*The Journal of Laryngology & Otology (2007), **121**, 676–679.*

doi:10.1017/S0022215107007104
Printed in the United Kingdom
First published online 3 April 2007

Main Article

Brushing cytology in cutaneous lesions of the head and neck

D Tamiolakis, E Proimos*, G E Perogamvrakis*, C E Skoulakis†, G C Georgiou, C E Papadakis*

Abstract

Background: Brushing cytology is a well established diagnostic procedure used by gynaecologists, physicians and surgeons to obtain representative samples from lesions. Our aim was to evaluate its reliability in ulcerative and tumour-like conditions arising in the skin of the head and neck.

Methods: Over 28 months, 86 patients with suspected cutaneous malignant lesions underwent a cytological examination with a cytobrush within the otolaryngology department.

Results: Cytological analysis identified 63 out of 64 histologically documented malignant tumours (60 primary basal cell and squamous cell carcinomas and three metastatic adenocarcinomas), and 21 out of 22 benign lesions. There was one false positive and one false negative result.

Conclusions: Brushing cytology of suspected cutaneous malignant lesions is a rapid and reliable diagnostic method which helps the clinician to decide on appropriate planning and treatment. The technique can be performed as an out-patient procedure, and smear preparation can be done in the laboratory, even at a peripheral hospital.

Key words: Cytology; Skin Neoplasms; Head and Neck

Introduction

There are two absolute indications for pre-operative diagnosis of tumours and tumour-like conditions of the skin, subcutaneous tissue and soft tissues: a primary lesion, and clinical suspicion of a recurrence or metastasis. The 'gold standard' for diagnosis is open biopsy of the lesion with histological examination of the excised tissue.

Pre-operative cytological evaluation is not a well recognised modality in this field, yet it offers several advantages.[1,2] The aims of cytological evaluation are to establish an aetiological and/or morphological diagnosis and thereby to establish a more accurate prognosis. Cytology is a useful tool for differentiating inflammatory and infectious lesions from those that are neoplastic. In many cases, cytology is also helpful in determining whether a tumour is malignant or benign. Cytology does however have its limitations, and these should be recognised. Problems may arise when an inflammatory response results in secondary dysplastic changes which can mimic those normally associated with neoplasia. It is also worth noting that, in poorly differentiated tumours, cytological examination may not identify the tissue of origin. Cytology, therefore, should not be regarded as a substitute for histopathological examination of biopsy specimens. Histology is more likely to provide a definite diagnosis and, since biopsies preserve tissue architecture, grading and classification of the tumour is usually possible.

Cytological examination of skin brushing material can be considered a rapid screening technique and may be used as an adjunct to biopsy. Patient anxiety can be relieved by providing an instant diagnosis, followed by discussion of treatment options. Surgery can be avoided if the lesion proves to be non-neoplastic, or delayed for convenience if it is benign. A diagnosis of malignancy allows pre-operative staging and planning of the extent of surgery. In addition, some cases may be managed either by radiotherapy[3] or local (intralesional) interferon treatment.[4,5] Furthermore, surgery in other cases may cause complications; for example, in older patients receiving systemic therapy, and in patients with multiple lesions for which restoration demands extensive skin allografting.

The most common malignant tumours arising from a chronic disease background are squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). Canti published, in 1979, a study of 1628 BCCs, which used scraping cytology and obtained very satisfying diagnostic results.[6] In contrast, we used brushing cytology in our work, using a rapid staining method

From the Departments of Cytopathology and *ENT, Chania General Hospital, Chania, Crete and the †ENT Department, General Hospital of Volos, Volos, Greece.
Accepted for publication: 19 April 2006.

(one minute duration) which was repeated when necessary, and we found that the sampling inadequacy rate was significantly diminished. This technical difference must be stressed; in the 1979 study, the sampling inadequacy rate was high due to inadequate exfoliation of cells. Correct smear preparation and proper fixation and staining techniques are also essential for optimal diagnostic results.[7]

Our study investigated the diagnostic accuracy, specificity and sensitivity of brushing cytology in head and neck cutaneous lesions.

Materials and methods

Eighty-six patients were examined in the department of otolaryngology, head and neck surgery of Chania General Hospital, over a 28-month period, and an equal number of lesions were documented in the files of the cytology department.

