Acta Derm Venereol (Stockh) 1997; 77: 292–295

Rapid Cytological Diagnosis of Primary Skin Tumours and Tumour-like Conditions

D. DASKALOPOULOU[1], K. GOURGIOTOU[2], E. THODOU[1], S. VAIDA[3] and S. MARKIDOU[1]

Departments of [1]Cytopathology and [3]Pathology, Regional Anticancer-Oncologic Hospital of Athens "St. Savas" and [2]Department of Dermatology, "A. Sygros" Hospital, Athens, Greece

This study presents the results of fine needle aspiration cytology performed on 1,263 skin lesions which were clinically suspicious for neoplasia.

The purpose of the study was to investigate the accuracy of fine needle aspiration cytology for the diagnosis of skin tumours and to assess its clinical value. Twenty-one to 27 Gauge needles were used and the specimens were stained by a quick Giemsa stain. The cytological examination reported 826 primary malignant tumours and 437 benign lesions. Five hundred and thirteen of the cytologically malignant cases and 123 of the benign ones had a subsequent histological examination. The correlation between cytology and histology revealed 6 false positive cytological results and one false negative.

Persuaded by our results, we believe that fine needle aspiration cytology can give highly reliable information concerning the histological type or primary skin tumours. It can also detect or exclude relapses of previously treated neoplasms. The procedure is non-traumatic, safe, quick, inexpensive and very well tolerated by the patients. ***Key word: fine needle aspiration.***

(Accepted December 9, 1996.)

Acta Derm Venereol (Stockh) 1997; 77: 292–295.

D. Daskalopoulou M.D., Regional Anticancer-Oncologic Hospital of Athens "St. Savas', 171 Alexandras Ave, 115 22 Athens, Greece.

Fine needle aspiration cytology (FNAC) is a well recognized modality of diagnosis of various organ systems (1). Although text books describe FNAC of skin lesions (2, 3), it has not become as yet widely practised, mainly because surgical excision and biopsy are relatively easy procedures. However, there are many cases in which an accurate diagnosis must be established in order to apply either radiotherapy (4–6) or local chemotherapy (7–9). These non-surgical treatment alternatives would be of significant value in selected patients: elderly persons with heart diseases or under systematic therapy, patients with multiple, extensive skin lesions in whom surgical treatment may cause complications, patients in whom more than 2–3 skin lesions occur at a considerable distance from each other on the head and neck, where restoration demands an extensive skin allograft, etc. In the above cases confirmation of malignancy as well as typing of the neoplasm can accurately be accomplished by FNAC. The procedure is non-traumatic, safe, inexpensive and very well tolerated by the patients. The cytological results, when there is considerable experience, are available within a few minutes.

The use of FNAC is justified especially in those cases which have to be investigated for recurrence of a previously treated neoplasm, particularly when multiple lesions are suspected of being recurrences. This is most frequently the case with basal cell carcinoma (BCC), a skin tumour notorious for relapses, since 40% of the patients with BCC present with a relapse within 10 years (10). When the surgical biopsy material is obtained from sites in which surgical excision, plastic surgery and even additional radiotherapy have been performed, the extremely difficult healing presents a serious problem. Harmful intervention in sensitive tissues can be avoided by using FNAC. The patient is spared unnecessary trouble when his problem is dealt with and solved in a very short time during his follow-up visit to the hospital.

Furthermore FNAC can be of value in specialized dermatology centres, where a rapid diagnosis must be established in cases where the clinical examination is equivocal, i.e. in differential diagnosis problems between BCC and solar or senile keratosis, sebaceous gland hyperplasia, radiodermatitis consequences, etc.

Finally, another important application of FNAC is in the follow-up of patients with chronic dermatoses, such as lichen sclerosus et atrophicus of the vulva, balanitis, xerotica obliterans and late radiation dermatitis scars from old thermal burns. In all the above cases, the development of a malignancy is possible.

MATERIALS AND METHODS

From 1990 to 1994, 2,608 cases of various skin lesions, diagnosed by FNAC, were documented in the files of the Cytology Department of our Institution. One thousand two hundred and sixty-three cases were primary skin lesions. The patients were referred to the outpatient clinic of the cytopathology department by physicians, dermatologists, surgeons and radiotherapists. The selection of cases was made according to a protocol: all patients presenting with persistent skin lesions, clinically suspicious for neoplasia, either flat or exophytic, ulcerated or subepidermal, were subjected to FNAC. According to the cytologic results further diagnostic or therapeutic decisions were made. The FNAC was performed by specially trained cytologists.

