

# Hypercalcemia and Strongyloides Superinfection in a Patient with Adult T-cell Lymphoma/Leukemia (ATLL)

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## INTRODUCTION

Adult T-cell leukemia/lymphoma is an uncommon hematologic malignancy in the United States. Patients with this disease present with variable symptoms; infection with HTLV-1 is central to pathogenesis. Even with chemotherapy, the majority of patients deteriorate rapidly, with survival frequently less than one year. Patients are highly susceptible to opportunistic infections.

In this case presentation, we describe a patient who was diagnosed with ATLL and whose hospital course was complicated by *Strongyloides* hyperinfection syndrome which contributed to his ultimate demise, even despite aggressive chemotherapy.

## CASE SUMMARY

A 55 year-old black male who emigrated from Belize six years ago presented with one week of altered mental status, decreased oral intake, and low back pain. He also reported 10-pound involuntary weight loss and night sweats over a two month period.

Two months prior, the patient had been admitted for abdominal pain and found by stool studies to be positive for *Strongyloides stercoralis*. He was given oral antimicrobials to be completed on an outpatient basis. Upper and lower endoscopies were scheduled but he was lost to follow-up.

On exam, patient was afebrile, hypertensive at 170/100, lethargic, oriented only to self, hypovolemic, and appeared wasted. Abdominal exam was notable for inguinal lymphadenopathy.

Laboratory studies on admission revealed BUN 60mg/dl, Cr 4.5mg/dl, serum calcium 18.2mg/dl, total protein 7.1g/dl, albumin 2.7g/dl, alkaline phosphatase 309U/L. Serum and urine protein electrophoresis and serum free light chain assays were negative. Urinalysis revealed 1+ proteinuria.

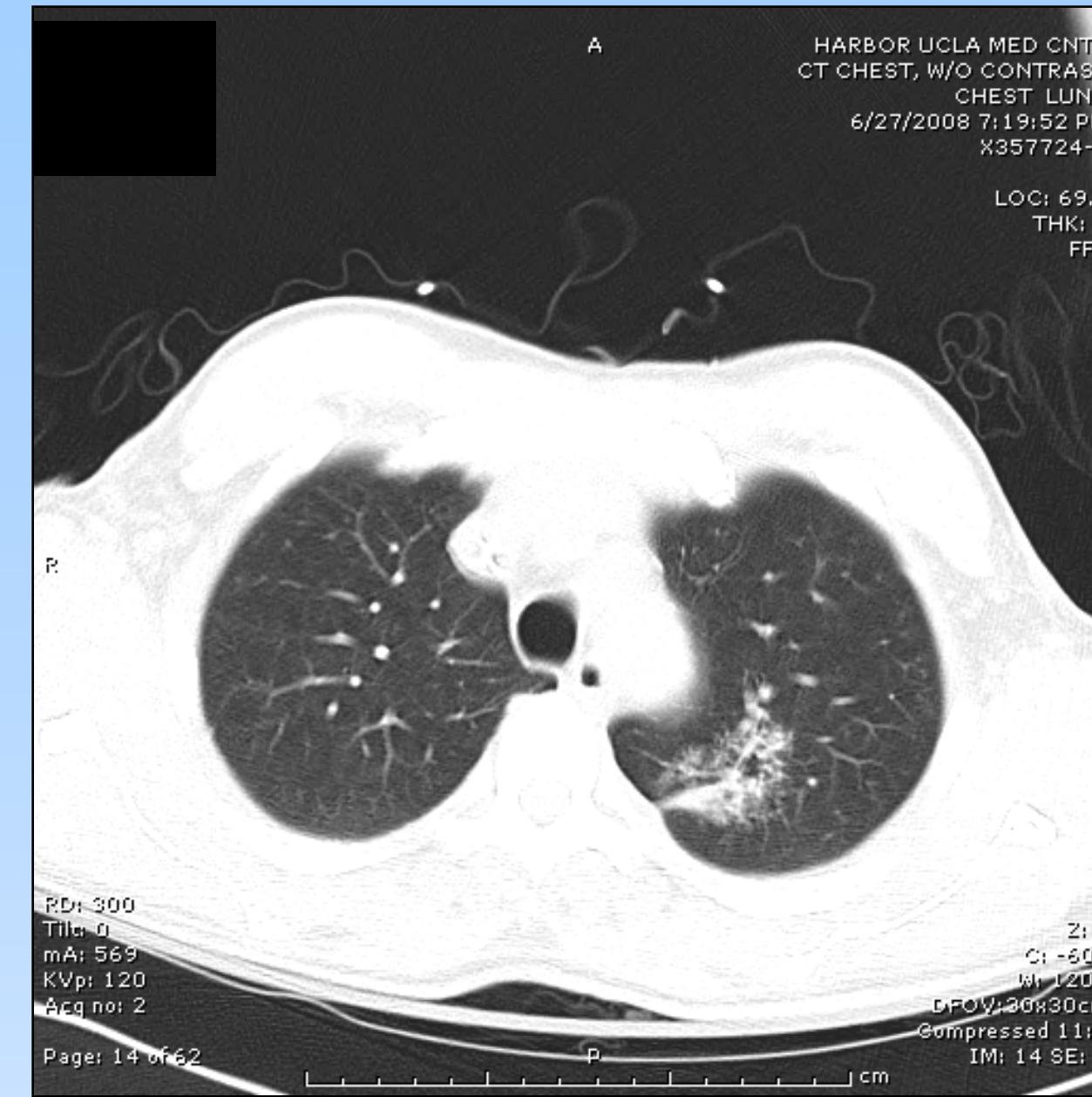
Computed tomography scan of the chest, abdomen, and pelvis showed multiple lytic lesions throughout the ribs, pelvis, and spine.

