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EDITORIAL

Preoperative diagnostic of parotid gland neoplasms: fine-needle aspiration cytology or core needle biopsy?

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Abstract

A preoperative cytologic or histologic diagnosis of parotid gland neoplasms is mandatory to decide which surgical procedure would be appropriate. Open biopsies are contraindicated because of the risk of recurrence secondary to tumour cell seeding; furthermore a subsequent curative parotid surgery can be complicated by a previous open biopsy. While fine-needle aspiration cytology (FNAC) was the only preoperative diagnostic procedure to distinguish benign versus malignant neoplasms over the past decades, core needle biopsy (CNB) has been increasingly used over the last few years. This created a debate as to whether FNAC or CNB should be the preoperative procedure of choice. The focus of this editorial is to analyse the advantages and disadvantages of FNAC and CNB, and to discuss which procedure is more appropriate in the preoperative work-up of parotid neoplasms.

Introduction

Salivary gland masses encompass a wide range of non-neoplastic lesions and of benign and malignant neoplasms. The malignancy rate for parotid tumours has been reported to be between 14–27% [1–3]. Age-standardized incidence rates per 100,000 in the US are 1.0 for males and 0.7 for females [4]. Signs and symptoms of malignancy such as pain, facial palsy and enlarged lymph nodes are present in approximately 25–35% of patients [5, 6]. After initial ultrasound evaluation, MR imaging is the modality of choice in the work-up of parotid neoplasms [7–9] if an additional imaging study is useful or necessary. Poorly defined tumour margins are the most accurate indicator of malignancy. However, such margins are present in up to 50% of malignant tumours on MR imaging [7], and small malignant neoplasms often resemble benign tumours on imaging studies [10, 11]. Neither clinical examination nor imaging studies can substitute for fine-needle aspiration cytology (FNAC) or core needle biopsy (CNB) in the preoperative diagnosis of parotid malignancies. Open biopsies are contraindicated because of the risk of tumour cell seeding, increasing the risk of recurrence of both malignant neoplasms and pleomorphic adenomas; furthermore, a subsequent curative parotid surgery can be complicated by a previous open biopsy [5]. Before 2000, all parotid neoplasms were treated by a formal parotidectomy: benign parotid neoplasms in the superficial lobe by

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a superficial parotidectomy and in the deep lobe by a total parotidectomy; malignant epithelial neoplasms were treated at least by a total parotidectomy. As the surgical options were restricted, the necessity and benefits of FNAC were questioned at that time [12]. But over the last two decades, new surgical procedures for benign tumours such as extracapsular dissection, partial superficial parotidectomy or deep lobe parotidectomy with preservation of the superficial lobe have been introduced [13–18]. Thus, in deciding which surgical procedure would be appropriate, it should be—whenever possible—known at the time of surgery whether the tumour to treat is, for example, a pleomorphic adenoma or a malignant neoplasm. For malignant neoplasms, it would be also desirable to know the histologic tumour type and grade since for several low-grade carcinomas, a deep-lobe parotidectomy can be avoided [19]. At present, the question is no longer—as 20–30 years ago—whether a preoperative cyto-/histo-logic diagnostic procedure is necessary and useful, but, which is more appropriate: FNAC or CNB. This is currently debated among head and neck surgeons and pathologists.

The present editorial aims to summarize the advantages and disadvantages of FNAC and CNB, and to discuss which of these preoperative diagnostic procedure may be the procedure of choice.

Fine-needle aspiration cytology

In experienced hands, FNAC is easy to perform and can be done in an outpatient setting with a 25–22 gauge needle; it causes little pain, does not require local anaesthesia and allows only limited histo/immunohisto-chemical analysis of the obtained material. Numerous studies on the utility and accuracy of FNAC have been published. Most of these are however retrospective and often do not mention whether samples are obtained by pathologists, radiologists or clinicians, nor whether the procedure is guided via palpation or ultrasound. In many studies, neither the sample removal technique nor the experiences and number of operators and pathologists involved are reported. In some studies, non-neoplastic lesions or recurrences of neoplasms are included while in others, they are not. On these grounds, it is difficult to compare the FNAC results.

