Ockham's razor is not so sharp

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Abstract

A 39-year-old male with newly diagnosed HIV had cavitary pneumonia initially attributed to *Pneumocystis jirovecii* but actually caused by *Rhodococcus equi.* After neurological deterioration, he was found to have intracerebral lesions caused by *Toxoplasma gondii*. This case underscores the inability to rely on the search for a unifying diagnosis (Ockham's Razor) in HIV-infected patients.

Case Report

A 39-year-old Caucasian male with no significant past medical history presented to the emergency room reporting a two-week history of a worsening cough associated with the production of rusty sputum, pleuritic chest pain, and intermittent fevers, as well as an unintentional 30-pound weight loss over the preceding several months. A chest X-ray revealed a large cavitary lesion in the superior segment of the left lower lobe and a smaller cavitary lesion in the right mid-lung (Figure 1). The presence of these cavities was confirmed on a computer tomography (CT) scan of the chest (Figure 2). He was started on empiric treatment with ceftriaxone and clindamycin, then placed in respiratory isolation until three sputum smears were negative for acid-fast bacilli. Blood cultures and sputum gram stain and culture were negative. HIV antibody was positive; his CD4 count was 19/μL and his viral load was 121,000/mL. Gram stain and acid-fast stain on bronchial washings were negative, but *Pneumocystis jirovecii* was revealed by silver staining. He was not hypoxic at rest and did not desaturate with exertion, so prednisone was not given. Trimethoprim/sulfamethoxazole (two double-strength tablets t.i.d.) was begun, after which he defervesced, his cough diminished, and he was discharged. However, culture of the bronchial washings also yielded *Brevibacterium*, which was initially considered to represent a contaminant.

He had been given an appointment at an HIV clinic to begin anti-retroviral therapy within his first week as an outpatient, but did not keep this appointment because he felt unwell. The patient returned eight days after discharge, complaining of persistent fevers of up to 104.5ºF. His neutrophil count had declined to 0/μL from 4,300/μL at discharge. Trimethoprim/sulfamethoxazole was immediately discontinued owing to concern that the drug had induced agranulocytosis. He had been started on azithromycin during his first hospital stay for prophylaxis against *Mycobacterium avium* and this drug was continued into his second hospitalization.

Early in his second hospital course, the bronchial cultures from his first admission returned from a state reference laboratory with a final speciation of *Rhodococcus equi*. At this point, the patient was started on imipenem/cilastatin, vancomycin, rifampin, and ciprofloxacin, all antibiotics with reported efficacy against this resistance-prone organism.[1] The organism was resistant to trimethoprim/sulfamethoxazole but sensitive to imipenem and ciprofloxacin, so these medications were continued as purposeful double coverage to maximize macrophage penetration and to avoid the development of resistance during monotherapy.[2] Coverage for co-infection with *Pneumocystis* could not be accomplished effectively because the patient became completely intolerant of oral intake in the setting of neutropenic colitis, and intravenous pentamidine caused a significant transaminitis. His inability to tolerate any medications by mouth also precluded the initiation of anti-retroviral therapy. Two weeks after re-admission, the patient began to experience intermittent right-sided weakness and paresthesias, with a contrast CT of the head demonstrating edema at the left posterior frontal corticomedullary junction. Magnetic resonance imaging (MRI) of the brain revealed a hyperintense 1.0×1.7×1.7-cm lesion centered within the subcortical white matter of the left posterior central gyrus, as well as other smaller multifocal lesions (Figure 3). He was started on steroids and phenytoin; neurosurgeons were consulted for a biopsy but recommended serial imaging because there are reports describing the dissemination of *Rhodococcus* to the brain,[3] and the patient was already on appropriate treatment for this pathogen. However, the patient's neurological status deteriorated over the next week and he developed a right lower facial droop and word-finding difficulties. A repeat CT scan showed interval worsening of the vasogenic edema around his left parietal and right occipital lesions. A nodule was surgically removed from the left parietal lobe, with the pathology showing cysts consistent with *Toxoplasma gondii* bradyzoites. Despite the commencement of pyrimethamine and the increase of azithromycin from prophylactic to treatment doses, his postoperative course was marked by further neurological decline. His final head CT revealed diffuse cerebral edema and interval development of leptomeningeal enhancement throughout the posterior fossa. His family decided to withdraw care five days after surgery, and he died.

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Discussion

This case illustrates several important pitfalls in the management of AIDS patients. First of all, *Pneumocystis jirovecii*, while still the most common opportunistic infection in AIDS patients,[4] is not the most frequent etiology of cavitary lung lesions in this immunocompromised population. The typical radiographic appearance of *Pneumocystis* pneumonia produces bilateral interstitial infiltrates.[5] When *Pneumocystis* cavities do arise, they may result from the outgrowth of cystic disease, from the breakdown of normal lung tissue by hyperactive elastase-elaborating macrophages, or from vascular invasion by the organism leading to intrapulmonary thrombosis and necrosis of down-stream tissues.[6,7] Various radiographic case series estimate the incidence of cavitary lesions in HIV-positive *Pneumocystis* patients at less than 10 percent,[8,9] although the advent of high-resolution CT scans has lowered the threshold for detection of cavities.[10,11] Lung cavitation in *Pneumocystis* patients still constitutes an uncommon manifestation of a common disease, and finding *Pneumocystis* in a patient with cavitary pneumonia should prompt widening of the differential diagnosis, while still recognizing the potential role of *Pneumocystis* as a co-pathogen. Other causes of cavitary disease include, but are not limited to: tuberculosis, *Mycobacterium kansasii*, invasive pulmonary aspergillosis, *Pseudomonas aeruginosa*, *Nocardia asteroides*, or

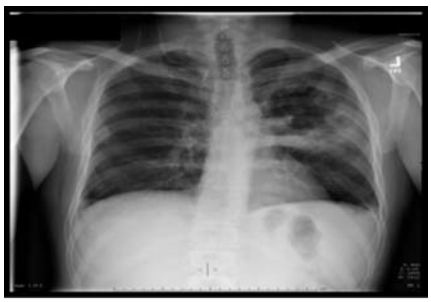

Figure 1. Chest X-ray on admission.

