Warthin’s tumor of parotid gland on Tc-99m pertechnetate scintigraphy with lemon juice stimulation: Tc-99m uptake, size, and pathologic correlation

Abstract The aim of this study was to evaluate the usefulness of technetium-99m (Tc-99m) pertechnetate scintigraphy with lemon juice stimulation in the diagnosis of Warthin’s tumor and its correlation with Tc-99m uptake, tumor size, and histologic subtype. Tc-99m pertechnetate scintigraphy before and after lemon juice stimulation and pathologic specimens of 34 Warthin’s tumors and 47 non-Warthin’s lesions were retrospectively evaluated. Tc-99m uptake of Warthin’s tumors before and after stimulation was visually graded as follows: absent; indeterminate; low grade; definite; and strong. Tumor size was defined as maximum diameter of the tumor measured from the surgical specimen. Warthin’s tumors were classified into three histologic subtypes according to the ratio of epithelial and lymphoid stromal components: predominant epithelial; intermediate; and low-grade epithelial types. Eighteen of 34 (53%) Warthin’s tumors and one benign lymphoepithelial cyst showed higher uptake than that of the normal parotid gland on Tc-99m scintigraphy before lemon juice stimulation. Thirty-two of the 34 (94%) Warthin’s tumors, one benign lymphoepithelial cyst, one pleomorphic adenoma, and one oncocytoma revealed higher uptake than that of the normal parotid gland on Tc-99m scintigraphy after lemon juice stimulation. The mean size was 37 mm in strong uptake Warthin’s tumors, 24 mm in definite uptake tumors, 19 mm in low-grade uptake tumors, and 12 mm in low-grade uptake tumors excluding those tumors with large cystic component. There was a significant correlation between tumor size and degree of Tc-99m uptake after lemon juice stimulation. However, there was no correlation between histologic subtype and Tc-99m uptake, and histologic subtype and tumor size in Warthin’s tumors. Our study concludes that Tc-99m pertechnetate scintigraphy with lemon juice stimulation is useful for the detection and diagnosis of Warthin’s tumor. The degree of uptake in Warthin’s tumor on Tc-99m scintigraphy with lemon juice stimulation depends mainly on tumor size and the presence of large cystic component in it.

Keywords Parotid neoplasm · Warthin’s tumor · Tc-99m pertechnetate scintigraphy · Lemon juice stimulation · Pathology

Introduction As surgical therapy is not always necessary because of no malignant potential in Warthin’s tumor, the accurate diagnosis of Warthin’s tumor is important. Technetium-99m (Tc-99m) pertechnetate scintigraphy is a simple, noninvasive, useful method for detection and diagnosis of Warthin’s tumor. Tc-99m pertechnetate retention
within the Warthin’s tumor is well differentiated from the normal parotid gland which drains Tc-99m pertechnetate after lemon juice stimulation. Some reports [1, 2, 3, 4, 5] concerning the further usefulness of Tc-99m pertechnetate scintigraphy after lemon juice stimulation in Warthin’s tumor have been published. The ability of epithelial cells in Warthin’s tumor to extract large anions, such as pertechnetate from the blood, is considered to be responsible for the Tc-99m pertechnetate accumulation in the tumor [6]. Seifert et al. [7] postulated that Warthin’s tumor evolved from the “stroma-rich type” through “typical type” to the “stroma-poor type” by adenomatous epithelial proliferation. There have been few reports relating to the degree of uptake on Tc-99m scintigraphy after lemon juice stimulation with regard to histologic subtype and tumor size in Warthin’s tumor [8]. Therefore, we retrospectively evaluated the relationship between the degree of Tc-99m uptake after lemon juice stimulation and histologic subtype, tumor size and histologic subtype, and the degree of Tc-99m uptake after lemon juice stimulation and tumor size in 34 Warthin’s tumors.