In most cases, clinical examination found an ulcer or exophytic mass. In a small number of cases, there was a healing or a flat, red-grey lesion surrounded by a small halo. The lesions were localised on the preauricular area (27), the temporal area (26), the lateral aspects of the neck (15), the orbit (five), the nose (three), the jugal-gingival groove (five) and the lips (five).

A gynaecological cytobrush was used to perform the examination (Figure 1). To test whether smears were satisfactory or not, a Giemsa quick-staining method (Hemacolor, Merck, Darmstadt, Germany) was applied, and if necessary the sampling was repeated. Subsequently, smears were stained with May–Grünwald–Giemsa and Papanicolaou stains.

Results

Of the 86 cases undergoing cytological analysis, 63 were reported as malignant (60 primary BCCs and SCCs (Figures 2 and 3), and three metastatic adenocarcinomas from the breast, kidney and gastrointestinal tract) and 21 were reported as benign (Table I). Cytological analysis resulted in one false negative result, a misdiagnosis of keratoacanthoma. Histological analysis documented a SCC arising on the jugal-gingival groove. Histological analysis also revealed one false positive result, concerning a case of endometriosis occurring in the nose, which was cytologically interpreted as a BCC (Figure 4).

Our cytological method showed a high rate of diagnostic accuracy, with 98.43 per cent sensitivity and 95.45 per cent specificity (95 per cent confidence interval).

FIG. 1
The cytobrush used to perform the examination.

Discussion

Disorders in the head and neck are accessible to inspection and palpation. Therefore, biopsy is the established diagnostic approach, providing the clinician with accurate histological evaluation. Cytological diagnosis of common primary cutaneous tumours, both benign and malignant, such as SCC and BCC, is well documented in the literature.[7] When faced with the differential diagnosis of cutaneous BCC versus cutaneous SCC, a reasonable first approach would be immunostaining for epithelial membrane antigen (EMA) and epithelial specific antigen Ab-9 (clone Ber-Ep4). Negativity for the former and positivity for the latter would favour a diagnosis of BCC. Cytology can almost always detect malignancy, so it plays an important role in the pre-operative investigation of primary skin tumours, as well as in the evaluation of possible metastasis from a previously documented neoplasm. This has been proven in our work too, with the exception of one case misdiagnosed as keratoacanthoma, and another one misdiagnosed as BCC. In cases of metastatic deposits, it is necessary to detect and manage the primary site. In our study, there were three cases of metastatic adenocarcinoma, primarily arising from the breast, kidney and gastrointestinal tract.

Distinguishing keratoacanthoma from squamous cell carcinoma is a persistent issue in pathology practice. Putti *et al.*[8] have reported that analysis of telomerase activity, cyclooxygenase isoenzyme 2 (COX-2) and p53 expression provides evidence that keratoacanthoma and squamous cell carcinoma are indeed distinct lesions and also helps differentiate the two lesions, despite their similarity on conventional morphology. Keratoacanthoma has recently been reclassified as squamous cell carcinoma-keratoacanthoma type to reflect the difficulty in histological differentiation as well as the uncommon but potentially aggressive nature of keratoacanthoma. The term 'squamous cell carcinoma-keratoacanthoma type' has been introduced for otherwise classical keratoacanthomas that reveal a peripheral zone formed

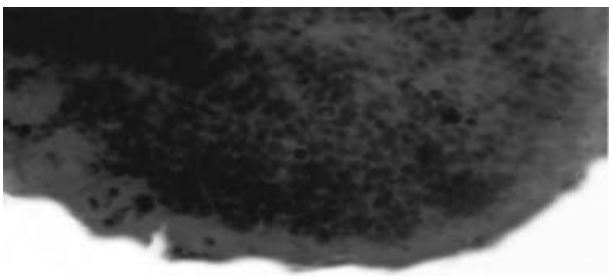

FIG. 2
Basal cell carcinoma arising in the temporal area (May–Grünwald–Giemsa; ×400).

https://doi.org/10.1017/S0022215107007104 Published online by Cambridge University Press

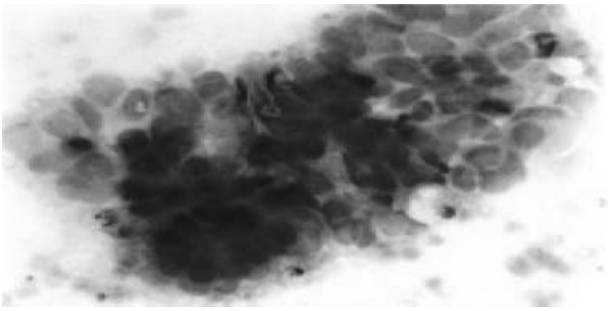

FIG. 3
Squamous cell carcinoma arising on the upper lip (Papanicolaou; ×400).