The 1,263 specimens were obtained from 1,189 patients, 668 men and 521 women with a median age of 61 years (range 29–91). FNAC of the usual exophytic lesions was performed using a 21–27 Gauge needle. Insulin needles were used to aspirate flat lesions and those suspicious for melanoma.

In the majority of cases a simplified cytological method of fine needle sampling without aspiration was performed (11). Withdrawal of the needle through the lesion alone yielded sufficient material for the establishment of the diagnosis. Usually 2–3 smears were prepared on each FNAC, which were stained with a quick Giemsa stain (Hemacolor-Merk-Germany). When in a few instances the air-dried smears were regarded as unsatisfactory (after immediate microscopic examination and careful scrutiny), the procedure was repeated in order to get sufficient material for the establishment of the diagnosis.

RESULTS

Table I presents the results of FNAC as well as the correlation between cytology and histology in the 636 cases where both examinations were available. A large number of cases which lack histological examination referred to relapses of previously

 ISSN 0001-5555

Table I. *Accuracy of cytologic diagnosis*

Cytology	No. of cases	Histology		
		Confirmed	Disproven	Not available
Malignant tumours				
Basal cell carcinoma (BCC)	501	300	4	197
Squamous cell carcinoma (SCC)	233	120	2	111
Carcinoma of sebaceous glands	1	1	0	0
Melanoma	62	57	0	5
Merkel cell tumour	3	3	0	0
Mixed (BCC+SCC)	6	6	0	0
Malignant fibrous histiocytoma	5	5	0	0
Primary cutaneous lymphoma	8	8	0	0
Kaposi's sarcoma	2	2	0	0
Untyped malignant tumours	5	2	3	0
Benign tumours				
Pilomatrixoma (Malherbe)	8	7	1	0
Cylindroma	8	8	0	0
Chondroid syringioma	3	3	0	0
Cutaneous meningioma	1	1	0	0
Granular cell tumour	4	3	0	1
Spindle cell lipoma	1	1	0	0
Lipoma	68	45	0	23
Pseudolymphoma	13	7	0	6
Benign histiocytoma	4	2	0	2
Nodular fasciitis	12	4	0	8
Epidermal cyst	28	21	0	7
Glomus tumour	1	1	0	0
Granuloma	11	1	0	10
Other benign conditions	275	18	0	257

treated neoplasms as well as in cytologically benign lesions which remained under follow-up.

As far as the cytological diagnosis is concerned, BCC (Fig. 1), SCC (Fig. 2) and melanomas were rather easily recognized. The diagnosis of malignant histiocytomas, Kaposi's sarcoma (Fig. 3), Merkel cell tumours, pilomatrixomas and cylindromas (Fig. 4) was based on cytologic criteria described in the literature but also on the experience gained in previous years by applying the imprint procedure on surgical biopsy material. Chondroid syringomas have the cytologic appearance of a mixed tumour of the salivary glands; thus they are easily recognized on smears. Cutaneous meningioma had exactly the same characteristics as primary meningial tumour, which is widely described in neurocytology. Granular cell tumour (myoblastoma) is a well-known entity to those who perform FNAC in breast tumours and tongue and gingivae lesions. In our cases the "myoblastoma' cells were typical, with foamy cytoplasm and prominent nucleoli. In the only case diagnosed as glomus tumour we aspirated a very cellular material from a reddish blue papule on the forehead of a 26-year-old woman. The cells were uniformly round with central nuclei and well-defined cell borders. They were arranged either separately or in small "nests' (Fig. 5) or

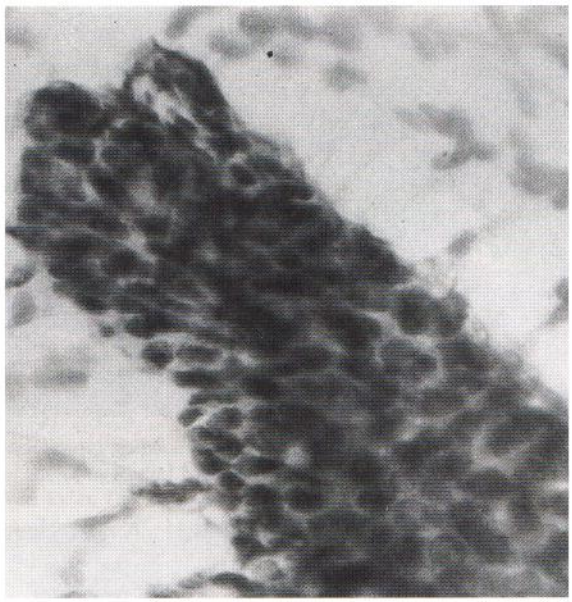

Fig. 1. Cytological smear of the BCC. Note the characteristic palisading of the cells.

