Hospital admissions for human T-cell lymphotropic virus type-1 (HTLV-1) associated diseases in Dominica

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See end of article for authors' affiliations

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Human T-cell lymphotropic virus type 1 (HTLV-1) is a retrovirus that is endemic in certain regions of the world. The global prevalence may be up to 11–20 million but it is highly endemic in certain areas of the world. In some parts of Southern Japan, prevalence may be as high as 30%, and 2%–6% in some islands of the Caribbean, while endemic foci are also described in some south eastern states of America, Latin America, and in Central Africa. The diseases associated with HTLV-1 infection in this areas include adult T-cell leukaemia/lymphoma (ATLL), tropical spastic paraparesis/HTLV-1 associated myelopathy (TSP/HAM), uveitis, infective dermatitis of childhood, polymyositis, Sjögren’s syndrome, polyneuropathy, arthropathy and immunosuppression. The lifetime risk of developing an HTLV-1 associated disease varies. The risk for ATLL is about 5% if infection occurs before age 20 years, and that of TSP/HAM is 2% if infection occurs at any age.

PATIENTS AND METHODS
A total of 298 inpatients in the medical wards of Princess Margaret Hospital, Commonwealth of Dominica suspected of having HTLV-1 associated diseases were screened for HTLV-1 using an enzyme linked immunosorbent assay (ELISA) technique between 1995 and 1999. Princess Margaret Hospital is a 200 bed secondary care centre in the Windward Island of Dominica (population 75 000). The spectrum of selected diseases screened for HTLV-1 included haematological malignancies, solid organ tumours, paraparesis and neuropathies, parasitic infestations, viral, bacterial and fungal infections, connective tissue disorders, arthritis, chronic renal failure, hepatic disease and dermatoses. Patients found to be HTLV-1 seropositive by ELISA had it confirmed by western blot testing at a referral centre, and were also screened for HIV by ELISA. All HTLV-1 seropositive patients were clinically examined with particular attention to the skin, lymphoreticular, rheumatological, and neurological systems. Laboratory investigations included a full blood count with differentials, stool microscopy for parasites, electrolytes, urca, creatinine, and calcium. Chest radiography, abdominal ultrasound, and tissue biopsy for histopathology was done as indicated.

RESULTS
Sex and age
There were 66 seropositive patients out of 298 hospitalised patients screened for HTLV-1 (22.15%). Thirty two (48.5%) of the patients were females and 34 (51.5%) were males. The mean age of clinical presentation was 56 years for all diseases and were in the age range of 9–89 years.

Associated diseases
Fifty eight patients were admitted for a single disease during the period of study, while eight patients had more than one disease. The seropositive cases included 12 cases of TSP/HAM (18.2%), which constituted 38.7% of all paraparesis/paraplegia screened, five cases of acute ATLL (7.6%), two cases of Hodgkin’s and eight cases of non-Hodgkin’s lymphoma (15.2%).

Table 1 Mean age of patients with HTLV-1 associated diseases

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Mean age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSP/HAM</td>
<td>60</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>46</td>
</tr>
<tr>
<td>Acute ATLL</td>
<td>38</td>
</tr>
<tr>
<td>Hyperinfective strongyloides</td>
<td>61</td>
</tr>
<tr>
<td>Crusted (Norwegian) scabies</td>
<td>57</td>
</tr>
</tbody>
</table>

Abbreviations: ATLL, adult T-cell leukaemia/lymphoma; ELISA, enzyme linked immunosorbent assay; HTLV-1, human T-cell lymphotropic virus type 1; TSP/HAM, tropical spastic paraparesis/HTLV-1 associated myelopathy
which made up 45.4% of all lymphomas, 27 cases of ectoparasitosis and endoparasitosis (40.9%); five cases of crusted scabies, 17 cases of hyperinfective strongyloidiasis, and two cases each of giardiasis and hookworm were seropositive.

The other seropositive cases were two patients with neuropathies of unknown aetiology (3.0%), three cases of pulmonary tuberculosis (4.5%), AIDS/HIV in three patients (4.5%), seronegative arthropathy in four patients (6.1%), and thrombocytopenia of unknown aetiology in two patients (3.0%) (tables 2, 3, and 4). There were nine other seropositive patients made up of chronic hepatitis (1) chronic renal failure (2), carcinoma of the oesophagus (1), myeloproliferative disease (1), infective dermatitis of childhood (1), Escherichia coli hepatic abscess (1), pneumonia (1), and optic atrophy (1).

HIV seropositivity
Forty nine HTLV-1 seropositive patients were screened for HIV. There were three seropositive patients (4.5%) of whom two had AIDS.

DISCUSSION
The retroviruses associated with diseases in man are HTLV-1, HTLV-2, HIV-1, HIV-2 and all are T-cell lymphotropic. HTLV-1 is endemic in Dominica with a seroprevalence of 2.66% in asymptomatic blood donors (in press). Altogether 22.15% of selected hospitalised patients in our study were seropositive and the main associated diseases are discussed.

Adult T-cell leukaemia/lymphoma
There are four clinical variants of ATLL: acute (55%), chronic (20%), lymphomatous (20%), and smouldering (5%). Acute ATLL is rapidly progressive with median survival of less than six months. There is marked leucocytosis, predominantly lymphocytes with lobulated nuclei (leukaemic cells), hypercalcaemia, skin infiltration, lymphadenopathy, and hepatosplenomegaly. Five patients in our study had the acute form of ATLL.