Reported results

In 2011, Schmidt et al. [20] published "a systematic review and meta-analysis of the diagnostic accuracy of FNAC for parotid gland lesions". They included 7 datasets for the assessment of non-neoplastic versus neoplastic lesions, with a total of 795 cases, and 64 datasets on the accuracy of FNAC for the diagnostic of malignancy versus benignancy, with a total of 6169 cases; 530 inadequate or indeterminate FNACs (8.6%) were reported. In distinguishing neoplastic from non-neoplastic lesions, the sensitivity and specificity were 96% and 98%, respectively. As for the distinction of malignant versus benign lesions, the sensitivity and specificity were 80% and 97%, respectively. They concluded that FNAC shows a quite high specificity for the diagnosis of neoplasia (98%) and malignancy (97%). The 64 analysed studies show more variability of sensitivity (33–100%) than specificity (88–100%), except one study with a specificity of 67%. A later meta-analysis performed by Liu et al. [21] included 70 studies with 6784 FNACs and reported 518 non-diagnostic and 385 indeterminate findings (13.3%). For the diagnostic of malignancy versus benignancy, 63 studies with 5647 FNACs were included. The sensitivity and specificity were 78% and 98%, respectively. In addition, Feinstein et al. [22] analysed 272 FNACs of parotid and 71 of submandibular neoplasms. There were 22 non-diagnostic and 39 indeterminate specimens (17.8%). The sensitivity and specificity in the detection of malignant neoplasms were for parotid 75% and 95% and for submandibular 91% and 94%, respectively. The most recent analysis, published in 2018 [23], included 477 parotid FNACs and reported a sensitivity and specificity for detecting malignancy of 82% and 90%, respectively. In 26 (5.5%) cases, the FNAC was non-diagnostic. There were 26 (5.5%) false-negative and 29 (6.4%) false-positive findings. The higher rate of false positives is in contrast to most studies reporting higher rates of false-negative than false-positive findings [24–27]. It is emphasized that only a few studies analysed tumour typing: the reported accuracy is 18–35% [26, 28].

Complications

Major complications such as tumour cell seeding or facial nerve paresis appear extremely rare. Shah et al. [29] analysed 575 studies including a total of 41,468 FNACs of head and neck masses. Only five cases of seeding were documented, three of which after FNAC of the parotid gland, thus corresponding to a risk of seeding of 0.00012%. The factors influencing the risk of cell seeding may be the needle size, the number of passes and the use of suction or capillary technique [29]. Interestingly, the risk of cell seeding seems to be greater in other organs such as thyroid gland (0.14%) [30] and liver (0.13%) [31]. There are no reported cases of facial nerve paresis after FNAC of the parotid gland.

Discussion (FNAC)

FNAC may be considered a safe and cost-effective procedure, with an extremely low rate of complications. The FNAC procedure does not require local anaesthesia but it is characterized by a relatively high rate of non-diagnostic and intermediate findings. The accuracy of FNAC

results is strongly related to the experience of the operator and cytologist. For distinguishing neoplastic versus non-neoplastic pathologies, the sensitivity and specificity of FNAC are high whereas for distinguishing malignant versus benign neoplasms, the sensitivity is much less satisfactory. The accuracy of tumour typing and grading is low. Possibly, histologic type, frequency of unusual lesions and experience of the cytologist influence these results. Accordingly, FNAC can be inappropriate to guide the extent of surgery for malignant neoplasms of the parotid gland. The accuracy of FNAC seems to be increased by an on-site microscopic evaluation of aspirates performed by a cytologist [32, 33] as well as by systematic ultrasound guidance. But it may be difficult in the daily practice, to have a cytologist available and most head and neck oncologists do not perform ultrasound examinations themselves.

Core needle biopsy

For many decades, core needle biopsies have been used in various oncological fields such as urology, hepatology, or breast diseases as an alternative to open biopsies. During the last decade, there has been a rise in the use of CNB for parotid gland lesions. CNB aims at obtaining an adequate sample of tissue with preserved histological architecture. This would enable the pathologist to apply a wider range of histochemical stains and immunohistochemical techniques, which may assist in tumour typing and grading in many cases [34]. Even extracapsular tumour growth has been occasionally detected in CNB specimens [35] but this is influenced by chance. The CNB is performed under ultrasound guidance after local anaesthesia with an 20–17 gauge needle, depending on the tumour size, localisation and the suspected disease process (e.g., lymphoma) [36].

Reported results

Kim et al. [37] in 2018 reported an update of two previous meta-analyses [34, 38] and a systematic review which included ten articles published between 2005 and 2016, encompassing 1315 CNBs. The rate of non-diagnostic specimens was 3.6% (46 out of 1268)—in one article the incidence of non-diagnostic specimens was not mentioned. There were 18 (1.3%) false-positive and 26 (2%) false-negative findings. The pooled sensitivity and specificity in detecting malignant neoplasms were 94% and 98%, respectively. In the two previous meta-analyses [34, 38] of CNB, the accuracy of specific histologic diagnosis was reported to be 96% and 95%.

Complications

In the meta-analysis by Kim [37], which as stated above included 1315 CNBs, 7 (0.5%) haematomas occurred and neither cell seeding nor permanent facial nerve paresis were reported; in one case, a temporary facial nerve weakness caused by local anesthesia was described. In 2016, Shah et al. [29] analysed 35 articles including 1803 CNB's of head and neck masses; only 2 cases of seeding were reported: one in the parotid gland [39] and one in a lymph node [40]. In 2016, Novoa et al. [41] investigated 103 excised needle tracks after CNB of salivary gland lesions, most located in the parotid gland. The examination revealed no tumour displacement in 65 cases and in 38 cases, the needle track was not identified.

