

ESMO Asia 2015 at the Suntec Singapore Convention & Exhibition Centre

Patient Cases and Tumor Board Discussion

11:00 - 12:30, Saturday, December 19, 2015, Hall 325

Peripheral T-Cell Lymphoma (PTCL)

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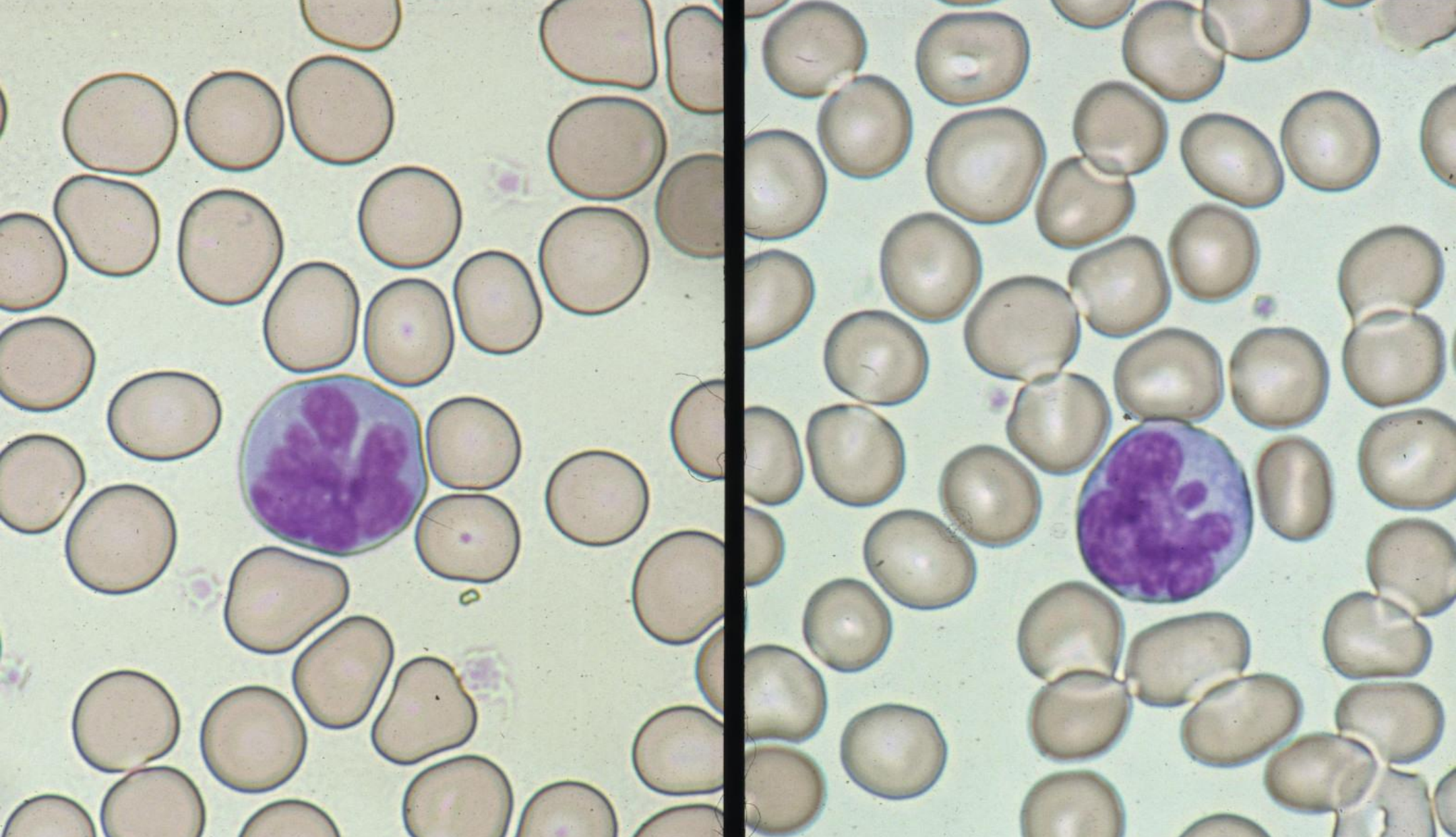
COI Disclosure Information

Kensei Tobinai, MD, National Cancer Center Hospital

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- Stockholder in: None
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- Other remuneration from: None
- Employee of: None

