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Symptoms associated with anthrax exposure: Suspected "aborted" anthrax

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Anthrax is a naturally occurring organism with a low incidence of infection. There are no known cases of human-to-human transmission. Bioterrorism-related anthrax in the United States has been seen in three high-risk groups: (1) postal workers, (2) politicians and their staffs, and (3) the press. It appears as though the bioterrorism-related anthrax cases of fall 2001 have been transmitted through the US Postal Service.

The authors present a case in which a person at high risk for anthrax exposure was inadequately treated and had symptoms that do not fall into any specific category of disease. It emphasizes the need for someone who has been started on prophylaxis for anthrax to complete a full 60-day course of treatment. It also shows the effectiveness of antibiotic therapy, even in those with high exposure to weaponized anthrax. Further, we would like to suggest that there may exist a new clinical entity of "aborted anthrax infection."

(Key words: anthrax, *Bacillus anthracis*, biological weapon, biological terrorism, biological warfare, biowarfare)

The *Bacillus anthracis*, or anthrax, spores we have seen in the United States since September 2001 have taken two forms: weaponized anthrax and conventional, nonweaponized anthrax. The spores of *B anthracis* have been sent to specific targets through the US Postal Service in the finely ground, "aerosolizable" form and also in the "clumpy," nonweaponized form.

This case presents a high-risk individual who was treated effectively after exposure to anthrax spores in a high-risk environment.

Report of case

An adult with no previous medical problems working as a postal inspector at a postal center involved in transferring letters known to contain anthrax[1] presented with complaints of cough, headache, and severe chest pain for 2 days. There was a remote history (1 month previous) of routine household fumigation. The cough was dry and nonproductive. The patient also had hot flashes, diaphoresis, chills, "body aches," and malaise. Mild photophobia was also present. No skin lesions were noted and the patient was afebrile. Initial chest radiograph raised the question of a widened mediastinum, an early sign of anthrax infection, while the computed axial tomography results were normal without signs of lymphadenopathy or hemorrhagic mediastinitis.

As an inspector for the US Postal Service, this patient evaluated the letter-sorting machine that processed a letter containing anthrax spores. Once the *B anthracis* spores were at the postal facility, but before the contamination was known, the spores were further spread in the workplace due to routine maintenance measures: "The use of compressed air to clean sorting machines may have contributed to the aerosolization and dispersion of *B anthracis* spores in the...facility."[1] In addition, as part of the investigation (and while wearing only a simple, store-bought face mask), the patient removed air filters in the area of contamination for evidentiary purposes. In the process of removing and changing these filters, the patient inhaled large quantities of dust particles. The patient also inspected about 10 packages at high risk for containing anthrax and for which culture results were still pending. This exposure was about 1 week before admission.

Three days after the initial exposure to the anthrax-contaminated machine, the patient's nose was swabbed for anthrax; the results were for epidemiologic reasons only. The patient was given a 10-day course of ciprofloxacin and sent home. The patient took the prophylactic antibiotic for 1 day and then missed 2 doses of the medication. Three days after the exposure, the patient had headaches and cough.

On the day of admission, the patient had worsening symptoms of cough and headache and complained of severe substernal chest pain, which appeared to be incapacitating. Although denying dyspnea, the patient did have worsening complaints of a dry hacking cough, hot flashes, diaphoresis, and chills. The patient's PO_2 level was 72.

The suspicion for anthrax was high due to repeated exposures and incomplete prophylaxis. Initial laboratory reports were normal with a leukocyte count of 5000 with 53% neutrophils, 36% lymphocytes, 8% monocytes, and 3% eosinophils.

The patient was admitted to the intensive care unit for presumptive anthrax and started on a regimen of ciprofloxacin,

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penicillin, and clindamycin hydrochloride. Narcotics were used successfully to alleviate severe chest pain. The patient's symptoms resolved over 2 days and the patient was subsequently discharged to complete a 60-day course of ciprofloxacin monotherapy. Blood culture results (obtained after ciprofloxacin prophylaxis was started) indicated no growth of the disease.

