molecular genetic evidence for a link may also be predisposed to lipomas. 


contrast, other researchers (12) have observed clonal chromosome abnormalities in only one of 58 lipomas in 18 patients with multiple lipomas. The high incidence of clonal chromosome abnormalities in our patient represents a particular feature of his lipomas that may be related to a germline RB1 mutation.

It is generally accepted that all patients with sporadic bilateral RB are heterozygous for an oncogenic RB1 mutation (2,3). In our patient, chromosome analyses on peripheral blood lymphocytes as well on skin fibroblasts revealed a normal karyotype, and FISH investigations on nuclei of skin fibroblasts by use of the above-mentioned RB1 probe demonstrated a normal signal distribution (Table 1).

Extensive screening for small mutations by use of heteroduplex analyses, single-strand conformation polymorphism analyses, and direct sequencing failed to disclose a RB1 mutation in peripheral blood mononuclear cell DNA. It is noteworthy that in a large study this screening procedure allowed for the detection of RB1 mutations in more than 80% of patients with hereditary RB (7,10). However, because of the complexity of the RB1 gene, mutations still may escape detection (6,10,14). Moreover, somatic mosaicism of RB1 mutations has been reported in patients with sporadic bilateral RB (15–17). On the other hand, recurrent loss of the same RB1 allele in two different lipomas of our patient further substantiates that a predisposing RB1 gene mutation, as was found in RBs and osteosarcomas from RB patients, may be involved in the development of this second primary neoplasm (18–23).

Ordinary lipomas almost never undergo malignant transformation (24). Nevertheless, the presence of lipomas in RB patients may indicate an increased susceptibility to second cancers (1). So far, no association could be demonstrated between particular RB1 gene mutations and specific second primary tumors (10). However, further studies aimed at the detection of an as yet un-

<table>
<thead>
<tr>
<th>Sample</th>
<th>Karotype [No. of metaphases]</th>
<th>FISH with a RB1 probe on interphase nuclei</th>
<th>Allelic representation of polymorphic RB1 STRs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of nuclei investigated</td>
<td>% of nuclei with respective spot counts</td>
<td>Rbl.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>46,XY [25]</td>
<td>nd</td>
<td>—</td>
</tr>
<tr>
<td>Skin fibroblasts</td>
<td>46,XY [25]</td>
<td>430</td>
<td>2.3</td>
</tr>
<tr>
<td>Lipoma 100/95</td>
<td>46,XY,del(13)(q12–13q31) [17]</td>
<td>205</td>
<td>68.3</td>
</tr>
<tr>
<td>Lipoma 314/96A</td>
<td>65–66,XXY,−4,−6,−9, add(9)(p21),−11,−12,−13, add(14)(p11),−15, add(18)(q23),−20, add(21)(p11),−22, −5,6mar [6]</td>
<td>210</td>
<td>19.0</td>
</tr>
<tr>
<td>Lipoma 314/96B</td>
<td>46,XY,del(13)(q12–13q14) [25]</td>
<td>217</td>
<td>92.2</td>
</tr>
</tbody>
</table>

*FISH = fluorescence in situ hybridization; RB1 = retinoblastoma gene; STRs = short tandem repeats; bp = base pairs; nd = not done; + = polymorphism present; − = polymorphism absent.
discovered germline RB1 mutation in our patient, as well as combined cytogenetic and molecular genetic analyses of additional lipoma samples, may clarify the molecular basis for the increased incidence of lipomas in patients with hereditary RB.

References


Note

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