Dr. Daniel Lee earned his BS in biology and his MD from the University of California at San Diego (UCSD) School of Medicine. Following his residency in Internal Medicine at the UCSD Medical Center and Veteran Affairs Medical Center, he completed an HIV/AIDS fellowship at the UCSD Owen Clinic, where he has continued to serve as an instructor and practicing clinician for nearly 20 years. Dr. Lee has served as a principal or co-principal investigator in numerous studies. His research focuses primarily on the metabolic complications of antiretroviral therapy. Dr. Lee is active in numerous professional organizations focused on HIV and other infectious diseases.

Clinical Conversations in HIV-Associated Wasting

A brief discussion with Daniel Lee, MD

INDICATIONS AND USAGE

Serostim® (somatropin) for injection is indicated for the treatment of HIV patients with wasting or cachexia to increase lean body mass and body weight, and improve physical endurance. Concomitant antiretroviral therapy is necessary.

IMPORTANT RISK INFORMATION

CONTRAINDICATIONS

Serostim® should not be used in patients with acute critical illness, active malignancy, hypersensitivity to somatropin or any of its excipients, or diabetic retinopathy. Increased mortality has been reported in patients with acute critical illness due to complications following surgery, multiple accidental trauma, or acute respiratory failure. Preexisting malignancies should be inactive and treatment completed prior to instituting therapy. Serostim® should be discontinued if there is evidence of tumor recurrence. Systemic hypersensitivity reactions have been reported with postmarketing use of somatropin products.

Please see additional Important Risk Information throughout and enclosed Full Prescribing Information.

A brief discussion with Daniel Lee, MD

Q: Do you think HIV-associated wasting is currently perceived as a concern?

A: There is certainly a preconceived idea that wasting was something we saw back in the 1980s and 1990s. But we still do see HIV-associated wasting these days. I think wasting is under-diagnosed. It requires clinicians to ask the right questions that will help uncover it—and this can be difficult in today's practice settings, where physicians have very little time.

Q: What type of questions do you ask your patients to determine if they may be experiencing HIV-associated wasting?

A: A patient may initiate a conversation about weight loss or more commonly, fatigue, which can open up the door to a discussion about wasting. But even in these cases, the medical providers needs to link a patient's report of fatigue or issues with their activities of daily living to loss of muscle mass and weight in order to properly evaluate for HIV-associated wasting. The most important questions to ask are around fatigue, difficulty with activities of daily living, or weight loss, whether they are newly diagnosed with HIV or well controlled on antiretroviral therapy.

Q: How do you typically assess patients for HIV-associated wasting?

A: The first step in assessing unintentional weight loss and decreased energy is determining the underlying cause or causes. Oftentimes it can be multiple issues—not necessarily one thing. I first ask the patient about their history. I ask how much weigh they have lost, how it happened, if it rapid or was it gradual, if they are having issues with nausea, vomiting, or diarrhea, how their appetite is, and for how long they've been experiencing the symptoms.

I'll ask what they eat and if they are eating enough. Many patients are not familiar with good nutrition. Sometimes not consuming enough calories can cause the weight and energy issues. I also ask about their ability to complete activities of daily living. Can they do the standard things that they need to do in life? Are they exercising? I may also ask about depression because many times depression may be linked to loss of appetite.

Next, during the physical exam, I usually have the patient undress and get into a gown so I can get a better look at everything. I look for evidence of muscle atrophy in the arms as well as in the legs. Typically, I assess a patient's strength in a standard neurologic motor exam with particular focus in the arms as well as in the legs.

Q: Can you tell us about a patient you diagnosed with HIV-associated wasting?

A: I had a 58-year-old male patient with a CD4-cell count of 570 cells/mm^3 and an undetectable viral load. He was a tall guy but was very thin and had a body mass index of 18.7. He was having trouble completing everyday activities such as walking up the steps to his apartment, cleaning, and food shopping. He would even get tired walking just a few blocks and had to take daily naps because of this fatigue. He followed a normal diet but his weight remained low and he had trouble gaining weight.

