Sternberg-Reed Cells in the Thoracic Duct Lymph of Patients with Hodgkin’s Disease

A Preliminary Report
Cytologic Studies in Connection with Lymphography

By A. Engeset, I. O. Brennhovd, I. Christensen, S. Hagen, K. Høeg, H. Høst, K. Liverud and A. Nesheim

The presence of Sternberg-Reed (SR) cells in routine peripheral blood smears of patients with Hodgkin’s disease is extremely rare. However, by the use of the flotation technique, Bouroncle1 found typical SR cells in leukocyte concentrations in 25 of 135 patients with Hodgkin’s disease. These cells were observed only in the advanced stages of generalized Hodgkin’s disease. The SR cells are supposed to be derived from the reticuloendothelial cells in the lymph nodes, liver, spleen or bone marrow. By which route the SR cells reach the peripheral blood is not known, but if the way is through the thoracic duct, it is likely that they will be present in greater concentration in the lymph than in the peripheral blood.

This preliminary study concerns the demonstration of SR cells in the thoracic duct lymph of patients with Hodgkin’s disease. The thoracic duct was cannulated in connection with lymphography.*

Material and Methods

Four individuals were studied, all with a histologically proven diagnosis of Hodgkin’s disease. Three patients (cases 1, 2 and 3) had advanced generalized disease with involvement of the lymph nodes on both sides of the diaphragm. One patient (case 4) had enlarged pathological lymph nodes only above the diaphragm.

The thoracic duct was cannulated during general anesthesia with a siliconized polythene tube nr. 160, as described by Werner.3 The lymph drainage was maintained for about 72 hours. Lymph samples for cytological studies were usually taken three times daily, but during the procedure of lymphography samples were taken every 10 minutes. The cytological studies were performed either on smears or on filter specimens.

Smears were prepared by centrifuging 5 ml of lymph at 1000 g for 10 minutes. The sediment was suspended in one drop of lymph, smeared in the usual manner, and stained.

*Appropriate consent to perform thoracic duct cannulation was asked for in every case.
Table 1.—Percentage distribution of cells in the thoracic duct lymph of patients with Hodgkin’s disease

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Neutrophils</th>
<th>Eosinophils</th>
<th>Basophils</th>
<th>Small lymphocytes</th>
<th>Lymphoblasts</th>
<th>Phagocytes</th>
<th>Smear cells &amp; naked nuclei</th>
<th>Sternberg-Reed cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.4</td>
<td>0.6</td>
<td>0.3</td>
<td>74</td>
<td>0.7</td>
<td>1.0</td>
<td>23</td>
<td>++</td>
</tr>
<tr>
<td>2</td>
<td>0.4</td>
<td>0.1</td>
<td>0.3</td>
<td>38</td>
<td>—</td>
<td>0.3</td>
<td>61</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>0.6</td>
<td>0.6</td>
<td>0.1</td>
<td>67</td>
<td>0.5</td>
<td>0.3</td>
<td>31</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>0.1</td>
<td>—</td>
<td>86</td>
<td>0.1</td>
<td>0.1</td>
<td>14</td>
<td>—</td>
</tr>
</tbody>
</table>

with May Grünwald and Giemsa. From each sample, two or three smears were examined for SR cells, and a differential count on 500–2000 cells was performed.

Samples of peripheral blood were taken three times daily for determinations of leucocyte counts, and differential counts and for study of buffy coat.

Lymphography was done by injection of 14–21 ml of Lipiodol Ultra Fluid® into the lymph vessels on the dorsum of each foot by a rate of 0.2 ml/minute.

**RESULTS**

The lymph flow varied from 0.3 ml/minute to 1.6 ml/minute. It increased during and after the meals, by physical exercise, and following the injection of the contrast. The latter increase may be caused partly by the injection itself and partly by the increased muscular activity during the moving of the patient from the stretcher to the X-ray table after the contrast injection had been finished. In one patient (case 1) severe coughing may have contributed to the increased flow during the procedure of lymphangiography.

**Cell Counts**

The total number of all cells in the thoracic duct lymph decreased during the period of the study, while the leukocytes in the peripheral blood tended to increase. These differences were not significant.

**Smears**

From Table 1, it appears that the small, mature lymphocyte was the most frequently observed cell type. “Smeared” cells, unclassified cells and “naked” nuclei were also present in large numbers. Many of the “naked” nuclei resembled the nuclei of the lymphocytes. The lymphoblasts, granulocytes and phagocytes comprised less than 2 per cent of the total cells.