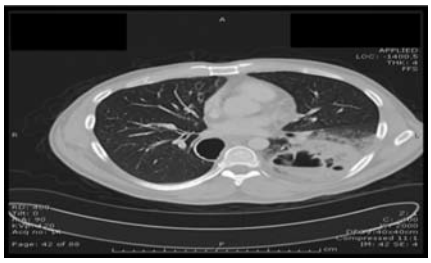

Figure 2. Computer tomography scan of the chest on admission.

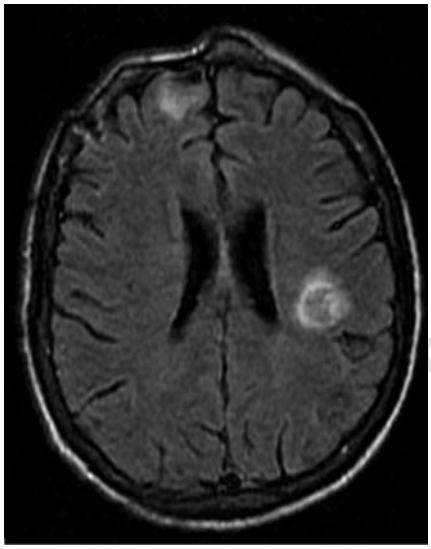

Figure 3. Magnetic resonance image of the brain two weeks after re-admission.

any complicated bacterial pneumonia, as well as neoplasms like Kaposi's sarcoma and non-Hodgkin's lymphoma.[12] As this case demonstrates, *Rhodococcus equi* should also be considered as an infectious cause of lung cavitation in an AIDS patient.

Identification of the *Rhodococcus* organism was delayed in our case owing to initial confusion of the pathogen with *Brevibacterium*. *Brevibacterium* and *Rhodococcus* both belong to the group of coryneform bacteria (indeed, *Rhodococcus equi* was originally known as *Corynebacterium equi* because of its morphology). However, while *Brevibacterium casei* has been associated with rare cases of sepsis in AIDS patients,[13,14] it is not known to have the same predilection for the lungs as *Rhodococcus*. *Rhodococcus equi* is a facultative aerobic, non-spore-forming gram-positive coccobacillus that classically produces a salmon-pink pigment and may manifest positive acid-fast bacilli stain results.[15] Because of the tendency to confuse *Rhodococcus* with other coryneform flora or mycobacteria, the microbiology laboratory should be alerted to the practitioner's concerns about the presence of this organism, especially in patients with compromised cell-mediated immunity who present with cavitary pneumonia.[16] A careful history should be taken to search for zoonotic exposure. In retrospect, our patient was found to have lived and worked in an area with plentiful livestock, almost certainly coming into contact with soil contaminated by herbivore manure. *Rhodococcus* is usually acquired in humans through inhalation of such soil, followed by hematogenous spread from the lungs to other sites. The organism does not necessarily show a *Nocardia*-like tropism for the central nervous system but the brain is one of the most common sites of extrapulmonary infection.[17]

In an HIV-positive or otherwise immunocompromised patient, the principle of Ockham's razor should be invoked cautiously. The propensity of AIDS patients to present with two or more synchronous infections can complicate diagnosis significantly and lead to inadequate treatment.[18] In this case, the presumption that the patient's lung cavities were caused by *Pneumocystis* led to treatment with high-dose trimethoprim/sulfamethoxazole, which is not uniformly effective against *Rhodococcus* and was demonstrably unsuccessful in this case. Then, the presumption that the patient's cerebral lesions arose from disseminated *Rhodococcus* delayed the proper diagnosis of *Toxoplasma gondii*, the most common opportunistic infection in the central nervous system of an AIDS patient.[19] The patient was treated with pyrimethamine and azithromycin after *Toxoplasma* was diagnosed, but drugs with sulfa moieties, such as sulfadiazine, were withheld owing to concern for further toxicity after he had already experienced agranulocytosis attributed to trimethoprim/sulfamethoxazole.

The unfortunate clinical course described in this case report may have been accelerated by both endogenous and exogenous insults to the immune system in a patient whose cell-mediated immunity had been decimated already by a previously unrecognized HIV infection. While trimethoprim/sulfamethoxazole is the preferred agent for *Pneumocystis jirovecii* pneumonia, it caused agranulocytosis in this patient. His neutropenic colitis further limited his treatment options and precluded the initiation of antiretroviral therapy, which could have led to a more favorable outcome by bolstering the lymphoproliferative response to his multiple infections, especially his fatal *Toxoplasma* encephalitis[20] This case is a sobering reminder of the iatrogenic harm that can stem from an incorrect diagnosis, and provides a cautionary tale for the practitioner who assumes parsimoniously that a single etiology explains the entirety of a patient's pathology.

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