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



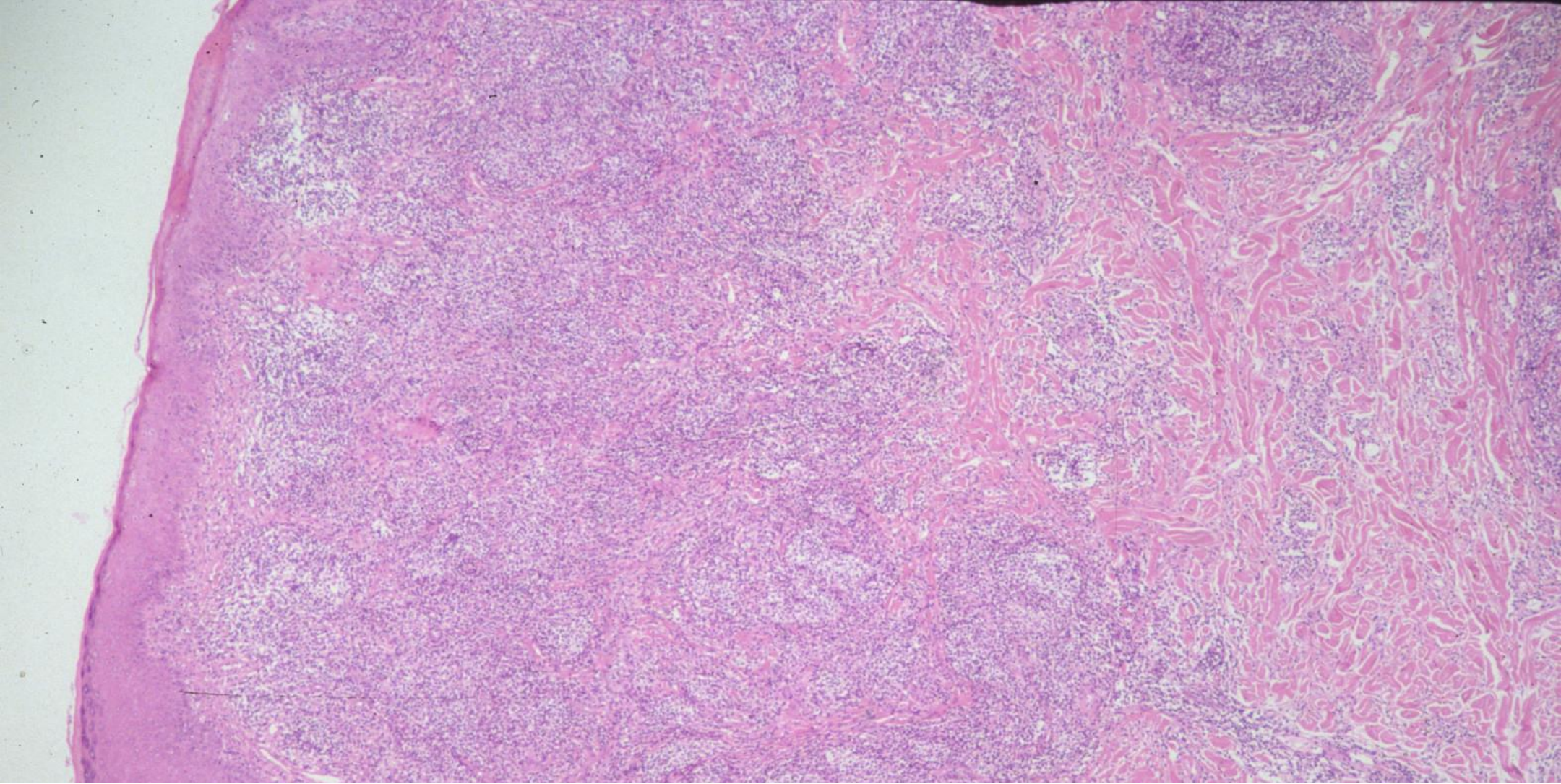
About 5% of the PB lymphocytes showed flower-like morphology with polymorphic nuclei.



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.

