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Pitfalls in preoperative work-up of parotid gland tumours: 10-year series

W. Fassnacht[1], S. Schmitz[1], B. Weynand[2], E. Marbaix[2], T. Duprez[3] and M. Hamoir[1]

[1]ENT Department, [2]Pathology Department, [3]Radiology Department, Head and Neck Oncology Program, Centre du Cancer des Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

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Abstract. *Pitfalls in preoperative work-up of parotid gland tumours: 10-year series. Problems/Objectives*: Preoperative fine-needle aspiration cytology (FNAC) and magnetic resonance imaging (MRI) are the two most widely accepted diagnostic techniques used for the assessment of parotid gland tumours. We retrospectively evaluated the ability of FNAC and MRI to predict malignancy in parotid gland tumours.
Methodology: Over a period of 10 years (2002-2011), parotidectomy for primary parotid gland tumours was performed in a consecutive series of 178 patients. Preoperative MRI was performed in 75% (133/178) of cases, and preoperative FNAC was performed in 70% of cases (124/178). Both modalities were applied in 53% (94/178) of patients. Sensitivity, specificity, and accuracy were analyzed retrospectively for each subgroup of patients.
Results: The sensitivity, specificity, and accuracy for predicting malignancy were 45%, 89%, and 84%, respectively, for FNAC (including only diagnostic cytology), and 40%, 88%, and 81%, respectively, for MRI. In the subgroup of patients who underwent both MRI and FNAC, sensitivity, specificity, and accuracy were 50%, 85%, and 80%, respectively. Preoperative MRI values improved significantly after introduction of diffusion-weighted (DW) acquisition in 2007 (71%, 93%, and 91%, respectively).
Conclusions: Compared to previously published results, the high number of nondiagnostic smears and the low sensitivity rates in our series were disappointing. In part, this can be explained by the low percentage of malignant tumours and the high number of low-grade tumours among these. We discuss possibilities for improving preoperative performance, such as ultrasound-guided FNAC.

Introduction

Primary parotid tumours constitute about 3% of all head and neck tumours. A high percentage (approximately 85%) are benign tumours.[1] Both benign and malignant lesions are characterized by a high diversity of histological types, which complicates their clinical assessment.[2-3] In general, clinical signs of malignancy include painful swelling, fixity or ulceration to skin or deep tissues, rapid growth, facial nerve paralysis, and enlarged pathologic lymph nodes.[2]

Magnetic resonance imaging (MRI) and fine-needle aspiration cytology (FNAC) are the two most widely accepted diagnostic modalities in the work-up of parotid lumps.

FNAC is a safe and simple technique at relatively low cost.[4] Interpretation of parotid mass cytology requires a high degree of experience from both the physician who performs the procedure and the cytopathologist, because the lesions tend to be highly variable and morphologically complex, and they often present a mix of cell types and growth patterns. In some cases, diagnosis of malignancy is established by tumour invasion and not cellular atypia, making diagnosis by cytology even more difficult.[5-8]

The role of MRI in the preoperative work-up of parotid masses is to map the lesion in order to define anatomical landmarks for surgery. It also serves to stage the neck and to assess the presumed histological nature of the lesion. In this regard, MRI

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is superior to other techniques such as computed tomography (CT) and ultrasound imaging.[9,10]

In daily practice, treatment for parotid lumps will be surgical in almost all cases. Therefore, criteria are necessary in order to determine the relative degree of urgency required to schedule surgery. In this retrospective study, we focused on the ability of MRI and FNAC to detect malignancy in a routine clinical setting at a university teaching hospital.

Material and methods

Patients

Over a period of 10 years (2002-2011), parotidectomy was performed in a consecutive series of 251 patients in the department of Head and Neck Surgery at Cliniques Universitaires St.-Luc, Brussels, Belgium. Among these patients, 178 underwent surgery for primary parotid gland tumours.

The remaining 73 patients were excluded from the present study, because they presented generalized diseases, secondary lesions, or tumour recurrence. In our series, we excluded seven patients with recurrent pleomorphic adenoma, six patients with generalized diseases such as lymphoma or Mikulicz syndrome, and 60 patients with intraparotideal metastasis of skin cancer. Among these patients, melanoma was diagnosed in 25 cases, squamous cell carcinoma in 22 cases, and Merkel cell carcinoma in six cases.

