Malignant lymphoma associated with simian Epstein-Barr virus infection in a Japanese macaque (Macaca fuscata)

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Introduction and objectives
Malignant lymphomas are common neoplasms in non-human primates as in humans [1]. Analyses of CD markers also help us to classify non-Hodgkin lymphoma in non-human primates and provide more information about the lymphomagenesis [2]. The simian Epstein-Barr virus (sEBV) is well known to play an important role in oncogenesis in macaques [3], and 98 % of Japanese macaques (Macaca fuscata) were seropositive for sEBV infection [4]. Recently, a Japanese macaque in our colony was found to have developed a malignant lymphoma and subsequently died. We here report the histopathological, virological and etiological data of the case.

Materials and methods
The animal was a male Japanese macaque aged 4.6 years old. Immunostaining for paraffin-embedded tissues was performed using antibodies to human CD markers, which had been confirmed cross-reactive with Japanese macaque's lymphoid antigens. To confirm the presence of sEBV in tumor cells, in situ hybridization was performed using fluorescein-conjugated oligonucleotides complementary to portions of the sEBV-encoded early RNA transcripts (sEBERs). Infection with STLV-1 was monitored by the detection of specific antibody to STLV-1 with an indirect immunofluorescence method. As for the sEBV infection status, the presence of anti-sEBV viral capsid antigen (sVCA) antibody and anti-sEBV early antigen (sEA) antibody were used as marker for the sEBV infection.

Results
Gross lesions were characterized by systemic swelling of various lymph nodes, a neoplastic mass in the nasal cavity and splenomegaly. Histopathological analyses revealed the presence of neoplastic cells classified into histiocytic Hodgkin-like cells and Reed-Sternberg (RS)-like cells. Immunohistochemical and virological results are shown in Table 1.

<table>
<thead>
<tr>
<th>Antibody to STLV-1 (titer)</th>
<th>sVCA</th>
<th>sEA</th>
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<tbody>
<tr>
<td>Nasal tumor</td>
<td>+</td>
<td>1:160</td>
</tr>
<tr>
<td>Iliac lymph node</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Liver</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Spleen</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*: RS-like cells were negative for all those markers.
**: CD16-positive cells were identical to EBERs-positive cells.

Discussion
Although morphological similarity to human Hodgkin lymphoma was observed in the present case, the majority of neoplastic cells were histiocytic cells with few inflammatory cells in the lesion. Hodgkin lymphoma in humans is characterized by a few RS cells with an inflammatory cell background. The appearance of CD20+ neoplastic NK/T-cells in the iliac lymph node corresponded to a previous observation in human T-cell lymphoma with an aberrant expression of CD20 and CD79a (both are B-cell markers) [5]. Antibodies to early antigen of sEBV were detected, while antibodies to simian T-cell leukemia virus-1 were negative. Those results suggested that the case may correspond to EBV-associated nasal type NK/T-cell lymphoma in humans [6] rather than Hodgkin lymphoma.

References