### Materials and methods

Tc-99m pertechnetate scintigraphy before and after lemon juice stimulation was performed in 114 patients, clinically suspected of having Warthin’s tumor, at our institution from June 1993 to August 1998. Eighty-one lesions (34 Warthin’s tumors, 47 non-Warthin’s lesions) in 65 patients (31 men, 34 women; age range 8–83 years, mean age 58 years) were confirmed pathologically after surgical removal and were investigated in our study. Twelve patients had a solitary Warthin’s tumor, 4 patients had 2 Warthin’s tumors, 3 patients had 3 Warthin’s tumors, 1 patient had 4 Warthin’s tumors, 1 patient had a Warthin’s tumor adjacent to a pleomorphic adenoma, 42 patients (30 pleomorphic adenoma, 2 basal cell adenoma, 1 oncocytoma, 2 benign lymphoepithelial cyst, 1 chronic lymphadenitis, 1 intraparotid lymph node, 2 adenoid cystic carcinoma, 1 adenocarcinoma, 1 mucoepidermoid carcinoma, 1 malignant lymphoma) had a solitary non-Warthin’s lesion, and 2 patients (pleomorphic adenoma, malignant lymphoma) had 2 non-Warthin’s lesions. Thirty-four Warthin’s tumors ranged in size from 9 to 60 mm (mean size 26 mm). Twenty-nine Warthin’s tumors and 41 non-Warthin’s lesions were solid, 4 Warthin’s tumors and 3 non-Warthin’s lesions had large cystic component more than 50%, and one Warthin’s tumor and 3 non-Warthin’s lesions were entirely cystic. Six patients with Warthin’s tumor and 1 patient with pleomorphic adenoma were bilateral.

Tc-99m parotid scintigraphy before lemon juice stimulation was performed 15 min after intravenous injection of 185 MBq (5 mCi) Tc-99m pertechnetate. Anterior and bilateral images of the parotid gland were obtained using GE MAXXUS (General Electric, Milwaukee, Wis.) gamma camera and low-energy high-resolution parallel hole collimator with a preset time of 5 min per view and 512 × 512 matrix. As soon as 10 ml of lemon juice was kept in the mouth for 1 min and gargled with a cup of water, ipsilateral image to the parotid mass was at first obtained and contralateral image was followed with a preset time of 5 min.

Tc-99m uptake before and after lemon juice stimulation was visually graded as follows: absent; indeterminate (the uptake in the tumor was not depicted); low grade (the uptake in the tumor was slightly higher than that in normal parotid gland); definite (the uptake in the tumor was definitely higher than that in normal parotid gland); and strong (the uptake in the tumor was marked). Grading was done by two radiologists (H. M. and H. K).

Before surgery, ultrasound was performed in all patients with a linear small-parts electronic sonographic scanner (6–13 MHz, LogiQ 500LA39, General Electric, Milwaukee, Wis.). The presence and the ratio of anechoic areas in the lesion were evaluated. “Large cystic component” was defined as the ratio of cystic component in the lesion that was more than 50% on ultrasound.

Each resected Warthin’s tumor was re-examined pathologically without knowledge of the result of Tc-99m pertechnetate scintigraphy by a pathologist. Warthin’s tumors were classified into three subtypes according to the ratio of epithelial tumor component to lymphoid stroma: predominant epithelial type (the epithelial component is more than 60% of the whole specimen); intermediate type (the epithelial component is between 40 and 60%); and low-grade epithelial type (the epithelial component is less than 40%).

Tumor size was defined as maximum diameter of the tumor measured on the surgical specimen.

Tc-99m pertechnetate scintigraphy, ultrasound, and surgical operation were performed in all patients after informed consent. An unpaired Student’s t-test for statistical analysis between Tc-99m uptake and tumor size and the Kruskal-Wallis test for statistical analysis between tumor size and histologic subtype, and Tc-99m uptake and histologic subtype, were used. A p-value < 0.05 was considered statistically significant.

### Results

The results of Tc-99m pertechnetate scintigraphic findings and histopathologic diseases in 81 lesions are shown in Table 1. Eighteen of 34 (53%) Warthin’s tumors and

#### Table 1 Tc-99m scintigraphic findings and histopathologic diseases in 81 lesions

<table>
<thead>
<tr>
<th>Tc-99m scintigraphy</th>
<th>Warthin’s tumor</th>
<th>Non-Warthin’s lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity on pre-stimulation</td>
<td>Activity on post-stimulation</td>
<td>(n = 34)</td>
</tr>
<tr>
<td>−1 or 0</td>
<td>−1 or 0</td>
<td>2 [1]</td>
</tr>
<tr>
<td>0</td>
<td>1+ or 2+ or 3+</td>
<td>14 [2]</td>
</tr>
<tr>
<td>1+</td>
<td>1+ or 2+ or 3+</td>
<td>8 [2]</td>
</tr>
<tr>
<td>2+</td>
<td>3+</td>
<td>10</td>
</tr>
</tbody>
</table>

3+ strong uptake; 2+ definite uptake; 1+ low-grade uptake; 0 indeterminate uptake; −1 absent; brackets no. of lesions with large cystic component; brackets no. of lesions with entire cyst.