



The role of fine-needle aspiration biopsy (FNAB) in Warthin tumour diagnosis and management

Alzbeta Jechova¹ · Martin Kuchar¹ · Stepan Novak¹ · Vladimir Koucky¹ · Lucie Dostalova¹ · Michal Zabrodsky¹ · David Kalfert¹ · Jan Plzak¹

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Abstract

Purpose Warthin tumour (WT) is the second most common benign tumour of the parotid gland. The aim of this study was to assess the value of the FNAB in the diagnosis and treatment decision in patients with WT.

Materials and methods We performed a retrospective study of patients treated for parotid gland mass between 2006 and 2016. Patients who underwent the surgery with preoperative FNAB were considered. The first group was comprised of patients with preoperative FNAB showing WT and the second group was formed by patients with definitive histology of WT.

Results 216 patients had FNAB with the result of WT and underwent surgery (98 women—45.4% and 118 men—54.6%). The definitive histology corresponded with the preoperative diagnosis in 201 cases (93.1%). The other way round, 222 patients were operated with definitive histology showing WT and we correlated this finding with preoperative FNAB. The result of FNAB corresponded with definitive histology of WT in 201 cases (90.5%). Counted sensitivity and specificity of the ultrasound-guided FNAB for the diagnosis of WT were, respectively: 96.63% (CI 93.19–98.64%) and 96.21 (CI 93.83–97.86%). The accuracy of this method was 96.36% (CI 94.54–97.70%).

Conclusion Ultrasound-guided FNAB is a safe, accurate and important method in WT diagnosis. The therapeutic approach can be chosen based on FNAB results correlated with other clinical findings. We propose that when WT is suspected, follow-up or enucleation of the tumour are appropriate treatments. Patient preferences should be also considered.

Keywords Warthin tumour · Cystadenolymphoma · Fine-needle aspiration biopsy · Ultrasound · Parotid gland tumours

Introduction

Salivary gland tumours are interesting for their histologic diversity. Approximately 80% affect the parotid gland, where most of them are benign [1]. The Warthin tumour (WT), or cystadenolymphoma, constitutes about one quarter of benign parotid tumours and therefore represents the second most common benign parotid tumour after pleomorphic adenoma [2, 3]. WT are more frequent in men, typically occurring in the fifth to seventh decades of life [4]. They are often associated with a history of smoking, tend to be multicentric and involve both parotid glands [5]. Roughly 90% of WT

are found in the superficial lobe of the parotid gland and present themselves as a slow-growing indolent mass [6, 7]. The precise aetiopathogenesis is not yet fully understood. The prevailing theory is that this tumour has its origins in heterotopic salivary parenchymal or ductal inclusions in the intraparotid and periparotid lymph nodes [4, 8]. The treatment of WT is surgical resection, but the extent of surgery is still discussed [9].

Ultrasound is a quick, accessible and reliable method of choice for the evaluation of parotid gland masses. It can be accompanied by fine-needle aspiration biopsy (FNAB) to obtain more information about the character of the mass and to choose the proper extent of surgery or observation. FNAB is a cytodiagnostic method based on the morphological findings of individual cells, groups of cells and micro-particles of tissue, acquired using a needle [10]. Multiple studies concerning the benefit of FNAB in the evaluation of the parotid gland masses have been carried out with wide range of sensitivities (67–92%) and specificities (82–99%)

✉ David Kalfert
david.kalfert@fnmotol.cz

¹ Department of Otorhinolaryngology and Head and Neck Surgery, First Faculty of Medicine, Charles University, University Hospital Motol, V Uvalu 84, 150 06 Prague, Czech Republic

[11, 12]. Generally, it is a safe, accurate and cost-effective method [13].

The aim of this study is to evaluate the utility of ultrasound-guided FNAB in the preoperative diagnosis of WT and its value in the decisional algorithm for the therapeutic approach.

Materials and methods

This retrospective analysis was conducted at the Department of Otorhinolaryngology and Head and Neck Surgery, First Faculty of Medicine Charles University, University Hospital Motol, Prague, Czech Republic.

The study included patients treated for WT between 2006 and 2016. Only patients with parotid gland involvement were considered. The patients were divided into two groups, which partially overlapped.

The first group of patients was comprised by those who had undergone preoperative FNAB with a result for WT and after which were operated so we could make the correlation with definitive histology. The second group consisted of patients operated for parotid gland mass with the definitive diagnosis of WT who had preoperative FNAB.