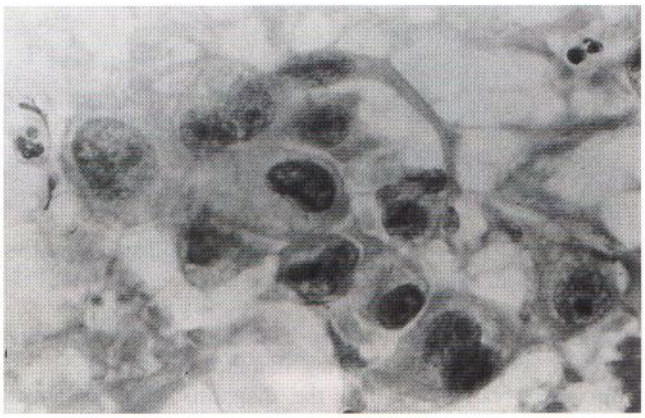

Fig. 2. Cytology of the SCC. Moderate differentiation.

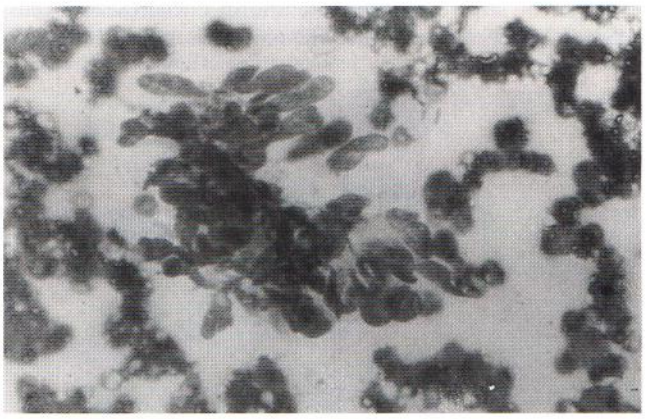

Fig. 3. Spinde-shaped cells in Kaposi's sarcoma.

surrounding small vessels. The diagnosis of lipomas, nodular fasciitis, epidermal cysts, granulomas and benign histiocytomas was based not only on cytological but also on clinical features

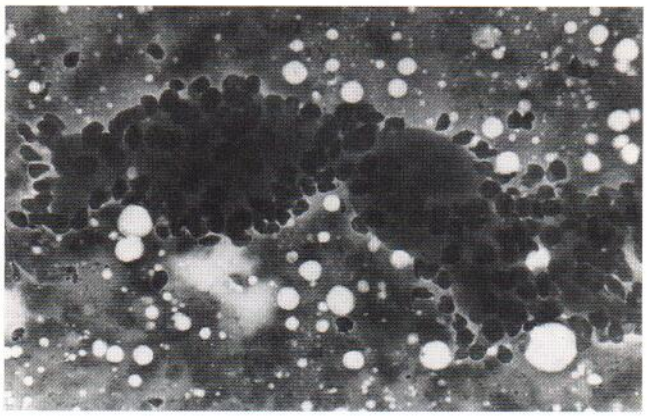

Fig. 4. Cylindroma. Small uniform cells surrounding typical hyaline droplets.

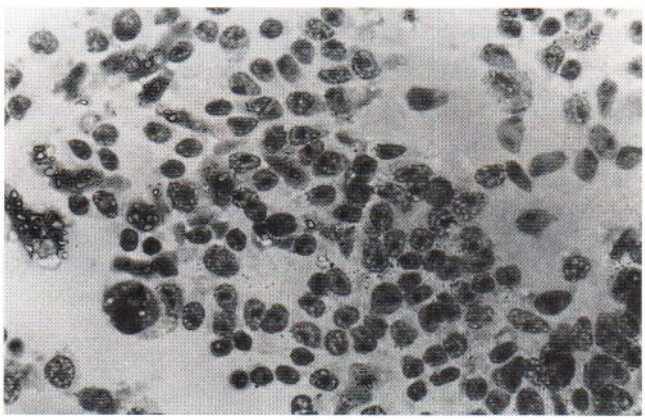

Fig. 5. Glomus tumour small "nests" and "Indian files" formed by tumour cells.

(location of the tumour, size and margins, growth rate, firmness, colour of the overlying skin etc).

