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Warthin's Tumor Multimodality Imaging. Anatomical and Scintigraphy Imaging Review, Including PET-CT and SPECT-CT

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Abstract

Salivary gland lesions discovered incidentally on various anatomic and molecular imaging modalities (-including PET-CT and SPECT-CT-) offer a clinical dilemma. The appropriate use of imaging techniques to diagnose a Warthin's tumor would be of utility. Anatomical and functional imaging modalities have been used with variable success. The evaluation of a suspected Warthin's tumor is challenging, each modality presenting with its benefits and limitations. No comprehensive review exists of the various ways to image Warthin's tumor. This review would help imaging experts to find ways to diagnose Warthin's tumors in difficult or indeterminate biopsies as well as cases where a biopsy is not indicated or not the first choice- for a variety of reasons. We propose to review different imaging techniques with the most recent advances, including PET-CT and SPECT-CT.

Keywords: Parotid; Warthin's; Salivary gland scintigraphy; MRI; Ultrasound; SPECT-CT; FDG PET

Introduction

Warthin's tumor is the second most common benign parotid tumor. It usually occurs in older patients (most often in the 6-7th decade of life). It most commonly presents incidentally on CT studies and nowadays on PET scans as well as in the work up of other processes involving the head and neck. This leads to a diagnostic dilemma. Is the parotid mass benign or malignant?

Historically, salivary gland imaging with [^{99m}Tc]-labeled sodium pertechnetate ([$^{99m}TcO_4^-$]) has been utilized to diagnose Warthin's tumors. [$^{99m}TcO_4^-$] scintigraphy has been used for the evaluation among other etiologies of Sjogren's syndrome, solitary parotid gland tumors (Warthin's tumor versus parotid malignancies), acute parotitis, and salivary gland ductal obstruction etc [1-20].

Other scintigraphic and anatomical imaging modalities have also been utilized to evaluate salivary gland pathology including ^{123}Iodine, ^{131}Iodine, and ^{67}Gallium scans or hybrid positron emission tomography (PET) with [^{18}F]-Fluorodeoxyglucose (FDG) [21-28], as well as the use of ultrasound, CT, and MRI.

Ultrasound has been able to identify a Warthin's tumor based on echo structure, margins and vascularity [23-25]. CT utilizes structure, margins, number of lesions, pattern of enhancement, washout time-frames and attenuation coefficients to differentiate between various parotid lesions [28]. The current role of MRI is predominantly in the pre-surgical delineation of facial nerve anatomy, although many investigators have attempted to use quantitative parameters in the evaluation of parotid masses including peak signal intensities, washout patterns, Apparent Diffusion Coefficient (ADC) cutoffs, and lesion-to-muscle magnetization transfer ratios [29-33]. However, these have had mixed results and are not commonly used in clinical practice.

When faced with the clinical dilemma of an indeterminate parotid gland lesion [$^{99m}TcO_4^-$] scans have been reported to have a high accuracy of about 87% (a sensitivity of approximately 78%, and a specificity of 91%); in addition, this test is also simple and quick to perform [7,14-20].

Discussion

Functional imaging

Salivary gland scintigraphy scans are usually performed by injecting 10 mCi of Na[$^{99m}TcO_4^-$] intravenously followed by immediate 5 minute anterior, right anterior oblique and left anterior oblique planar images (up to 500000 counts per image). A secretory challenge is then performed with lemon juice and another set of planar images is obtained. Then, SPECT-CT imaging may be performed immediately thereafter using a dual head hybrid gamma camera with a 180 degree circular orbit and a 15 second per stop acquisition of SPECT data immediately followed by a low dose CT (120 kVp/80 mAs). The SPECT-CT acquisition can be useful in cases where there are multiple known parotid lesions and the results can be used to diagnose a Warthin's tumor or direct an FNA or biopsy towards certain lesions.

Salivary gland scintigraphy has been extensively used to resolve the presence of a parotid mass discovered clinically or by anatomic imaging and successfully utilized to confirm the presence of a Warthin's tumor or oncocytoma [7,14-20]. Miyake et al. published a series of 34 patients. They found a high accuracy for this technique as almost all patients had significantly increased uptake following lemon juice stimulation with a delayed washout pattern [18]. Murata et al. also looked at 23 Warthin tumors and 45 non Warthin tumors and they reported an overall diagnostic accuracy of 87%, a sensitivity of 78% and a specificity of 91% [19]. Shinohara et al. reported a similar accuracy for this technique in a much larger series of 275 patients, which included 207 ^{67}Gallium scans used as a surrogate marker for malignancy. The study reported a sensitivity of 75% and specificity of 88% for Warthin tumors, while the lack of ^{67}Gallium uptake excluded malignancy with a negative

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predictive value of 95% [20]. Many other reports beginning as early as in the 1970's have described the high positive predictive value of this pattern for detecting a benign lesion such as a Warthin's tumor or oncocytoma [7,14-20]. The pattern of increased radiotracer retention following lemon juice stimulation and a delayed washout pattern was diagnostic for a Warthin's tumor and confirmed by further biopsy.

