Cytologic Evaluation of the Enlarged Neck Node: FNAC Utility in Metastatic Neck Disease

I Bagwan, S Kane, R Chinoy

Citation

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Abstract

Introduction: Fine Needle Aspiration Cytology not only confirms the presence of metastatic disease, but also gives clues regarding the nature and origin of the primary tumour.

Study Design: The study material comprised of all aspirates (1978 aspirates from 1255 patients) from the neck lymph nodes during the period January 2003 to December 2003. All hematolymphoid neoplasms were excluded. The FNA results were reviewed, the morphology of the individual cells and their patterns in the smears were studied in detail and the FNA diagnosis was correlated with the histology.

Results: Cytology results were unsatisfactory in 184 specimens (9%), negative or reactive in 495 specimens (25%) and suspicious or positive for malignancy in 1299 specimens (65.67%). The most common metastasis to the neck nodes was of squamous carcinoma arising in the oral cavity.

Conclusion: FNA of head and neck masses proved to be a useful tool in diagnosing metastasis with good certainty.

INTRODUCTION

A neck mass in an adult, that is present for longer than a week is pathological until proven otherwise.[1] In our country, tubercular lymphadenitis is not at all uncommon but even so, a large percentage of all persistent adult neck masses turn out to be malignant, whereas in the pediatric population neck masses are only rarely malignant.

The use of Fine Needle Aspiration Cytology (FNAC) for the diagnosis of metastatic malignancies in the lymph nodes is a well-established method.[2] Lymphadenopathy may be the first sign of malignancy in a patient. FNAC not only confirms the presence of metastatic disease, but also gives clues regarding the nature and origin of the primary tumour. In patients with enlarged lymph nodes and previously documented malignancy, FNAC can obviate further surgery performed merely to confirm the presence of metastasis. However, regional lymphadenopathy is not always due to metastatic tumour, and not every nodule represents a lymph node. Cysts (congenital or acquired), abscesses, subcutaneous benign and malignant tumours may also raise the question of lymph node metastasis, especially in patients with a known tumour.[3]

The false- positive rate of lymph node FNAC for the detection of metastasis is quite low (in the range of 0.9-1.7%). [2] Avoiding false-positive diagnosis is of obvious importance since therapeutic and surgical decisions are often based exclusively on cytology results. Cystic metastasis and aspirates of unusual low grade malignancies compose most of the false-negative cases.[3,4,5] Moreover; the procedure is very cost effective, simple, and free of complications, well tolerated by the patient, done on an outpatient basis and repeatable. India is imminently suited to use this procedure, & this is borne out by the fact that it has flourished both in large institutions, in peripheral small community hospitals & in private clinics. Increased exposure and routine audits have improved the sensitivity and the accuracy of FNAC in all anatomic sites, particularly so in head and neck masses.[6,7,8]

The present study will address metastatic lesions occurring in the adult population. These are generally metastatic from the upper aero digestive tract and salivary glands or may present as occult primaries. Occasionally a neck metastasis from a distant site springs from the gastrointestinal tract,

kidney or the lung. Other primary sites below the clavicle, which may appear in the neck, are the cervix, ovary and sometimes even the bladder.

MATERIAL AND METHODS

The study material comprised aspirates from the neck lymph nodes during the period January 2003 to December 2003 (12 months). All hematolymphoid neoplasms were excluded. This made up a total of 1978 aspirates from 1255 patients. In the design of the present study, each aspirate was considered as one case.

FNAC was performed using a 23-gauge needle. An average of 2 passes was performed and minimum 3 slides were prepared. One slide was air dried and stained by Giemsa stain, while the remaining 2 slides were fixed in alcohol ether mixture and then stained with PAP stain. Smears showing enough cellular material to provide a diagnosis were considered satisfactory. The FNA results were reviewed and the morphology of the individual cells and their patterns in the smears were studied in detail. These smears were later reported as either negative or positive for malignancy or inadequate for any opinion. In the final report, in the case of occult primaries, a statement regarding the likely site of origin was usually documented. In this study the FNAC diagnoses were correlated with the histological findings, wherever available, or the clinical correlation was obtained.

RESULTS

During this period, a total of 7088 FNAC's from all sites were performed in the institute. Of these, 1978 aspirations (27.90%) were obtained from enlarged lymph nodes in the head and neck region. This group constituted 1255 patients (840 males & 415 females) ranging from 18 to 75 years of age.

