中文題目：老年人罹患HTLV-1合併僵直性脊椎炎的個案報告

英文題目：A case of HTLV-1 infection and Ankylosing Spondylitis in an elderly woman

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Abstract

Chronic lower back pain is a common musculoskeletal symptom in the community especially for the elderly patients. One of the most important considerations are any types of inflammation of the joints. The human T-cell lymphotropic virus type 1 (HTLV-1) infection is a rare but invasive viral infection associated with poor outcome. Some HTLV-1 related disorder including HTLV-1 related myelopathy/ tropical spastic paraparesis (HAM/TSP) and adult T-cell leukemia/lymphoma (ATL) mimic the features of AS. In this report, we describe an interesting case of an elderly woman suffering from chronic lower back pain. Her clinical manifestations shared features of AS. To our knowledge, this is the first report with AS in combination with HTLV-1 infection which has not been reported to date.

Introduction

The human T-cell lymphotropic virus type 1 (HTLV-1) infection is a special virus infection which can cause many diseases including adult T-cell leukemia/lymphoma (ATL) and HTLV-1 related myelopathy/ tropical spastic paraparesis (HAM/TSP). We describe a young woman who developed severe lower back pain with ankylosing spondylitis(AS) and HTLV-1 infection that eventually caused HAM/TSP and ATL. Treatment of AS were unsatisfied and with a good response to danazol, steroid and interferon –α treatment added. HTLV-1 infection related HAM/TSP can remain undiagnosed or can be misdiagnosed, leading to erroneous treatment decisions as we report in this case report.

Case Report

A 68-year-old female patient presented with chronic lower back pain for more than 40 years of duration. The low back pain started since she was 25-year-old. The severe back pain was worse in the morning and improved after some light exercise or taking a bath. Two year prior to admission, the patient was diagnosed as Ankylosing

Spondylitis (AS) at another hospital and had been treated with pulse therapy. From 1992, long term use of non-steroid anti-inflammatory drug (NSAID) and steroid was noted.

In November 2003, she presented with severe back pain with refractory to steroid and NSAID. Clinical examination showed anterior tibialis atrophy, symmetrical paresthesias and weakness of the lower limbs.

Neurological examination at admission showed normal mental status and cranial nerves. In the motor examination, muscle strength, bulkan tone were normal in both upper extremities. In the lower extremities, however, strength was Grade 3/5 in the left and Grade 2/5 in the right flexor muscles, Grade4+/5 in the left and Grade 4/5 extensor muscles. Muscle tone was increased in both lower extremities with elicited sustained in both ankle clonus. In the sensory examination, upper extremities were normal. Pin prick and light touch were normal, but position and vibration sense was mildly impaired in the lower extremities. Other finding included spasticity of both legs together with hyperreflexia and waddling gait. She also had the symptoms of voiding difficulty and constipation.

Laboratory data at the time of her first admission is summarized in Table 1. Basic laboratory investigation revealed mild leukocytosis with lymphocyte predominant (White Blood Count 10600/uL [Normal: 4-10 $X10^3$], lymphocyte 64% [Normal:20-40%]). Rheumatic factor 36.1IU/ML (Normal:<20IU/ML), HLA-B27 was positive. No obvious inflammatory process with CRP 0.17 mg/dl (Normal: <0.8 mg/dl), ESR 4 mm/HR (Normal: <12 mm/HR). Other investigations showed , ANA: Speckled 160X +, C3 91 mg/dl (Normal: 90-150 MG/DL), C4 14 mg/dl (Normal: 17-37 MG/DL), CH50 23.8 CH50/ML (Normal:32.6-39.8 CH50/ML), CK 327 U/l (Normal: 25-175 U/L) and LDH 197 U/L (Normal:90-200 U/L). MRI of the whole spine revealed periarticular marrow edema, irregularity especially wavy appearance of cartilages with enhancement of bilateral sacroiliac joint and syndesmophyte formation (Figure 1).

By the modified New York Criteria, this patient fit the diagnosis of Ankylosing Spondylitis. We prescribed the NSAID based therapy for as AS. In the mean time, we also arrange some examinations for her due to the previous poor response and lymphocytosis.