In the 8 cases in which the diagnosis of a malignant lymphoma was established, the monotonous cell population had all the characteristics of lymphoid derivation. One case was characterized as "probably mycosis fungoides" due to the presence of large cells with cerebriform nuclei (Sézary cells) (Fig. 6). The later performed immunophenotyping confirmed the initial diagnosis. Three of the cases were high-grade non-Hodgkin's lymphomas (NHL), all of T-cell origin, and 4 were low-grade NHL. Only one out of the 8 cases of primary cutaneous NHL was of B-cell origin. The characterization of the 8 above cases as "primary cutaneous NHL" was finally based on clinical and other diagnostic parameters. In the 13 cases cytologically reported as pseudolymphomas, the diagnosis was based on the reactive appearance of the lymphoid population, i.e. the presence of tingible body macrophages and the full range of small and transformed lymphocytes, including several monocytoid cells.

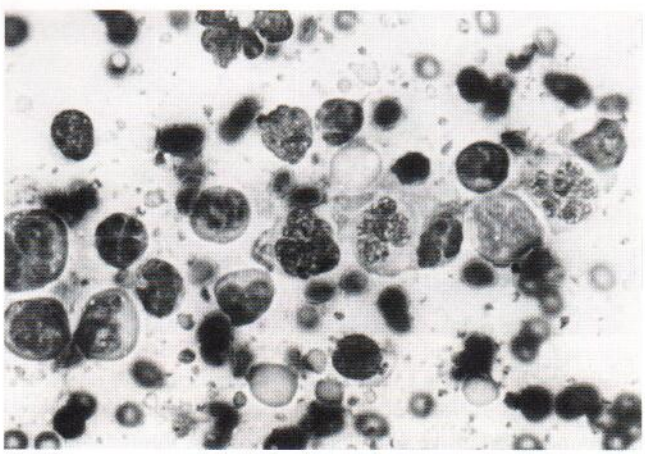

Fig. 6. Typical convoluted nuclei of tumour lymphocytes in mycosis fungoides.

As far as the accuracy of the method is concerned, out of 304 cases cytologically diagnosed as BCC only 4 were disproved histologically (Table II). In the first 2 cases histology revealed a low-differentiated SCC, in the third a mixed carcinoma (BCC+SCC), and in the last case papillary hyperplasia. There were only two false positive cytological diagnoses of SCC: the first was actually a keratoacanthoma and the other solar keratosis. One case cytologically misdiagnosed as calcifying epithelioma of Malherbe was in fact an adenoid BCC. The glandular shape and arrangement of the cells made them resemble the basophilic cells of Malherbe. Aggregates of shadow cells were also present in the smears.

In the category of "cytologically untyped malignant neoplasms" correlation with histology revealed three false positive cytodiagnoses: the first was a desmoplastic trichoepithelioma, the second a papillary syringocystadenoma and the third was eccrine gland epithelioma. The remaining 2 cases (Table I) were indeed malignant neoplasms: a melanoma and an angiosarcoma.

The diagnostic accuracy of the method was 98%, the sensitivity 99.8% and the specificity 94.3%. It must be stressed that in none of our cases did FNAC cause any problem for the patient or obscure the subsequent histological study.

DISCUSSION

The histological confirmation of the cytological results on skin tumours revealed a high sensitivity for the FNAC method. In 1979 Canti (13) reported his study based on scraping of 2,547 skin lesions. His results were considered very satisfactory. In our experience the method of scraping a lesion can produce a number of non-diagnostic smears. This technical problem can

Table II. *Discrepancies between cytology and histology*

No. of cases	Cytology	Histology
1	BCC	SCC low-differentiated
2	BCC	SCC low-differentiated
3	BCC	Mixed carcinoma (BCC+SCC)
4	BCC	Papillary hyperplasia
5	SCC	Keratoacanthoma
6	SCC	Solar keratosis
7	Epithelioma Malherbe	BCC adenoid variant
8	Untyped malignant neoplasm	Desmoplastic trichoepithelioma
9	Untyped malignant neoplasm	Papillary syringocystadenoma
10	Untyped malignant neoplasm	Eccrine gland epithelioma

be solved by using FNAC. In the present study, fine needle sampling was the method of choice. Furthermore, with the application of the quick Giemsa staining, immediate examination of the material for its adequacy and repetition of FNA if needed, cases with diagnostically insufficient material were almost absent (0.6%: 8 out of 1,271 cases).