Patient Profile-2 and Questions

- 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

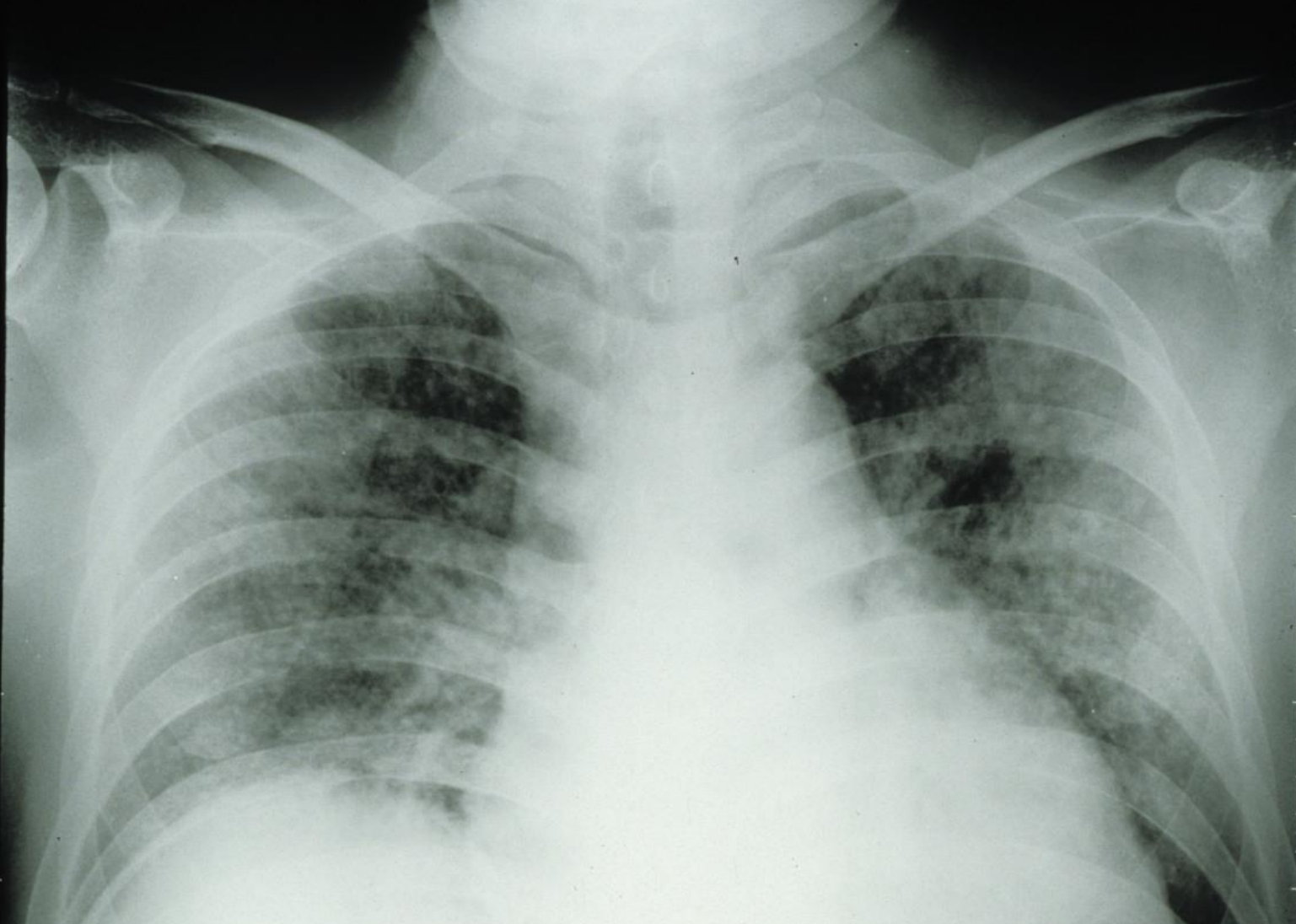
Patient Profile-3 and Questions

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.