Patient developed worsening hypercalcemia and leukocytosis, and bone marrow aspirate was performed, revealing hypercellularity with findings suggestive of adult T-cell leukemia and lymphoma. Simultaneously, peripheral blood smear demonstrated marked lymphocytosis with "flower cells".

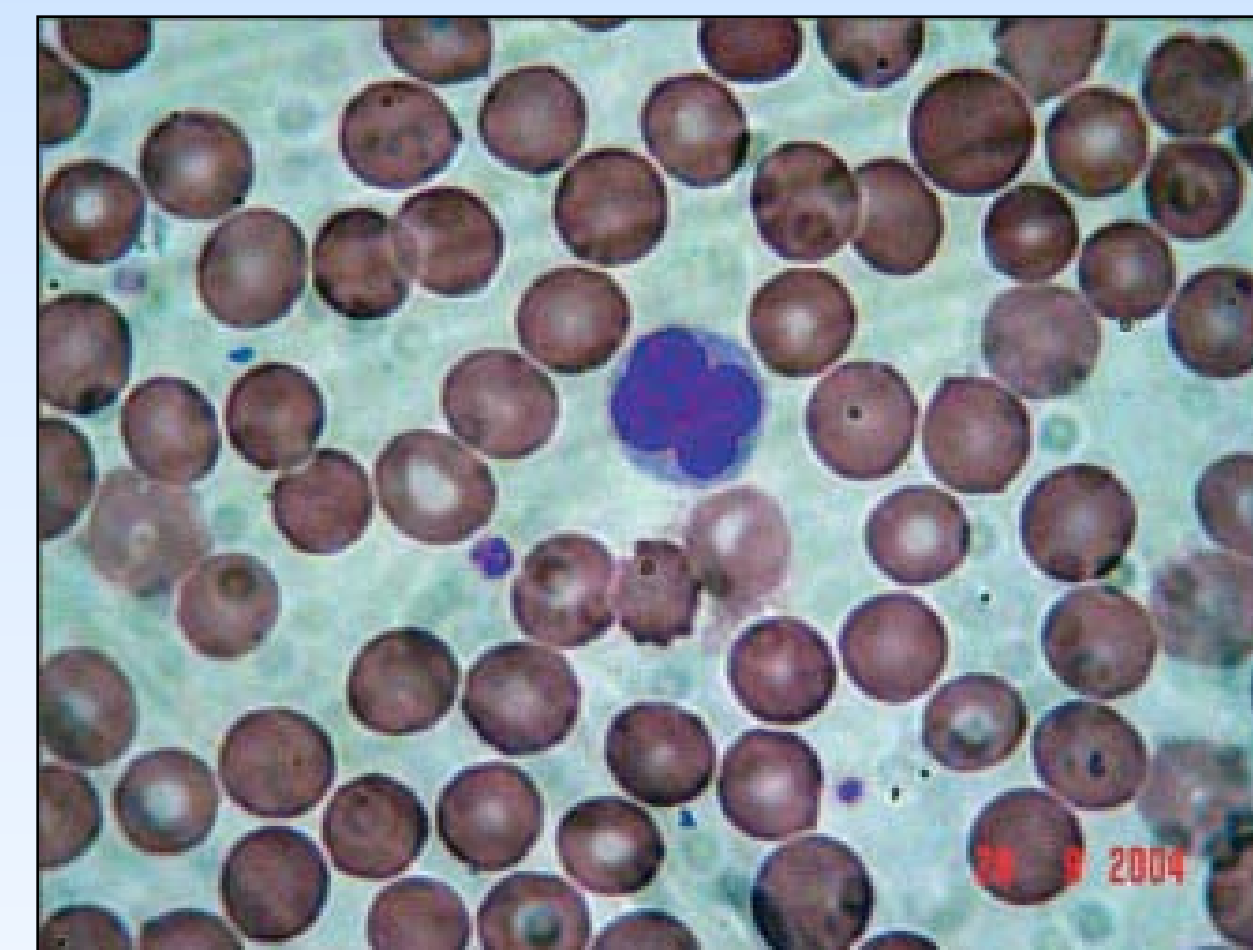
Due to refractory hypercalcemia and leukocytosis, patient was started on dexamethasone therapy, and subsequently developed respiratory distress that required monitoring in the intensive care unit. Bronchoscopy revealed *Strongyloides* hyperinfection. Stool studies confirmed a *Strongyloides* infection.