They all presented with marked leucocytosis with atypical lymphocytes while hypercalcaemia on admission occurred in four patients as well as hepatosplenomegaly. The lymphomatous form of ATLL may present like acute ATLL but leucocytosis and atypical cells are usually absent or minimal. There were eight seropositive patients with non-Hodgkin’s lymphoma in our study out of which seven can be classified as lymphomatous ATLL. The eighth patient was a 60 year old woman who presented with well defined skin patches over her trunk and abdomen (fig 1). She was initially referred to us as a case of extensive tinea corporis, but histology of a skin biopsy specimen showed features of mycosis fungoides. She developed multiple skin nodules on the upper limb, generalised lymphadenopathy, and severe ichthyosis of the lower limb four months later (figs 2 and 3). The histopathology of a skin nodule biopsy specimen showed non-Hodgkin’s lymphoma. We classified her as a case of chronic ATLL, which usually has an insidious onset and natural history is more prolonged than acute and lymphomatous ATLL. We did not identify any smouldering ATLL in our study. The mean age of presentation of the acute ATLL and lymphomatous ATLL in our study (table 1) is consistent with the 43 years found in cases of ATLL in Jamaica, suggesting an early life exposure to the virus through maternal to child transmission as leukaemogenesis may take 20–40 years.18

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**Table 2** HTLV-1 associated diseases

<table>
<thead>
<tr>
<th>Diseases</th>
<th>No of cases</th>
<th>% of HTLV-1 seropositive (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSP/HAM</td>
<td>12</td>
<td>18.2</td>
</tr>
<tr>
<td>Neuropathies of unknown aetiology</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>10</td>
<td>15.2</td>
</tr>
<tr>
<td>ATLL (acute)</td>
<td>5</td>
<td>7.6</td>
</tr>
<tr>
<td>Ectoparasites/endoparasites</td>
<td>27</td>
<td>40.9</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>3</td>
<td>4.5</td>
</tr>
<tr>
<td>AIDS/HIV</td>
<td>3</td>
<td>4.5</td>
</tr>
<tr>
<td>Seronegative arthropathy</td>
<td>4</td>
<td>6.1</td>
</tr>
<tr>
<td>Thrombocytopenia of unknown aetiology</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
<td>13.6</td>
</tr>
</tbody>
</table>

**Table 3** Prevalence of diseases

<table>
<thead>
<tr>
<th>Diseases</th>
<th>No of cases screened (n=298)</th>
<th>No (%) of HTLV-1 seropositive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraparesis</td>
<td>31</td>
<td>12 (38.7)</td>
</tr>
<tr>
<td>Acute ATLL</td>
<td>5</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>22</td>
<td>10 (45.4)</td>
</tr>
<tr>
<td>Other haematological malignancies</td>
<td>24</td>
<td>1 (4.2)</td>
</tr>
<tr>
<td>Solid organ tumours</td>
<td>8</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>Parasitosis</td>
<td>66</td>
<td>27 (40.9)</td>
</tr>
<tr>
<td>Other infections</td>
<td>55</td>
<td>4 (7.3)</td>
</tr>
<tr>
<td>Other diseases</td>
<td>87</td>
<td>17 (19.5)</td>
</tr>
</tbody>
</table>

**Table 4** HTLV-1 and parasitic infestation

<table>
<thead>
<tr>
<th>Parasites</th>
<th>No (%) of cases (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongyloidiasis</td>
<td>18 (66.7)</td>
</tr>
<tr>
<td>Crusted (Norwegian) scabies</td>
<td>5 (18.5)</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>2 (7.4)</td>
</tr>
<tr>
<td>Hookworm</td>
<td>2 (7.4)</td>
</tr>
</tbody>
</table>

**Figure 1** Extensive well demarcated patches in a 60 year old HTLV-1 seropositive woman with initial diagnosis of mycosis fungoides (all photos published with patient’s permission).
observed two cases each of intestinal giardiasis and hookworm infestation. One patient with hookworm had severe iron deficiency anaemia with a haemoglobin concentration of 36 g/l. Robinson et al in Jamaica found an increased prevalence of *Giardia lamblia* in HTLV-1 carriers (9.1%) when compared with HTLV-1 seronegative patients (3.3%).

**HIV/AIDS**

There were three HIV seropositive patients out of 49 HTLV-1 seropositive cases of whom two had AIDS. One patient with severe wasting died from rapidly progressive pneumonia with chest radiography findings of bilateral interstitial pneumonitis suggestive of *Pneumocystis carinii* pneumonia, while the other had extensive tinea capitis and later died from lobar pneumonitis.

Some authors have suggested that coinfection of HTLV-1 and HIV can accelerate progression of HIV to AIDS.

The exact mechanisms by which HTLV-1 causes diseases is not conclusively known. The tax gene products of HTLV-1 induces expression of interleukin-2, interleukin-2 receptors, and other transcription factors and may lead to leukaeemia/lymphoma. The mechanism of TSP/HAM may involve myelin damage by cytotoxic T-cell directed against HTLV-1 in tissues, damage by cytokines, and neutralising antibodies directed against HTLV-1 infected cells.

Immune response to the virus may explain inflammatory diseases associated with HTLV-1. Low levels of IgE and IgA are found in asymptomatic HTLV-1 carriers. This may result in hyperparasitaemia especially in strongyloides and scabies infestation as observed in our study.

We have documented both infective and non-infective diseases associated with HTLV-1 in Dominica. Routine blood screening in blood transfusion services is the right step in endemic regions and in immigrants from such regions. Further efforts should be made at intensifying both physician and public awareness on HTLV-1 associated diseases.

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