Within days of discharge from the hospital on ciprofloxacin monotherapy, the patient began to complain of paroxysmal chest pain and dyspnea. The patient also complained of continued malaise and diaphoresis. The patient's monotherapy was changed from ciprofloxacin to doxycycline but symptoms persisted and worsened.

One month after the initial hospital admission, the patient was readmitted for these symptoms. Repeat evaluation revealed continued hypoxia with a PO_2 level of 67, results for a ventilation perfusion scan were negative, erythrocyte sedimentation rate was elevated to 35, and there was small pleural effusion. There was also a suspicion of lymph node calcification in the mediastinum based on results of a computed tomographic scan.

The chest pain and dyspnea, along with intermittent fevers up to 39.2° C (102.6° F), persisted until the patient was given triple-antibiotic therapy with ciprofloxacin, clindamycin hydrochloride, and doxycycline.

Discussion

Our patient clearly had a significant exposure to the weaponized form of anthrax.[1] The patient's coworkers at the contaminated facility were culture positive for inhalational anthrax. Although the prophylactic treatment was appropriate, the patient did not complete the prescribed regimen. A previously healthy and active individual, the patient was unable to return to normal daily activities after the anthrax exposure. Although the patient's exposure history to household fumigation must be considered as a possible cause of patient deterioration, that cause is considered less likely as a result of confirmed workplace exposure to *B anthracis*.

Although a complete set of vital titers were not done, the presence or absence of these titers would not change our feeling, based mainly on temporal relations, that the anthrax exposure is responsible for this patient's change in health status. Further, while the patient never met the criteria of positive blood cultures for the diagnosis of anthrax, it is our belief that, despite being culture negative, the patient manifested definite physiologic changes that do not have any other valid explanation—despite extensive inpatient work-up. Again, these changes were temporally related to the time of the patient's workplace exposure to the anthrax bacillus. We strongly believe that there is a relation between the patient's exposure to anthrax and the symptoms displayed. In the absence of an alternative diagnosis for this patient, and because an anthrax diagnosis was not made definitively, we suggest that there may exist a clinical entity of "aborted anthrax infection." Serial serologic testing may be helpful in determining the presence of this entity.

Epidemiology

Anthrax has affected animals for thousands of years. Hundreds of thousands of agricultural animals—primarily cattle, sheep, goats, and horses—used to die each year from the disease until the introduction of anthrax vaccinations for animals, which has decreased the number of outbreaks in the United States in the past 3 decades.[2]

Traditionally, inhalational anthrax was acquired from contaminated animal hides, including wool and fur. Since 1900, there have been only 18 naturally occurring reported cases in the United States.[3] The last recorded natural inhalational anthrax case was in 1978.[4] One case of naturally occurring cutaneous anthrax was documented in a North Dakota farmer in 2001.[5] As of December 7, 2001, a total of 22 cases of anthrax (11 each of the inhalational and cutaneous forms) have been confirmed in the United States as being the result of intentional release in fall 2001.[6]

Most incidents of anthrax in animals are found in countries outside of the United States. Chad has approximately 548 cases per 1 million head of cattle, while Guinea has 163; Ethiopia, 141; Mongolia, 119; and Cambodia, 108.[2]

Pathophysiology

There are three forms of anthrax: cutaneous, inhalational, and gastrointestinal. The type of anthrax a person contracts is determined by the form of contact he or she had with *B anthracis* spores. Skin contact results in cutaneous anthrax; respiratory tract exposure results in inhalational anthrax. Eating meat that is not sufficiently cooked from infected animals causes the rarest form of anthrax, gastrointestinal anthrax. Toxin release (lethal toxin and edema toxin) causes local edema and necrosis. As the spores accumulate and germinate in the lymph nodes, regional hemorrhagic lymphadenitis can develop.[7] *Bacillus anthracis* can spread systemically via lymph nodes and blood to cause septicemia—and, rarely, to the central nervous system to cause meningitis.[4]

Diagnosis

For people with suspected anthrax infection, laboratory testing is essential to make the diagnosis. In the absence of a titer culture or postinfection serologic evidence, as in this case, the diagnosis of anthrax can only be suspected. The diagnosis in this case is not confirmed. This is a suspected case of anthrax where a diagnosis is not definite.

