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Skin Scrape Cytology in the Diagnosis of Nodular Basal Cell Carcinoma for Treatment by Photodynamic Therapy

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Photodynamic therapy is a new mode of cancer treatment with promising results for basal cell carcinoma. The current study aims to investigate the accuracy of skin scrape cytology in the diagnosis of basal cell carcinoma as an integrated part of the treatment procedure. A total of 107 nodular basal cell carcinomas of the skin from 90 patients were examined and cytological and histological diagnoses were compared. Compared with histopathology, cytopathology gave 3 false benign results (2.8%) and no false malignant diagnoses. Three lesions were benign by both methods. We conclude that basal cell carcinoma is reliably diagnosed with both techniques. However, cytology is simpler and faster, allowing treatment to be instituted shortly after the first consultation. ***Key words: skin tumours; cytology; basal cell carcinoma; photodynamic therapy.***

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We have recently demonstrated that photodynamic therapy (PDT) may be a simple and cost-effective treatment for basal cell carcinoma, which gives good cosmetic results (1). PDT is based on the use of a photosensitizer and light to induce tumour cell damage with no post-treatment scar tissue formation (2). Scarring following a pre-treatment biopsy is undesirable, particularly on the face. Strangely, cytodiagnosis is rarely performed as an alternative method of diagnosis, although reports by Brown et al. (3), Derrick et al. (4) and Barton et al. (5) conclude that skin scrape cytology may reliably diagnose BCC. In our institution debulking by curettage is included in the protocol for PDT treatment of nodular BCC and no confirmatory histology would be available after successful therapy. The aim of the study was to compare the diagnostic accuracy of cytology with that of histopathology of minute tumour fragments removed with a curette from lesions that were clinically suspected of being nodular BCCs.

MATERIALS AND METHODS

Specimens

A total of 112 lesions from 90 patients with lesions on the head, thorax or abdomen clinically suspected of being nodular BBCs were included in the current study. Specimens from 5 of the 112 lesions were inadequate by cytology and/or histopathology and were excluded from the study. The 5 lesions excluded were distributed equally among the participating clinicians (AS, TW). From each lesion a comparative cytological and histological specimen was taken. After removal of the epidermal keratin layer using the point of a needle, cytology specimens were taken by scraping a scalpel blade or curette over the lesion and smearing the cells on to a glass slide. The specimens were air-dried and stained with Diff-Quick. Minute tumour fragments of sizes 1–3 mm were subsequently removed from the lesions with a curette and placed in a Shandon cytoblock cassette before fixation in 4% buffered formalin. The tumour fragments were removed without damaging neighbouring skin and without the use of anaesthesia.

The histological specimens were examined by one pathologist (AB) and the cytological specimens by three cyto-pathologists at Cytological Unit, Department of Pathology, The Norwegian Radium Hospital. All histological and cytological specimens were reported blindly and independently.

Cytology

Any surface crust was always removed before the smear was made. The cytological diagnosis of BCC was based on a cellular smear with the presence of small dissociated hyperchromatic cells in cohesive sheets (Fig. 1A). The cells have scanty cytoplasm, indistinct cell borders and the cohesive sheets often demonstrate palisading.

Histology

The minute tissue fragments were fixed in 4% buffered formalin before embedding in paraffin. Sections 5 μm thick were cut at 3 levels and stained with haematoxylin and eosin. The histological diagnosis of BCC was based on the criteria defined by WHO (6) (Fig. 1B).

RESULTS

In 94 of the 107 cases, both histology and cytology confirmed the clinical diagnosis of BCC (Table I). In 3 cases both methods were reported as benign, and one lesion was diagnosed as squamous cell carcinoma by both techniques. Subtyping of the carcinoma was not possible in 3 tumours due to scanty biopsy material. However, 2 of the 3 cases were correctly classified as BCC by cytology. Another 3 cases recorded as atypical squamous hyperplasia in biopsy material were reported as BCC, suspected BCC, and irregular epithelial hyperplasia, respectively, in corresponding smears from skin scrapes. Compared with histology, cytology gave 3 false benign results (2.8%) and no false malignant results.

DISCUSSION

Correct diagnosis is an essential part of clinical practice; however, unwanted side-effects of the diagnostic test and the use of medical resources have to be taken into consideration. In the current study all lesions were clinically evaluated to be nodular BCCs with a tumour thickness of 2 mm or more excluding superficial and sclerotic lesions. This report demonstrates a high diagnostic accuracy of the 2 participating clinicians (AS, TW) in diagnosing BCC, partly facilitated by macroscopic inspection of the tumour material obtained by the scrape technique described.