All the patients were preoperatively subjected to clinical examination and ultrasound evaluation with ultrasound-guided FNAB. Some of the patients underwent magnetic resonance imaging and computer tomography. Facial nerve function was assessed clinically using House–Brackmann grading before and after surgery. Since this was a retrospective study, data on smoking history, Frey's syndrome and sensory impairment were not available for all the patients, so we did not include them in our results. The extent of the surgery varied from enucleation of the mass (removal only of the tumour with intact capsule) to the total parotidectomy.

Preoperative FNAB results were compared with histopathological findings and the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and likelihood ratio were stated. Sensitivity was calculated based on the ratio of positive cytology results to all histopathologically confirmed WT. Specificity was calculated as the ratio of histopathologically confirmed other type tumours to all negative FNAB. Accuracy was calculated by dividing the total number of true-positive and true-negative tumours by the total number of tumours.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics (version 22.0; SPSS, IBM, Armonk, NY, USA). Mean, median, standard deviation, and range were counted. The statistical results were calculated using the Fisher's exact test (two-tailed); *p*-values equal or to less than 0.05

were considered as significant. Sensitivity and specificity, PPV and NPV, and positive likelihood ratio (LR+) and negative likelihood ratio (LR−) were calculated with their corresponding 95% confidence intervals (CI).

Results

In the monitored 10-year period (2006–2016) a total of 748 patients were operated at our department for parotid gland tumour. Women predominated (429; 57.4%) over men (319; 42.6%). The median age was 57 years (range 12–96 years). In 651 (87%) patients' preoperative FNAB was performed. 604 (92.8%) patients were diagnostic and 47 (7.2%) cases were non-diagnostic. 216 (35.8%) patients were diagnosed with WT according to FNAB.

Sensitivity and specificity of the ultrasound guided FNAB for the diagnosis of WT were, respectively: 96.63% (CI 93.19–98.64%) and 96.21 (CI 93.83–97.86%). The positive likelihood ratio was 25.51 (CI 15.52–41.94) and the negative likelihood ratio 0.03 (CI 0.02–0.07). Our data showed PPV 93.06% (CI 89.07–95.66%) and NPV 98.20% (CI 96.33–99.12%). The accuracy of this method was 96.36% (CI 94.54–97.70%). All results are shown in Table 1.

Group 1

A total of 216 patients underwent FNAB with the result of WT followed by surgery between 2006 and 2016 [98 women (45.4%) and 118 men (54.6%)]. At the time of the surgery their median age was 63 years (33–83 years) (Table 2). The majority of patients were treated by simple enucleation of the tumour [109 (50.5%)], followed by extracapsular extirpation [53 (24.5%) patients], 44 (20.4%) patients had superficial parotidectomy, 5 (2.3%) patients had subtotal parotidectomy and 5 (2.3%) patients had total parotidectomy (Table 2).

Facial nerve palsy was seen in 20 cases (9.3%), due mostly to a temporary lesion of the marginal branch. In

Table 1 Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value, negative predictive value and accuracy of ultrasound-guided FNAB in the diagnosis of WT

	Value	95% CI
Sensitivity	96.63%	93.19–98.64%
Specificity	96.21%	93.83–97.86%
Positive likelihood ratio	25.51	15.52–41.94
Negative likelihood ratio	0.03	0.02–0.07
Positive predictive value	93.06%	89.07–95.66%
Negative predictive value	98.20%	96.33–99.12%
Accuracy	96.36%	94.54–97.70%

Table 2 Group 1 (patients with preoperative FNAB result of WT), evaluation of the surgical approach and facial nerve palsy

Surgical approach	N	%	Facial nerve palsy (postoperative)			
			No		Yes	
			N	%	N	%
Enucleation	109	50.5	104	95.4	5	4.6
Extracapsular extirpation	53	24.5	51	96.2	2	3.8
Superficial parotidectomy	44	20.4	35	79.5	9	20.5
Subtotal parotidectomy	5	2.3	3	60.0	2	40.0
Total parotidectomy	5	2.3	3	60.0	2	40.0

relation to the extent of the surgery 5 (4.6%) of 104 patients had facial nerve palsy after enucleation, 2 (3.8%) of 53 patients after extracapsular extirpation, 9 (20.5%) of 44 patients after superficial parotidectomy, 2 (40.0%) of 5 patients after subtotal parotidectomy and 2 (40.0%) of 5 patients after total parotidectomy (Table 2). Hence facial nerve palsies were statistically more frequent in patients with more extensive surgery compared with extirpation (enucleation and extracapsular extirpation) ($p = 0.00008$).

