomycosis developed two to four weeks following exposure to a severe natural dust storm. The population at risk consisted of 26,000 residents of the San Joaquin Valley with access to health care at the Naval Hospital, Lemoore, Calif. Eight patients were white, and ten were nonwhite. The number of cases per 100,000 was estimated to be 36 for the white group and 254 for the nonwhite group. The disease was disseminated in four patients, and all were from the nonwhite group. One patient with disseminated disease, a black man, died. These data suggest that nonwhites may be relatively more susceptible to acquiring primary disease, in addition to developing disseminated disease. Dust storms of this magnitude must be considered a threat to health for populations living within areas endemic for coccidioidomycosis.

The fungus, Coccidioides immitis, is endemic to the lower Sonoran life zone, including the San Joaquin Valley. This fungus can cause either asymptomatic infection or symptomatic respiratory disease ("valley fever"). Occasionally, the infection disseminates, producing significant morbidity and mortality. Previous reports have substantiated that the Naval Air Station at Lemoore, Calif, lies within the area endemic for C immitis, with an annual incidence of coccidioidal infection approximating 1.5 percent.

Materials and Methods

Eighteen new cases of symptomatic valley fever were diagnosed at the Naval Hospital, Lemoore, Calif, following a severe natural dust storm that occurred from Dec 20 to 22, 1977. This storm arose from the southeast near Bakersfield, Calif, an area of high endemicity. The storm lasted approximately 48 hours. Visibility during the storm decreased to approximately 0.25 mile. The wind velocity rose to 34 mph. The dust was ubiquitous. It seeped through windows, depositing a layer of dust on car seats and household furniture, making it virtually impossible to avoid exposure to the dust. Measurement of the total suspended particulates from samples of air taken at Lemoore, Calif, on Dec 21, 1977 revealed 2,434 μg of particulate matter per cubic meter. This compares with a yearly average measurement for this area of 120 μg/cu m to 140 μg/cu m (Kings County Air Pollution Control District, personal communication, December 11, 1978). For comparison, Primary National Ambient Air Quality Standards call for a maximum level of total suspended particulates of 250 μg/cu m.

The Naval Air Station at Lemoore, Calif, is located in the central part of the San Joaquin Valley, 35 miles south of Fresno, Calif. The Naval Hospital at Lemoore, Calif, serves approximately 20,500 dependents and retired individuals. One-third of this population is under 15 years of age. There are 5,558 individuals on active duty who are attached to the Naval Air Station. Whites comprise 84 percent of the population on active duty, and nonwhites comprise 16 percent. The nonwhite racial distribution is as follows: blacks, 7 percent; Filipinos, 5 percent; and other racial groups (including Oriental, Spanish-American, and native American), 4 percent. The precise racial breakdown of dependent and retired populations is unknown but is thought to approximate that of the population on active duty.

Criteria for Inclusion in the Study

The criteria for inclusion of patients in the group under study were as follows: (1) all patients had a history of direct contact with the dust storm; (2) all patients developed symptoms within the known period of incubation for valley fever (one to four weeks); (3) all patients, except two patients with disseminated disease, had positive cutaneous reactions to either coccidioidin or spherulin; (4) all patients, except one (who declined to have a chest x-ray film), had abnormalities on the chest x-ray film that were consistent with pneumonia due to coccidioidomycosis; and (5) all patients had serologic evidence of active coccidioidal infec-

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tion, and in the majority of cases, both precipitin tests and immunodiffusion serologic tests were positive.

RESULTS

In all 18 cases (nine male and nine female patients), symptoms of valley fever developed within two to four weeks after exposure to the dust storm. Initial symptoms generally consisted of low-grade fever, nonproductive cough, fatigue, and pain in the chest. Eight patients were white, and ten patients were nonwhite (two blacks, two Mexican-Americans, one Oriental, four Filipinos, and one Samoan). There were four cases of disseminated disease (three men and one woman), all in nonwhites (one black, who died of fulminant disseminated disease; one Mexican-American; one Filipino; and one Oriental). The number of cases per 100,000 persons is estimated to be 36 for the white group and 254 for the nonwhite group. Sixteen of the 18 patients were between 20 and 49 years of age. The remaining patients were a 15-year-old boy and a 62-year-old man, both whites. There were no pediatric cases.