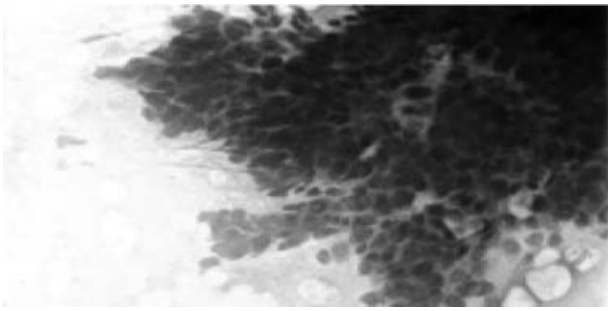

FIG. 4
Endometriosis, misdiagnosed as basal cell carcinoma (Papanicolaou; ×400).

by squamous cells with atypical mitotic figures, hyperchromatic nuclei and loss of polarity to some degree. These marginal cells may also penetrate into surrounding tissue in a more aggressive pattern.

In the case of endometriosis misdiagnosed on cytological analysis as BCC, the smears contained fragments of palisading epithelial cells resembling those of BCC, with uniform nuclei and a bland chromatin pattern. No stromal cells were recognised.[7]

In theory, cutaneous metastases may result from any neoplasm; this is borne out in practice.[9] To make a diagnosis of sweat gland carcinoma, one should first establish that the tumour shows sweat gland differentiation, as recognised by identification of extracellular ductal or intracytoplasmic lumen formations. This can be highlighted by their diastase-resistant periodic acid-Schiff, EMA, and carcinoembryonic antigen positivity. Demonstration of S-100 protein may be a useful pointer to sweat gland differentiation. Distinction of some types of sweat gland carcinoma from metastatic adenocarcinoma is not possible on morphological grounds. Immunohistochemical analysis does not allow distinction between a primary adnexal tumour and a metastatic tumour, except in a few cases (i.e. prostate and thyroid). Malignant sweat gland tumours are often positive for oestrogen and progesterone receptors, and these markers are therefore of limited usage in the differential diagnosis. Finally, there are some benign lesions which can be cytologically diagnosed.[10–13] Cytological analysis can rule out metastasis from a documented neoplasm in followed-up patients with newly arisen skin lesions. Cytological analysis can also diagnose uncommon cystic lesions (e.g. keratin cysts) and inflammatory processes.

Significant indications for the brushing cytology method are as follows (Table II). Firstly, in cases in which rapid diagnosis is needed; a skin brushing can be stained and accurately interpreted in a few minutes, and this simple method requires no freezing, paraffin embedding or microtome. Secondly, in cases in which a biopsy is not possible: this may be due to patient refusal, lack of tissue-processing facilities, inaccessibility of the lesion or the danger of biopsy complications. Thirdly, in cases in which a biopsy is not needed; the physician need only to confirm a clinical diagnosis with a minimum of trauma or pain (e.g. a cutaneous lesion which is obviously benign and needs no biopsy but is of unknown aetiology, or a lesion for which the possibility of occult malignant change must be ruled out). Fourthly, in cases in which follow up of treated lesions is required, and in which repeated biopsies would be wasteful and/or poorly tolerated by the patient; cytology is usually highly sensitive in the diagnosis of recurrence when a good specimen is obtained. Fifthly, brushing cytology may be indicated as an adjunct to excisional biopsy frozen section, for example, in order to evaluate the persistence of tumour cells in the margins of an excision. Sixthly, brushing cytology may be indicated for its safety; biopsy of certain tumours (e.g. malignant melanoma) may release neoplastic cells into lymphatic and blood vessels, whereas gentle brushing for cytological analysis decreases the chances of such an occurrence.[14]

TABLE I
RESULTS

Method	Total cases (*n*)	+ve (*n*)	−ve (*n*)
Cytology	86	63	21
Histology	86	63	23

True positives = 63; true negatives = 21; false positives = 1; false negatives = 1. +ve = positive; −ve = negative

TABLE II
INDICATIONS FOR BRUSHING CYTOLOGY

Rapid diagnosis required
Biopsy not possible
Biopsy not needed
Follow up of treated lesions
Adjunct to biopsy
Safety*

*Avoiding dissemination of disease.

