

Four cases of Warthin's tumor of the parotid gland detected with FDG PET

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In the cancer screening with FDG PET for 1,872 medical health club members, high FDG accumulation in the parotid gland was found in four males (age, 57-70 years). Warthin's tumor was confirmed by surgical pathology. The exact mechanism of high FDG accumulation in Warthin's tumor is not yet known. This tumor may be found incidentally during FDG PET studies. When high FDG accumulation is found in the parotid gland, integrated consideration of the results of the physical examination, medical history and ^{99m}Tc -pertechnetate scintigraphy makes it possible to differentiate Warthin's tumor from other lesions.

Key words: Warthin's tumor, ^{18}F -fluorodeoxyglucose (FDG), positron emission tomography (PET)

INTRODUCTION

WE HAVE CONDUCTED membership-based medical health check-ups, by up-to-date imaging methods including whole-body positron emission tomography (PET) with ^{18}F -fluorodeoxyglucose (FDG) at the HIMEDIC Imaging Center at Lake Yamanaka since October, 1994.¹ In these examinations we found four cases of Warthin's tumor in the parotid gland detected with FDG PET. Because glycometabolism increases in malignant tumors, FDG PET takes advantage of this in the detection of malignant tumors and metastasis.² However, FDG is known to accumulate even in some benign lesions. Recently, it has been reported that although Warthin's tumor grows slowly and is benign, FDG uptake can be found in the tumor.³⁻⁶ This finding is important in discriminating between benign and malignant in extracranial head and neck tumors by means of FDG PET, and therefore we studied this in our cases.

MATERIAL AND METHODS

We conducted whole-body PET examination with FDG for cancer screening in 1,872 members (1,214 males and 658 females) during the period from October, 1994 to March, 1997. The mean age was 52.49 ± 10.17 years. Among these members four examinees in whom FDG accumulation was found in the parotid gland were studied.

A whole-body PET camera (ECAT EXACT 47, Siemens/CTI, USA) was used. Following fasting for four hours after a light breakfast, or overnight, FDG 260-270 MBq was infused intravenously and the emission scan was started 45 minutes later. The transmission scan for attenuation correction was omitted. For examinees who were suspected of having tumors in the parotid gland, magnetic resonance imaging (MRI, Siemens, Impact Dash) was performed in four subjects and ultrasonography (US, Toshiba, SSA 250A) in three. The examinees were asked about their smoking habit.

RESULTS

Table 1 shows the four cases in which abnormal FDG accumulation was found locally in the parotid gland (Fig. 1 and Fig. 2). The age ranged from 58 to 70 years and all were male smokers. Two examinees did not notice the mass in the parotid gland, but the other two examinees had

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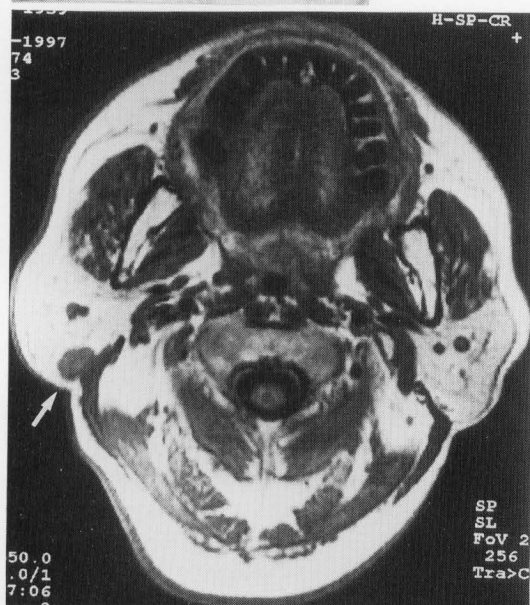
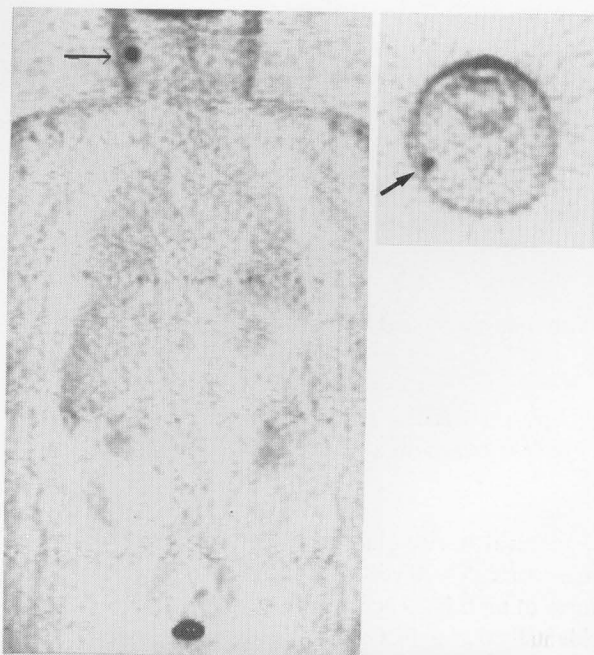


