Unusual and rare complication described in San Francisco

5 December 2013

HIV infection has always been associated with changes in weight and body shape. In the early 1980s when this infection was new and did not yet have an official name, in parts of southern Africa it was called “slim disease” because of the dramatic impact it had on people’s weight and appearance. There are many reasons untreated HIV infection can have such an effect, including the following:

- HIV infection can damage the lining of the intestinal tract and impair its ability to absorb nutrients from food. Over time this can lead to unintentional weight loss, commonly called wasting.
- HIV can cause the body to decrease production of the hormone testosterone in men and women. This can result in weaker muscles and loss of muscle tissue.
- In HIV infection, the body may not respond appropriately to the effects of another hormone—growth hormone. In some cases, production of growth hormone may fall below normal, which also affects muscle strength and the maintenance of muscles.
- The body—particularly the intestines—becomes more prone to infections, inflammation and diarrhea. These also cause weight loss.

Once on potent anti-HIV therapy (commonly called ART or HAART), weight gain usually occurs. In some people, at least initially, some of the increased weight is mostly fat, so ART may be fingered as a potential cause of this problem. However, in the time before ART was available, doctors who studied weight changes in HIV-positive people noticed that with intensive feeding (and treatment of underlying infections) weight gain was possible, but the increased weight seemed to be mostly fat. Perhaps this was due to underlying hormonal dysfunction caused by HIV—insufficient testosterone and/or growth hormone—or inflammation caused by the chronic nature of HIV infection.

The emergence of the HIV lipodystrophy syndrome

In the mid-to-late 1990s, when potent ART first became available, patients and doctors noticed a strange collection of signs and symptoms involving changes in body shape and facial appearance. These changes seemed to be caused by the loss of the fatty layer just under the skin (subcutaneous fat) and particularly affected the following parts of the body:

- cheeks and temples of the face
- arms and legs
- buttocks

The loss of fat is called lipoatrophy.

Some patients also developed deposits of fat in the belly, and in women, in the breasts. Less often, fat was deposited around the shoulders and neck—commonly referred to as a “buffalo hump.” The increase in fat in some parts of the body is called lipohypertrophy. The changes in body shape, in particular the loss of fat, were linked to exposure to the following nukes (nucleoside analogues):

- d4T (Zerit, stavudine)
- AZT (zidovudine, Retrovir and found in Combivir and Trizivir).

In the present era, the nukes commonly used as part of the initial therapy for HIV are as follows:
Kivexa— a fixed-dose formulation of two drugs: abacavir (Ziagen) and 3TC (lamivudine)
Truvada— a fixed-dose formulation of two drugs: tenofovir (Viread) and FTC (emtricitabline)

These drugs do not cause loss of fat in the face or other parts of the body. Indeed, studies have found that there is even a small increase in subcutaneous fat when abacavir or tenofovir is used in place of d4T or AZT.

Internal changes

The changes we have described are physical. However, inside the body there are also metabolic changes revealed by blood tests—increased levels of fatty substances such as bad cholesterol (LDL-C) and triglycerides, as well as increased levels of blood sugar and the hormone insulin. This hormone is produced by the pancreas gland and helps move sugar from the blood into cells. However, over time, cells may gradually become less sensitive to insulin and may need ever-increasing amounts of this hormone to help control blood sugar—a process called insulin resistance. If left untreated, insulin resistance can become serious, leading to the development of type 2 diabetes.

A report from San Francisco

Doctors in this city have reported an unusual and rare finding—an apparently harmless but disfiguring condition called cutis verticis gyrata (CVG) on the heads of four HIV-positive men. In CVG, the skin on the head becomes raised in parts and depressed in others, forming ridges and furrows. What appears to be unique about the San Francisco report is that CVG has not been previously reported in HIV-positive people. All of the men had longstanding HIV infection, as well as the HIV lipodystrophy syndrome prior to the development of CVG. Generally, the cause of CVG in adults is unknown, though some doctors suspect disturbances in hormones may play a role.

Cases and details

Key points:

- all four men were between 50 and 61 years old
- they were HIV positive for between 13 and 30 years
- their most recent CD4+ counts were between 400 and 560 cells
- their viral loads were less than 50 copies/ml
- doctors classified participants as being overweight or obese

These patients had used many different HIV drugs from different classes, as would likely be typical of people who were treated over many years. Doctors noted that all patients had been exposed to thymidine analogues, a group of nukes linked to the HIV lipodystrophy syndrome:

- d4T – used by two patients
- AZT – used by three patients

All four men had signs of facial lipodystrophy and enlarged bellies. Two had deposits of fat around their shoulders and neck.

After the development of CVG, two patients used testosterone replacement therapy for up to two years and a third patient used growth hormone for less than a year. No other use of anabolic steroids was disclosed by patients.

Looking back

When interviewed by the doctors, three patients recalled first noticing the initial signs of CVG about a decade ago, as ridges appeared on their scalp. In the fourth patient, the ridges appeared two years ago. However, all patients noticed that ridges appeared on their scalps only after they developed the HIV lipodystrophy syndrome. These ridges did not go away when massaged.

Is there a link with blood sugar and insulin?

In most cases, lab analyses of the men’s blood were within normal ranges for cholesterol, liver enzymes, protein, testosterone, estrogen and thyroid-stimulating hormone (TSH). However, doctors discovered that all the men had relatively high levels of glucose (sugar) in their blood; three patients were approaching pre-diabetic levels or even
higher, and one patient’s glucose levels were within the range seen in people with diabetes. All assessments of blood glucose were done when the men were fasting. Furthermore, levels of the hormone insulin in the blood (drawn when the patients were fasting) were higher than the upper limit of normal in three patients.

**What was done?**

Surgery is a standard approach for treating CVG in HIV-negative people. However, surgery, particularly in HIV-positive people, carries the risk of infections developing in places where the skin was cut. As an alternative, in one patient a doctor injected his scalp with the substance poly-L-lactic acid (PLA, Sculptra, NewFill). This is commonly used in plastic surgery as, once it is emplaced in the skin, PLA can trigger the formation of collagen and helps to raise depressions. After several injections given five weeks apart, the man’s furrows decreased in depth, without the appearance of any complications. PLA tends to degrade within a couple of years after emplacement so repeated injections may be necessary.

**An elusive cause**

CVG is relatively rare in people, with only 500 cases reported prior to the year 2003. The reasons for the four cases of CVG in these HIV-positive adults are not known, but it is possible that a combination of several factors—including disturbances of insulin and other hormones, perhaps related to the HIV lipodystrophy syndrome and even unknown genetic factors—may have played a role. CVG does not appear to have been previously reported in HIV-positive people in the English language medical literature.

Now that the San Francisco doctors have published their report, hopefully other doctors caring for HIV-positive people may be more vigilant for any appearance of CVG and more research into this strange condition can be conducted.

**Resource**

[Body Weight and Body Shape Changes](#) from *A Practical Guide to HIV Drug Side Effects*  
—Sean R. Hosein

**REFERENCES:**

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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

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