Furthermore, and due to a higher metabolic rate head and neck cancers are routinely staged with [^{18}F]-FDG PET-CT scans. Increased uptake has been described in malignant parotid lesions in the literature [26], however FDG is a nonspecific radiotracer and it's uptake is also increased in inflammatory conditions and other benign conditions. This suggests that this may not be an adequate modality for excluding or including benign or malignant parotid lesions on the sole basis of increased or lack thereof FDG uptake [23-30]. On the other hand Motoori et al. [14,26,36] described a combined FDG PET-CT and [$^{99m}TcO_4^-$] salivary gland scintigraphy approach as a potential way to distinguish benign parotid tumors in a series of 72 patients especially in the setting of a non-diagnostic fine needle aspiration and reported a sensitivity of 75% and a specificity of 80% of the joint approach [30]. This approach could be easily translated clinically on all incidental parotid lesions found on routine staging FDG PET scans. Horiuchi et al. recently described increased FDG uptake in several but not all pleomorphic adenomas related mostly to an over expression of GLUT1 transporters, again stressing the limitation of the FDG PET-CT scan when used alone [24].

Anatomical imaging

At the present time parotid gland tumors can be diagnosed by FNA with a high accuracy (90-98%) and a low cost [33]. However, some parotid gland tumors are small or deep, thus making it difficult to obtain an adequate sample and the possibility of using a noninvasive technique to confirm the benign nature of a parotid lesion becomes attractive and economical. Ultrasound has been used to improve the diagnostic yield from FNA biopsies of parotid lesions. On ultrasound, Warthin tumors are usually oval, hypoechoic, hypervascular, well-circumscribed, and contain multiple anechoic areas [34]. According to the North American literature, ultrasound cannot definitively distinguish benign from malignant parotid lesions opposing the European view [34,35].

On the other hand preoperative ultrasound imaging is usually obtained to evaluate for malignant features (ill defined margins or infiltration into adjacent structures) and to determine the exact location/extent of the lesion, hence guiding the surgical procedure that is performed. If the mass appears benign, local excision or superficial parotidectomy is the treatment of choice, however, if the mass shows malignant features, then a total parotidectomy ± facial nerve resection is performed [36]. Typically in patients with a suspected Warthin's tumor then enucleation or superficial parotidectomy with preservation of the facial nerve is recommended [37].

On CT and MRI Warthin tumors typically appear well circumscribed with homogenous, cystic or solid lesions, in the parotid or peri-parotid region, most commonly involving the inferior pole of the gland. The appearance of multiple or bilateral parotid or periparotid masses is suggestive of a Warthin's tumor, but not diagnostic.

Although MRI is more commonly used to evaluate parotid masses, CT imaging has also shown promise in elucidating parotid tumors. A study by Choi et al. found that Warthin tumors (8/9) showed strong early phase enhancement with a decrease in attenuation on delayed imaging (120 seconds) as opposed to the pleomorphic adenomas (30/35) which predominately showed increased delayed enhancement [38]. The mean Hounsfield units (HU) measured in the early phase CT's (30 second delay) from patients with Warthin tumors was 96 HU (± 22 SD), as opposed to the pleomorphic adenomas with HU of 66 (± 24) [38]. The ratio of tumoral CT numbers (mean delayed HU/mean early HU) of Warthin tumors (0.82 ± 0.15) significantly differed from those of pleomorphic adenomas (1.33 ± 0.24) and malignant tumors (1.16 ± 0.22) [38].

MR imaging is commonly used for parotid tumors because it allows for facial nerve identification, Unfortunately on traditional MR imaging, Warthin tumors, which are benign tumors, can mimic malignant tumors with low, intermediate, or mixed signal on T2 images [36]. Therefore, traditional MRI sequences have been purported not to be useful although Ikeda et al. found that short tau inversion recovery sequences (STIR) and T2-weighted sequences produce significantly lower mean minimum signal intensity ratios in the hypo-intense areas of Warthin tumors (STIR 0.29 ± 0.22 SD; T2 0.28 ± 0.09) compared to malignant parotid tumors (STIR 0.53 ± 0.19; T2 0.48 ± 0.19) [36].

