A case of HTLV-1 associated adult T-cell lymphoma presenting with cutaneous lesions and tropical spastic paresis

Purva V Sharma1,*, Michael Witteman1, Swethika Sundaravel1, Tulisa Larocca1, Yuanming Zhang2, Harry Goldsztajn3

1 Department of Internal Medicine, University of Miami Palm Beach Regional Consortium, Atlantis, Fl, USA;
2 Department of Pathology, JFK Medical Center, Atlantis, Fl, USA;
3 Department of Hematology/Oncology, JFK Medical Center, Atlantis, Fl, USA.

Summary

Adult T cell lymphoma (ATL), is a peripheral T cell neoplasm associated with infection by human T-lymphotropic virus (HTLV). This is a case of a 28-year-old lady who presented with back pain for the past month and recent onset weakness in her lower extremities bilaterally. She has a history of T-cell lymphoma secondary to HTLV-1 under remission since 2014 and systemic lupus erythematosus complicated by lupus nephritis. On physical examination patient had hyper-reflexia in both knees, ankle clonus bilaterally and spasticity in both her lower extremities. She also had a diffuse, scaly, macular rash in her upper and lower extremities and ulcer-like lesions on the plantar surface of both feet. Her lumbar puncture showed lymphocyte predominance. The Western Blot test was positive for HTLV antibodies in the CSF. The patient was started on IV Methylprednisolone which considerably improved her symptoms. The biopsy of her skin lesions showed an immunophenotype of T-cells similar to the cells in the bone marrow at the time of diagnosis of the lymphoma. HTLV infection is an etiologic agent for ATL as well as for tropical spastic paresis. One should have a high degree of suspicion for tropical spastic paresis in patients with HTLV-1 infection as it can easily go undiagnosed. Indolent forms of ATL can also present in the form of skin lesions in later stages. It is also important to distinguish between skin manifestations of ATL and cutaneous T cell lymphomas, and the importance of skin biopsies for the same cannot be undermined.

Keywords: HTLV infection, T-cell lymphoma, tropical spastic paresis, cutaneous lymphoma

1. Introduction

Adult T cell leukemia-lymphoma (ATL), according to the most recent World Health Organization (WHO) classification of lymphoid neoplasms, is defined as a peripheral T cell neoplasm associated with infection by the human T-lymphotropic virus (HTLV), type I (HTLV-I) (1). Although it is considered as one of the most highly aggressive T cell non-Hodgkin lymphoma (NHL) variants, the disease course is variable and sometimes quite indolent.

Infection with HTLV-1 is endemic in islands of Japan, Caribbean islands such as Trinidad and Jamaica and some parts of southeastern United States. In the United States as a whole, the incidence of ATL is approximately 0.05 cases per 100,000 people (2). Since ATL is associated with HTLV-1 infection, patients with ATL are also at risk for HTLV-1-associated myelopathy, also known as tropical spastic paraparesis.

We present a case of a young lady with known history of Adult T-cell lymphoma presenting with new skin manifestations of ATL as well as tropical spastic paresis.

2. Case Report

A 28-year-old Haitian female patient presented to the
emergency department in March 2017 with complaints of back pain for one month prior to presentation and recent onset weakness in her lower extremities bilaterally.

She has a history of T-cell lymphoma secondary to HTLV-1 infection. This was diagnosed the very first time with a bone marrow biopsy in 2013 in her oncologist’s office. She completed 5 cycles of chemotherapy (CHOP), the last one being in March 2014, after which the T-cell lymphoma was under remission. However, she did not maintain follow-up post chemotherapy and her current state of disease during this presentation to the hospital was unknown.

On admission, the patient was afebrile, with a heart rate of 88/min and a blood pressure of 110/70 mmHg. Patient’s neurological examination revealed hyper-reflexia in both knees, as well as ankle clonus bilaterally. There was also spasticity appreciated in both her lower extremities. On skin examination, the patient was found to have a diffuse, scaly, macular rash in her upper and lower extremities and also in her sub-mammary region. She also had ulcer-like lesions on her soles.

A lumbar spine MRI did not show spinal cord compression and was negative for acute disease process. At this stage, there was concern for tropical spastic paraparesis secondary to HTLV infection and indolent course of the disease. She had a lumbar puncture which revealed 12 white blood cells with lymphocyte predominance, normal protein and glucose (Table 1). The Western Blot test was positive for HTLV antibodies in the CSF. The patient was started on IV Methylprednisone 40 mg every 8 hours which was tapered over the next 2 weeks. The patient experienced gradual improvement in her lower extremity weakness over the next 2-3 weeks, after starting the high-dose steroids. The infectious disease team agreed with this treatment because there is no definitive treatment for tropical spastic paresis.

As the diagnosis of T-cell lymphoma was already established, a repeat bone marrow biopsy was not performed during this admission. However, she had a biopsy of one of the skin lesions on her right lateral thigh which showed atypical T-cells, positive for CD3 and CD8 and showing markedly decreased expression of CD5 and CD7. (Figures 1, 2, and 3).

The immunophenotype of the T-cells in the skin biopsy findings was similar to the cells found in the bone marrow in a repeat bone marrow biopsy in 2016 which showed an atypical T-cell population consistent with a T-cell lymphoproliferative disorder which is the previously diagnosed T-cell lymphoma (Figure 4). The findings raised suspicion of involvement by a mature T-cell lymphoma.