His medical history included opportunistic infections, hypertension, hypertriglyceridemia, and neuropathy in his feet starting in 2002. He also had depression related to his HIV diagnosis since 2001.

Q: When did you conclude that this patient was likely experiencing wasting?

A: I was able to zero in on wasting after evaluating this patient and ruling out other possible causes of his weight loss. His CBC, chemistry panel, and EKG were all normal, so the most likely explanation was HIV-associated wasting. I decided this patient would benefit from treatment given his weight loss, fatigue, and difficulty with activities of daily living.

Q: How did you use diagnosis of exclusion to determine this patient was wasting and a candidate for treatment with Serostim® (somatropin) for injection?

A: The treatment of HIV-associated wasting should be individualized and focused on the cause or causes of wasting. Thus we must rule out other causes of wasting including inadequate oral intake/nutrition, anorexia, or oral or esophageal pathology—none of which this patient had. He also did not have gastrointestinal obstruction, malabsorption, or diarrhea. We excluded altered metabolism, which is associated with increased resting energy. We ruled out untreated infections. From an HIV standpoint, this patient was in pretty good shape, and he did not have any current opportunistic infections or malignancies.

In addition, we consider the economic and psychological issues such as poverty or depression that might interfere with his access to food or desire to eat. However, those were not issues for this patient. Given that the patient did not appear to have any of the other causes of wasting, I felt he may benefit from the use of Serostim®.

Q: How did the patient respond to treatment with Serostim®?

A: Treatment with Serostim® provided my patient with improvements in energy and the ability to complete the daily tasks he was struggling with before. The ability to complete daily tasks is probably the most important benefit and something that is not often talked about. If you do not have energy, it is obviously quite impactful. For many of our patients, this is their biggest challenge.

Patient Case

Clinician's observation: "He was having trouble completing everyday activities, such as walking up the steps to his apartment, cleaning, and food shopping. He followed a normal diet, but his weight remained low."

PATIENT PROFILE

58-year-old male diagnosed with HIV in 2001 who reported persistent fatigue that impacted his ability to perform everyday activities. Though the patient had been adherent to antiretroviral therapy since diagnosis and had maintained adequate caloric intake with oral supplements, his weight and energy continued to decrease. After a thorough workup ruled out potential causes, the patient was determined to have HIV-associated wasting. An anabolic steroid was initiated, but later discontinued when patient developed drug-induced hepatitis. The patient was then prescribed Serostim® (somatropin) for injection for HIV-associated wasting.

ReLeVAnt MeDICAL HISto Ry

- HIV+ (2001)
- Opportunistic infections (PJP and CMV retinitis)
- Drug-induced hepatitis
- Hypertension
- Hypertriglyceridemia
- Peripheral neuropathy
- Active depression

So CIAL HISto Ry

- Relationship status: Single
- Unemployed on disability
- Activity level: Exercised 2-3x/week when he had enough energy
- Enjoyed running as exercise
- No recreational drug use

o Ve RVIe W of Sy Mpto MS At t IMe of HIV-ASSo CIAte D WASt Ing DIAgno SIS

- Fatigue often necessitating naps during the day
- Inability to complete daily living tasks, such as walking up stairs and food shopping
- Unintentional weight loss

We Ig Ht HISto Ry

- Height: 6'0"
- Premorbid weight: 165 lbs
- Premorbid BMI: 22.4
- Weight at HIV-associated wasting diagnosis: 138 lbs
- BMI at HIV-associated wasting diagnosis: 18.7

p Hy SICAL ex AM

- Thin male with slight bi-temporal wasting
- Decreased muscle mass in extremities
- Decreased strength on neurologic exam in his arms/legs
- Hypersensitivity to light touch consistent with peripheral neuropathy

LABo RAt o Ry Re Su Lt S

- CD4-cell count: 570 cells/mm^3
- Viral load: Undetectable
- WBC: Within normal limits
- Hgb: Within normal limits
- TSH: Within normal limits
- Vitamin D: Within normal limits
- Testosterone levels: Within normal range
- EKG: Normal

tR e At Ment H ISto Ry

- High-calorie oral supplements
- Anabolic steroids

This case study represents a real patient of Dr. Lee, however, it may not be a complete representation of the individual's entire medical case or include his full experience with Serostim®. Certain details such as concomitant medications, dose adjustments, and adverse reactions may not be reflected. For more information obtained from clinical trials and unsolicited post-marketing reporting of adverse experiences, refer to the Important Risk Information throughout and see enclosed Full Prescribing Information.