PDT with photosensitizing drugs activated by visible light is a new mode of cancer therapy (7). This treatment has given promising results for superficial and nodular BCC, with a

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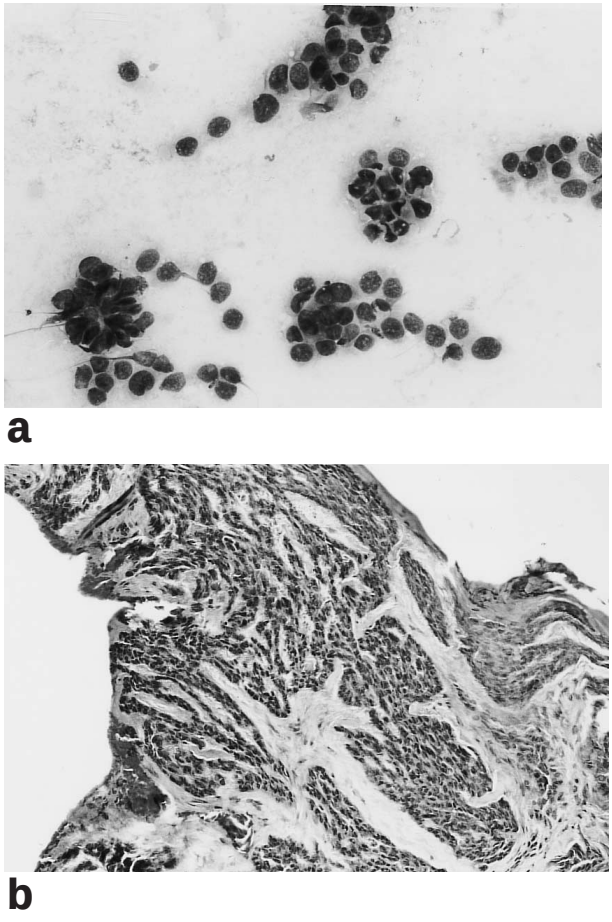

Fig. 1. Nodular BCC. *(A)* Diff-Quick stained smear with dissociated carcinoma cells in clusters (×400). *(B)* Curettage specimen from the same lesion demonstrating infiltrating cords of BCC (×80).

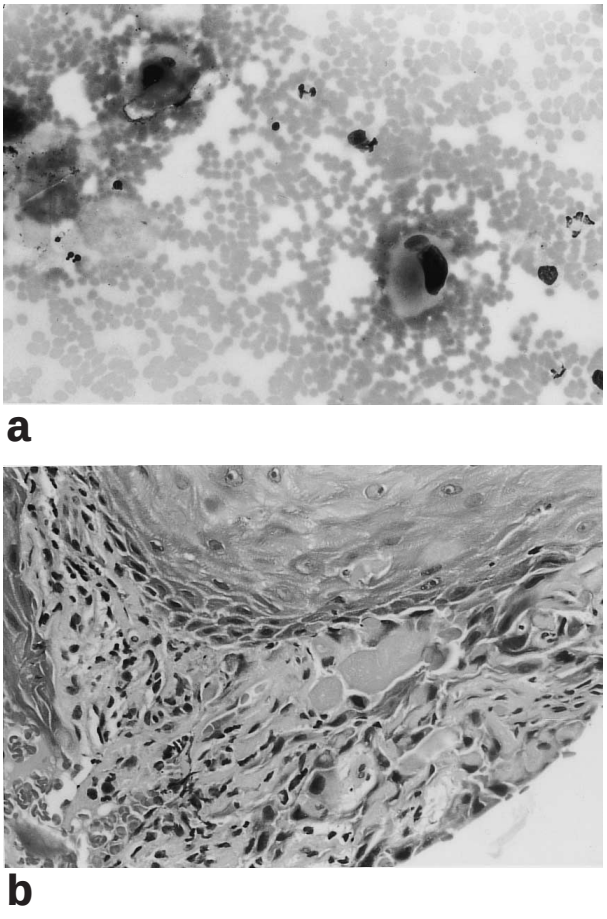

Fig. 2. Squamous cell carcinoma. *(A)* Diff-Quick stained skin scrape with single lying carcinoma cells with pleomorhic nuclei and dense homogeneous cytoplasm (×400). *(B)* Tissue fragment from the same lesion demonstrating microinvasive growth of atypical cells with squamous differentiation (×170).

complete response in almost 90% of cases (1, 2). The cosmetic outcome of patients with cured lesions was considered excellent to good in about 80% of cases. Noodt et al. (8) reported that PDT killed tumour cells by apoptosis which did not result in scarring. This may explain the good cosmetic outcome of patients with cured lesions.

