

## Clinical dilemmas in palliative care for HIV infection

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In several respects, palliative care in late HIV disease tends to differ from that in other terminal diseases such as cancer, and special difficulties arise in alleviation of pain and suffering. The following story is illustrative:

### *The case of Dona*

Dona, age 33, is the widow of Ed, who was diagnosed with HIV when incarcerated in 1991 for possession of marijuana. Almost at the same time, Dona was admitted to hospital with pneumonia which proved to be tuberculous. Not until she was discharged did she discover that she was infected with HIV, acquired from her husband, an intravenous drug user. Both Ed and Dona were started on zidovudine, the only anti-HIV drug then readily available. Ed soon developed *Pneumocystis* pneumonia and candida oesophagitis, complicated by anaemia due to the zidovudine. When new drugs for HIV became available, Ed and Dona were switched to these. Ed developed AIDS-related dementia, becoming paranoid and abusing Dona mentally and physically. She filed for divorce but continued to look after him until he died in 1995. Within two months of his death, Dona developed ataxia and a right-sided paralysis from what proved to be a central nervous system lymphoma—a condition that at that time was expected to cause death within 90 days. Three weeks after this diagnosis the first protease inhibitors were released, and she has been on triple therapy for over 4 years. She now has neuropathy, lipodystrophy, abnormal cervical smears and hearing loss, and has been in hospice care for 4 years. However, her brain lymphoma has regressed and recently, for the first time, she had a 'negative viral load'.

### UNEVEN TRAJECTORY OF ILLNESS

As the above case demonstrates, HIV disease may not follow a predicted timetable. Providers may not be able to predict outcome of the highly active antiretroviral therapies (HAART). The impact of HAART is equally uncertain for the incidence of new cases of AIDS-defining illness as it is on existing conditions. The most common AIDS-related malignancies are Kaposi's sarcoma, non-Hodgkin lymphoma (NHL) and cervical carcinoma. The only malignancies that have decreased in incidence since the introduction of HAART have been Kaposi's sarcoma and primary brain lymphoma; there seems to be no change in the incidence of NHL, Hodgkin's lymphoma or

invasive cervical carcinoma<sup>1</sup>. NHL is typically diagnosed at a time when the immune system is not severely depressed<sup>2</sup>. The incidence of certain non-AIDS-defining cancers, such as anal cancer, multiple myeloma, and cancers of the stomach, lung and larynx may even be increasing with the increasing longevity conferred by HAART<sup>3</sup>. Wasting syndrome has emerged as the most frequent initial clinical diagnosis among people already on HAART<sup>4</sup>.

From this we may conclude that, even though current antiretroviral therapy is much more successful at prolonging reasonably good health, severe illnesses are likely to emerge eventually in this patient population. These may well differ in frequency from the AIDS-defining illnesses seen in the early years of the epidemic.

### DISCOMFORTS OF ANTIRETROVIRAL THERAPY

Drugs for HIV can have side-effects that spoil enjoyment of life and hamper adherence to complex treatment regimens. Three types of disturbance are of special note.

Peripheral neuropathy is the most frequent neurological complication associated with HIV infection. It can cause burning, numbness, tingling, or pain. Sometimes the neuropathy is due to the HIV infection itself, sometimes to the antiretroviral agents (most commonly didanosine, zalcitabine or stavudine). Pain may vary from mild discomfort to inability to ambulate. If it is medication-induced, drug holidays or medication changes may be indicated; but for patients who have experienced multiple drug failures, medication change may not be feasible. Neuropathies seldom respond well to treatment<sup>5</sup>.

Alterations in body fat distribution can lead to changes in physical appearance which can be very disturbing to patients. Several syndromes have been identified, and in some studies these have been linked to protease inhibitor use—though in others over half the patients with lipodystrophy had no history of antiretroviral use<sup>6</sup>. Lipodystrophy may show itself with loss of subcutaneous fat in the face or extremities, an increase in abdominal girth (known as the protease paunch), dorsocervical fat pad enlargement on the back of the neck (buffalo hump), or increase in breast size in women. Strategies ranging from hormone therapies to switching of antiretrovirals have met with mixed success.

Other conditions that have been attributed to long-term antiretroviral therapy include diabetes, advanced cardiovascular disease, lipid abnormalities and hair loss. The exact incidence of these conditions in the treated population is still debated. We can expect to see more long-term complications of antiretroviral therapy in the future as patients live longer.

### PALLIATIVE OR CURATIVE?

HIV presents an especially difficult challenge when the patient becomes severely ill. The virus hampers the ability to resist not only opportunist infections but also those due to common pathogens, and many of the symptoms that arise will be potentially treatable. For example, when an individual with severe wasting syndrome suddenly loses vision, the cause may be an opportunistic viral infection such as cytomegalovirus. However ill the patient, prevention of blindness may become a major concern, requiring aggressive diagnostic procedures. These in turn generate ambiguities in clinical decision-making. Box 1 lists some symptoms that are especially troubling to patients.