Discussion (CNB)

With the use of CNB, a sample of tissue with preserved histological architecture is obtained. The rate of indeterminate or inadequate specimens is low; the sensitivity and specificity in detecting malignant versus benign neoplasms are high. CNB is accurate in distinguishing carcinoma from lymphoma and, often, in tumour typing and grading. The procedure requires a local anaesthesia. Major complications are rarely reported but further data is desirable. The risk of tumour cell seeding after CNB seems to be related to the needle diameter, the tumour type and the anatomic site of puncture [42]. While needle track recurrences after CNB of breast cancer, thyroid cancer, etc., are described in the literature [43], no such recurrences after CNB of parotid gland neoplasms have been reported. Authors who are reluctant to endorse regular use of CNB argue that the number of analysed CNBs of parotid gland neoplasms may be too small and the follow-up too short for detecting needle track recurrences.

The risk of injuries of facial nerve branches may potentially be increased in CNBs of neoplasms in the periphery of the parotid, where nerve branches are quite superficial and in some cases lateral to the neoplasm. However, such lesions were never reported.

Comparison between FNAC and CNB

CNB is superior to FNAC in the preoperative diagnosis of parotid masses. CNB has a higher sensitivity in diagnosing malignant neoplasms and allows tumour typing and grading in most cases. The specificity of both procedures for discriminating benign from malignant lesions is quite similar. The rate of indeterminate and non-diagnostic specimens is lower with CNB than with FNAC. CNB requires a local anaesthesia and is, therefore, more time-consuming than FNAC. The number of passes is generally higher in

FNAC than in CNB. The rate of major complications such as tumour cell seeding or facial nerve paresis is extremely low for both procedures. Several authors [44, 45] who performed both FNAC and CNB compared their own experience in retrospective studies and made the same observations. Novoa et al. [41] analysed in 2016 in a prospective study comparing FNAC with CNB 103 patients with salivary gland lesions; they received ultrasound-guided FNAC and CNB; a cytologist was present during the FNAC procedure. The sensitivity and specificity in detecting malignant neoplasms for FNAC and CNB were 64 and 94% versus 95 and 100%. The results of CNB were clearly superior to that of FNAC despite ultrasound guidance and in situ of a cytologist during the latter.

Conclusions

Due to the rarity of malignant salivary gland neoplasms, the variety of carcinoma types and the similarity of several cytological findings of benign tumours and low-grade carcinomas, FNAC diagnosis is challenging; optimal evaluation requires cytologists experienced in salivary pathology. Since FNAC has a high specificity and a high sensitivity in distinguishing non-neoplastic lesions versus neoplastic masses, it could be used as first diagnostic procedure in lesions with a low probability to be a neoplasm.

In the preoperative diagnosis of parotid neoplasms, CNB is superior to FNAC. CNB preserves tissue architecture allowing a wider range of histochemical and immunohistochemical techniques than FNAC; the microscopical assessment should be performed by head and neck pathologists preferably with proven record in salivary glands. CNB has a high diagnostic potential (tumour typing and grading) compared to frozen section (FS) [28, 38, 46], thus, intraoperative FS may be avoided in selected cases by performing a preoperative CNB, which could diminish costs and allow optimal planning of surgery and counselling of the patient. Finally, the evolving molecular testing in the diagnosis of salivary gland neoplasms seems feasible with CNB material [47, 48]. A disadvantage of CNB is the local anaesthesia, with greater time consumption and discomfort for the patient.

Nevertheless, CNB may be the procedure of choice in the preoperative work-up of parotid neoplasms; it must be performed by experienced operators as sonographic examination of head and neck is recognized as challenging. Furthermore, in case of pleomorphic adenoma or malignant neoplasm, the needle track may be resected during curative surgery [41].

It is noted, that relevant current knowledge is based mainly on retrospective studies variously performed: ultrasound versus palpation guided and different specialists involved (pathologists, clinicians or radiologists). Furthermore, the experience and number of involved operators and pathologists, as well as the size of the needle and the number of passes, are not mentioned in many studies. Schmidt RL et al. [49] analysed 95 studies on FNAC or CNB and concluded that verification bias is common; most analyses overestimated sensitivity and underestimated specificity.

A prospective study with a statistically optimal number of cases of both FNAC and CNB and a precisely defined protocol (inclusion criteria; experience of operators and pathologists; needle size; number of passes, etc.) is needed to properly evaluate the ideal use of FNAC and CNB in the work-up of parotid masses. Furthermore, detailed histopathological evaluation of needle tracks of both FNAC and CNB are desirable.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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