The definitive histology showed WT in 201 cases (93.1%). Surprisingly, three definitive histologies turned out to be carcinomas, 1 (0.5%) case of mucoepidermoid carcinoma, 1 (0.5%) case of adenocarcinoma not otherwise specified and 1 (0.5%) case of cribriform cystadenocarcinoma. The remaining histology revealed MALT lymphoma (two cases; 0.9%), other type lymphoma (two cases; 0.9%), oncocytoma (two cases; 0.9%), other benign lesion (5 cases; 2.3%) and pleomorphic adenoma (one case, 0.5%). All results are in Table 3.

Group 2

The other way round we operated 233 patients with definitive histology of WT in the same period of time. 11 patients were excluded from this study, because they did not have preoperative FNAB. Out of the remaining 222 patients

there were 124 (55.9%) men and 98 (44.1%) women. At the time of the surgery their median of age was 63 years (39–83 years).

We performed simple enucleation of the tumour in 114 (51.4%) cases, extracapsular extirpation in 54 (24.3%), superficial parotidectomy in 44 (19.8%), subtotal parotidectomy in 5 (2.3%) and total parotidectomy in 5 (2.3%) cases, respectively.

Facial nerve palsy was observed in 21 patients (9.5%), in the majority of cases it was only a temporary lesion of the marginal branch. In relation to the extent of the surgery 4 (3.5%) of 110 patients had facial nerve palsy after enucleation, 1 (1.9%) of 54 patients after extracapsular extirpation, 12 (27.3%) of 44 patients after superficial parotidectomy, 2 (40.0%) of 5 patients after subtotal parotidectomy and 2 (40.0%) of 5 patients after total parotidectomy (Table 4). As in the previous set of patients' facial nerve palsies were statistically more frequent in patients with more extensive surgery compared with extirpation (enucleation and extracapsular extirpation) ($p < 0.0001$).

The results of FNAB corresponded with definitive histology of WT in 201 cases (90.5%). Fourteen (6.3%) results were nondiagnostic, 4 (1.8%) were suspicious of carcinoma and 3 (1.4%) showed other benign lesions (Table 5).

All patients with definitive histology of WT are disease-free with no recurrence (observation time 2–12 years).

Table 3 Group 1 (patients with preoperative FNAB result of WT), evaluation of the definitive histology, gender and age

Definitive histology	FNAB results— WT (216; 100%)		Gender		Age (years)		
	N	%	Female	Male	Median	Min	Max
WT	201	93.1	91	110	63	39	83
PLA	1	0.5	0	1	36	–	–
Oncocytoma	2	0.9	2	0	69	56	82
Other benign lesion (cystitis etc.)	5	2.3	1	4	54	33	79
MALT lymphoma	2	0.9	2	0	63	60	65
Other type of lymphoma	2	0.9	1	1	66	57	74
Mucoepidermoid carcinoma	1	0.5	1	0	58	–	–
Adenocarcinoma	1	0.5	0	1	64	–	–
Cribriform cystadenocarcinoma	1	0.5	0	1	59	–	–

Table 4 Group 2 (patients with definitive histology of WT), evaluation of the surgical approach and facial nerve palsy

Surgical approach	N	%	Facial nerve palsy (postoperative)			
			No		Yes	
			N	%	N	%
Enucleation	114	51.4	110	96.5	4	3.5
Extracapsular extirpation	54	24.3	53	98.1	1	1.9
Superficial parotidectomy	44	19.8	32	72.7	12	27.3
Subtotal parotidectomy	5	2.3	3	60.0	2	40.0
Total parotidectomy	5	2.3	3	60.0	2	40.0

Table 5 Group 2 (patients with definitive histology of WT), evaluation of the preoperative FNAB result, gender and age

FNAB results	Definitive histology results—WT (222; 100%)		Gender		Age (years)		
	N	%	Female	Male	Median	Min	Max
WT	201	90.5	91	110	63	39	83
Non-diagnostic	14	6.3	3	11	56	44	77
Other benign lesion (cystitis etc.)	3	1.4	1	2	60	48	67
Suspicion carcinoma	2	0.9	1	1	75	69	81
Squamous cell carcinoma	1	0.45	1	0	61	–	–
Adenocarcinoma	1	0.45	1	0	66	–	–

Discussion

The WT is the second most common benign tumour of the parotid gland, the typical characteristics are; male gender predominance, manifestation in older ages (5–7th decade), smoking history and multicentricity [14]. Although some studies have found an increased incidence in women, decreased patient age and a significant increase in percentage of WT over pleomorphic adenomas [14–17]. Our results show 1.3:1 male-to-female ratio, meaning only a slight male preponderance, which is in concordance with the recent findings.