- **This study investigated the use of brushing cytology in cutaneous lesions of the head and neck**
- **Cytology correctly identified 63 of 64 histologically documented malignant tumours of the skin of the head and neck**
- **Brushing cytology was a rapid and reliable diagnostic method which could be performed in an out-patient setting**

https://doi.org/10.1017/S0022215107007104 Published online by Cambridge University Press

Brushing cytology has some limitations, including: the absence of a cell pool in which cells may accumulate and remain moist; the difficulty of penetrating the superficial, horny, squamous layers to access diagnostic cells in deeper lesions; the comparative ease of obtaining punch biopsies; and cytologists' unfamiliarity with this type of specimen.

Conclusions

Despite the exponential interest and growth in dermatopathology over the years, and the fact that the skin is the largest desquamating organ in the body, interest in cutaneous cytology has in the past been limited. Although not a substitute for standard histological analysis, in the hands of an experienced cytopathologist, brush smears can aid in establishing the clinical diagnosis with ease and rapidity and can serve as an adjunct to routine histological study. The technique is cheap, easy to perform and does not cause any discomfort to the patient. In remote areas where facilities for full histopathological examination are unavailable, brushing cytology may represent a simple and useful diagnostic adjuvant. Brushing cytology's reliability, rapidity and easy performance without anaesthesia warrant serious consideration of its application within the field of head and neck surgery.

References

1 Orell S, Sterrett G, Walters M, Whitaker D. Supporting tissues. In: Orell S, Sterrett G, Walters M, Whitaker D, eds. *Manual and Atlas of Fine Needle Aspiration Cytology*, 2nd edn. New York: Churchill Livingstone, 1992;300–34
2 Linsk JA, Franzen S. Melanomas and skin nodules. In: Linsk JA, Franzen S, eds. *Clinical Aspiration Cytology*, 2nd edn. Philadelphia: JB Lippincott, 1989;319–36
3 Reisner K, Haase W. Electron beam therapy of primary tumors of skin. *Radiol Med* 1990;**8**:114–15
4 Dogan B, Harmanyeri Y, Balooglu H, Oztek L. Intralesional Alfa-2a interferon therapy for basal cell carcinoma. *Cancer* 1995;**91**:215–19
5 Greenway T, Cornell C, Tanner J, Peets E, Bordin M, Wagi C. Treatment of BCC with intralesional interferon. *Acad Dermatol* 1986;**15**:437–43
6 Canti G. Skin cytology and its value for rapid diagnosis. *Acta Cytol* 1979;**23**:516–17
7 Orell S, Sterrett G, Walters M, Whitaker D. The techniques of FNAC. In: Orell S, Sterrett G, Walters M, Whitaker D, eds. *Manual and Atlas of Fine Needle Aspiration Cytology*, 2nd edn. New York: Churchill Livingstone, 1992;8–23
8 Putti T, Teh M, Lee YS. Biological behavior of keratoacanthoma and squamous cell carcinoma: telomerase activity and COX-2 as potential markers. *Modern Pathology* 2004;**17**:468–75
9 Reingold IM. Cutaneous metastases from internal carcinoma. *Cancer* 1966;**19**:162–9
10 Duperrat B, Badillet G. Cytological examination of Bullae and Vesicles [in French]. *Rev Cytol Clin* 1971;**4**:9–16
11 Dey P, Das A, Radhika S, Nijhawan R. Cytology of primary skin tumors. *Acta Cytol* 1996;**40**:708–13
12 Rege J, Shet T. Aspiration cytology in the diagnosis of primary tumors of skin adnexa. *Acta Cytol* 2001;**45**:715–22
13 Cheng L, Binder SW, Cajjar NA, Hirchowitz SL. Fine needle aspiration as an adjunct to the diagnosis of a rare adnexal tumor of hair follicle origin: trichoblastoma. *Diagn Cytopathol* 2003;**29**:225–8
14 Naib Z. The vulva and the skin. In: Naib Z, ed. *Cytopathology*, 4th edn. Boston: Little, Brown & Co, 1996;199–217

Address for correspondence:
Dr Chariton E Papadakis,
1 Akrotiriou St,
Chania,
Crete 73133, Greece.

Fax: +30 2821055654
E-mail: papch@otenet.gr

Dr C E Papadakis takes responsibility for the integrity of the content of the paper.
Competing interests: None declared