Preoperative MRI was performed in 75% (133/178) and preoperative FNAC in 70% (124/178) of patients. For FNAC, 63% (78/124) of the smears were diagnostic. Both modalities combined were applied in 53% (94/178) of patients, and 59% (55/94) of smears in this subgroup diagnostic.

Fine-needle aspiration cytology

Depending on the clinical examination, we performed palpation-guided FNAC for palpable parotid masses and ultrasound-guided puncture for ambiguous cases. A 23 gauge needle and a 10 ml syringe holder with 5 ml of air was used. In order to avoid contamination, aspiration was passive, by means of capillarity.[11] Two to three pricks were carried out, with several passes into the tumour each time. The clinician then placed all material in a tube that contained an alcohol-based fixation solution.

From 2002 to 2010, samples were then processed by placing 4 ml of the solution in a centrifugation chamber in order to obtain a spot on a slide. From 2010 onward, a liquid-based technique was used (ThinPrep Cytyc Corporation, Marlborough, MA, USA). Material was captured after aspiration of the solution through a filter and transferred to a slide. Slides were then Papanicolaou stained. The remaining material was embedded in paraffin, which permitted complementary stainings by immunocytochemistry or PCR. In our series, there were no cases of local complications, such as local infection, bleeding, or tumour spread.

Magnetic resonance imaging

Pretherapeutic MRI examinations were all performed with a standardized protocol that included the following: (1) Sagittal fast spin-echo (FSE) T2-weighted (W) views and precontrast coronal spin-echo (SE) T1-W views that covered the whole neck for both tumour and nodal evaluation. (2) Axial precontrast SE T1-W, FSE T2-W with fat saturation (FS) option, and post-contrast axial SE T1-W with FS views in similar slice locations covering whole parotid glands. (3) Isotropic diffusion-weighted (DW) acquisition in the axial transverse plane using the spin echo-echo planar imaging (SE-EPI) technique with automated calculation of ADC maps, which was introduced in 2007.

Additional sequences were acquired in an "à la carte" mode, mainly contrast-enhanced (CE) coronal T1-W with FS images. Standard slice thickness was 4 mm, with a 10% (0.4 mm) interslice gap. Different magnetic resonance systems with static B_0 field strengths ranging from 1.5 to 3 Teslas from two manufacturers (Philips Health-care, DA Best, The Netherlands & Siemens Medical Solutions, Brussels, Belgium) were used throughout the study period. The paramagnetic contrast agent was gadoterate (Dotarem) administered intravenously at the standard dose of 0.1 mM/kg.

A suspicion of malignancy was reported in cases in which invasion of surrounding structures and an irregular margin were observed. In some cases, other criteria, such as atypical signal intensity or tumour heterogeneity, led to a suspicion of malignancy.

Statistical analysis

The FNAC results were classified as nondiagnostic if low cellularity or contamination did not allow for a cytological diagnosis. Diagnostic smears were compared with the final histology and classified as

follows: true positive (malignancy was correctly diagnosed or suspected), true negative (absence of malignancy was correctly diagnosed), false positive (malignancy was incorrectly diagnosed or suspected), and false negative (failure to detect malignancy). The MRI results were compared with the final histology and classified as follows: true positive (malignancy was correctly diagnosed, including suspicion for malignancy), true negative (absence of malignancy was correctly diagnosed), false positive (malignancy was incorrectly diagnosed or suspected), and false negative (failure to detect malignancy). In the subgroup of 55 patients who underwent both MRI and FNAC, the results were compared with the final histology and classified as follows: true positive (malignancy was correctly diagnosed or suspected in at least one modality), true negative (absence of malignancy was correctly diagnosed in both modalities), false positive (malignancy was incorrectly diagnosed or suspected in at least one modality), and false negative (failure to detect malignancy in both modalities). Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were analyzed retrospectively for each subgroup of patients.