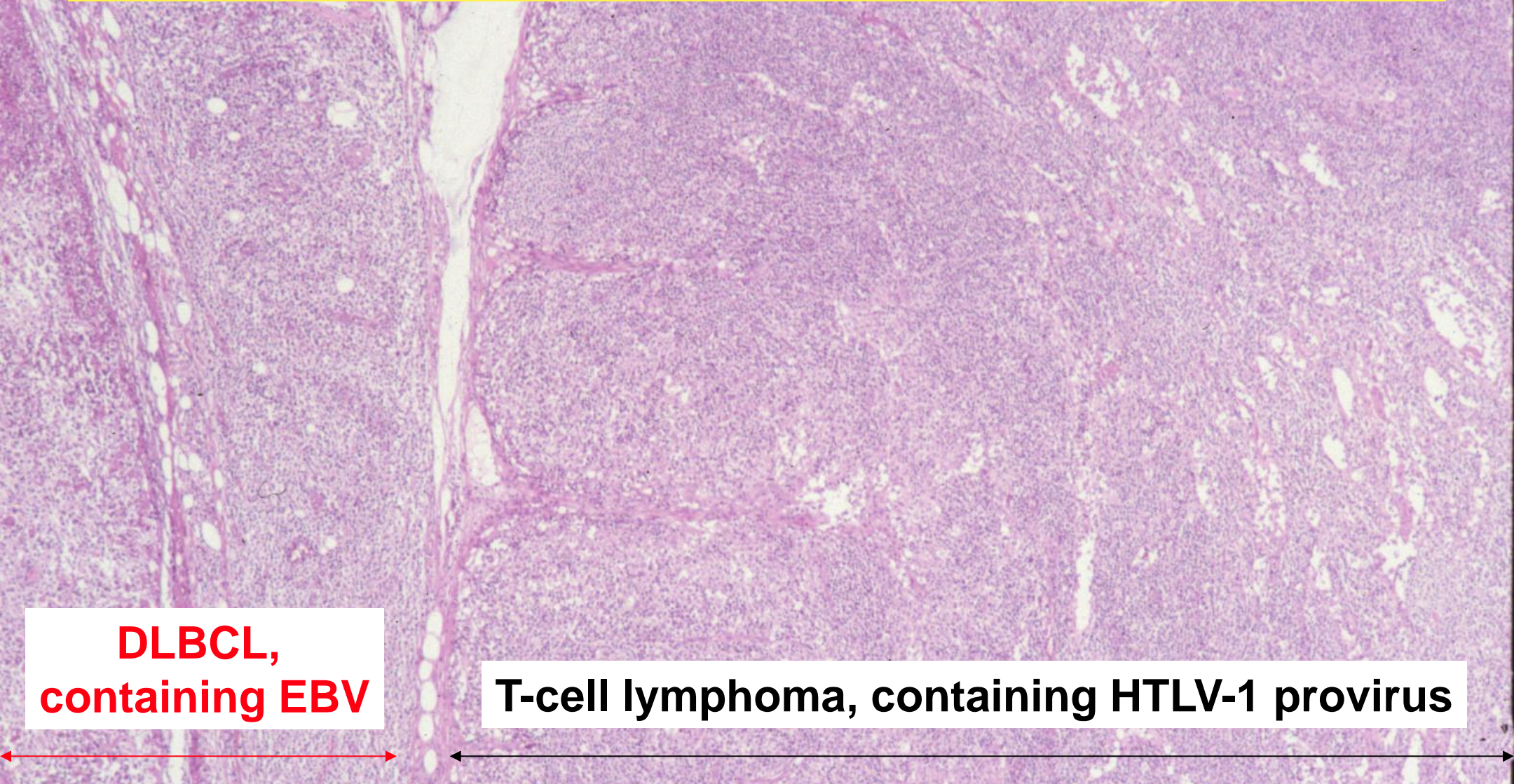
How should we consider this situation?

- 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



**DLBCL,
containing EBV**

T-cell lymphoma, containing HTLV-1 provirus

It is suggested that the immunodeficient state in an ATL patient allows the emergence of EBV-related B-NHL.