The cellular content of the lymph varied from patient to patient. In case 4, which had Hodgkin’s disease at a localized stage, the cells in the lymph were predominately small, mature lymphocytes and “smeared” cells. In the other patients, more eosinophils and phagocytes were observed, and the relative number of these cells increased following the injection of the contrast medium. Furthermore, in these patients with generalized Hodgkin’s disease, reticulum cells were observed in all smears, and in most of them some typical SR cells were also found (Fig. 1). In one patient (case 1), the number of SR cells in the smears increased significantly during and following the lymphography. However, injection of the contrast medium did not influence the number of
Fig. 1.—Sternberg-Reed cell in lymph smear of case I (May-Grünwald and Giemsa; $\times$ 1000).

SR cells occurring in the smears obtained from the two remaining patients with generalized disease (cases 2 and 3).

"Smeared" cells were most frequently observed in case 2. The nucleoli of the latter resembled those in the lymphocytes in the same smears, and probably the "smeared" cells and the lymphocytes represented the same cell.
In the filter specimens, quantitation was performed only on the SR cells. In one patient (case 3) no characteristic SR cell was found in spite of the fact that these cells were frequently demonstrated in the ordinary lymph smears. This discrepancy may be explained partly by difficulties in producing some of the filter specimens caused by the presence of the contrast medium in the lymph following the lymphography. Otherwise, the findings in the filter specimens were consistent with those in the lymph smears.

Peripheral Blood Studies

The percentage distribution of the cell types in the leukocyte concentrations was in agreement with that in the routine smears, except for the presence in the former of lymphoblasts (in all patients) and of some reticulum cells (in case 1 and 2). SR cells were not found in the routine smears nor in the smears of the leukocyte concentrations.

Complications

The polythene tube accidentally slipped out of the thoracic duct in one patient about five hours after it was introduced. Thus, further study had to be discontinued. In two patients (cases 3 and 4), a non-distressing chylothorax occurred, which disappeared spontaneously in a few days. No deleterious or beneficial effects of the procedure were observed on the clinical course of the patients studied.

Discussion

The lymph nodes have normally a well-defined microscopic appearance. The predominant cells are the reticulum cells and the lymphocytes. The latter are free and mobile cells which may escape with the efferent lymph. Thus the lymph of the thoracic duct contains mainly lymphocytes.

In Hodgkin's disease, the normal structure of the lymph nodes is partly destroyed, and there is a heterogeneous histologic picture with increase in the number and size of the reticulum cells, the occurrence of SR cells and increased numbers of eosinophils, lymphocytes, monocytes and plasma cells. The cellular content of the efferent lymph will probably reflect the cellular changes in the lymph nodes. Thus, if many lymph nodes are involved, the above-mentioned cell types may be present even in the central lymph. The findings in the present study support this hypothesis, as these cell types were present in the thoracic duct lymph in our patients with generalized disease.

In one patient, however, the number of SR cells in the lymph increased during and following the lymphography. Thus, the question arises whether the injection of the contrast medium per se may detach SR cells from the lymph nodes. Further studies are necessary to clarify this problem.

We were not able to demonstrate SR cells in the peripheral blood in spite of their frequent occurrence in the lymph smears of three patients. The technique employed was the same in the blood and in the lymph smears. Previously, Engeset and Nesheim\(^2\) were unable to demonstrate SR cells in the leukocyte concentrations of peripheral blood in a series of patients with advanced stages of Hodgkin's disease. Bouroncle\(^1\) suggested that the SR cells are so frequently
absent in peripheral blood because of their large size which militates against their remaining in circulation. Presumably they will be filtered by the capillaries of the lungs.

It should be emphasized that our data were obtained on relatively few patients, and thus may not be representative. However, our findings indicate that SR cells may occur in the thoracic duct in advanced Hodgkin's disease, and this may suggest a lymphatic spread of this disease.

**Summary**

Typical Sternberg-Reed cells were found in the thoracic duct lymph in three of four patients with a histologically proven diagnosis of Hodgkin's disease, but in none of the patients were these cells demonstrated in the peripheral blood. The findings are discussed.

**SUMMARIO IN INTERLINGUA**

Typic cellulas de Sternberg-Reed esseva trovate in le lympha del ducto thoracic in tres de quatro patientes con un histologicamente provate diagnose de morbo de Hodgkin. Tammen, nulle tal cellulas esseva demonstrate in ulle del patientes in le sanguine peripheric. Le constatationes es commentate.

**REFERENCES**

Sternberg-Reed Cells in the Thoracic Duct Lymph of Patients with Hodgkin’s Disease: A Preliminary Report Cytologic Studies in Connection with Lymphography

A. ENGESET, I. O. BRENNHOVD, I. CHRISTENSEN, S. HAGEN, K. HØEG, H. HØST, K. LIVERUD and A. NESHEIM