CYTOLOGICAL DIAGNOSIS OF CUTANEOUS BASAL CELL CARCINOMA

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Abstract- Basal cell carcinoma (BCC) is the most common cancer of the skin. Definite diagnosis usually requires histological examination but recently it has been suggested that cytological examination of skin smear can be used as an alternative. To evaluate sensitivity and specificity of cytological examination, a total of 125 skin lesions, clinically suspected to be BCC were studied. Cytological samples were taken by scraping a scalpel blade over the lesion and smearing the cells on to a glass slide. The specimens were air-dried and stained with May-Grünwald-Giemsa. An incision biopsy was performed for histopathological study. The cytological results were compared with the histopathological results of the lesions. Histopathology revealed BCC in 102 lesions (81.6%), squamous cell carcinoma (SCC) in 11 lesions (8.8%), seborrheic keratosis in 6 lesions (4.8%), actinic keratosis in 5 lesions (4%) and keratoacanthoma in 1 lesion (0.8%). Cytological examination reported BCC in 90 (72%), SCC in 13 (10.4%) and seborrheic keratosis in 6 lesions (4.8%) and was non-diagnostic in 16 lesions (12.8%). The sensitivity and specificity of the cytology in identifying all of the BCC types were 87.3% and 95.3%, respectively. In conclusion, cytological examination is easy to perform, saves time, requires a minimum of equipments and can be considered a reliable method in the diagnosis of suspected cutaneous BCC.

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Key words: Basal cell carcinoma, scraping, cytology,

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignant tumor of the skin and generally is diagnosed by clinical features which must be confirmed by histological examination before any therapeutic maneuver; hence, a biopsy for histopathological evaluation must be performed. This requires local anesthesia, is time consuming and expensive. Several studies have suggested that cytological examination of the skin smears from the suspected BCC lesions can be a useful alternative method of diagnosis (1-6).We performed this study to examine the sensitivity and specificity of cytology in the diagnosis of BCC.

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MATERIALS AND METHODS

From Januarary 2002 to Januarary 2003, 125 lesions clinically presumed to be a BCC from 104 patients (73 male and 31 female) with the mean age of 62.5 years were included in this study. These lesions were located predominantly on the head and neck. Samples for cytologic examination were

collected by scraping a scalpel blade over the surface of the lesion without local anesthesia. In ulcerated lesions, crusts were carefully removed first with a sterile forceps and then the cellular material was collected. In non-ulcerated lesions the skin surface was broken first with the scalpel. The cellular materials were spread onto a glass slide and air-dried. The specimens were stained with May-Grünwald-Giemsa and then examined under the microscope. Histopathological specimens were obtained with an incisional biopsy under local anesthesia. The biopsies were fixed in 10% formaldehyde for at least 24 hours, routinely processed and embedded in paraffin.

After cutting 5 µm sections, we stained specimens with Hematoxylin and Eosin and examined them under microscope. The cytologic and histopathologic specimens were examined by different pathologists and cytological and histopathological diagnoses were assessed independently, without awareness of clinical details.

Criteria for the cytological diagnosis of BCC were 1) high intercellular cohesion in tissue fragments, 2) high nuclear-cytoplasm ratio of tumor cells with the cytoplasm forming a very narrow basophilic rim around the nucleus, 3) small size of the tumoral cells, 4) morphologically uniform tumor cells, 5) oval or fusiform and sometimes round nuclei with blurred chromatin structures, 6) presence of pink amorphous material in some lesions, 7) nucleoli usually not evident and 8) some fragments with distinct sharp borders. The presence of tight groups of uniform small cells with narrow basophilic cytoplasm was considered the most consistent diagnostic feature for the cytological diagnosis of BCC. Squamous cell lesions showed less cellular adhesion, more nuclear pleomorphism, less nuclear-cytoplasm ratio and no pink material.

RESULTS

Of the 125 lesions investigated in this study, 112 lesions were primary and 13 lesions were recurrent. Histopathological findings showed BCC in 102 lesions (81.6%), squamous cell carcinoma (SCC) in 11 lesions (8.8%), seborrheic keratosis in 6 lesions (4.8%), actinic keratosis in 5 lesions (4%) and keratoacanthoma in 1 lesion (0.8%).

Of the 102 lesions histologically diagnosed as BCC, cytological study showed BCC in 89 (87.3%), SCC in 1 (0.9%) and was non-diagnostic in 12 lesions (11.8%). Cytological examination of SCC lesions showed correct diagnosis in 7 lesions (63.6%) and was non-diagnostic in 4 lesions (36.4%).

All 6 lesions histologically diagnosed as seborrheic keratosis were confirmed by histological examination. In 5 cases of actinic keratosis, cytological examination was reported SCC in 4 cases and BCC in 1 case (Table 1).