Cytology results from 1978 lymph node aspirates were unsatisfactory in 184 specimens (9%), negative or reactive in 495 specimens (25%) and suspicious or positive for malignancy in 1299 specimens (65.67%). The unsatisfactory smears were reportef as inadequate for opinion. The common causes for these 184 non-diagnostic smears were (i) very scanty cellularity; (ii) technically suboptimal quality of the smears due to drying artefacts or admixture with blood. In 90% of cases, the pathologist performed the FNAC, while in the remaining 10% the clinician performed it. Repeat aspirations (47 cases) and excision biopsies (28 cases) revealed the presence of metastasis in 75/184 (40%) originally non-diagnostic lymph nodes. The most common tumors metastasizing to the lymph nodes originated in the head and neck region (tongue, alveolus, maxilla, buccal mucosa, nasal cavity, palate, larynx, etc.), followed by the respiratory system and then tumors of unknown origin.

Figure 1

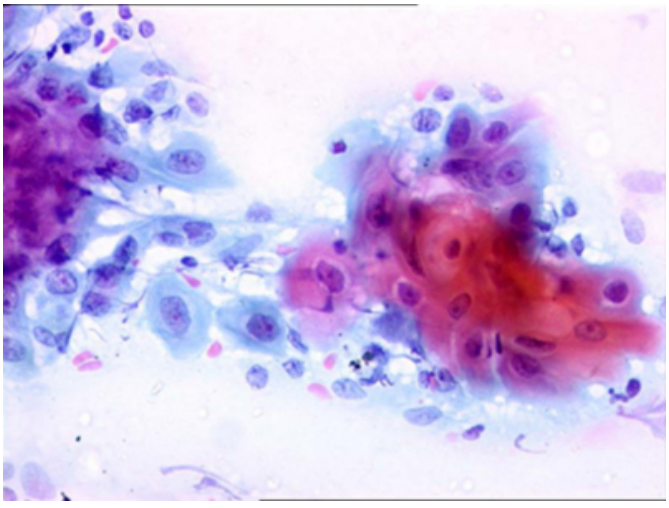
Table 1: Distribution Of Cytology Results Of Head & Neck Lymph Node Aspirates

SR NO.	CYTOLOGY RESULTS	NUMBER OF FNACs	%
	Squamous carcinoma	728	36.81
	Adenocarcinoma	145	07.33
	Poorly differentiated carcinoma	241	12.18
	Small cell carcinoma	18	00.91
	Non Small cell carcinoma	31	01.57
	Undifferentiated carcinoma (Nasopharyngeal type)	36	01.82
	Salivary gland tumor	14	00.70
	Thyroid carcinoma	56	02.83
	Negative for metastasis/ reactive node	495	25
	Inadequate aspirate	184	9
	Uncommon metastasis	30	01.52
	TOTAL	1978	100.00

The most common tumor metastatizing to the neck nodes was the squamous carcinoma arising commonly in the tongue, alveolus, buccal mucosa and palate (728/ 1978 cases). These constituted keratinizing squamous carcinoma cells in 406 aspirates (20.52%). (Fig.1).

Figure 2

Figure 1: Cytology smear showing clusters of keratinizing squamous carcinoma indicating metastasis in the lymph node. (MGG X 400)



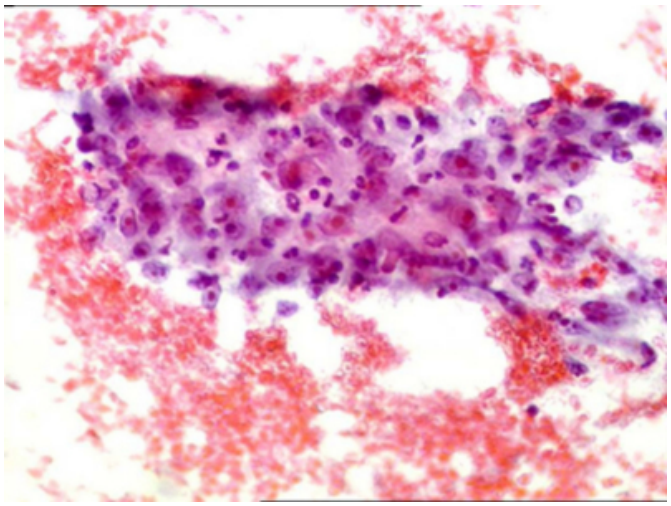
Necrosis, liquefaction or cystic change was noted in 30

cases. Poorly differentiated carcinoma cells were noted in 228 nodal aspirates (11.52%), these posed difficulties in determining the site of origin. Other primary sites included the lung (65 cases), oesophagus (38 cases), gall bladder (5 cases) and cervix (4 cases). Of the 728 nodal aspirates that showed metastatic squamous carcinoma cells, the primary site of origin was not known in about 64 cases.