Cultures of sputum that were positive for C. immitis were obtained from only three patients; two had disseminated disease, and one had localized pulmonary involvement. The majority of patients were not able to produce adequate specimens of sputum.

Five patients initially had erythema nodosum, and one patient exhibited a maculopapular eruption. None of these cases was disseminated.

Nine of our patients had blood of group O (two with disseminated disease), four had blood of group A (one with disseminated disease), and three had blood of group B (one with disseminated disease). One patient had blood of group AB and did not have disseminated disease.

CASE REPORTS

The following case reports illustrate the unusual manner in which disseminated disease can occur.

CASE 1

A 35-year-old black man came to the Naval Hospital at Lemoore, Calif, in early February 1978, with a one-month history of progressive cough, myalgia, severe headache, pain in the neck, a 9-kg (20-lb) loss of weight, and accompanying anorexia. Years before, he had received one year of therapy with isoniazid for tuberculin skin test conversion. A right middle lobe infiltrate was noted on his chest x-ray film, and the patient was begun on intravenous therapy with methicillin on the basis of a Gram stain of sputum that was suspicious for staphylococci. His respiratory status further deteriorated. Cutaneous tests with sphenin and Tricophyton were negative. Cocccidioidal serologic samples were drawn. The patient was transferred to the Naval Regional Medical Center at Oakland, Calif, for further diagnostic work-up.

At the time of admission to the Naval Regional Medical Center, the patient appeared to be in moderate distress, complaining of pain in the chest, head, and neck, with a temperature of 39.4°C (103°F), pulse rate of 150 beats per minute, and blood pressure of 125/90 mm Hg. He was fully oriented. There was minimal mucosal rigidity, with moderate discomfort on passive range of movement of the head. Decreased breath sounds were noted over both pulmonary bases, with associated rales. Cardiac examination revealed a regular tachycardia with an S1 gallop. The edge of the liver was palpable 2 cm below the right costal margin.

Laboratory data on admission included a white blood cell count of 15,000/cm3, with 17 percent eosinophils. The hematocrit reading was 29 percent, the platelet count was 60,000/cm3, and the erythrocyte sedimentation rate was 70 mm/hr. The prothrombin time and partial thromboplastin time were normal. The findings from urinalysis were unremarkable. The results of tests of hepatic function were normal, except for a moderate elevation of the concentration of alkaline phosphatase at 180 IU/L. The levels of urea, nitrogen, creatinine, and electrolytes were normal.

On admission, analysis of arterial blood gas levels revealed a pH of 7.41, an arterial oxygen pressure of 56 mm Hg, an arterial carbon dioxide tension of 35 mm Hg, and a bicarbonate level of 22 mEq/L with the patient breathing room air. Gram stains and cultures of sputum were nondiagnostic. A chest x-ray film demonstrated diffuse pulmonary infiltrates in the right middle and lower lobes and the left lower lobe, with increased pulmonary vascular markings. Lumbar puncture was performed, which was normal. Precipitins to C. immitis antigens were present, and the coccidioidal immunodiffusion titer was positive at 1:32. Subsequently, C. immitis was grown from the blood, a concentrated specimen of urine, and the bone marrow.

The patient received a total of 76 mg of amphotericin B before this therapy was terminated because of acute renal deterioration. He was subsequently treated on an experimental protocol using intravenous therapy with miconazole; and after a short initial stabilization, his condition deteriorated rapidly. The patient developed hypercalcinia of unclear etiology, which responded to intravenous therapy with saline solution and furosemide. He later suffered cardiorespiratory arrest, coma, and progressive renal failure. The patient died on March 15, 1978.