This study also showed that cytological examination can be useful in all clinical and histopathological subtypes of BCC (Tables 2 and 3).

Table 1. Relationship between the cytological and histopathological results

	Cytologic results			
Histopathologic results	**BCC**	**SCC**	**Seborrheic keratosis**	**Nondiagnostic**
BCC (n=102)	89 (87.2%)	0 (0.0%)	0 (0%)	12 (11.8%)
SCC (n=11)	0 (0%)	7 (63.6%)	0 (0%)	4 (36.4%)
Seborrheic keratosis (n=6)	0 (0%)	0 (0%)	6 (100.0%)	0 (0%)
Actinic keratosis (n=5)	1 (20.0%)	4 (80.0%)	0 (0%)	0 (0%)
Keratoacanthoma (n=1)	0 (0%)	0 (100.0%)	0 (0%)	0 (0%)
Total (n=125)	90 (72.0%)	13 (10.4%)	16 (12.8%)	16 (12.8%)

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma.
*Data are given as number (percent).

Table 2. Cytological results according to histopathologic subtype of BCC

Histopathologic subtype of BCC	Cytologic results		
	BCC	**SCC**	**Nondiagnostic**
Solid type (n=72)	62 (86.1%)	0 (0.0%)	10 (13.9%)
Sclerotic (n=9)	8 (88.9%)	0 (0.0%)	1 (11.1%)
Superficial (n=12)	11 (91.6%)	0 (0.0%)	1 (8.3%)
Adenoid (n=3)	3 (100.0%)	0 (0.0%)	0 (0.0%)
Micronodular (n=4)	3 (75.0%)	1 (25.0%)	0 (0.0%)
Keratotic (n=1)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Squamous differentiation (n=1)	1 (100.0%)	0 (0.0%)	0 (0.0%)
Total (n=102)	88 (87.2%)	1 (1.0%)	12 (11.8%)

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma.
*Data are given as number (percent).

DISCUSSION

Cytological examination is a quick and easy procedure to perform which needs minimum of especial equipments and requires little training. It can be considered, in experienced hands and is reliable for the confirmation and differentiation of malignant skin tumors.

The high diagnostic accuracy of the cytologic examination in the diagnosis of BCC was first reported by Ruocco, in a study comprising 500 cases. Comparing to histopathological results, the cytodiagnosis of BCC was correct in 98.8% of positive cases and 98.4% of negative cases (7).

Powell *et al.* performed a study on 82 skin tumors, and reported that the sensitivity and specificity of cytological examination in the diagnosis of BCC were 91 % and 87%, respectively. They concluded that cytology could be considered reliable in the diagnosis of BCC (4).

It is difficult to distinguish benign from malignant basal cells, but basal cells rarely appear on a smear obtained from normal skin. The cytological diagnosis of BCC may also be difficult to distinguish from Merkel cell carcinoma and metastatic oat cell carcinoma (8). However, it is possible to distinguish BCC from SCC cytologically (Figures 1 and 2). Seborrheic keratosis differs from BCC by its possession of exfoliated superficial squamous cells and horn cysts (Fig. 2).

In contrast to BCC, malignant melanomas have larger cells, with a pronounced nuclear enlargement and macronucleoli, as well as high cellular dissociation. Nevi rarely supply enough cells for exfoliative diagnostic cytology and therefore generally results in insufficient smears (9). In our study only one BCC was misdiagnosed as SCC on cytological examination, which was a micronodular BCC with pleomorphic basal cells, and a case of actinic keratosis with basal cell hyperplasia misdiagnosed as BCC.

Table 3. Cytological results according to clinical subtype of BCC

Clinical subtype	Cytologic results			
	BCC	**SCC**	**Seborrheic keratosis**	**Nondiagnostic**
Nodular (n=81)	70 (86.4%)	1 (1.2%)	0 (0.0%)	10 (12.3%)
Sclerotic (n=8)	7 (87.5%)	0 (0.0%)	0 (0.0%)	1 (12.5%)
Superficial (n=12)	10 (83.3%)	0 (0.0%)	1 (8.3%)	1 (8.3%)
Total (n=101)	87 (86.1%)	1 (1.0%)	1 (1.0%)	12 (11.9%)

Abbreviations: BCC, basal cell carcinoma; SCC, squamous cell carcinoma.
*Data are given as number (percent).