Several new techniques have been advocated to help discriminate Warthin tumors from other parotid lesions. Time-intensity curves (TIC) for Warthin tumors consistently show delayed washout, whereas pleomorphic adenomas show a persistent or plateau pattern [37].

Mirroring this, dynamic MRI shows that the peak signal intensity for Warthin tumors is at 0-30 seconds, but pleomorphic adenomas and malignant tumors showed peak signal intensities ranging from 30-210 seconds or a gradual increase in signal for up to 5 minutes [33]. Dynamic contrast enhanced MRI has also shown that Warthin tumors typically demonstrate ≥ 30 % washout, whereas the malignant tumors demonstrate low washout <30% [37]. Ikeda et al. found similar findings with 44.0% ± 20.4 average washout ratio of Warthin tumors, compared to malignant tumors with washout ratios of 11.9% ±11.6 [36].

Several studies have advocated using ADC cutoff values to separate parotid lesions into probable tumor subtypes, although there is some debate as to the reproducibility of ADC values among institutions. The studies that specifically focused on Warthin tumors found that Warthin tumors have low ADC values. Ikeda found that the average ADC value on diffusion weighted images of Warthin tumors (0.96 ± 0.13×10^{-3} mm^2/s, N=19) was significantly lower than the average ADC value of malignant tumors (1.19 ± 0.19×10^{-3} mm^2/s, N=17) [39-42]. Habermann et al. and Eida et al. additionally corroborated this data [40,41]. One study by Wang et al. lumped 3 Warthin tumors (low ADC) with 10 pleomorphic adenomas (high ADC) as solid benign tumors, likely artificially inflating the ADC value for Warthin tumors [42]. By the Wang et al. criteria (ADC values smaller than 1.22×19×10^{-3} mm^2/s indicate malignancy) and therefore every Warthin tumor in the Ikeda study would have been considered malignant [37,42]. Yabuuchi et al. recommended using an ADC cutoff value of 1.0×10^{-3} mm^2/s to distinguish between carcinoma (greater than 1.0×10^{-3} mm^2/s) and Warthin tumor (generally less than 1.0×10^{-3} mm^2/s) in parotid lesions showing delayed washout [37,43].

Furthermore, according to a study by Sakamoto et al., a heavily T2 weighted sequence can help distinguish a pleomorphic adenoma (which usually appears more heterogeneous) from Warthin tumors (which usually appear more homogenous) [43]. Using heavily weighted T2 sequences also rendered statistically significant differences in the signal intensities of the solid portion of pleomorphic adenomas compared to Warthin tumors [43].

Lastly, lesion-to-muscle magnetization transfer ratios has been suggested by Takashima et al. as a technique to help improve diagnostic MRI accuracy when evaluating the parotid gland for malignancy [33].

Conclusion

Anatomical and functional imaging modalities have been used to distinguish Warthin tumors with a myriad of techniques and variable success. The adequacy of the technique used is crucial to appropriate characterization. Ultrasound and FNA can be challenging in the case of multiple lesions and sampling errors. CT and MRI frequently require contrast administration or even advanced quantitative techniques -not routinely available-. Salivary gland scintigraphy has proven to be an accurate, simple and reproducible test. SPECT-CT can resolve cases where multiple lesions are noted. Ultimately, our era of multimodality imaging offers clinicians and radiology experts the necessary tools to noninvasively diagnose Warthin tumors.

