Sixteen haplotypes were associated with the disease in the 10 families studied. In two subjects it was not possible to identify the haplotypes. A3B7 was the haplotype found most frequently in the patient group (17.6%). This was significantly higher than that observed in the control population (1.8%), representing a relative risk of 12.46.

The haplotype A3B14, which has also been shown in association with idiopathic haemochromatosis in certain regions, was not found to be linked to the disease in this patient population; this haplotype, however, was not represented in the control population studied.

The phenotype prevalence of the HLA antigens in the control population was determined in 203 healthy, unrelated blood donors from the blood bank of the Hospital Geral de Santo António-Porto.

HLA haplotype prevalence in the control population was calculated in a control group of unrelated subjects from the north of Portugal, including the spouses of some family members in whom the disease was excluded, heterozygous family members (only the non-idiopathic haemochromatosis associated haplotype was considered), and normal subjects previously HLA genotyped.

The significance of the differences observed between the prevalence of antigens and haplotypes in the patient and control groups was determined by the \( \chi^2 \) test. The relative risk was calculated by the method of Woolf.

The comparison of the phenotype prevalences of HLA antigens showed a significantly higher prevalence of the A3 and B7 (p < 0.01) in the patient group. The antigen A3 was represented in 52.9% of the subjects in the patient group and in 21.7% of the controls. The antigen B7 was represented in 35.3% of the cases in the patient group and in 8.9% of the controls. These figures correspond to relative risks of 4.065 and 5.606 for A3 and B7, respectively. Among the other antigens tested, high prevalences of A2 and B12 were also found, but they were seen as often in the control group.

### References


**Angioinmunoblastic lymphadenopathy associated with thyroid disease**

Between 1979 and 1983, nine patients with angioinmunoblastic lymphadenopathy were seen in Norwich Health District. Of these, two patients were found to have associated thyroid disease.

### Case 1

A 74 year old widow was admitted because of lack of energy for four weeks, a "flu-like" illness and a rash on the arms and legs. She had been well, but was receiving fenticon 600 mg three times a day for cervical spondylosis.

On examination she was pale and ill, with widespread lymphadenopathy and hepatosplenomegaly. Investigations showed mild normocytic normochromic anaemia, a normal erythrocyte sedimentation rate, and a white cell count; a direct Coomb's test was positive and reticulocyte count was 2%.

Serum protein electrophoresis showed polyclonal increase in gamma globulins, but otherwise serum biochemistry was normal. An infracapsular lymph node biopsy specimen showed features of angioimmunoblastic lymphadenopathy.

She was treated with prednisolone 10 mg four times a day, but in spite of this she became increasingly anaemic and required transfusions. Her condition rapidly deteriorated and she died of uncontrollable disease and haemolytic anaemia three weeks after admission.

Necropsy showed widespread generalised lymphadenopathy and an enlarged liver and spleen. The thyroid gland (30 g) was firm and showed a nodular, greyish cut surface, suggesting either Hashimoto's disease or tumour infiltration.

Histological examination of the thyroid gland showed follicular atrophy and lymphocytic and plasma cell infiltration consistent with advanced Hashimoto's disease.

Lymph nodes were examined from the mesentry hilar regions of lungs, tonsils, and inguinal regions. They had shown the former appearance of angioimmunoblastic lymphadenopathy but with terminal immunoblastic transformation. Immunoperoxidase preparation of necropsy tissue was unsatisfactory as it was not possible to determine whether there was a T or B cell preponderance.

Necropsy showed regression of the lymphadenopathy, an ostitis fibrosa-like appearance of vertebrae, and metastatic calcification of blood vessels and alveolar walls.

The parathyroids were normal. The thyroid showed residual papillary carcinoma confined to the gland. There was no histological evidence of thyroiditis and no macroscopic evidence of generalised lymphoma.

### Case 2

A previously fit 75 year old housewife was admitted with bilateral swelling of the ankles and a generalised purpuric rash of three
weeks’ duration. She was taking diclofenac 50 mg twice a day for osteoarthritis of the hips.

On examination she was pale, ill, and had generalised lymphadenopathy and hepatosplenomegaly. Investigations showed a normocytic normochromic anaemia with an erythrocyte sedimentation rate of 117 mm/first hour. The white cell count was 17 × 10⁹ with an absolute lymphocytosis. The direct Coomb’s test was positive and the reticuloocyte count was 4%. The bone marrow was hypercellular, but otherwise normal. Serum protein electrophoresis showed a large polyclonal increase in gamma globulins. Serum electrolytes and renal function tests were normal, but the corrected calcium was 3-1 mmol/l (normal 2-25-2-65 mmol/l) and phosphate was 1-22 mmol/l (normal 0-80-1-45 mmol/l). Hypercalcaemia persisted. Serum parathormone concentrations were inappropriately high and varied from 0-22 μg -0-26 μg/l (normal range less than 0-01-0-73 μg/l) over a period of six months.