Serologies for HTLV-1 were positive, and patient subsequently received combination chemotherapy with cyclophosphamide, vincristine, doxorubicin and prednisone (CHOP). After an initial hematologic response with decrease in lymphoma cells in the peripheral blood over several days, patient's lymphocytosis and hypercalcemia recurred. Patient subsequently developed, fever, lactic acidosis, myocardial infarction, and expired after being placed on comfort measures.

## DATA/IMAGES



CT chest of this patient during hospitalization



This image adapted from another patient, showing similar manifestations in the peripheral blood smear, including atypical lymphocytes with a "flower cell" appearance.

### Comparing ATLL subtypes

	Acute	Lymphomatous	Smoldering	Chronic
Proportion of ATL cases	55%	20%	5%	20%
median survival	6 months	10 months	>4 years	24 months
4-year survival	5%	6%	66%	27%
lymphocyte count	variable	< 4000 /mL	<4000 /mL	>4000 /mL
Flower cells present	present	not present	occasional	occasional
Calcium, corrected	variable	variable	<5.5 mEq/L	<5.5 mEq/L

Adapted from Verdonck, Human T-lymphotropic virus 1: recent knowledge about an ancient infection. *The Lancet*. Volume 7, Issue 4, April 2007, Pages 266-281

## DISCUSSION

Adult T-cell lymphoma/leukemia is a non-Hodgkin's T-cell lymphoid neoplasm of varying clinical manifestations and prognosis. ATLL results from HTLV-1 infection and its incidence is strongly associated with areas endemic to the virus, such as Japan, the Caribbean, western Africa and Peru.

HTLV-1 may be transmitted by blood or sexual contact but it is more often transmitted through breastfeeding, thereby infecting many individuals at a young age. Pathogenesis of ATLL requires HTLV-1 infection, but only four to five percent of HTLV-1-infected individuals develop the malignancy, typically 10 to 30 years following infection.

The acute and lymphomatous variants are more common but carry poorer prognoses. Median survival range from 8 to 10 months even with chemotherapy. The acute variant often presents with leukocytosis, generalized lymphadenopathy, hepatosplenomegaly, and hypercalcemia with lytic bone lesions. The lymphomatous variant is manifested by lymphadenopathy without peripheral blood involvement. Cutaneous lesions are more prevalent in the chronic variant and smoldering variants.

Diagnosis is made by serologic confirmation of HTLV-1 infection and identification of morphologically proven malignant cells with T-cell surface antigens.

Typically, chronic and smoldering variants may be monitored without therapy. Acute and lymphomatous variants benefit from combination chemotherapy, most commonly with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone).

Prognosis for acute and lymphomatous variants is poor, with median survivals ranging from 8 to 10 months, even with chemotherapy. Chronic and smoldering variants have a median survival typically 2 and >5 years, respectively, without treatment.

ATLL patients invariably develop immunosuppression, and can present with opportunistic infections such as *Strongyloides stercoralis* and *Pneumocystis jiroveci*. *Strongyloides stercoralis* is a helminthic parasite with the potential for dissemination through autoinfection. Immunosuppression and HTLV-1 infection are important risk factors for *Strongyloides hyperinfection* syndrome. Common manifestations of this infection are fever, gastrointestinal and pulmonary complaints, which may lead to organ failure and septic shock. Ivermectin is the standard treatment.

## REFERENCES

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