IMPORTANT RISK INFORMATION (CONTINUED)

WARn Ing S An D p Re CAut Ion S

Acute Critical Illness: Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with [pharmacologic amounts of] somatropin.

Concomitant Antiretroviral Therapy: Somatropin has been shown to potentiate HIV replication in vitro, however there was no increase in virus production when antiretroviral agents were added to the culture medium. All patients received antiretroviral therapy for the duration of treatment during Serostim® clinical trials and no significant increase in viral burden was observed.

Neoplasms: Patients with preexisting tumors should be monitored for progression or reoccurrence. Monitor patients on somatropin therapy carefully for preexisting nevi.

Please see additional Important Risk Information continued on the back and enclosed Full Prescribing Information.

HIV-associated wasting can have long-lasting negative effects on physical function and can ultimately impact survival

- Weight loss is still an independent and important predictor of mortality in patients receiving HAART
- As one study revealed, weight loss correlated to an increase in mortality compared to subjects who maintained or gained weight
- When patients with HIV lose weight unintentionally, they also lose LBM, which can be associated with a decline in strength and functional performance
- Reduced functional capacity can decrease the ability to complete tasks requiring a certain level of physical endurance

Lean body mass (LBM) is depleted in HIV-associated wasting. LBM is composed of:

Skeletal Muscle

Blood and blood constituents

Organ tissue

Intracellular and extracellular water

IMPORTANT RISK INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

Impaired Glucose Tolerance/Diabetes: Cases of new onset impaired glucose tolerance, new onset type 2 diabetes, and exacerbation of preexisting diabetes have been reported in patients receiving Serostim® (somatropin) for injection. Some patients developed diabetic ketoacidosis and diabetic coma. Patients with risk factors for hyperglycemia and glucose intolerance should be monitored closely and those using antidiabetic agents may require dose adjustment.

Intracranial Hypertension: Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea, and/or vomiting has been reported. Funduscopic examination should be performed prior to initiating treatment with Serostim® and periodically during the course of treatment. If papilledema is observed, treatment should be stopped and restarted at a lower dose after IH-associated symptoms have resolved.

Severe Hypersensitivity: Serious systemic hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with postmarketing use of somatropin products. Patients and caregivers should be informed that such reactions are possible and that prompt medical attention should be sought if an allergic reaction occurs.

Fluid Retention/Carpal Tunnel Syndrome: Swelling (particularly in the hands and feet), musculoskeletal discomfort, or carpal tunnel syndrome may occur during treatment with Serostim®. Symptoms may resolve spontaneously, with analgesic therapy, or after reducing the frequency of dosing. If symptoms of carpal tunnel do not resolve by decreasing the weekly number of doses, it is recommended that Serostim® treatment be discontinued.

Skin Atrophy: Rotate the injection site to avoid tissue atrophy.

Pancreatitis: Cases of pancreatitis have been reported rarely. Consider pancreatitis in patients who develop persistent severe abdominal pain.

ADVERSE REACTIONS

In clinical trials in HIV-associated wasting or cachexia the most common adverse reactions (incidence >10%) were increased tissue turgor, arthralgia, myalgia, and arthrosis, which may be responsive to dose reduction. Other common adverse reactions (incidence >5%) included nausea, fatigue, gynecomastia, paresthesia, generalized edema and hypoesthesia.

SPECIAL POPULATIONS:

Somatropin should be used during pregnancy only if clearly needed and with caution in nursing mothers because it is not known whether somatropin is excreted in human milk. The safety and effectiveness of somatropin in patients with hepatic or renal impairment or in patients aged 65 years and over have not been evaluated in clinical studies.

Please see the enclosed Prescribing Information for full disclosure.

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