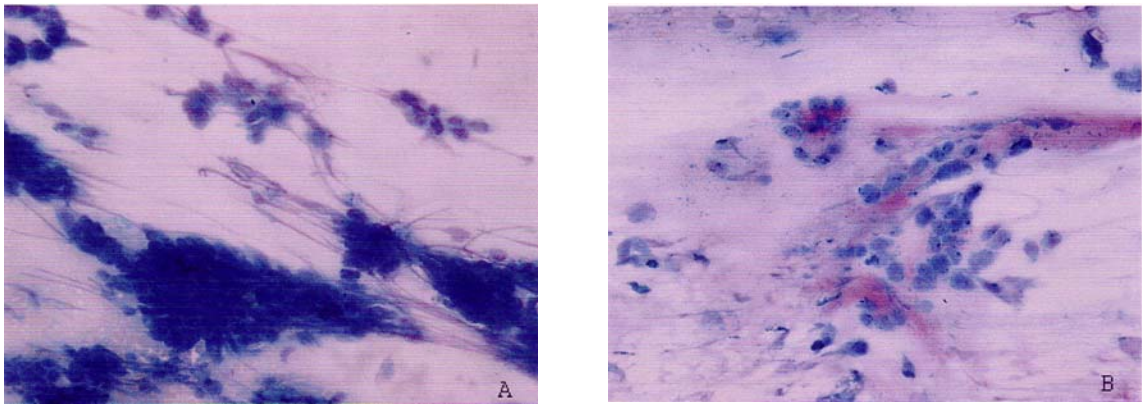

Fig. 1. A and B: Smears from basal cell carcinoma. There are fragments of syncytial sheets and small closely packed cohesive cells with little polarity; palisading occurs focally at the periphery of some of the clumps. There are monomorphic cells with round, oval and elongated nuclei along with fine granular chromatin patterns; also there is light eosinophilic amorphous material (as a stroma component) within the tumoral cells.

Also it was not possible to distinguish SCC from actinic keratosis and keratoacanthoma in cytologic examination. In 16 cases (12.8%) the cytology was not diagnostic because of either not enough material or insufficient diagnostic criteria. Therefore, our results confirm a high degree of sensitivity (89/102, 87.3%) and specificity (22/23, 95.7%) for cytological diagnosis of BCC.

The diagnostic accuracy of the cytologic examination of BCC lesions is due to characteristic and specific diagnostic criteria. These criteria allow differentiation of BCC from most benign epidermal lesions, as well as from other malignant skin tumors, such as SCC and malignant melanoma. The cytopathologist must insist on smears with qualitatively and quantitatively sufficient cellular material. The clinician must remember that an insufficient smear does not exclude a malignant tumor of skin, which may be proven by another exfoliative smear or invasive diagnostic procedures.

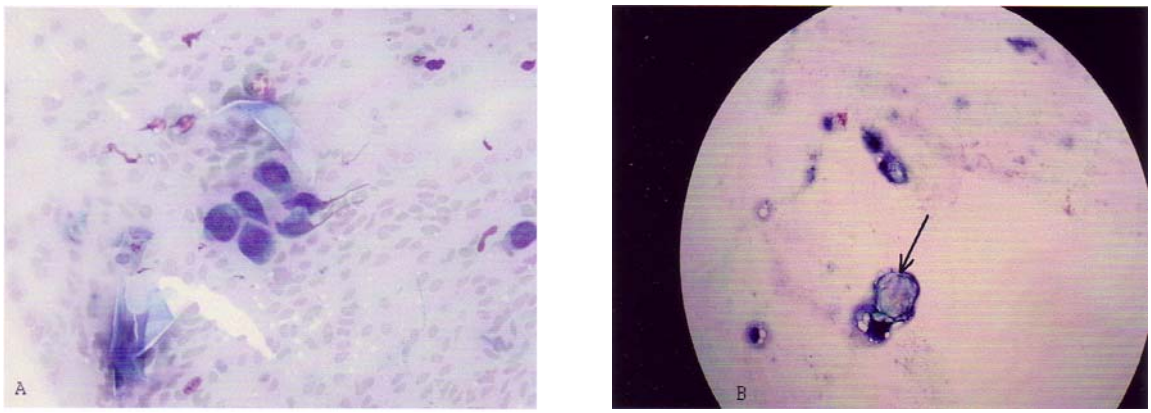

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Fig. 2. A: smear form squamous cell carcinoma shows small clusters of malignant squamous cells with no evidence of palisading. The nuclei of malignant cells are large with coarse clumping chromatin. B: smear from seborrheic keratosis shows a few scattered degenerated and keratinized there is also a structure of horny cyst (arrow).

The major disadvantage of using cytology in the diagnosis of BCC is that it cannot give much information about the pattern of tumor.

In conclusion, exfoliative-cytologic examination is very simple and useful. It requires minimum of equipments, and can be performed in outpatient's clinics. Minimal bleeding may be seen after scraping the lesion, but it causes no problem and requires only the application of local pressure. It reduces both the time and cost in clinics and laboratory. It is more acceptable to the patient as it does not require local anesthesia or sutures and leaves no scar.

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