Metastasis of adenocarcinoma (Fig.2) was observed in 145 aspirates (7.33%) with lung being the commonest primary site (40 cases), followed by stomach (28 cases), colon/ rectum (22 cases), pancreas (9 cases), gall bladder (4 cases), ovary (4 cases), salivary gland (3 cases) and unknown primary site (25 cases).

Figure 3

Figure 2: Cytology smear showing metastasis of adenocarcinoma. Note the neutrophils sticking around the mucin of the tumor cells. (MGG X 400)

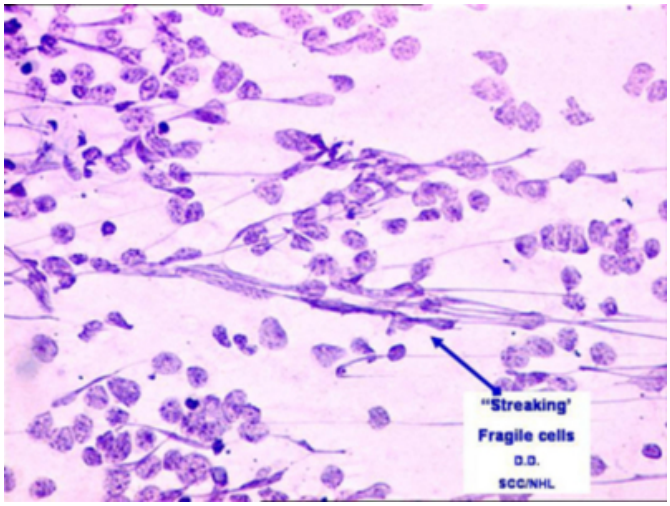


In addition to cases with definite metastasis of squamous and adenocarcinoma of lung, 18 smears showed features suggestive of metastasis of small cell carcinoma of lung. In 31 aspirates it was not possible to differentiate metastatic squamous carcinoma from adenocarcinoma and hence was labeled as metastasis of non-small cell carcinoma. Sub typing of metastatic carcinoma cells into either small cell or non-small cell type could not be achieved in 13 cytology smears due to lack of differentiating features. These cases were lumped into poorly differentiated category. The primary site of origin was not known in about 25 cases.

Cytological examination of 36 nodal aspirates revealed presence of large, primitive looking tumour cells with round vesicular nuclei, prominent nucleoli and ill defined cytoplasm showing streaking effect. (Fig.3) These features were in keeping with spread from undifferentiated nasopharyngeal carcinoma in 27 cases, while in 9 cases the primary site was not known.

Figure 4

Figure 3: Cytology smear showing the streaking effect commonly seen with metastasis of nasopharyngeal carcinoma, small cell carcinoma and lymphoma. (MGG X 200)



Definite or suspicious metastasis from a known primary in thyroid was reported in 56 lymph node aspirations. This comprised metastasis from papillary carcinoma in 32 cases, medullary carcinoma in 10 cases, anaplastic carcinoma in 5 cases and there was suspicion of metastasis in 9 cases. Spread from a primary salivary gland tumour was suspected in 14 cases. The features were suggestive of metastatic mucoepidermoid carcinoma in 5 cases, metastasis of adenoid cystic carcinoma in 6 cases and adenocarcinoma of salivary duct origin in 4 cases.

In addition to these common tumours metastasizing to the neck nodes, there were also certain unusual tumours, which did spread to the neck nodes and posed difficulty in diagnosis. These tumours are enumerated in Table 2. In cases where the primary was not known, differentiation of a poorly differentiated adenocarcinoma from a melanoma or a germ cell tumour was the most common problem encountered. (Fig.4)

