Peripheral T-Cell Lymphoma (PTCL)

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Patient Profile-1

- 41-year-old, asymptomatic Japanese male
- He noticed skin nodules 15 years ago, and they increased in size and in number, recently.
- Neither LN-swelling nor hepatosplenomegaly
- Mild leukocytosis with 5% atypical lymphocytes showing flower-like morphology
- Serum LDH and serum Ca; WNL
About 5% of the PB lymphocytes showed flower-like morphology with polymorphic nuclei.
Small skin nodules were noticed on his left year lobe 15 years ago, and they gradually have increased in size and in number.
Questions

• What examinations should we perform?

1) Flow cytometric analysis on PBMNC
2) Histopathologic analysis of skin nodules
3) Serological analysis on human T-lymphotropic virus type-I (HTLV-1)
4) *Southern blot analysis of HTLV-I provirus*  ----optional
The biopsied skin nodule disclosed the infiltration of T-cells, and Southern-blot analysis revealed monoclonal integration of HTLV-I provirus.
Based on the histopathologic analysis on the skin nodules as T-cell lymphoma and seropositivity for HTLV-1, a diagnosis of adult T-cell leukemia-lymphoma (ATL) was made.

What disease subtype for ATL should we diagnose?

1) Acute type
2) Lymphoma type
3) Chronic type
4) Smoldering type
Patient Profile-3 and Questions

Two years later he visited again because of progression of skin lesions, and a gradual increase in leukocytes was recognized thereafter. His subtype of ATL was judged to progress to chronic type, and pentostatin (DCF) induced PR.

After the treatment for the complicated miliary tuberculosis, bilateral cervical LN-swelling suddenly appeared.

How should we consider this situation?

1) LN-swelling due to ATL involvement
2) LN-swelling due to other causes
Mycobacterium tuberculosis was isolated from the broncho-alveolar lavage, and a diagnosis of miliary tuberculosis was made. Thereafter, he suffered from adenovirus type 11-induced hemorrhagic cystitis, indicating a marked immunodeficient state.
Composite lymphoma of ATL and EBV+ DLBCL

It is suggested that the immunodeficient state in an ATL patient allows the emergence of EBV-related B-NHL.
Bands of low density in LN are seen, probably due to the low percentage of ATL cells in the composite lymphoma.
Clonal rearrangement of IgH gene in LN cells, indicating a monoclonal B-cell lymphoma.
Definite presence and monoclonal origin of EBV genome in LN cells (B-lymphoma cells)

EBV terminal repeat can be used to analyze clonal populations in EBV-infected cells

Monoclonal EBV Genomes in LN Cells

Probe: EBV terminal repeat digested with BamHI
Summary of Southern Blot Analysis

1) Clonally rearranged TCR-β gene and monoclonal integration of HTLV-I provirus in ATL cells

2) Clonal rearrangement of IgH gene in lymphoma cells, indicating a monoclonal B-cell lymphoma

3) Definite presence and monoclonal origin of EBV genome in lymphoma cells
Conclusions

1) This is the first report of secondary EBV genome carrying monoclonal B-cell lymphoma in an ATL patient.

2) It is suggested that the profound immunodeficient state in the ATL patient allows the emergence of EBV-related B-cell lymphoma.