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 [99mTc]-labeled sodium pertechnetate ([99mTcO4–]) has been utilized to diagnose Warthin’s tumors. [99mTcO4–] 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 123Iodine, 131Iodine, and 67Gallium scans or hybrid positron emission tomography (PET) with [18F]-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 timeframes 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 [99mTcO4–] 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[99mTcO4–] intravenously followed by immediate 5 minute anterior, right anterior oblique and left anterior oblique planar images (up to 50000 counts per image). A secretary 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 oncocyteoma [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 67Gallium 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 67Gallium 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 [18F]-FDG PET-CT scans. Increased uptake has been described in malignant parotid lesions in the literature [26], however FDG is a nonspecific radiotracer and its 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 [111mTcO4] 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. Horiuichi 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 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 mm2/s, N=19) was significantly lower than the average ADC value of malignant tumors (1.19 ± 0.19×10-3 mm2/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 mm2/s indicate malignancy) and therefore every Warthin tumor in the Ikeda study would have been considered malignant [37,42]. Yabuichi et al. recommended using an ADC cutoff value of 1.0×10-3 mm2/s to distinguish between carcinoma (greater than 1.0×10-3 mm2/s) and Warthin tumor (generally less than 1.0×10-3 mm2/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