References

1. Vinagre F, Santos A, Santos M, Prata A, Oliveira A, et al. (2008) Salivary gland scintigraphy in the evaluation of patients with sicca complaints. Acta Reumatol Port 33: 422-428.
2. Vivino FB, Hermann GA (2008) Role of nuclear scintigraphy in the characterization and management of the salivary component of Sjögren's syndrome. Rheum Dis Clin North Am 34: 973-986, ix.
3. Frallonardo P, Ramonda R, Salaffi F, Carotti M, Andretta M, et al. (2008) Sjögren's syndrome: comparison among the main imaging techniques in the study of major salivary glands. Reumatismo 60: 141-149.
4. Vinagre F, Santos MJ, Prata A, da Silva JC, Santos AI (2009) Assessment of salivary gland function in Sjögren's syndrome: the role of salivary gland scintigraphy. Autoimmun Rev 8: 672-676.
5. De Jager JP, Choy D, Fleming A (1984) Salivary scanning in rheumatoid arthritis with sicca syndrome. Ann Rheum Dis 43: 610-612.
6. Katz WA, Ehrlich GE, Gupta VP, Shapiro B (1980) Salivary gland dysfunction in systemic lupus erythematosus and rheumatoid arthritis. Diagnostic importance. Arch Intern Med 140: 949-951.
7. Parret J, Peyrin JO (1979) Radioisotopic investigations in salivary pathology. Clin Nucl Med 4: 250-261.
8. Su YX, Xu JH, Liao GQ, Zheng GS, Cheng MH, et al. (2009) Salivary gland functional recovery after sialendoscopy. Laryngoscope 119: 646-652.
9. Macioszek A, Baczyk M, KopeÄ‡ T, SowiÅ„ski J (2008) [Salivary gland damage after 131I therapy in patients with differentiated thyroid cancer. Preliminary report]. Endokrynol Pol 59: 403-410.
10. Kapanen M, Collan J, Saarilahti K, Heikkonen J, Kairemo K, et al. (2009) Accuracy requirements for head and neck intensity-modulated radiation therapy based on observed dose response of the major salivary glands. Radiother Oncol 93: 109-114.
11. Voordeckers M, Everaert H, Tournel K, Verellen D, Baron I, et al. (2008) Longitudinal assessment of parotid function in patients receiving tomotherapy for head-and-neck cancer. Strahlenther Onkol 184: 400-405.
12. Kodaira T, Tomita N, Tachibana H, Nakamura T, Nakahara R, et al. (2009) Aichi cancer center initial experience of intensity modulated radiation therapy for nasopharyngeal cancer using helical tomotherapy. Int J Radiat Oncol Biol Phys 73: 1129-1134.
13. Rudat V, Münter M, Rades D, Grötz KA, Bajrovic A, et al. (2008) The effect of amifostine or IMRT to preserve the parotid function after radiotherapy of the head and neck region measured by quantitative salivary gland scintigraphy. Radiother Oncol 89: 71-80.
14. Motoori K, Ueda T, Uchida Y, Chazono H, Suzuki H, et al. (2005) Identification of Warthin tumor: magnetic resonance imaging versus salivary scintigraphy with technetium-99m pertechnetate. J Comput Assist Tomogr 29: 506-512.
15. San Pedro EC, Lorberboym M, Machac J, Som P, Shugar J (1995) Imaging of multiple bilateral parotid gland oncocytomas. Clin Nucl Med 20: 515-518.
16. Gates GA (1977) Sialography and scanning of the salivary glands. Otolaryngol Clin North Am 10: 379-390.
17. Higashi T, Murahashi H, Ikuta H, Mori Y, Watanabe Y (1987) Identification of Warthin's tumor with technetium-99m pertechnetate. Clin Nucl Med 12: 796-800.
18. Miyake H, Matsumoto A, Hori Y, Takeoka H, Kiyosue H, et al. (2001) Warthin's tumor of parotid gland on Tc-99m pertechnetate scintigraphy with lemon juice stimulation: Tc-99m uptake, size, and pathologic correlation. Eur Radiol 11: 2472-2478.
19. Murata Y, Yamada I, Umehara I, Okada N, Shibuya H (1998) Diagnostic accuracy of technetium-99m-pertechnetate scintigraphy with lemon juice stimulation to evaluate Warthin's tumor. J Nucl Med 39: 43-46.
20. Shinohara S, Yamamoto E, Tanabe M, Maetani T, Fujiwara K, et al. (2001) [Evaluation of RI scintiscanning to parotid gland tumors]. Nihon Jibiinkoka Gakkai Kaiho 104: 852-858.
21. Meltzer DE, Gebara NV, Goel SR, Ghesani M, Kuriloff DB, et al. (2008) Asymmetric I-131 uptake in the submandibular gland in the setting of thyroid carcinoma. Clin Nucl Med 33: 638-640.