Fig. 1 Case 4. Intense FDG accumulations are noted at the level of the right parotid gland on the axial and coronal tomographic images (arrow). An axial T2-weighted MR image shows a well-demarcated tumor (arrow). The signal intensity is low compared with that the parotid gland.

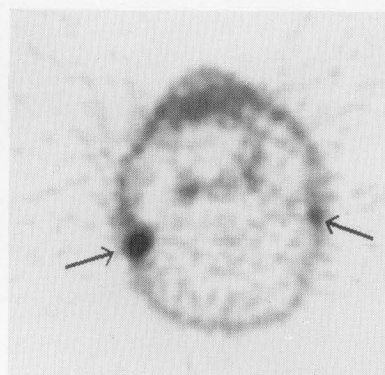


Fig. 2 Case 2. At the level of the parotid gland of the axial tomographic image, intense FDG accumulation in the right and slight FDG accumulation in the left are visualized (arrow). A bilateral Warthin's tumor was considered although pathological confirmation was not obtained in the left.

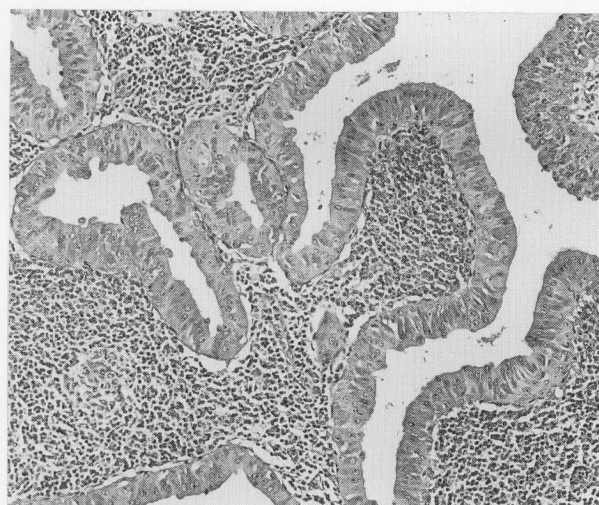


Fig. 3 Case 4. Microscopically, the tumor is composed of glandular epithelium and lymphoid stroma. The epithelial cells formed two cell layers show papillary and cystic arrangements. Lymphoid stroma has a lymphoid follicle.

noticed it four to six years ago, but did not seek treatment. In case 2, FDG accumulation was seen in both parotid glands (Fig. 2), and US revealed a palpable tumor in right parotid gland (2.6 cm in diameter). The other three examinees had showed FDG accumulation in one parotid gland. In MRI (Fig. 1), in agreement with the PET findings, all cases were found with a low signal on the T2-weighted images. All masses located within the inferior side of the gland had a clear smooth margin without infiltration to the surrounding parotid gland. In case 3, the

physical examination, PET and MRI showed a mass in the right parotid gland, and US showed two masses (1.8 cm and 0.8 cm in diameter) in the same gland. ^{99m}Tc -pertechnetate scintigraphy performed at another facility showed a hot spot, which was compatible with Warthin's tumor.

From the above findings, Warthin's tumor in the parotid glands was suspected because of the positive FDG result. The patients were then introduced to an otolaryngologist and underwent partial parotidectomy including the tumors. In case 2 who had tumor in both parotid glands, only right gland, in which the tumor was palpable, was treated surgically. Although two tumors

Table 1 Four cases of Warthin's tumor

Case No.	Age Sex	FDG PET	MRI	US	Awake to mass	Smoking	Partial parotidectomy
1	68 M	L (+++)	T1 low T2 slt low	—	no	2 packs 30 years	L
2	70 M	R (+++) L (+)	T1 low T2 slt low	R 2.6 cm L 1 cm*	4 years ago	2 packs 50 years	R only
3	64 M	R (+++) one spot	T1 low	R 1.8 cm 0.8 cm*	6 years ago	3 packs 30 years	R
4	58 M	R (+++)	T1 low	R 1.8 cm	no	under 1 pack 30 years	R

M: male, L: left parotid gland, R: right parotid gland, slt low: slightly low, US: ultrasonography, *: not palpable physically, (+++): high FDG accumulation, (+): slight FDG accumulation

were detected with US at the right parotid gland in case 3, only one was found during surgery. Histopathological examination of the resected specimens confirmed Warthin's tumor in all patients (Fig. 3).