As far as the diagnosis is concerned, it seems that the false negative or the false positive rate is generally very low (13). In some specific tumours like trichoepithelioma, pilomatricoma (Malherbe) (14) papillary hidradenoma (15), chondroid syringoma (16), Merkel cell carcinoma (17), Kaposi's sarcoma, glomus tumour, cylindroma and granular cell tumour, although specific cytologic features have been described, the diagnosis is possible only when there is considerable experience of skin lesions. This experience may be obtained by routinely performing the imprint procedure on excised tumours. Since the material is taken directly from the lesion and many imprints can be taken from different sites, comparison between histology and cytology reveals direct common cytologic features. When applied to cytological smears, these can lead to the correct diagnosis even though the architecture of the lesion is missed.

In rare cases the identification of the tumour type presents difficulties even for the more experienced cytologist. The morphologic features of a "metatypical' BCC can mislead cytologists to the diagnosis of a low-differentiated SCC and vice versa. Keratoacanthoma as well as solar keratosis can present with a considerable cell atypia; pigmented BCC must be differentiated from melanoma etc.

In conclusion the cytologic examination of primary cutaneous tumours and tumour-like conditions is a sensitive and safe diagnostic method. Reliable results are accessible on technically satisfactory smears and by adequately experienced cytologists. When the cases are carefully selected (only skin lesions clinically suspected for neoplasia, not all the spectrum of dermatologic diseases), FNAC can be particularly useful both to the patient and to preoperative or non-surgical treatment planning in centres dealing with similar cases. We would like to stress that FNAC cannot replace histology in the diagnosis of skin tumours, as there is a considerably large number of lesions in which tissue architecture is of paramount importance for the accurate diagnosis. FNAC has its place in a well-defined clinical protocol, taking into account that in the context of benign primary cutaneous neoplasms FNAC has little to offer in terms of taxonomic diagnostic accuracy. On the other hand, it can almost always detect malignancy.

REFERENCES

1. Koss L, Woyke S, Olszewski W. Aspiration biopsy. Cytologic interpretation and histologic bases. 2nd edn. New York, Tokyo Igacu-Shoin: 1992.
2. Orell S, Sterrett G, Walters M, Whitaker D. Supporting tissues. In: Manual and atlas of fine needle aspiration cytology. 2nd edn. Churchill Livingstone, 1992: 300–334.
3. Linsk JA, Franzen S. Clinical aspiration cytology. 2nd edn. Philadelphia: JB Lippincott Co, 1989: 319–336.
4. Lovett RD, Perez CA, Shapiro SJ, Garcia DM. External irradiation of epithelial skin cancer. Int J Radiat Oncol Biol Phys 1990; 19 (2): 235–242.
5. Reisner K, Haase W. Electron beam therapy of primary tumors of the skin. Radiol Med 1990; 8: 114–115.
6. Von Essen CF. Indications for radiation therapy of skin cancer. In: Tumours of the skin. Year Book Medical Publishers, 1984: 88–128.
7. Greenway T, Cornell C, Tanner J, Peets E, Bordin M, Nagi C. Treatment of basal cell carcinoma with intralesional interferon. J Am Acad Dermatol 1986; 15: 437–443.
8. Dogan B, Harmanyeri Y, Baloglu H, Oztek I. Intralesional alfa-2a interferon therapy for basal cell carcinoma. Cancer 1995; 91: 215–219.
9. Edwards MJ, Soong SJ, Boddie AW. Isolated limb perfusion for localized melanoma of the extremity. Arch Surg 1990; 125: 317–381.
10. Schubert H, Wolfran G, Guldner G. Basaliorezidive nach Behandlung. Dermatol Monatsschr 1979; Vol. 165: 89–96.
11. Zajdela A, Zillhard P, Voillemot N. Cytological diagnosis by fine needle sampling without aspiration. Cancer 1987; 59: 1201–1205.
12. Canti G. Rapid cytological diagnosis of skin lesions. In: Koss IE, Coleman DV, eds. Advances in clinical cytology. Vol. 2. N.Y.: Masson Publishing, 1984.
13. Canti G. Skin cytology and its value for rapid diagnosis. Acta Cytol 1979; 23: 519.
14. Unger P, Watson C, Phelps R, Danque P, Bernard P. Fine needle aspiration cytology of pilomatrixoma. Acta Cytol 1990; 6: 847–850.
15. Hustin J, Donnay M, Hamels J. Indentification of papillary hidradenoma of the vulva by imprint cytology. Acta Cytol 1980; 5: 466–467.
16. Masood S, Hardy N. Fine needle aspiration cytology of chondroid syringoma. Acta Cytol 1988; 4: 482–484.
17. Skoog L, Schmitt F, Tani E. Neuroendocrine (Merkel-cell) carcinoma of the skin. Diagn Cytopathol 1990; 1: 53–57.