FNAB is a useful method in the diagnosis of major salivary gland masses. It helps distinguish between neoplastic and non-neoplastic lesions and it aids in the proper planning of required surgery, according to the biological behavior of the tumour [18].

The potential of malignant transformation of WT is extremely low (below 1%) and only a few cases have been reported in the literature so far [19–21]. Some authors even question its neoplastic origin, claiming that WT would be more accurately classified as tumour-like lesions and not benign tumours [14, 22, 23]. Regarding these facts raises the question of what kind of surgical procedure would be appropriate for the treatment of WT and if simple follow-up would not be enough. On the other

hand, Laco et al. reported two cases of metastasis of lung and renal carcinoma to the WT, but such phenomenon is extremely rare [24]. The literature proposes many different approaches, from follow-up to total parotidectomy with the preservation of the facial nerve in multifocal cystadenolymphoma [19, 25, 26]. But most authors propose superficial parotidectomy or extracapsular extirpation [1, 9, 27]. The work of Ciuman et al. demonstrates a statistically significant positive correlation between the extent of surgery and Frey's syndrome, sensory impairment, transient and permanent facial nerve palsy and aesthetic outcome [28]. In our cohort of patients, facial nerve palsies were also statistically less frequent ($p < 0.0001$) in patients who underwent enucleation (4.6 and 3.5%) or extracapsular extirpation (3.8 and 1.9%) compared with more extensive surgeries (20.5 and 27.3% facial nerve palsies among superficial parotidectomies, 40% among subtotal parotidectomies and 40% among total parotidectomies).

The majority of our patients with FNAB showing WT were treated with enucleation (50.5%) or extracapsular extirpation of the lesion (24.5%). Superficial parotidectomy was performed when the tumour was in close relation to the facial nerve, so the main trunk of the nerve had to be identified to ensure the safety of the procedure. The subtotal parotidectomy and total parotidectomy were done when there was a suspicion of malignancy during the surgery. In our cohort, the enucleation turned out to be safe and our procedures

were sufficient in taking into account the facial nerve function and the recurrences. Hence, we suggest it as a method of choice when the surgical approach is chosen and reliable FNAB is available. The precedent exists, in 1988 Heller and Attie proposed enucleation as a treatment of WT [29].

The diagnosis of the WT should be based on multiple findings such as FNAB result, location in the superficial lobe of the parotid gland, namely its tail, ultrasound characteristics (well-margined, homogeneous, hypoechoic lesion with often well-perfused intralesional septations, possibly total anechoic or cystic with a distal sound enhancement, multifocal or bilateral) [9, 17]. Espinosa and collective proposed a diagnostic algorithm based on typical MRI findings with sufficient specificity to avoid surgery if WT is suspected [30].

Most patients diagnosed with WT are older, often with many comorbidities, so surgery under general anesthesia is riskier. Yuan et al. discovered an increased risk of postoperative facial nerve palsy in patients with diabetes mellitus [31]. So, if the preoperative diagnosis of the WT would be accurate enough, management could be conservative, especially when surgery presents serious risks regarding patients' comorbidities, or when the patient does not want the surgical treatment. Our data show that ultrasound-guided FNAB has very good sensitivity and specificity (respectively, 96.63% and 96.21%) in the WT diagnosis. Combined with other clinical findings named above, it is a highly accurate and reliable method.

Therefore, at our department, if the FNAB shows WT, we discuss the possibilities with the patient-limited surgery (enucleation) or follow-up. If the conservative therapy is chosen, we perform a control after approximately 3 months, and we evaluate the growth rate. If there is no progression, we can continue with the follow-up strategy. Literature data show that WT can have a wide range of growth rates, reduction in size being a possibility [15].

Conclusion

Based on our findings we propose that ultrasound-guided FNAB is an accurate and reliable method in the WT diagnosis. Enucleation is an appropriate and safe surgical technique if the tumour is in a favorable location in the superficial lobe of the parotid gland, with low occurrence of facial nerve palsy and no reported recurrence at our department. Moreover, the surgical approach can be modified based on the preoperative finding and if there is any suspicion of malignancy, preoperative histology can be performed and the enucleation can be converted into a more extensive surgery. Non-surgical management of the parotid gland mass with typical characteristics of WT, confirmed by FNAB result is also possible when the patient is unwilling or unable to undergo the surgery. It is important to regard the fact that

WT mostly occurs in older patients which are likely to have more comorbidities. However, it is also important to mention that the accuracy of FNAB depends also on the experience of the physician performing the procedure and on the availability of a capable pathologist to assess the cytological findings.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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