Parotid Incidentaloma Identified by Positron Emission/Computed Tomography: When to Consider Diagnoses Other than Warthin Tumor

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Abstract
Introduction Parotid gland incidentalomas (PGIs) are unexpected hypermetabolic foci in the parotid region that can be found when scanning with whole-body positron emission/computed tomography (PET/CT). These deposits are most commonly due to benign lesions such as Warthin tumor.

Objective The aim of this study was to determine the prevalence of PGIs identified in PET/CT scans and to assess the role of smoking in their etiology.

Methods We retrospectively reviewed all PET/CT scans performed at our center in search of PGIs and identified smoking status and standardized uptake value (SUVmax) in each case. We also analyzed the database of parotidectomies performed in our department in the previous 10 years and focused on the pathologic diagnosis and the presence or absence of smoking in each case.

Results Sixteen cases of PGIs were found in 4,250 PET/CT scans, accounting for 0.4%. The average SUVmax was 6.5 (range 2.8 to 16). Cytology was performed in five patients; it was benign in four cases and inconclusive in one case. Thirteen patients had a history of smoking. Of the parotidectomies performed in our center with a diagnosis of Warthin tumor, we identified a history of smoking in 93.8% of those patients.

Conclusions The prevalence of PGIs on PET/CT was similar to that reported by other authors. Warthin tumor is frequently diagnosed among PGIs on PET/CT, and it has a strong relationship with smoking. We suggest that a diagnosis other than Warthin tumor should be considered for PGIs in nonsmokers.

Introduction
It is not unusual to find unexpected hypermetabolic foci as a result of scanning using whole-body positron emission/computed tomography (PET/CT). Known as incidentalomas, such findings are not necessarily related to the tumor or disease being studied. Parotid gland incidentalomas (PGIs) are defined as new focal intraglandular deposits of radiotracer in patients without prior history of parotid disease.¹ These deposits are most commonly due to benign lesions such as Warthin tumor (WT),¹ ² ³ ⁴ ⁵ but they can also be caused by metastatic lymph nodes or malignant tumors.⁶

The parotid gland is the salivary gland that most commonly develops tumors, most of which are benign. After pleomorphic...
adenoma, WT is the second most prevalent parotid tumor. It presents as a slow-growing mass in the tail of the gland, and is usually asymptomatic. It generally occurs between the sixth and seventh decades of life, predominantly in men. It has a strong association with smoking, which is therefore considered a risk factor for its development.\textsuperscript{7–10} WT can be multicentric or bilateral, and it rarely becomes malignant.

To our knowledge, only two previous studies have reported the prevalence of PGI, and both were performed in Asia.\textsuperscript{2,11} Furthermore, clinical features such as the role of smoking have not been considered in their etiology. The present study aimed to determine the prevalence of parotid incidentalomas in \textsuperscript{18}F-fluorodeoxyglucose (\textsuperscript{18}F-FDG) PET/CT and evaluate the presence of smoking in this group of patients. We also reviewed the database of parotidectomies performed in our hospital to assess the relationship between WT and smoking.

Materials and Methods

Patients

We conducted a retrospective review of the reports of PET/CT performed in 4,250 patients in our hospital between June 2009 and February 2013. We identified 16 cases of parotid focal uptake in patients without known disease of the parotid glands. The group consisted of 10 men and 6 women, 48 to 88 years of age. In most cases, PET-CT was indicated as an extension study of diagnosed neoplasms or to confirm locoregional relapse after treatment. In two cases, it was indicated to rule out giant cell arteritis.

We reviewed the history of smoking in the 16 cases: 13 had smoked or were current smokers. We identified additional studies performed on the parotid masses, finding that only 5 patients underwent cytologic analysis by fine needle aspiration cytology (FNAC). In 8 of the 16 cases, the lesion was located in the right parotid gland, in 7 cases it was located on the left, and in 1 case it was bilateral. Two patients had more than one deposit within the same gland.

We analyzed the database of parotidectomies performed in our department in the previous 10 years and focused on the pathologic diagnosis and the presence or absence of smoking in each case.

