Testicular Ultrasound and Biopsy Findings in Cases of Acute Lymphoblastic Leukemia

Introduction

Involvement of the testes - one of the most common sites of relapse in Acute Lymphoblastic Leukemia (ALL) - usually presents with painless enlargement of one or both testes. Testicular involvement occurs in 10% to 23% of boys during the course of the disease at a median time of 13 months from diagnosis. Occult testicular involvement is recognized in 10% to 33% of boys undergoing bilateral wedge biopsies performed during the first 3 years of treatment or any time after cessation of the therapy (1). In a study in which biopsies were done in boys with newly diagnosed ALL, microscopic testicular involvement was reported to be 21% (2).

Since the clinical incidence of testicular relapse varies widely from 1 to 40%, and since microscopic infiltrates in autopsies have been reported to be 64 to 92% in boys, it is suggested that testicular infiltration escapes clinical detection until the organ is several times its normal size (2).

In light of these data, testicular infiltration was evaluated by testicular ultrasonography (USG) and biopsy and the correlation analyses between these methods were carried out in a group of boys with ALL followed up at Dr. Behçet Uz Children’s Hospital.

Among 154 ALL patients, 25 boys aged between 2 and 14 years, followed up at Dr. Behçet Uz Children's Hospital between 1985 and 1996 were included in the study. Seventeen underwent testicular USG and biopsy just after the cessation of the therapy, whereas in 8 boys these procedures were performed whenever clinical involvement was suspected. Testicular biopsies were performed as bilateral open wedge biopsies and were evaluated histologically.

Ten of the 17 patients were in the standard (SRG), 5 were in the intermediate (MRG) and 2 were in the high risk group (HRG). UKALL, BFM 90 and LSA2L2 treatment regimens were given to these patients. Remission induction therapy and radiotherapy at 18 Gy were given to all of the patients according to the UKALL therapy protocol.

All of the subjects were evaluated clinically. Eight boys having painless testicular enlargement underwent testicular USG and biopsy immediately. All cases were evaluated in light of the clinical, ultrasonographic and biopsy findings. Specificity, sensitivity, positive predictivity and negative predictivity values were detected.

In 17 cases with no clinical evidence of testicular involvement, USG revealed a hypoechoic area in one, and a metastatic mass image in another. However their biopsies showed no pathology histologically.

Four cases showing testicular infiltration were evaluated in 8 cases with painless testicular enlargement. In 8 cases in which testicular infiltration was suspected according to the ultrasonographic findings, 3 cases showed no evidence of infiltration at the biopsy.

Risk groups, time of involvement and the results are summarized in table 1.

Four cases showing testicular infiltration were in the HRG. Except one case, time for testicular relapse varied
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between 6 months and one years. Remission was achieved in all of the cases by residue BFM 90 ALL therapy protocol. Radiotherapy at 18 Gy was given in addition to chemotherapy. Hematologic relapse occurred in one case one month after the remission and he died during the induction therapy. The other two cases were at the follow-up stage for 1 to 2 years. Contact with one case was lost after 1 year follow up.

Testes are the second common site of relapse in boys with ALL. Testicular relapse may be the first recognized site for recurrent leukemias. In the study of Stoffel and coworkers, testicular involvement was the first site of relapse in 8 out of 13 patients (67%) (3). Overt disease is most often seen within 2 years of stopping therapy, irrespective of the duration of the therapy (1). Incidence of testicular relapse is different in different studies (4-9).

In our study, none of our 17 patients in whom biopsies were performed after the cessation of the therapy, showed pathologic findings and testicular relapse did not occur during the followup. Five of the 8 cases with evidence of clinical testicular involvement had also microscopic evidence of testicular disease. Thus, testicular biopsy may be a more valuable method if it is performed whenever involvement is suspected clinically. Frequent and detailed testicular examination, evaluation of their size and hardness should be preferred to routine biopsies.

Testicular USG was performed on all of the cases before the biopsy, and the clinical findings, ultrasonographic and biopsy results were compared. Eric et al. compared the clinical, USG, magnetic resonance (MR) and biopsy findings in 8 cases. USG and MR results were negative in all cases, but 4 cases showed leukemic infiltration in biopsy. This study suggested that USG and MR were not successful in evaluating the presence of testicular involvement (10). In our study, the specificity for the positivity of clinical findings and biopsy was 85%, sensitivity was 100%, the positive predictive value was 62.5% and the negative predictive value was 100%. When the relationship between USG and biopsy was evaluated, sensitivity, specificity, positive predictivity and negative predictivity values were 100%, 75%, 50% and 100% respectively. According to these results we conclude that if there is clinical suspicion of testicular involvement, it is appropriate to perform testicular biopsy directly without an ultrasonographic examination.

### Table 1. Risk groups, time of testicular involvement and the results of the cases with testicular infiltration

<table>
<thead>
<tr>
<th>Case</th>
<th>Risk Groups</th>
<th>Time of relapse</th>
<th>The other relapses</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HRG</td>
<td>6 months after diagnosis</td>
<td>Bone Marrow (BM)</td>
<td>In remission. At follow-up stage for 1.5 years</td>
</tr>
<tr>
<td>2</td>
<td>MRG</td>
<td>1 year after therapy</td>
<td></td>
<td>Follow up discontinued after 1 year</td>
</tr>
<tr>
<td>3</td>
<td>HRG</td>
<td>1 year after diagnosis</td>
<td>CNS+BM</td>
<td>Exitus</td>
</tr>
<tr>
<td>4</td>
<td>HRG</td>
<td>At the diagnosis</td>
<td>BM</td>
<td>In remission. At follow-up stage for 1 year</td>
</tr>
<tr>
<td>5</td>
<td>HRG</td>
<td>1 year after diagnosis</td>
<td></td>
<td>In remission. At follow-up stage for 2 year</td>
</tr>
</tbody>
</table>

### References