### ETHNIC/RACIAL DIFFERENCES

Deaths among people with AIDS in the USA began to fall in 1996, for the first time in the history of the epidemic. The incidence of AIDS also decreased in the same year. In States that have HIV reporting, HIV diagnosis rates have been stable for several years but a higher proportion of cases are now being seen among women and people from minority groups. Women in New York had a shorter survival time than men, and the explanation was thought to lie in several factors, including poverty, difficulty with the healthcare system, and the role of women as caregivers (often for HIV-infected spouses or children)<sup>7</sup>. Other analyses of the New York data indicate that survival time has increased more for younger people than for older people, and for heterosexuals and men who have sex with men than for intravenous drug users<sup>8</sup>. After hospital admission, Hispanics seem to have a worse survival rate than white or African Americans<sup>9</sup>. The combined impact of drug use and sexually transmitted diseases, especially in patients aged 18–24, is a trend of great concern. Access to care is a great and growing issue in these groups<sup>10</sup>.

### MENTAL ILLNESS

Several studies have documented the increased frequency of mental illness in patients with HIV disease<sup>11,12</sup>—notably, depression, substance abuse, anxiety and dementia. Dementia is still a common initial symptom in the diagnosis of AIDS<sup>11</sup>. Depression is of particular importance since as

#### Box 1 Common symptoms of concern to patients

##### Confusion/dementia

This usually demands rigorous examination to ensure that the cause is not a central nervous system infection, tumour medication or other condition such as hypoxia. The precipitating factor may prove to be underlying anxiety or depression

##### Diarrhoea

In the early stages this is commonly secondary to medication and may reduce adherence to therapy. But *Salmonella*, *Shigella* and *Campylobacter* infections can be the cause in patients with only modest immunosuppression or none<sup>17</sup>

##### Dysphagia

Frequent in the terminally ill, dysphagia or odynophagia commonly has an infectious origin. Other aetiologies include medications and gastro-oesophageal reflux

##### Dyspnoea

Many causes of this distressing symptom, from anaemia to acute lung infection, must be considered

##### Fatigue/asthenia

Particularly in the late stages of HIV disease, this symptom is highly prevalent<sup>19</sup>. Causes to be excluded include adrenal insufficiency, depression, hypogonadism and medication side-effects.

##### Fever

Fever is especially troubling when accompanied by profuse sweating, rashes or arthritis. Assessment depends on the state of immune function: tuberculosis may occur at any level of immunosuppression. *Mycobacterium avium* complex infection is almost confined to patients with very low CD4 counts.

##### Nausea/vomiting

Nausea and vomiting are commonly due to medication and can interfere not only with drug bioavailability but also with the patient's adherence to treatment. Most antiretrovirals and many of the medications used to prevent opportunistic infections have this side-effect, sometimes via hepatitis or lactic acidosis. Intrinsic gastrointestinal disease, central nervous system disease and other causes must be ruled out

##### Pruritus

Though commonly due to the generalized xerosis (dry skin) of HIV disease, pruritus may be medication-related or secondary to one of the conditions exacerbated by HIV such as eczema or scabies

##### Pain

Pain is common in both early and late stages of HIV disease: among hospice patients with HIV, as many as half have pain from peripheral neuropathy, arthritis, headache or other sites<sup>18</sup>. Pain of new onset may demand special investigations to rule out infection or a tumour

well as predisposing to suicide it can influence immune function. Fortunately, HIV-infected patients seem to respond to antidepressant regimens at about the same frequency as the non-HIV-infected.

## CAREGIVER STRESS

Certain features of the HIV epidemic impose exceptional stresses on caregivers. In one US study of informal caregiving, over 6% of the population in central cities had provided care to HIV-infected persons, as opposed to 3.2% for the entire country. Two-thirds of these people had performed domestic tasks but just over a quarter had provided personal care. With HIV the caregivers differed from others in being more likely to be young, male and providing care that was emotionally stressful<sup>13</sup>.

When the caregiver of an HIV patient is a family member, special difficulties arise. Issues of sexual or drug behaviour may emerge simultaneously with the information on the HIV diagnosis, and be met by fears of social stigma, contagion, infection, abandonment, guilt, and overwhelming fatigue<sup>14</sup>. In many instances, several members of the family are HIV-infected, and the stress of anticipatory grief may be exacerbated if the caregiver has already lost numerous friends to HIV. The caregiver, if a partner, may also be angry at having been exposed unwittingly to the infection. Finally, when the caregiver is a gay man, he may face the prospect of losing his home, possessions or money as well as that of having no say in decisions about care in the terminal stage of his partner's illness.

Women who are HIV-infected tend to neglect their own care if they also have HIV-infected children in the home<sup>15</sup>. In one rural county in the southern USA most HIV-infected children were still being looked after by their HIV-positive mothers<sup>16</sup>. For an infected caregiver, daily involvement with the patient brings home his or her own likely fate.

## CONCLUSION

Despite the increased survival rates achieved in the past five years, perplexing issues remain for delivery of care in HIV infection. By becoming more of a chronic disease it creates new medical challenges, in which palliation and attempts at cure cannot be separated. Disparities of geography, risk group, gender and ethnicity deprive some patients of the full benefits of medical advances. Even when access is readily available, the patient is not cured and there is the ever-present threat of infection or tumour. These concerns will persist until we have a cure, available and affordable to all, and methods to ensure that unsuspecting individuals will not become infected.

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