During her illness, the serum thyroxine (T4) concentration fell from 57 nmol/l to 15 nmol/l (normal range 50-150 nmol/l) and thyroid stimulating hormone activity remained normal. A thyroid scan showed no abnormality and there were no thyroid antibodies in the serum. A cervical lymph node biopsy specimen showed deposits of papillary thyroid carcinoma and a striking lymphoproliferative reaction, thought possibly to be an immune response to the tumour, or angioimmunoblastic lymphadenopathy.

She was discharged home, but returned nine days later, having deteriorated rapidly and was sleepy and confused. On readmission she had widespread, large, firm, tender, generalised lymphadenopathy. A right axillary lymph node biopsy specimen showed features of angioimmunoblastic lymphadenopathy. She was treated with prednisolone 20 mg four times a day with a good response and was well for five months. She then became lethargic and there was a rapid deterioration of renal function. A renal biopsy specimen showed focal segmental proliferative glomerulonephritis. She died of renal failure and bronchopneumonia three weeks later.

Comments

The first patient is the fourth reported example of histologically confirmed Hashimoto’s disease, associated with angioimmunoblastic lymphadenopathy, and there have been reports of associated abnormal thyroid function tests in this disease. The patient was taking fenoprofen before the onset of the disease and it is well known that acute T cell leukaemia can be precipitated by a variety of drugs, and a patient who already has autoimmune disease would be particularly susceptible to developing abnormal lymphoproliferative reactions to foreign antigens such as drugs. It is also reasonable to speculate that an abnormal immune system might predispose to both conditions.

The second patient with papillary carcinoma of the thyroid shows an association which has not been previously described. There was no coexistent thyroiditis. This patient also exhibited a segmental proliferative glomerulonephritis and this may have been due to circulating antigen and antibody complexes. It has been described only once before in association with acute T cell leukaemia. The gross hypercalcaemia with normal parathyroid glands strongly suggests that the abnormal lymphoid cells are responsible for secreting a parathyroid hormone-like substance and this association has been described before. This patient was, however, unique in showing the changes of advanced osteitis fibrosa cystica. Hypercalcaemia is also common in acute T cell lymphoma/leukaemia associated with HTLV-1 infection.

The nature of angioimmunoblastic lymphadenopathy is now believed to be a variety of peripheral T cell lymphoma, but displaying features of a disordered immune system.

Autoantibodies occur in angioimmunoblastic lymphadenopathy but the precise nature of association with thyroiditis is unknown.

It is uncertain whether thyroid carcinoma in case 2 is mere coincidence, but altered immunity might predispose to carcinoma, and malignant disease has been reported in association with angioimmunoblastic lymphadenopathy.

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References


Prevalence of HTLV1 in Zimbabwe: a pilot survey

Researchers have shown that human T cell leukemia/lymphoma virus (HTLV1) infection is common in Japan and among certain black populations in the Caribbean and other well defined areas of the world, and that it is associated with a high incidence of adult T cell leukemia/lymphoma. Because of concern with diseases acquired after transfusion, the Blood Transfusion Service carried out a survey to identify the possible presence of HTLV1 in Zimbabwe, and to determine the need to do routine HTLV1 screening on all blood donations.

Random samples were collected from normal blood donors as well as from a sample of patients with lymphoma and those sent for human immunodeficiency virus (HIV) exclusion because of symptoms. The survey, conducted in December 1987, showed no evidence of HTLV1 antibodies in the group with lymphoma or normal blood donors. There was an 0-4% positivity rate found among the patients sent for HIV exclusion (table). The Dupont HTLV1 and Serodia ATL test kits were used in this survey. The four positive specimens found using the Dupont test kit were retested using the Serodia ATL kit; only two were found to be positive.

The sample size was adequate to detect a true population prevalence of 1%, but with this prevalence most of the positive tests would be expected to be false positive, even with a test sensitivity and specificity of 99%. As no confirmatory test method is available in Zimbabwe, we are unable to confirm these results. In view of the findings presented above we conclude that screening for HTLV1 antibodies is not indicated in Zimbabwe at present, but suggest continued sample

Table: Results of HTLV1 testing

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<tr>
<th>Type of specimen</th>
<th>No of specimens</th>
<th>HTLV1 antibodies</th>
<th>No (%)</th>
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<tbody>
<tr>
<td>Normal blood donors</td>
<td>578</td>
<td>26</td>
<td>4 (1-4)</td>
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<tr>
<td>Patients with lymphoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Patients sent for HIV exclusion</td>
<td>296</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>900</td>
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