22. Caglar M, Tuncel M, Usubutun A (2003) Increased uptake on I-131 whole-body scintigraphy in Warthin tumor despite false-negative Tc-99m pertechnetate salivary gland scintigraphy. Clin Nucl Med 28: 945-946.
23. Nguyen BD, Roarke MC (2008) Salivary duct carcinoma with perineural spread to facial canal: F-18 FDG PET/CT detection. Clin Nucl Med 33: 925-928.
24. Horiuchi C, Tsukuda M, Taguchi T, Ishiguro Y, Okudera K, et al. (2008) Correlation between FDG-PET findings and GLUT1 expression in salivary gland pleomorphic adenomas. Ann Nucl Med 22: 693-698.
25. Subramaniam RM, Durnick DK, Peller PJ (2008) F-18 FDG PET/CT imaging of submandibular gland oncocytoma. Clin Nucl Med 33: 472-474.
26. Uchida Y, Minoshima S, Kawata T, Motoori K, Nakano K, et al. (2005) Diagnostic Value of FDG PET and Salivary Gland Scintigraphy for Parotid Tumors. Clinical Nuclear Medicine 30: 170-176 .
27. Enomoto A, Nakahara H, Uchihashi T, Tsuji H, Hamada S (2011) Fluorodeoxyglucose-positive Warthin tumor in a neck node mimicking metastasis in primary intraosseous left posterior mandibular cancer staging with positron emission tomography/computed tomography. Journal of oral and maxillofacial surger, 69: 2052-2054.
28. Iwai T, Baba J, Shibasaki M, Omura S, Hirota M, et al. (2012) 18F-fluorodeoxyglucose-positive Warthin tumor in a contralateral cervical lymph node mimicking metastasis in tongue cancer staging with PET/CT. J Craniofac Surg 23: e507-509.
29. Klijanienko J, Petras S, De Bosschere L, Paulmier B, Le Tourneau C, et al. (2012) False-positive FDG PET/CT uptake in Warthin tumor in head and neck oncological patients confirmed by a fine needle aspiration. Diagn Cytopathol 40: 282-284.
30. Nguyen VX, Nguyen BD, Ram PC (2012) Bilateral and multifocal Warthin's tumors of parotid glands: PET/CT imaging. Clin Nucl Med 37: 175-177.
31. Higasi T, Nakayama Y, Murata A, Sugiyama M, Nakamura K (1972) Clinical evaluation of 67 Ga-citrate scanning. J Nucl Med 13: 196-201.
32. Collins RD Jr, Ball GV, Logic JR (1984) Gallium-67 scanning in Sjögren's syndrome: concise communication. J Nucl Med 25: 299-302.
33. Takashima S, Wang J, Takayama F, Momose M, Matsushita T, et al. (2001) Parotid masses: prediction of malignancy using magnetization transfer and MR imaging findings. AJR Am J Roentgenol 176: 1577-1584.
34. Bialek EJ, Jakubowski W, Zajkowski P, Szopinski KT, Osmolski A (2006) US of the major salivary glands: anatomy and spatial relationships, pathologic conditions, and pitfalls. Radiographics 26: 745-763.
35. Madani G, Beale T (2006) Tumors of the salivary glands. Semin Ultrasound CT MR. 27(6): 452-64.
36. Ikeda M, Motoori K, Hanazawa T, Nagai Y, Yamamoto S, et al. (2004) Warthin tumor of the parotid gland: diagnostic value of MR imaging with histopathologic correlation. AJNR Am J Neuroradiol 25: 1256-1262.
37. Yabuuchi H, Matsuo Y, Kamitani T, Setoguchi T, Okafuji T, et al. (2008) Parotid gland tumors: can addition of diffusion-weighted MR imaging to dynamic contrast-enhanced MR imaging improve diagnostic accuracy in characterization? Radiology 249: 909-916.

38. Choi DS, Na DG, Byun HS, Ko YH, Kim CK, et al. (2000) Salivary gland tumors: evaluation with two-phase helical CT. Radiology 214: 231-236.

39. Yousem DM, Kraut MA, Chalian AA (2000) Major salivary gland imaging. Radiology 216: 19-29.

40. Habermann CR, Gossrau P, Graessner J, Arndt C, Cramer MC, et al. (2005) Diffusion-weighted echo-planar MRI: a valuable tool for differentiating primary parotid gland tumors? Rofo 177: 940-945.

41. Eida S, Sumi M, Sakihama N, Takahashi H, Nakamura T (2007) Apparent diffusion coefficient mapping of salivary gland tumors: prediction of the benignancy and malignancy. AJNR Am J Neuroradiol 28: 116-121.

42. Wang J, Takashima S, Takayama F, Kawakami S, Saito A, et al. (2001) Head and neck lesions: characterization with diffusion-weighted echo-planar MR imaging. Radiology 220: 621-630.

43. Sakamoto M, Sasano T, Higano S, Takahashi S, Iikubo M, et al. (2003) Usefulness of heavily T(2) weighted magnetic resonance images for the differential diagnosis of parotid tumours. Dentomaxillofac Radiol 32: 295-299.