False-Positive MIBG Scans With Normal Computed Tomography Imaging in Patients With High-Risk Neuroblastoma

To the Editor: Kushner et al\(^1\) investigate the most sensitive modality for early detection of relapse in patients with asymptomatic high-risk neuroblastoma who had previously achieved complete remission or very good partial remission. They demonstrate that iodine-\(^{123}\) \((123^\text{I})\) metaiodobenzylguanidine (MIBG) scanning was the only positive surveillance scan in 27\% of patients and conclude that \(^{123}\text{I-MIBG}\) scanning is the most reliable test for detection of clinically unsuspected tumor recurrence in this population. However, it is difficult to fully assess the reliability of \(^{123}\text{I-MIBG}\) scanning based on the unexpected tumor recurrence in this population. The authors do not indicate how the diagnosis of recurrence was confirmed. This is a particularly important question for the 27\% of patients who had no indication of relapse on any other form of imaging or surveillance. If there was no histopathologic confirmation of relapse, it may be possible that some patients had false positive \(^{123}\text{I-MIBG}\) scintigraphy scans. This may partly explain the improved survival rate seen in this cohort. No data is provided on the number of patients with positive \(^{123}\text{I-MIBG}\) scans who were found not to have relapsed. In absence of this information, the clinical utility and reliability of \(^{123}\text{I-MIBG}\) scanning in this population remains unclear.

The potential for a false-positive MIBG result has been described in a variety of clinical settings, including evaluation at diagnosis or relapse. Specific cases have been reported in an accessory spleen,\(^2\) urinoma,\(^3\) benign liver tumors,\(^4\) and pyelonephritis.\(^5\) Pfluger et al\(^6\) quote a specificity of 85\% for MIBG alone that increases to 95\% when used in conjunction with magnetic resonance imaging in their study of 50 newly diagnosed patients. It therefore seems likely that some patients under post-treatment surveillance who develop MIBG changes only with no changes on computed tomography (CT) imaging will have false-positive scans.

To further address the specificity of \(^{123}\text{I-MIBG}\) changes in the absence of CT changes we retrospectively evaluated the post-treatment surveillance at our institution over the last 10 years in a similar population to that described by Kushner et al.\(^1\) Since 1999, our institution has had 13 patients with high-risk neuroblastoma who were treated with intensive induction therapy, autologous transplant, and radiation therapy\(^6\) and achieved complete or very good partial remission status. During post-treatment surveillance imaging, five patients had positive \(^{123}\text{I-MIBG}\) uptake with no evidence of evolving mass disease on concurrent CT. The patient details are described in Table 1. One patient with focal \(^{123}\text{I-MIBG}\) uptake in the liver (patient 2) had a biopsy performed that did not show any evidence of recurrent neuroblastoma. The remainder were followed with observation alone. All are currently alive with no evidence of disease at a median of 5 years follow-up (range, 7 to 100 months). One patient has long-term morbidity as a result of his treatment but no active NB disease. The remainder are well.

Our results suggest that when following high-risk neuroblastoma patients who are in complete or very good partial remission status, the presence of a positive MIBG scan in the absence of changes in other surveillance scans needs to be interpreted with caution. While three of the patients were between 12 and 18 months.

### Table 1. High-Risk Patients With Neuroblastoma With False-Positive MIBG Scans Postautologous Transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at Diagnosis (months)</th>
<th>Sex</th>
<th>Stage</th>
<th>(\text{nMyc} ) Status</th>
<th>Induction Response</th>
<th>MIBG Status Prior to Transplantation</th>
<th>Location of Positive MIBG Uptake During Follow-Up</th>
<th>Time Until Positive Scan Post-Transplantation (months)</th>
<th>Concurrent CT Findings</th>
<th>Biopsy</th>
<th>Follow-Up (months)</th>
<th>MIBG Status at Last Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.5</td>
<td>Female</td>
<td>3</td>
<td>Amplified</td>
<td>Very good partial remission</td>
<td>No uptake</td>
<td>Liver</td>
<td>3</td>
<td>Normal</td>
<td>Not done</td>
<td>7</td>
<td>Unchanged</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>Male</td>
<td>4</td>
<td>Not amplified</td>
<td>Complete remission</td>
<td>No uptake</td>
<td>Liver and ribs</td>
<td>8</td>
<td>Normal</td>
<td>Normal liver</td>
<td>60</td>
<td>No longer avid</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
<td>Male</td>
<td>4</td>
<td>Not amplified</td>
<td>Complete remission</td>
<td>No uptake</td>
<td>Tumor bed</td>
<td>13</td>
<td>Small calcified mass unchanged from previous CTs</td>
<td>Not done</td>
<td>100</td>
<td>No longer avid</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>Female</td>
<td>4</td>
<td>Not amplified</td>
<td>Complete remission</td>
<td>No uptake</td>
<td>Right lung base</td>
<td>11</td>
<td>Area of consolidation suggestive of pneumonia</td>
<td>Not done</td>
<td>35</td>
<td>No longer avid after pneumonia treatment</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>Male</td>
<td>4</td>
<td>Not amplified</td>
<td>Complete remission</td>
<td>No uptake</td>
<td>T5 vertebra (site of presenting disease)</td>
<td>36</td>
<td>Soft tissue suggestive of scar; unchanged from previous</td>
<td>Not done</td>
<td>60</td>
<td>No longer avid</td>
</tr>
</tbody>
</table>

Abbreviations: MIBG, metaiodobenzylguanidine; CT, computed tomography.
months of age, and would not currently be treated on high-risk protocols, their results in combination with the other two patients, suggest a limitation on the reliability of $^{123}$I-MIBG scanning as a stand-alone surveillance test. Further, while $^{123}$I-MIBG scanning may help detect relapsed disease at an earlier time point, precise specificity needs to be understood in order to mitigate the risks of biopsy, to reduce unnecessary stress for patients and their parents, and to avoid the risk of initiating unnecessary treatment. Ultimately, further large multi-institutional studies may assist to precisely define the sensitivity and specificity of $^{123}$I-MIBG scanning for this patient population.

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**AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**
The author(s) indicated no potential conflicts of interest.

**REFERENCES**

DOI: 10.1200/JCO.2009.24.0036; published online ahead of print at www.jco.org on November 2, 2009