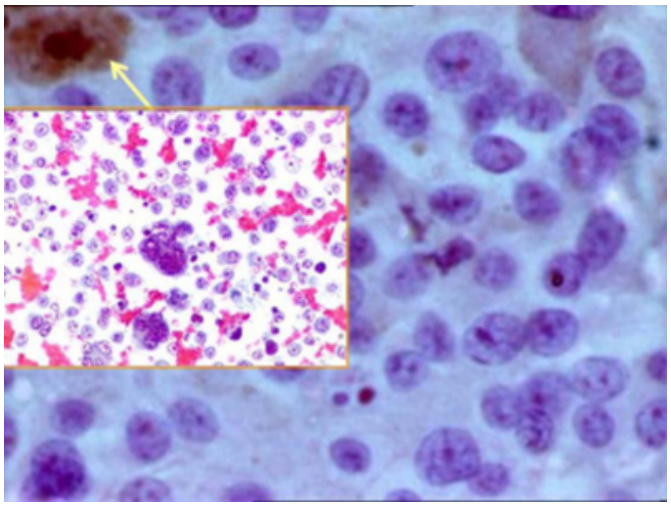
Figure 5

Table 2: Uncommon Metastasis To Head & Neck Lymph Nodes

	UNCOMMON METASTATIC LESIONS	NO. OF FNAC
1.	Germ cell tumour	12
2.	Melanoma	10
3.	Small round cell tumour	03
4.	Transitional cell carcinoma	01
5.	Renal cell carcinoma (clear cell type)	02
6.	Myoepithelial carcinoma of salivary gland	02
	TOTAL	30

Figure 6

Figure 4: FNA smear showing metastasis of malignant melanoma. Note the presence of giant cells (inset) and the presence of melanin pigment. (MGG X 400)



Histological correlation was possible in 540 positive aspirates. It was observed that FNAC had an accuracy rate of 83.5 % thus proving to be a useful diagnostic test. One case diagnosed as metastasis of well-differentiated squamous carcinoma on FNAC, turned out to be an epidermal cyst on histology following excision. This was the only false positive case. In one patient with supraclavicular lymphadenopathy, a differential diagnosis of either a non-Hodgkin's lymphoma or metastasis of germ cell tumour was offered. Following excision biopsy, this was observed to be a metastasis of neuroendocrine carcinoma with a primary in lung.

In 54 positive FNAC from patients with no known history of primary malignancy, cytology showed strong evidence of malignancy but no biopsy was subsequently performed.

DISCUSSION

Lymph nodes that are clinically suspicious for metastasis are one of the most common indications for FNAC. FNAC has a significantly lower risk of subsequent complications, including tumor recurrence, as compared to excisional biopsy.[3,6] FNAC is of considerable value in disease staging and documentation of recurrence. More than 90% of lymph node metastases are diagnosed by initial aspiration.[3]

One very important aid in working up the neck mass, and head and neck oncology in general is the looking at the neck level of involvement. For example, cancers of oral cavity and submandibular gland commonly involve Level 1 nodes (nodes in the submandibular and submental triangles of the neck); Level 2 nodes (nodes along the upper one-third of the sternocleidomastoid muscle) are involved nasal, pharyngeal and laryngeal cancers.[2]

In the present study, metastasis of squamous carcinoma to the lymph nodes was the most common lesion encountered, seen in 728 of 1978 aspirates (36.81%). In differentiated squamous carcinomas, tight clusters or loosely scattered single cells showing various degrees of keratinization are seen. (Fig. 1) Most of the aspirated cells tend to be mature but a careful search for hyperchromatic irregular nuclei showing more malignant features is important for a confident diagnosis. This is because on rare occasions, the branchial or epidermal cyst aspirate with its content of mature squamous cells may closely mimic a differentiated metastatic carcinoma.[3] The less differentiated squamous carcinomas are more difficult to diagnose but cells with abundant dense opaque cytoplasm, arranged in mosaic sheets with occasional keratin pearl formation and giant cell reaction to keratin are useful diagnostic clues. (Fig.1)

In our study, one case of epidermal cyst was misdiagnosed as metastasis from a well-differentiated squamous carcinoma. The presence of mature squamous cells against a lymphoid background was misinterpreted as metastatic well differentaited carcinoma cells. Many metastatic nodes undergo liquefaction necrosis with central cavitations. FNA smears of these nodes reveal abundant neutrophils, histiocytes, necrotic debris and stray individually scattered keratinized cells. The differential diagnosis includes an acute suppurative pathology, a Warthin's tumour, infected branchial cleft cyst, epidermoid cyst and necrotizing squamous carcinoma. A re-aspiration from the edge of the mass rather than from the center is more contributory.[3,4,6] Cystic change in metastatic nodes was noted in about 8% of

our cases. This is one of the most common causes of false negative and, rarely, false-positive diagnosis.[3] The tumour cells of non-keratinizing variant of squamous carcinoma appear in sheets and have round to oval nuclei with coarse granular chromatin and prominent nucleoli. Sometimes differentiation from poorly differentiated adenocarcinoma becomes difficult or even impossible. A mucin stain may be helpful in select cases. When cells are singly scattered and much undifferentiated the possibily of Non Hodgkin's lymphoma has also to be considered.[8,9]