Results

Fine-needle aspiration cytology

Overall, 79 patients who underwent diagnostic FNAC were included. Histopathological analysis after surgery revealed 70 cases (89%) of benign tumours and nine cases (11%) of malignant tumours. Among the benign lesions, cytological diagnosis was true negative in 62 cases (89%) and false positive in eight cases (11%). In the nine cases of malignant histology, we found four cases (45%) of true positive and five cases (55%) of false negative results. Sensitivity, specificity, accuracy, PPV, and NPV were 45%, 89%, 84%, 33%, and 93%, respectively. FNAC correctly typed 22% of the malignant tumours (2/9) and 60% of the benign tumours (42/70).

Magnetic resonance imaging

Overall, 133 patients who underwent preoperative MRI were included. Histopathological analysis after surgery revealed 113 cases (85%) of benign tumours and 20 cases (15%) of malignant tumours. Among the benign lesions, we found a true negative

Table 1

Preoperative diagnostic value of FNAC

FNAC	**Malignant histology**	**Benign histology**	**Predictive value**
FNAC positive for malignancy (suspicious or malignant)	4	8	Positive predictive value: 33%
FNAC negative for malignancy (benign cytology)	5	62	Negative predictive value: 93%
Performance	Sensitivity: 45%	Specificity: 89%	

FNAC: fine-needle aspiration cytology.

Table 2

Preoperative diagnostic value of MRI

MRI	**Malignant histology**	**Benign histology**	**Predictive value**
MRI positive for malignancy (suspicious or malignant)	8 (3, 5)	13 (9, 4)	Positive predictive value: 38% (25%, 55%)
MRI negative for malignancy (benign diagnosis)	12 (10, 2)	100 (45, 55)	Negative predictive value: 89% (81%, 96%)
Performance	Sensitivity: 40% (23%, 71%)	Specificity: 88% (83%, 93%)	

Numbers and calculated percentages in parentheses: up to and including 2007, and from 2008 onward, respectively.
MRI: magnetic resonance imaging.

Table 3
Preoperative diagnostic value of FNAC and MRI combined

FNAC and MRI	Malignant histology	Benign histology	Predictive value
FNAC or MRI positive for malignancy (suspicious or malignant)	4	7	Positive predictive value: 36%
FNAC and MRI negative for malignancy (benign diagnosis)	4	40	Negative predictive value: 91%
Performance	Sensitivity: 50%	Specificity: 85%	

FNAC: fine-needle aspiration cytology; MRI: magnetic resonance imaging.

result in 100 cases (89%) and a false positive result in 13 cases (11%). In the 20 cases with malignant histology, we found eight cases (40%) of true positive and 12 cases (60%) of false negative results. In the overall period from 2001 to 2011, sensitivity, specificity, accuracy, PPV, and NPV were 40%, 88%, 81%, 38%, and 89%, respectively. Detailed analysis was performed for two subgroups, before and after DW-MRI was introduced. Predictability of malignancy improved significantly after 2007, with a sensitivity of 71% in patients who had surgery after January 2008, compared to only 23% in 2001–2007. A correct histological diagnosis based on radiological criteria was proposed in 0% (0/20) of malignant tumours and 59% (67/113) of benign tumours.

Magnetic resonance imaging and fine-needle aspiration cytology

Fifty-five patients underwent both preoperative MRI and diagnostic FNAC. Histopathological analysis after surgery revealed 47 cases (85%) of benign tumours and eight cases (15%) of malignant tumours. Among the benign lesions, we found a true negative result in 40 cases (85%) and a false positive result in seven cases (15%). In the eight cases with malignant histology, we found four cases each (50%) of true positive and false negative results. Sensitivity, specificity, accuracy, PPV, and NPV were 50%, 85%, 80%, 36%, and 91%, respectively.

Discussion

FNAC and MRI are important and complementary tools in the preoperative work-up of parotid gland tumours. Our data show that FNAC preoperatively predicts the pathological diagnosis of malignant tumours more accurately, while MRI provides valuable additional anatomical information for the surgeon. In our hands, the combination of both modalities did not yield a significantly better diagnostic value in detecting malignancy than either modality alone.