The flow cytometric immunophenotyping report indicated the malignant cells were significant elevated for CD3, CD4 and decreased in CD19. Her serum anti-HTLV-1

antibody level was 8192. Bone marrow exam showed unremarkable. The peripheral blood smear showed a few lymphocyte of hyperlobulated nuclei with less than 5%. Cerebrospinal fluid (CSF) examination also revealed positive with anti-HTLV-1 antibodies. Base on the laboratory result, flow cytometric immunophenotyping, clinical features and histological finding, she fitted the diagnostic criteria of chronic type of adult T-cell lukemic/lymphoma (ATL)[1] and HAM/TSP. The diagnostic criteria from the WHO description of HAM/TSP are listed in table 2 [2]. Danazol, corticosteroid and interferon –α was started and her symptoms improved dramatically after the use of danazol, corticosteroid and interferon –α. She maintained this therapy with relative stable condition for 5 years. We also checked her family members and her father, mother and brother were also HTLV-1 carriers.

Table 1 Initial laboratory result of her first admission

	2003/11/13
Hb	12.4 g/dl
WBC	10600 /ul
Lym	64%
Platelet	221000 /ul
Na	141 meq/l
K	3.7 meq/l
Ca	8.3 mg/dl
AST	34 IU/L
ALT	43 IU/L
LDH	197 U/L
Rheumatic factor	36.1 IU/ML

C3	91 mg/dl
C4	14 mg/dl
CD2	89.2%
CD3	85.5%
CD4	80.3%
CD8	4.6%
CD10	0.1%
CD19	5.7%
CD25	69.1%

Table 2.Criteria for diagnosis of HAM

Present features
Primary
● Hyperreflexia, often with spasticity and clonus
● Presence of HTLV-I or HTLV-II antibodies or antigens in blood and/or CSF
Supportive
● Lower extremity weakness
● Neurogenic bladder and/or bowel dysfunction
Absent features
● Family history of spastic paraparesis

● Cranial nerve or cognitive impairment
● Upper extremity weakness
● Laboratory abnormalities that would explain examination findings
● Spinal cord lesions that would explain examination findings

Five years later the disease then developed from chronic type ATL into acute type of ATL. Her laboratory examination showed severe leukocytosis with lymphocyte predominant (WBC: 159800/ul, Lym: 92%). The hyperlobulated nuclei of lymphocyte markedly increase in her peripheral blood (Figure 2). She died 5 years after the initial diagnosis of HTLV-1 infection due to Listeria monocytogenes pneumonia.

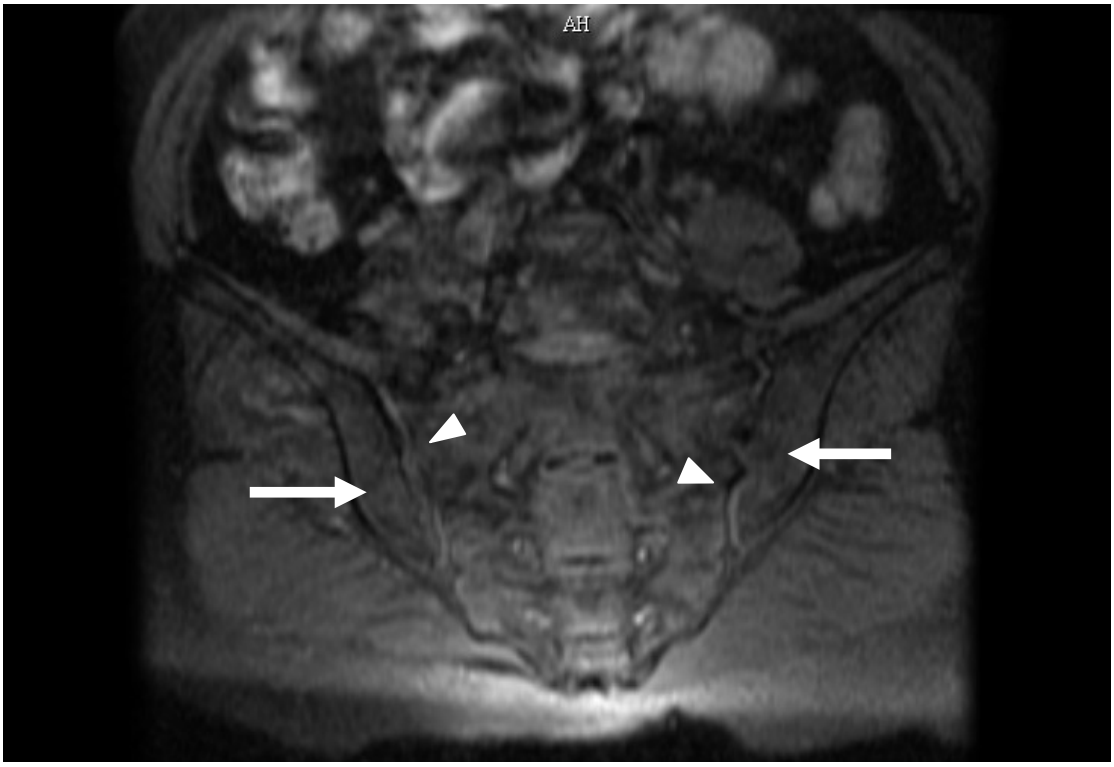

Figure 1. Magnetic resonance image of the patient's sacroiliac joint.