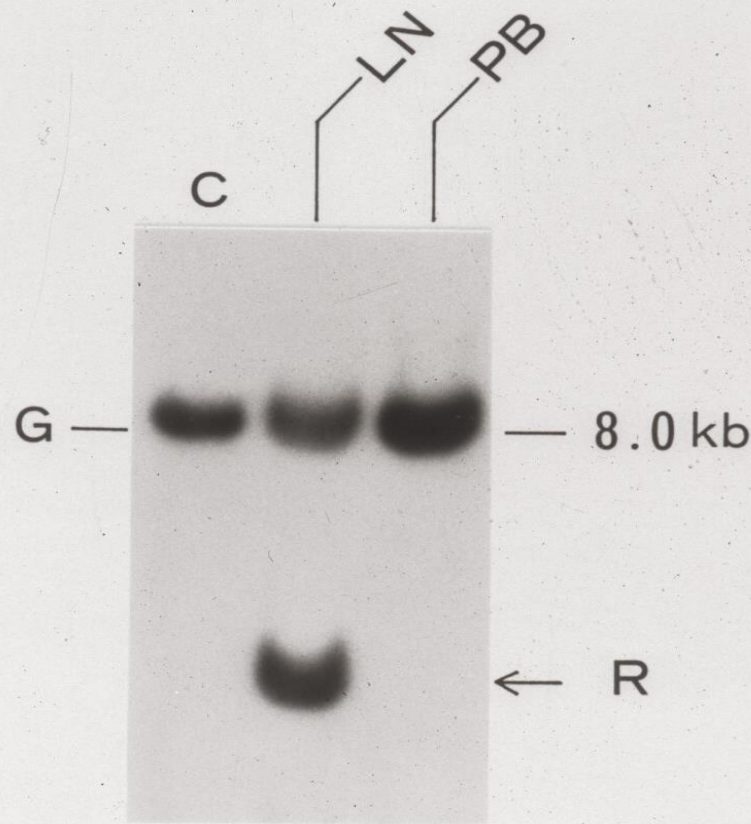
Detection of HTLV-I Provirus DNA in Case XX



Bands of low density in LN are seen, probably due to the low percentage of ATL cells in the composite lymphoma.

digested with *Eco*RI

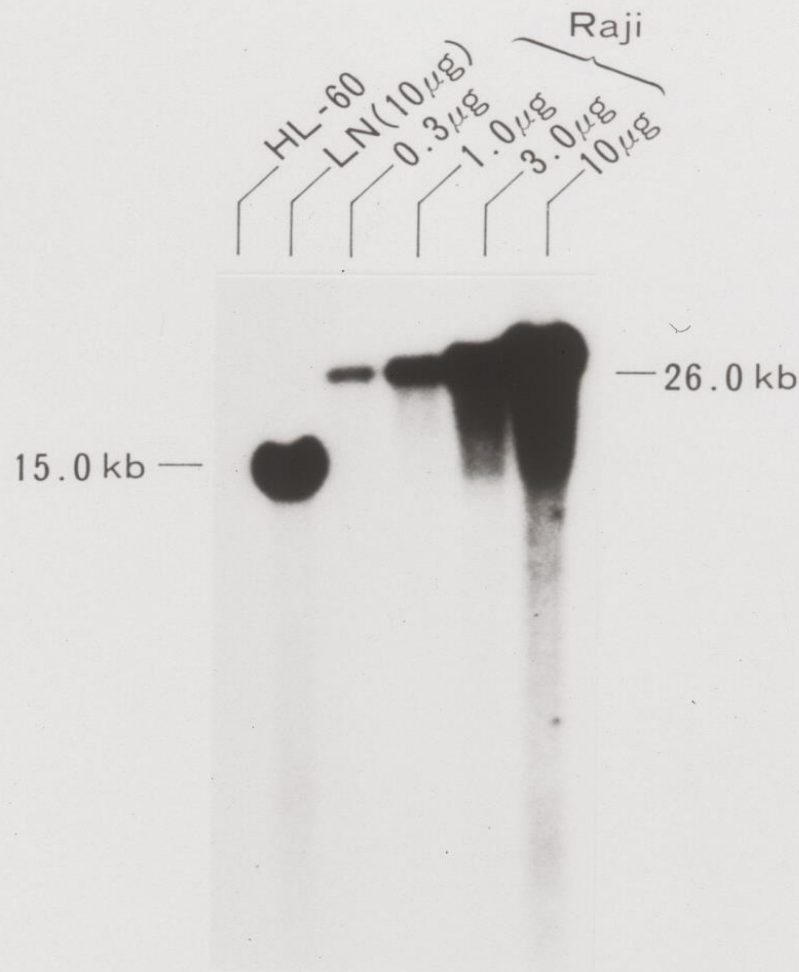
Gene Rearrangement of Immunoglobulin Heavy Chain Gene (JH)



digested with Hind III

**Clonal rearrangement of
IgH gene in LN cells,
indicating a monoclonal
B-cell lymphoma**

Monoclonal EBV Genomes in LN Cells



Probe : EBV terminal repeat
digested with *Bam*HI

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

**Definite presence and
monoclonal origin of
EBV genome in LN cells
(B-lymphoma cells)**

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.

(Tobinai K, et al.: Leuk Res 1991;15:837-46)