Analysis of the diagnostic performance of MRI showed a significant improvement in preoperative values after the introduction of isotropic DW acquisition in 2007: from 23% to 71%. Further analysis of consecutive patients might render the specificity more precisely, as there were only seven patients with a malignant diagnosis after 2007. This finding confirms data from previous studies, which suggest that DW-MRI helps to distinguish between benign and malignant parotid gland tumours and to characterize the different histological types of benign tumours.[12]

In our series, the high rate of nondiagnostic smears and the low sensitivity for the detection of malignancy in either modality were disappointing. Indeed, previously reported sensitivity rates vary from 56% to 90% for FNAC and from 81% to 87% for MRI.[3,6,9,11-16] These findings might reflect a routine setting in a university teaching hospital. In contrast to other studies, repeated smears were not performed in cases of nondiagnostic or low cellular smears. In our institution, because the procedure is performed by the surgeon and not by the pathologist, no immediate feedback regarding slide quality was possible. Among the previously published studies, those reporting similarly low sensitivity rates were performed in a similar routine clinical setting where no on-site pathologist was available.[15,16]

In our series, we have to emphasize the lack of diagnostic FNAC in patients with parotid malignancies. Diagnostic cytology was available in only 41% (9/22) of cases, whereas it was nondiagnostic

Table 4
Results of preoperative FNAC in all 22 patients with malignant diagnosis

Histology	***N***	**FNAC benign**	**FNAC indeterminate or malignant**	**FNAC not performed or not diagnostic**
Salivary duct carcinoma	3	0	3	0
Polymorphous low grade adenocarcinoma	1	1	0	0
Acinic cell carcinoma	6	1	0	5
Adenoid cystic carcinoma	3	2	1	0
Squamous cell carcinoma	1	0	0	1
Carcinoma ex pleomorphic adenoma	3	0	0	3
Mucoepidermoid carcinoma	5	1	0	4

FNAC: fine-needle aspiration cytology.

or not performed in 59% (13/22). Data might therefore have been insufficient for a representative sample.

Although high-grade carcinomas were usually detected by FNAC, low-grade carcinomas were often missed. Malignancy was detected in all three cases of salivary duct carcinoma, a highly aggressive carcinoma. On the other hand, FNAC failed to detect malignancy in low-grade carcinomas such as polymorphous low-grade adenocarcinoma, low-grade mucoepidermoid carcinoma, and acinic cell carcinoma.

Even so, our findings fall behind the results previously reported in other studies. A standardized work-up procedure will therefore be introduced for all patients who present with parotid lumps in our outpatient clinic. Routine MRI protocols should include isotropic DW acquisition, and FNAC with ultrasonographic guidance should be performed in all patients. Our results and those of previously published studies suggest that the ideal setting for FNAC is an interdisciplinary head and neck tumour clinic, with an experienced radiologist performing ultrasound and an on-site pathologist evaluating slide quality in real time. In ultrasound-guided cytology clinics, accuracy is greatly improved and the number of inadequate specimens is significantly reduced.[17]

Another possibility is to perform ultrasound-guided core biopsy, which is well tolerated and has been demonstrated to have a high degree of diagnostic accuracy. However, there is a potentially higher risk of tumour seeding in the needle tract and hemorrhage.[18]

A better diagnostic rate would be helpful in the development of appropriate treatment plans for individual patients. This is of particular interest in patients who present with Warthin tumour. This tumour is the second-most common benign tumour of the parotid gland, and it is closely associated with smoking.[19] Some authors suggest that this tumour should be classified as a tumour-like lesion, since both the epithelial and lymphoid tumour components are polyclonal in origin and recurrence and malignant transformation are extremely rare.[20] Whenever the preoperative work-up is conclusive for Warthin tumour, conservative management may be proposed, especially in elderly patients with high comorbidity.

Conclusions

Our data suggest that in a routine clinical setting, the sensitivity of the preoperative work-up for parotid gland malignancies may not be as high as was suggested by previous studies in specialized salivary gland centers. Considering the great variety of tumours and the high rate of low-grade carcinomas, this seems to be of particular importance in salivary gland pathology. We believe that all head and neck centers should be aware of this fact and, if necessary, should critically review their own experiences and work-up procedures.

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Dr. Wolfram Fassnacht
Université Catholique de Louvain,
Cliniques Universitaires Saint-Luc
Service ORL – Chirurgie cervico-faciale
Av. Hippocrate 10
1200 Brussels, Belgium
Tel.: 0032-2-764-1942
Fax: 0032-2-764-8935
E-mail: Wolfram.Fassnacht@uclouvain.be