In our institution intratumoural debulking by curettage is included in the protocol for PDT of nodular BCC and the removed tumour material was used for subsequent histopathological examination. Some squeeze artefacts were seen after curettage, but the histopathological evaluation was disturbed in only 1 case (Fig. 2B). The specimens were obtained by minimal invasive scraping and curettage, thus avoiding the more invasive punch biopsy. Any damage to adjacent normal tissues may in our experience interfere with the clinical evaluation of the treatment response after PDT. Almost half of the lesions were located on the head and face and intra-tumoural curettage was the only method of collecting histopathological specimens without damaging adjacent tissues. Neither cytological skin scrape nor intra-tumoural curettage leaves any scar.

The non-invasive skin scrape is a cytodiagnostic method

Table I. *Correlation cytology and histology in 107 skin lesions clinically diagnosed as BCC*

Histology					Cytology	
	Basal cell carcinoma	Suspected of basal cell carcinoma	Squamous cell carcinoma	Irregular	Benign	Total
Basal cell carcinoma	94				2	96
Squamous cell carcinoma			1			1
Carcinoma, type not specified	2	1			1	4
Atypical	1	1		1		3
Benign				1	2	3
Total	97	2	1	2	5	107

currently used for superficial skin lesions including nodular BCC (9 – 11), whereas the deeper lesions are best sampled by fine needle aspiration cytology (12). Although the skin scrape was first introduced in the late 1920s (13), only a few authors have described this technique in the differential diagnosis of a BCC (3 – 5, 9 – 11), the most frequent skin tumour. Skin scrape cytology is particularly useful in diagnosing superficial BCC as it is almost impossible to resect tumour tissue from such lesions by curettage or by punch biopsy without damaging adjacent tissues. Cytology has the advantage of being faster and simpler and may be used as a standard procedure in the diagnosis of superficial and nodular BCC.

In the present series cytology did not confirm 3 cases of BCC. However, atypical epithelium was not seen by reviewing the smears and the skin scrapes were regarded as unrepresentative. In an extensive study of 240 cases of BCC, Derrick et al. (4) reported that cytopathology gave a false negative and false positive diagnosis in 0.42%, respectively. In the current study only 1 erroneous cytological diagnosis of BCC was made (Fig. 2A), and the corresponding biopsy demonstrated microinvasive atypical squamous epithelium compatible with squamous cell carcinoma (Fig. 2B). Another 2 cases of BCC in cytological smears were reported as carcinoma of undetermined type by histopathology. The tissue specimens were, however, too small to classify the tumours in more detail. The embedded tissue specimens measured 2 mm on the sections and were possibly not representative of BCC.

It may be difficult to distinguish between a benign tumour originating in skin adnexal tissues and BCC when the skin scrape contains relatively few cells and the biopsy specimen is small. Particularly pilomatrixoma has morphological features similar to BCC and always has to be ruled out when in doubt. However, contrary to BCC cells from benign adnexal skin tumours are mostly cohesive and without atypia. In the current study all specimens were reviewed blindly and independently by 1 cyto-pathologist (AB) and only 1 diagnosis was changed retrospectively. A skin scrape primarily reported as BCC contained tumour cells with evidence of squamous differentiation (Fig. 2A), and the original diagnosis was changed to squamous cell carcinoma.

The skin scrape technique is rapid and requires a minimum of equipment and no local anaesthetic. Microscopy of formalin-fixed and paraffin-embedded specimens usually requires 1 – 2 days and the only alternative method whereby a confirmed diagnosis can be achieved quickly is by use of frozen section histology. However, the frozen section technique usually requires specimens larger than 3 mm. Using Diff-Quick rapid stain, the smear can be evaluated immediately with the patient sitting in the consulting room, and the costs are kept to a minimum. Papanicolaou stain is usually recommended when dealing with tumours with squamous differentiation. However, squamous differentiation may be identified in Diff-Quick stain due to the characteristic intense blue cytoplasm (royal blue) which is seen in keratinizing lesions. A few atypical cells with distinctive "royal blue" cytoplasm (Fig. 2A) were seen by reviewing the smear, and the histology was reported as suspicious of squamous cell carcinoma (Fig. 2B). Also, if scraping yields insufficient material, repeated scraping or subsequent curettage may follow.

In conclusion, both histopathological examination of removed tumour tissue by curettage and cytological examination of air-dried and Diff-Quick stained skin scrapes are reliable in the diagnosis of BCC, and are without unwanted side-effects. Skin scrape cytology has, however, the advantage of being inexpensive and faster. We believe that PDT within soon will become available to dermatologists as a standard treatment for BCC and that the simple skin scrape has a high probability of being the method of choice for the confirmation of the diagnosis.

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