The New York Case: Lessons Being Learned

Recently, a case of HIV infection in New York City gained wide public attention because of the possibility that it represented a novel and “superaggressive” virus, capable of causing rapid clinical disease and broadly resistant to available drugs (1). Publicizing this case before careful epidemiologic investigations were completed has been criticized as an overreaction that led to unnecessary public fear. The physicians and public health authorities involved argue that the unusual nature of this case—a transmitted drug-resistant virus and an apparently rapid disease course—required wide disclosure to find or prevent additional cases. At the recently concluded 12th Conference on Retroviruses and Opportunistic Infections, these vigorous debates prompted many press comments and a special 1-hour session to review the New York case and its implications. My purpose in this commentary is to place this case into the perspective of the broader experience with HIV infection and to explore the implications of how it was revealed to the public.

In the New York case, a middle-aged man who had been HIV negative in May 2003 was retested and found to be HIV positive in December 2004. Possible exposures included multiple instances of unprotected sex with men and abuse of methamphetamine. The patient described a 1-week illness with fever, pharyngitis, weakness, and fatigue about 6 weeks before his HIV diagnosis. However, at his first positive test result in mid-December, his HIV enzyme-linked immunosorbent assay showed full antibody reaction against viral antigens, which would be unusual for an acute HIV infection. Because the symptom complex of acute HIV is so nonspecific (and often absent), the timing of the patient’s infection is uncertain. However, it could not have been much earlier than his previous HIV test in May 2003, which had yielded negative results. In mid-December 2004, the patient’s CD4 cell count was 0.080 × 10^9 cells/L and his plasma viral load was 280,000 copies/mm^3.

In mid-January 2005, the patient was referred to an HIV research clinic for possible acute or recent infection. There, additional testing showed the virus to have numerous mutations and reduced sensitivity to many antiretroviral drugs. It was sensitive to only 2 approved agents. Furthermore, the virus was unusual in its ability to use each of the 2 most common co-receptors for HIV, CCR5 and CXCR4. In summary, this patient was probably infected within the previous 20 months with a multiple drug class-resistant virus and had experienced a rapidly progressing immune deficiency, perhaps due to a more aggressive variant of HIV.

The HIV research clinician who made these observations contacted state and local health authorities about this case. The authorities decided to alert the public by issuing a press release and holding a press conference attended by many leading HIV physicians and scientists, as well as health officials.

The reaction to the public announcement was immediate, widespread, and, at least in some cases, clearly exaggerated. The case was immediately featured on local, national, and international news, in some cases with alarming headlines suggesting a possible outbreak of a new and much more aggressive “strain” of HIV. Implied in the most extreme reports was the possibility that this virus might be more contagious as well as more rapidly fatal, reminding us of similar groundless speculations early in the HIV epidemic about “casual transmission” of HIV. In the midst of this media-inspired public concern, health professionals must try to understand the public health implications of this case and reflect on the consequences of a public announcement with all-too-predictable consequences.

What are the key features of this case, and how unusual are they? This patient was infected with a virus resistant to most available antiretroviral drugs. Often, HIV is resistant to 1 or more drugs when transmitted (2). As is true with other infections, HIV variants that emerge in the community reflect incomplete suppression with antiretroviral agents, which selects for viruses with resistance mutations. When transmission occurs, the transmitted virus may carry some or all of the mutations from the original host. These mutations may weaken the virus in the original host—as measured by a reduced “replication capacity” in a commercial assay—but in the new host the virus grows more normally and has a higher replicative capacity (3). The prevalence of transmitted drug resistance is usually rather low and extends to only 1 or 2 drug classes. Transmission of virus resistant to 3 classes, as in the New York case, is much less common, but it has been reported many times (4).

Another question that sparked attention in the New York case was the unusual dual-tropic nature of the patient’s virus. In almost all cases of recent HIV infection, the acquired virus uses a protein on the surface of cells, the CCR5 chemokine receptor, to gain entry into these cells (5). This variant is therefore common in earlier-stage HIV disease. It is transmitted even if the source is infected with a mixture of HIV variants, some that use the CCR5 receptor and others that use another protein, the CXCR4 receptor. Most people infected with HIV that uses the CXCR4 receptor (as in the New York case) have been infected for a considerable period of time. Instances of initial infection with the CXCR4 variant are rare and are seen only in persons who lack the gene for the CCR5 receptor (6), which was apparently not the situation in the New York case. The case was, in fact, even more unusual because the patient had a virus that could use either type of receptor to infect cells. These “dual-tropic” strains seem to prefer to...
use the CXCR4 receptor in vivo (7, 8) and are therefore associated with either a more advanced disease stage or a higher rate of clinical progression (9). Although seen in more advanced stages of HIV disease, however, viruses that use CXCR4 seem less transmissible than the common CCR5 form. Therefore, the type of HIV in the New York case is more consistent with a long-standing infection, not a recent one, or is the result of genetic susceptibility to infection by this unusual virus. Either explanation, if true, would decrease the public health significance of the reported case. If not a recent infection, the virus would resemble many others that have developed drug resistance in patients with advanced-stage disease. If the rapid appearance of the dual-tropic virus reflects a unique host susceptibility, others might not be readily infected after exposure.