Currently, cultures of nasal swabs are used to detect *B anthracis* spores that may be resting in the nose. However, a negative test result of a nasal swab does not mean that exposure has not occurred. Similarly, a positive test result of a nasal swab does not mean that the person has the disease. The value of these test results lies in their use as epidemiologic tools during investigation of exposure. *Bacillus anthracis* endospores

"do not divide, have no measurable metabolism, and are resistant to drying, heat, ultraviolet light, gamma radiation, and many disinfectants."[4] The spores can also remain dormant for more than 50 years. It is this resilience that makes *B anthracis* a desirable germ for biowarfare.[8]

According to the Centers for Disease Control and Prevention's November 1, 2001, *MMWR: Morbidity and Mortality Weekly Report*, if inhalational anthrax is suspected, it should be determined if the patient has already had 2 to 5 days of flu-like symptoms. If so, a leukocyte count, chest radiograph, and blood cultures should be obtained. A computed tomographic scan of the thorax should be ordered if the results of the chest radiograph are abnormal. Rapid diagnostic testing for influenza may also be considered.[9]

If pleural effusion is present, a thoracentesis should be performed, according to the Centers for Disease Control and Prevention, and the fluid sent for Gram staining and culture, polymerase chain reaction, and cell block for immunohistochemistry. If signs of meningitis or altered mental status are present, a lumbar puncture should be performed to analyze cerebrospinal fluid. Antibody testing is available but not diagnostic; rather, it is more frequently used for surveillance of an environmental exposure.[9]

Treatment

Among the antibiotics recommended for treatment of inhalational anthrax are ciprofloxacin, doxycycline, and penicillin G procaine—although doxycycline is contraindicated in disease involving the central nervous system. Monotherapy is not recommended for treatment of anthrax except in its mild cutaneous form. We treated our patient with ciprofloxacin, penicillin, and clindamycin, as per recommendations on the Center for Civilian Biodefense Strategies Web site (see *http://www.hopkins-biodefense.org/*) based at The Johns Hopkins University, Schools of Public Health and Medicine. It is thought that ciprofloxacin targets *B anthracis* itself, penicillin helps to penetrate the central nervous system, and clindamycin hydrochloride serves to interrupt protein synthesis by *B anthracis*.[10]

Prophylaxis is given to any person known to have been in an area contaminated by anthrax spores, irrespective of his or her clinical condition.

Surveillance

Nasal swabs are used during investigations of known or suspected anthrax exposures because they may provide clues to help investigators assess the exposure circumstances.

Antibody tests can be used to measure reactions in patients with anthrax infection and others who have received the anthrax vaccine. Antibody testing also helps investigators make estimates of the number of exposures in a population affected by an outbreak, but it is not validated as a diagnostic tool for anthrax disease.[9]

Two sequential tests are necessary to interpret the antibody test results. Individuals presumed to have some exposure to anthrax may be asked to return for a second test to measure any changes in the antibody level over time. Results from the second antibody test help care providers judge the significance of the initial test and assess the extent of exposure (eg, location in a building, number of persons exposed).[9]

Comments

With the threat of bioterrorism, our sensitivity to the clinical syndrome associated with anthrax is heightened. There are various bioterrorism workgroups and government agencies that are monitoring the incidence of disease and the most effective means of prophylaxis and treatment. As a result, we were able to act efficiently and effectively by monitoring and successfully treating our high-risk patient, possibly aborting another case of anthrax infection.

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