Irregularity and wavy appearance of cartilages (arrow heads) of bilateral sacroiliac joint with subcondral sclerosis; Periarticular marrow edema (thick arrows) and

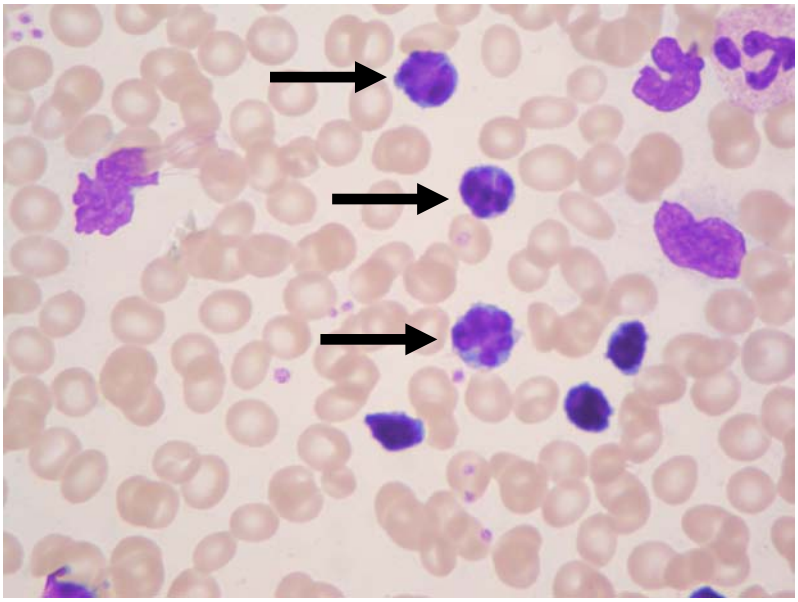

Figure 2. Peripheral blood smear at the time of progressed into acute type ATL. Note the hyperlobulated lymphocytes which are also so called the "flower cells" (arrows).

Discussion

This case highlights a number of interesting points. Co-occurrence of sacroiliitis and HTLV-1 infection is rarely reported, to our knowledge, this has never been previously described.

It may cause diagnostic confusion due to the both of them share some symptoms in common. HAM/TSP has higher prevalence in female. It affects less than 2% of the HTLV-1 carriers with the time of onset may rang from 4 months to 30 years since infection [3]. The risk factor of HAM/TSP is still not fully clear. One important risk factor would be associated to the provirus load [4, 5].

In most cases, of HAM/TSP is characterized with insidious onset of progressive weakness and spasticity of the lower limbs with signs of pyramidal tract involvement,

which progresses slowly [6-8]. In many patients especially the elderlys, bladder disorders and sexual problems are the first symptoms of the disease. Other features included hyperreflexia, ankle clonus, constipation and lumbar pain [9, 10].

There were no effective treatment HAM/TSP, some studies showed that danazol and corticosteroid may show some improvement [2, 11]. Management of HAM/TSP is based on two mechanisms which is the direct modulation of the immune response that was induced by HTLV-1 and decreasing the HTLV-1 viral load, which in turn should lead to a reduction in HTLV-1-specific cytotoxic lymphocyte activity. Interferon-α and Interferon-β1a showed some benefits and a slight improvement in motor function [12, 13]. A recent andomised, double-blind, placebo-controlled study by using the combination of zidovudine and lamivudine had showed that there were no significant changes in provirus load and no clinical improvement [14].

This disease has poor prognosis, according to a previous study of 14-year follow-up it may cause a median of 21 years from the disease inset to wheelchair confinement [15].

A diagnosis of HAM/TSP, ATL or AS should be very careful and a close needs monitoring is recommended. If chemotherapy, immunosuppressant or immune modulate agent was given to a patient who is not fully confirmed may have cause the patient's possible underline disorder to flare up again.

In summary, we present a rare case of the coexistence of chronic ATL, HAM/TSP and AS in an elderly patient. HAM/TSP should be listed in the differential diagnosis of any patient presenting chronic lower back pain with poor response to therapy, even with a radiological picture suggestive of a structural spinal cord lesion, should have a screening test for HTLV-I, especially in the elderly patient in the endemic area.

Disclosures

The author declare that there are no conflicts of interest

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