When a tumor looks very bizarre or anaplastic in a setting of an occult primary, sites such as upper aerodigestive tract, lung, thyroid and pancreas should be seriously considered as the likely sources of the primary. Pseudo sarcomas or spindle cell carcinomas should never be forgotten in a site where epithelial tumors are common.[2]

Metastatic adenocarcinomas of the head and neck region can originate from either salivary glands or thyroid. Other primary sites include breast, lung, kidney, prostate and gonads, etc. The individual cells are large cuboidal to columnar with abundant lacy cytoplasm, often with a pale blue extra cellular mucinous fluid background. (Fig.2) Some cells may even exhibit vacuoles with definite signet ring cell morphology. The nuclei are round to oval with irregularly thickened nuclear membranes and prominent nucleoli. Sometimes it gets increasingly difficult to rule out a poorly differentiated squamous carcinoma.[6,8] Metastatic clear cell carcinoma should raise the suspicion of a primary in the kidney or the salivary gland (myoepithelial cell tumors). Aspirates with papillary branching, three-dimensional groups of cells may originate from thyroid, salivary glands, breast, lung and rarely even the ovary. All these sites were encountered as primary tumour sites in one or many cases in the present study. Psammoma bodies have been in thyroid, lung, pancreas and ovarian metastasis.[2]

In case of metastatic undifferentiated carcinoma, nasopharynx followed by lung should be considered as the most common primary tumour sites. Aspirates of metastatic nasopharyngeal carcinomas shed cells, which smear or streak easily. (Fig.3) This streaking artefact is also seen in case of small cell lung carcinoma and lymphomas. Cells of nasopharyngeal carcinoma are large, primitive looking with round vesicular nuclei, prominent nucleoli and illdefined cytoplasm. Whereas in case of small cell carcinoma, the cells appear naked with scant cytoplasm and have ovoid nuclei, about twice the size of mature lymphocytes, with indistinct nucleoli. The chromatin is salt and pepper type. Nuclear dust, individual cell death and pyknotic nuclei are visible in the background. Nuclear moulding is a useful sign to look for.[7,9] It is very difficult to rule out lymphoma on FNAC under these circumstances. Clinical history of generalised lymphadenopathy might be helpful in differentiation.

Table 2 shows distribution of certain unusual tumours metastatizing to neck nodes. These cases were diagnosed with the help of relevant clinical data and by comparing with reference material.

Melanomas arising in the eyeball, scalp or head and neck region may metastasize to neck nodes, but occasionally it presents as a metastasis from an occult primary. Cytologically these aspirates are highly cellular with loosely scattered pleomorphic cells and binucleate and multinucleate forms. (Fig.4) The cells have eccentrically placed nuclei, irregular nuclear outlines, intranuclear vacuoles and large prominent nucleoli. Melanin pigment is seen only in 25% of all aspirates.[7,8] All the above mentioned features may not be present in every case. In the absence of intracytoplasmic pigment, melanomas are often mistaken for a spindle cell carcinoma, sarcoma or as an anaplastic carcinoma. An uncommon tumour in neck nodes is metastatic seminoma. The tumour cells are usually scattered or in loose aggregates showing streaking effect. The cells are large, deeply stained and the nuclei have granular chromatin with prominent nucleoli. In the background, lymphocytes and histiocytes may be seen. Undifferentiated or embryonal carcinomas have a primitive or blastemal morphology.[2,7]

In conclusion, FNA of head and neck masses proved to be a useful tool in diagnosing metastasis with good certainty. It helped in planning surgery for malignant cases, where definitive operative intervention can be performed in one session. A thorough study of the morphological details of the individual metastatic tumour cells can help in suggesting the most likely primary sites of tumour. Moreover, the procedure is simple and cost effective. It is suitable for developing countries and small secondary care hospitals with limited resources.

CORRESPONDENCE TO

ROSHNI F. CHINOY, MD, DCP Professor & Head, Tata Memorial Hospital, Parel, Mumbai- 400 012 India Email: roshchinoy@gmail.com

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Author Information

Izhar N. Bagwan, M.D., D.N.B.
Ex Senior Registrar in Pathology, Tata Memorial Hospital

Shubadha V. Kane, M.D.
Professor of Pathology, Tata Memorial Hospital

Roshni F. Chinoy
Professor & Head of Pathology, Tata Memorial Hospital