The final feature of the case that seems unusual is the patient’s apparently rapid progression to AIDS in a matter of weeks to months. The patient’s disease stage was advanced according to CD4 cell count and HIV viral titer criteria, although he had been infected for no more than 20 months. However, this feature, while unusual, is not unprecedented. In fact, the natural history of HIV disease progression varies widely. Although several excellent cohort studies document a typical progression from initial infection to clinical AIDS in about a decade, the course of HIV disease, like that of other diseases, is roughly normally distributed. Some patients show no evident progression even after 15 to 20 years of infection, while others die rapidly (10, 11). An overview of 2 of the large cohort studies, the Multicenter AIDS Cohort Study (MACS) and the Women’s Interagency HIV Study (WIHS), showed that rates of disease progression vary widely, with several percent of patients dying within 1 year of becoming infected. The New York patient is clearly at the forward edge of this curve, progressing to a CD4 cell count well below 0.200 × 10^9 cells/L in a matter of months to 2 years, but he is not unique.

In the end, the patient in the New York case is infected with a virus that shows drug resistance, which is not a novel finding. His virus has the unusual feature of dual-receptor tropism, which is consistent with either long-standing infection or unusual host susceptibility, and a rate of disease progression that is rapid, but not more so than has been previously reported. This case, while unfortunate for the individual, poses no proven public health risk. His virus may not be readily transmissible, and his rapid disease progression may be principally a function of his own host response rather than due to a highly virulent virus. At a minimum, clarifying any public health risk awaits more extensive and careful research. At the moment, we don’t even know if this virus has been transmitted to any other person.

Given the characteristics of this case, what were the concerns of the physicians and health authorities? Was their decision to publicize the case understandable and appropriate, or exaggerated and misguided? In contrast to the case itself, the answers to these questions are even more subjective and open to debate. We can only speculate on goals and motivations and don’t yet know whether the net result of informing the public about this case in this manner and before more research was completed will be positive or negative.

Almost immediately, the HIV research clinicians notified the health authorities about the combination of highly resistant HIV and apparently rapid disease progression in this patient. After the patient’s multiple unprotected sexual contacts were appreciated—apparently more than a month after the original HIV diagnosis—health officials decided to issue a public alert. Assuming the health authorities were concerned about identifying possible similar infections connected to the index case, a more typical approach would involve an effort to find sexual contacts of the original case-patient and, in turn, the contacts of those individuals. This contact tracing would not have required, or benefited from, a public health alert and would have avoided understandable and predictably exaggerated public and media response to a public announcement.

The advantages of a public alert in this case seem limited. The identity of the index case-patient could not be revealed publicly, and he apparently did not know many of his sexual contacts. Physicians may have been more diligent in diagnosing acute HIV infection as a result of the alert, but many previous efforts to educate physicians to recognize acute cases of HIV infection for treatment or research referral have had little effect. Issuing a public alert and holding a press conference seem to have been unnecessary in this case, frightening the public while having little potential benefit. The press alert and press conference certainly did not facilitate the much more important epidemiologic investigation warranted by this unusual or even unique case. This investigation is now in progress.

Is, then, the New York case important from a biological or public health risk perspective, or is it merely an unusual juxtaposition of several findings that have been reported singly but not together? We simply don’t yet know. As summarized, each central aspect of the case—transmitted highly resistant HIV, dual-tropic virus, and apparently rapid disease progression—is uncommon, and their simultaneous occurrence is extremely rare. But until more is known, this case remains only an interesting instance of HIV infection, albeit one that demands further investigation. When was the actual transmission? Can we find the source of this virus? Has it been transmitted, and if so did it share any of the features of the virus in the original case? These are crucial questions and do warrant pursuit.

Lost in much of the media-driven controversy in this case are the really important public health concerns. The following concerns, unfortunately, rarely generate headlines. Why are people still putting themselves at risk for transmission when we have expended so much effort to educate people that condoms offer excellent protection?
from HIV? Have our prevention efforts failed, or have we even really committed as a society to support efforts to prevent HIV transmission? All HIV infection comes from an infected source. Why are some persons with this virus not protecting others from this scourge? Was the source of this case-patient’s infection aware that he was infected? Why have we failed so miserably to reduce the barriers to HIV diagnosis? Why are we failing to diagnose acute HIV infection even though we have reason to believe the high viral titers during the earliest days of infection dramatically increase transmission risk?

And what of the coepidemic of methamphetamine abuse? First a massive problem on the West Coast, addiction to this drug is now common across the United States. Methamphetamine, often consumed in repeated and frequent binges, is deeply linked to failure to observe safe methods of preventing HIV transmission, and methamphetamine use by those taking antiretroviral therapy for HIV infection is strongly associated with the type of poor medication adherence that often leads to the selection of drug-resistant mutations (11). These conditions create almost a perfect storm for both HIV drug resistance and for virus transmission.

Let’s hope that we move quickly away from guessing or finger-pointing about the handling of New York case. Clearly, rigorous epidemiologic investigation is preferred over public alerts that cause only fear. But we should just as firmly insist that the true crises of HIV transmission—failure to use condoms, poor case finding of acute infection, and control of epidemic methamphetamine abuse—are the real issues in cases like this patient. While the true crises seem destined for the back pages of our press rather than the front pages, they are the true and continuing challenges even after more than 2 decades of the HIV epidemic. If the New York case allows us to question our failure in transmission prevention and to demand better performance, we may someday see some redeeming value in the high viral titers during the earliest days of infection dramatically increase transmission risk?

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