At autopsy, the lungs were firm and contained multiple milliar abscesses that microscopically were replete with C. immitis. Grossly apparent abscesses were also present in the spleen and multiple lymph nodes. Microscopic foci were present in the liver, pleura, thyroid gland, heart, kidneys, and bone marrow. The brain was grossly unremarkable but contained microscopic abscesses in which no spherules were found. No cutaneous lesions were identified. Within the kidneys, definite glomerular and tubular changes were present, including glomerulosclerosis, tubular atrophy, chronic interstitial inflammatory infiltration, and occasional small foci of calcification with granulomas containing spherules.

CASE 2

A 48-year-old woman of Japanese descent came to the outpatient clinic on Jan 12, 1978, complaining of headaches, intermittent fever to 38°C (100.4°F) orally, chills, and a nonproductive cough. The findings from physical examination were normal, except for mild respiratory difficulty. The chest x-ray film showed a right perihilar and upper lobe interstitial infiltrate. A cutaneous test with sphenin was negative, but the serum complement-fixation test for coccidioidomycosis was positive at a dilution of 1:2.

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The patient was treated with rest and decongestants, and her condition improved slightly. She returned on Feb 6, 1978, with a weeping, erythematous fungating lesion of the right external ear and smaller but similar lesions on the right side of the forehead, the right anterior portion of the chest wall, and left thigh. The patient had been treated by a dermatologist with antibiotics and local care of the skin, without improvement. Disseminated coccidioidomycosis was suspected and was confirmed by cutaneous biopsy. A serologic test by immunodiffusion was positive at this time at a dilution of 1:512. A bone scan was abnormal in the areas of the cutaneous lesions only. The findings from analysis of the cerebrospinal fluid and urinalysis were normal. A culture of sputum was positive for C immitis.

Therapy with amphotericin B was begun, and all areas of known disease resolved over a six-month period of treatment, with minimal cosmetic deformity. When therapy with the drug was stopped, the patient had received 3,111 mg of amphotericin B, the immunodiffusion titer had dropped to 1:16, and the patient's only symptom was chronic fatigue.

The other two patients with disseminated coccidioidal infection were a 40-year-old Mexican-American man and a 39-year-old Filipino man. In both patients the coccidioidal infection was disseminated only to the skin. Both patients were successfully treated with intravenous therapy with amphotericin B.

Discussion

A previous study alluded to soil or dust contaminated with C immitis as the "vehicle of natural infection." More recent epidemiologic studies at archaeological sites have confirmed the relationship between inhalation of fungus-contaminated soil and infection. Zoologists whose work brings them into contact with rodent burrows are also likely to become infected. Coccidioides immitis has been isolated from samples of air collected during dust storms. Smith and Beard stated in 1940 that "when susceptible human beings stir up dust in highly infected areas, veritable epidemics occur." Goldstein et al reported an epidemic of 75 cases of symptomatic pulmonary coccidioidomycosis among a group of men performing military maneuvers in an endemic area during World War II. These men were "subjected to miniature dust storms or 'dust devils' ... created by the movement of vehicles. . . ."

In the present study, there was a direct temporal relationship between the dust storm of Dec 20 to 22, 1977, and a marked increase in the incidence of symptomatic valley fever. For comparison, the monthly incidence of new cases of valley fever at the Naval Hospital at Lemoore, Calif, that were serologically diagnosed prior to and subsequent to the dust storm is shown in Figure 1.

The outbreak of dust storm-related coccidioidomycosis in January 1978 was not isolated to Lemoore, Calif, but involved a large area of the San Joaquin Valley and extended out of the endemic area into regions of northern California. In a recent symposium, Pappagianis reported 379 cases of primary coccidioidomycosis following this dust storm. These cases were diagnosed by serologic testing on samples referred to his laboratory in Davis, Calif, from a large area of central California. Of these cases, 4 percent were reported to have developed dissemination. No racial breakdown was given. Einstein, in the same symposium, commented that "... this represents our first experience with a known natural dust-borne outbreak." We suspect that the higher incidence of dissemination in our study (22 percent) was due to a larger percentage of non-whites in our population.