\textsuperscript{18}F-Fluorodeoxyglucose Positron Emission/Computed Tomography

Combined \textsuperscript{18}F-FDG whole-body PET/CT (Gemini TF, Philips, Amsterdam) with 64-slice CT was performed. Standard patient preparation included: 6-hour fasting, hydration, and serum glucose level of less than 150 mg/dL before tracer injection. Patients were asked to rest quietly in supine position, and vesical evacuation was done before the acquisition of images.

A dose of 3.7 MBq/kg of \textsuperscript{18}F-FDG was intravenously injected. Low-dose CT and PET from the base of the skull to the proximal thighs were performed, with an additional acquisition of head and neck images. The total examination time was \(\sim\)20 minutes. An abnormal PET-CT finding was defined as a significant increased uptake, higher than that of the surrounding normal tissue.

Results

We found PGIs in 16 patients who underwent PET/CT between June 2009 and February 2013, corresponding to 0.4% of patients undergoing PET/CT. The incidentalomas were more frequent in men (62.5%, 10 cases), and the average age at diagnosis was 68 years.

The most common indication for the test was lung cancer (7 cases, corresponding to 43.75%), followed by breast cancer (3 cases), giant cell vasculitis (1 case each of Horton disease and Takayasu arteritis), and 1 case each of locally advanced oropharyngeal cancer, gallbladder carcinoma with liver metastasis, peritoneal carcinomatosis of gynecologic origin, and retroperitoneal lymphoma. (See Table 1.)

Five of the 16 patients underwent FNAC of the parotid mass. Three of five masses had an inflammatory component without a malignant component, one was considered a mixed tumor suggestive of pleomorphic adenoma, and the other was inconclusive. Of the 16 patients, only the patient with the pleomorphic adenoma underwent surgery; a superficial parotidectomy was performed and the histology was confirmed. In the remaining 11 cases, FNAC was not performed but the mass was monitored by periodic clinical follow-up. Thirteen patients (81.25%) had a history of smoking. One of the three nonsmokers was the patient with the pleomorphic adenoma.

The average standardized uptake value of parotid tumors was 6.51, ranging from 2.87 to 16.1. The term used to describe the lesions was hyperintense or hypermetabolic intraglandular nodule.

A review of the database of parotidectomies performed in our department revealed that 311 patients were surgically treated for parotid gland tumors in the previous 10 years and 80 cases (25.7%) were identified as WT. This was the second most frequent tumor after pleomorphic adenoma. A history of smoking was identified in 93.8% of patients with WT (75 cases). This percentage was high compared with the prevalence of smoking in pleomorphic adenomas, which was 38.8%. (See Table 2.)

Discussion

Our findings show that the prevalence of PGIs on PET/CT in our institution is similar to that reported in the two previous studies in Asia. When analyzing the presence of cigarette smoking in our patients with PGIs, we found it was a common factor in 81.25% of the patients.

In our study, FNAC was performed in five cases. Three were negative for malignancy without typing the lesion. One case was a pleomorphic adenoma and the other had a nondiagnostic smear. The remaining patients did not undergo additional testing on the PGI due to the advanced stage of the primary tumor, the absence of symptoms, or the unlikelihood of metastasis based on clinical and tomographic features.

In the largest series published to date, Wang et al found 58 PGIs in 19,333 patients, representing a prevalence of 0.3%.\textsuperscript{11} They obtained histologic confirmation in 51 patients, 41 with benign lesions (mainly represented by pleomorphic adenomas and WT) and 10 with malignant tumors. In a smaller
sample, Horiuchi et al detected four cases of abnormal parotid FDG uptake in 1,872 PET scans, with an estimated prevalence of 0.2%; all four cases were diagnosed with WT.\(^2\) Other series of cases also found WT as the main cause of PGI.\(^1,3\)