DISCUSSION

Conventionally, it has been said that pleomorphic adenoma (benign mixed tumor) accounts for 55% of all tumors in the parotid glands, cancer for 25%, and Warthin's tumor (papillary cystadenoma lymphomatosum) for 15%. Cancer in pleomorphic adenoma is rare and cancer in Warthin's tumor is very rare (0.3–1.0%).⁷⁻⁹

Among 1,872 medical health club members, four were found with Warthin's tumors. Since FDG accumulation is seen in all cases of Warthin's tumor, this disease is not to be overlooked. The incidence of Warthin's tumor in Japanese aged 52 ± 10 years is 0.21%.

A common site where Warthin's tumor occurs is the lower pole of the parotid gland, and it is usually 1–3 cm in diameter and growth is very slow. The number of patients is greater in males than in females, and the literature consistently cited of the ratio of males to females as being at least 5 : 1.^{10,11} It is noted that the tumor occurred in the 60s and 70s⁹ and in smokers¹² most frequently. The results for our four cases correspond to those reports: all were males with a long smoking history, and included three heavy smokers.

During development, the salivary tissue of the nascent parotid gland intermingles with the adjacent lymphoid tissue of the nascent lymph nodes. Histologically, Warthin's tumor consists of an epithelial (papillary duct) parenchyma and a lymphoid stroma.^{8,9} In Warthin's tumor, heterotopic salivary ducts within preexisting lymphoid tissue show signs of focal metaplasia due to chronic irritation such as that caused by tobacco. The lymphoid tissue undergoes subsequent reactive changes in response to the neoplastic epithelium. Plasma cells distribute to the periphery of proliferated epithelial tumor cells.⁸ This

pattern indicates an immunological reaction by the lymphoid stroma and excludes a reaction to local inflammation.^{8,10,13}

As for mechanisms causing FDG accumulation to be seen in Warthin's tumor, there are two hypothesis. One is that the epithelial cells in the ductal inner layer contain a large number of mitochondria^{10,13} and immunoglobulin A^{14,15} and FDG may accumulate in these cells. Another is that FDG may accumulate in the lymphoid stroma in a tumor. There are two versions of the hypothesis. One opinion is that FDG accumulates in the physiological lymphoid element, similarly to polyclonal tonsillar tissue.^{8,17} The other is that FDG may accumulate in the active infiltrated lymphocytes,^{16,18} similarly to Hashimoto's thyroiditis. Although FDG accumulates in these patients,^{19,20} it is unlikely that Hashimoto's thyroiditis and Warthin's tumor have similar pathophysiologic characteristic. Whether FDG uptake occurs in the epithelial cells or in the lymphoid tissue remains to be determined.

Preoperative determination of malignancy in parotid tumor is a goal which head and neck surgeon have long had. In Warthin's tumor, a lot of FDG³⁻⁶ and ^{99m}Tc-pertechnetate^{11,21,22} accumulates in all cases. Our case 3 was positive for ^{99m}Tc-pertechnetate at another facility. In parotid carcinoma, a lot of FDG accumulates, but ^{99m}Tc-pertechnetate dose not accumulate. In pleomorphic adenoma, both FDG and ^{99m}Tc-pertechnetate do not accumulate or only accumulate mildly.^{3-6,10,11,21,22} In salivary gland scintigraphy with intravenous infusion of ^{99m}TcO₄⁻, the substance is positive in Warthin's tumor and is a cold defect in other parotid tumors.⁶ In the diagnosis of Warthin's tumor, ^{99m}Tc-pertechnetate is superior to FDG PET. In terms of parotid mass, integrated consideration of the physical examination, medical history and ^{99m}Tc-pertechnetate scintigraphy allows surgeon to differentiate preoperatively a benign parotid mass from a malignant mass, but in interpreting FDG PET images of extracranial head and neck, it is important to understand FDG uptake in normal tissue in this area.²⁰

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