Dust storms of this magnitude must be considered a threat to health for populations living within endemic areas. It seems appropriate to advise individuals living within these areas to avoid going outdoors in dust storms unless necessary and, if necessary, to wear a protective mask to minimize infection as much as possible. The use of these devices has been previously recommended to protect construction workers excavating large areas of land in endemic sites and archaeological students at "digs."
It is well known that blacks and Filipinos have an increased tendency for disseminated disease following pulmonary infection. Gifford et al.\(^9\) calculated a rate of disseminated cases per 100,000 of the population at risk for various races. They found that Mexican-Americans were three times, blacks 14 times, and Filipinos 175 times as likely to have disseminated disease as whites; their respective death rates from the disease were 5, 23, and 192 times that of whites. In a ten-year series of autopsies, Huntington\(^14\) reported that Mexican-Americans were three times, blacks ten times, and Filipinos 14 times as likely to die of disseminated disease as whites. In their excellent review of coccidioidomycosis, Drutz and Catanzaro\(^14\) point out that there are no extensive studies of the relative susceptibility to coccidioidal dissemination among various Oriental populations. In a study by Sievers,\(^16\) the incidence of dissemination among Mexican-Americans approximated that of southwestern native Americans, with an incidence about three times that of whites. All of the patients with disseminated disease in our study were from the nonwhite group.

Although the size of the sample in our study is too small to make any definite conclusions, nonwhites appeared to be relatively more susceptible to developing primary disease, as well as disseminated disease, from exposure to the dust storm. As far as could be determined from historical data, there was no difference in the degree or duration of exposure to the dust storm between white and nonwhite groups. The higher incidence of symptomatic infection in nonwhites could not be explained by occupational differences or by differences in housing standards, hygiene, or nutritional status. Whereas it is well documented in the literature that dissemination is more likely to occur in nonwhites, to our knowledge, there are no previous data suggesting that nonwhites may be more likely to develop symptomatic primary disease.

We propose that especially susceptible racial populations residing in coccidioidal endemic areas should be advised of the following information: (1) a potentially serious endemic fungal disease exists; (2) an atypical or prolonged respiratory illness should lead them to seek medical attention early; and (3) excessive exposure to dust from natural dust storms or mechanical disruption of the soil should be avoided unless natural immunization has occurred, as determined by positive cutaneous tests.

A recent report\(^17\) has demonstrated a relationship between blood group B and dissemination. This blood group is reportedly more common in persons of black and Filipino ancestry. One out of three patients with blood group B in our series had disseminated disease. The size of the sample is too small to derive any conclusions, although this blood group had the highest rate of dissemination in our study.

It is interesting to speculate whether dissemination might have been avoided in the nonwhite group by early short-course therapy with amphotericin, with close monitoring for toxic effects. It is conceivable that such use of amphotericin could prove justifiable in terms of a risk-to-benefit ratio. To our knowledge, there are no reports in the literature describing such a prophylactic regimen.

Ajello\(^18\) estimated that there are 100,000 cases of coccidioidomycosis per year in the United States, with approximately 53 deaths annually. In spite of these impressive numbers, there has not been rapid advancement either in prophylaxis or therapy. A vaccine produced from spherules of *C. immitis* killed with formaldehyde solution (formalin) has been developed by Levine et al.\(^19,20\) and has been shown to be safe and effective in a variety of animals. Limited testing in humans also indicates that the vaccine is probably safe, but its protective efficacy has not yet been determined.\(^21\) Additional trials of human safety followed by efficacy studies are needed. Considering the scope of the problem, albeit regionalized, it would be reasonable to invest more research in these areas.

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REFERENCES