As PGIIs are likely benign lesions, metastatic disease should not be suspected initially without histopathologic confirmation, even in patients with known malignancy elsewhere.\(^1,4,5\) Nevertheless, these lesions warrant further radiologic and histopathologic correlations. Ultrasonography and FNAC are useful tools to characterize parotid masses, avoiding erroneous staging of primary malignancies.\(^6\) The objective of cytologic diagnosis of parotid masses is the differential diagnosis between benign and malignant lesions.\(^12\) Complex histopathology and heterogeneity of cellular patterns of salivary gland tumors explain why typing of primary salivary malignancies by FNAC is a challenge. The accuracy of FNAC depends on the experience of the clinician who performs the procedure and the pathologist who evaluates cytologic material.\(^12\)

We found the prevalence of smoking in parotid tumors surgically treated in our hospital was significantly higher in patients with WT than in patients with other tumors \((p < 0.001)\). More than 90% of patients with WT were smokers, and cigarette use in patients with other benign and malignant neoplasms was lower, 38 and 55.4%, respectively. Several other authors have studied the relation between WT and smoking. According to their publications, between 80 and 94% of patients with WT smoke,\(^7\)–\(^9,13\) and the risk for development of WT correlates with the level and duration of smoking.\(^7,9\) Sadetzki et al found a remarkably high odds ratio \((15.3)\) for developing WT in the presence of smoking.\(^9\)

### Conclusion

Based on the high prevalence of WT as PGI on PET/CT and the strong relationship with smoking, we suggest diagnosis other than Warthin tumor should be considered for PGI in

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Smoking</th>
<th>SUV(_{\text{max}})</th>
<th>Cytology (FNAC)</th>
<th>PET/CT indication</th>
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<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>Male</td>
<td>Yes</td>
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<td>Negative for malignancy</td>
<td>Lung cancer</td>
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<td>2</td>
<td>48</td>
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<td>Yes</td>
<td>16.1</td>
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<td>Horton disease</td>
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<td>3</td>
<td>64</td>
<td>Female</td>
<td>No</td>
<td>5.1</td>
<td>Not performed</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>Female</td>
<td>No</td>
<td>4.55</td>
<td>Not performed</td>
<td>Breast cancer</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
<td>Male</td>
<td>Yes</td>
<td>4.03</td>
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<td>Gallbladder cancer</td>
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<td>6</td>
<td>88</td>
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<td>8</td>
<td>74</td>
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<td>9</td>
<td>79</td>
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<td>15.9</td>
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<tr>
<td>12</td>
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<td>3.5</td>
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<tr>
<td>13</td>
<td>85</td>
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<td>14</td>
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<td>6.8</td>
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<tr>
<td>15</td>
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<td>16</td>
<td>70</td>
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<td>4.29</td>
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<td>Lung cancer</td>
</tr>
</tbody>
</table>

Table 1 Data of 16 patients with parotid incidentalomas detected by PET/CT

Abbreviations: FNAC, fine needle aspiration cytology; PET/CT, positron emission/computed tomography; SUV\(_{\text{max}}\), standardized uptake value.

<table>
<thead>
<tr>
<th>Histologic diagnosis</th>
<th>Number of cases (%)</th>
<th>Smoking status (%)</th>
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<tbody>
<tr>
<td>Pleomorphic adenoma</td>
<td>134 (43.1%)</td>
<td>52 (38.8%)</td>
</tr>
<tr>
<td>Warthin tumor</td>
<td>80 (25.7%)</td>
<td>75 (93.8%)</td>
</tr>
<tr>
<td>Malignant tumors</td>
<td>56 (18%)</td>
<td>31 (55.4%)</td>
</tr>
<tr>
<td>Other diagnosis</td>
<td>41 (13.2%)</td>
<td>17 (41.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>311 (100%)</td>
<td>175 (56.3%)</td>
</tr>
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</table>

Table 2 Data of parotidectomies performed in our department in the previous 10 years

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nonsmokers. Further studies with histologic diagnosis and larger samples are warranted to confirm our hypothesis.

References
1. Lee SK, Rho BH, Won KS. Parotid incidentaloma identified by combined 18F-fluorodeoxyglucose whole-body positron emission tomography and computed tomography: findings at grayscale and power Doppler ultrasonography and ultrasound-guided fine-needle aspiration biopsy or core-needle biopsy. Eur Radiol 2009;19(9):2268–2274