She has a known history of systemic lupus erythematosus (SLE) since 2013, diagnosed by positive ANA as well as ds-DNA and low complement c3 and c4 levels. It was complicated by lupus nephritis and end stage renal disease requiring hemodialysis. Patient also had a history of hyperthyroidism and was diagnosed with Graves’ disease.

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<th>Table 1. Results of CSF fluid analysis</th>
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Another significant finding in our patient was the presence of HTLV-1 in the malignant cells of ATL, which can be determined by testing for the antibody in the blood. Since HTLV-1 DNA testing in tissues is a useful tool to differentiate between skin manifestations of ATL and cutaneous T cell lymphomas, and a key differentiating feature is the HTLV positivity in the malignant T cells of ATL. HTLV-1 DNA testing in tissues is a useful tool to establish that the skin lesions are one of the manifestations of the ATL.

The immunophenotype of the T cells infiltrating the skin lesions was very similar to the ones in the bone marrow, establishing that the skin lesions are one of the manifestations of the ATL. A key differentiating feature between skin lesions of ATL and other forms of cutaneous T-cell lymphomas is the presence of HTLV-1 in the malignant cells of ATL, which can be determined by testing for the antibody in the blood.

Another significant finding in our patient was the presence of HTLV-1 in the malignant cells of ATL, which can be determined by testing for the antibody in the blood. Her medical records showed that she was hospitalized on two occasions in the past for similar complaints of lower extremity weakness. Given the patient's history and the CSF findings, the likely etiology of the weakness and spasticity on examination was thought to be tropical spastic paresis due to infection with HTLV-1. Almost 10% of carriers of HTLV-1 develop HTLV-1 associated myelopathy/tropical spastic paresis (9). Also our patient had antibodies to HTLV-1 in serum as well as CSF, and she could likely be developing a slowly progressive myelopathy defined as 'definite' tropical spastic paresis (10). One of the radiologic findings is diffuse muscle atrophy of the extremities on MRI which was not performed on our patient (11). Other findings include atrophic changes in the spinal cord and multifocal high-signal-intensity lesions in the cerebral white matter on T2-weighted images which were also not seen in our patient (12,13). However, our patient had a positron-emission tomography (PET) scan in 2016 which reported multifocal uptake in thoracic spine, lumbar spine and pelvis, which has been reported in some patients with tropical spastic paresis (14).

Tropical spastic paresis is more common in females than in males, in keeping with the high prevalence of HTLV infection in females. It affects less than 2% of HTLV-1 carriers, so our patient was among the less than 2% population with spastic paresis.

Another important association of HTLV-1 is with autoimmune diseases such as rheumatoid arthritis, Sjogren's syndrome and SLE and has been studied extensively at the molecular level. HTLV-1 virus infects CD4+ T lymphocytes, which can in turn lead to changes in their behavior and can trigger inflammatory reactions that can break immune system tolerance, leading to autoimmunity (15). Our patient has a history of SLE, and the association between SLE and HTLV infection is thought to be based on molecular mimicry. A recent study concluded that there is no real association between SLE and HTLV infection and that geographical and environmental factors should be taken into consideration.

3. Discussion

Adult T-cell lymphoma (ATL) is an uncommon neoplasm of the peripheral T lymphocyte cells and it is etiologically associated with HTLV (3). About 5% of the carriers of the HTLV virus can develop adult T-cell lymphoma after a long latent period (4). As per the Shimoyama Classification, Adult T-cell lymphoma can present as different subtypes such as acute, smoldering lymphoma and chronic (5). Among these, the smoldering and chronic forms of ATL follow a more indolent course (6). Our patient's disease course could also be considered indolent as she was in remission for almost 3 years after her last cycle of chemotherapy with no active disease, until her presentation during this hospital admission.

Skin manifestations occur in almost one-third of the patients of ATL (3). They are also seen more commonly in patients with a more indolent course of the disease, as seen in our patient (7). Skin lesions in ATL mimic various other skin conditions, including certain types of cutaneous T-cell lymphomas. Some of these presentations include leukocytolytic purpura, plaques, erythro-derma and a papulo-squamous eruption (8). Often times it is seen that, when patients present with a skin lesion as the first manifestation of ATL, the diagnosis can be missed. In our patient, however, as her diagnosis of ATL was already established, an immediate biopsy of her skin lesions was done upon presentation. The immunophenotype of the T-cells infiltrating the skin lesions was very similar to the ones in the bone marrow, establishing that the skin lesions are one of the manifestations of the ATL.

A key differentiating feature between skin lesions of ATL and other forms of cutaneous T-cell lymphomas is the presence of HTLV-1 in the malignant cells of ATL, which can be determined by testing for the antibody in the blood.

4. Conclusion

HTLV infection is an etiologic agent for ATL as well as for tropical spastic paresis. Indolent forms of the disease can also present in the form of skin lesions in later stages. It is important to distinguish between skin manifestations of ATL and cutaneous T cell lymphomas, and a key feature is the HTLV positivity in the malignant T cells of ATL. HTLV-1 DNA testing in tissues is a useful tool to study T-cell lymphomas.

References


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