Utility of FNAC in Dermatological Manifestations of Metastatic Cancer with the Review of the Literature

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Abstract

Objectives: Cutaneous metastasis (CM) though rare, indicates a terminal event in any malignancy and has a grave outcome. The present study reiterates the role of fine needle aspiration cytology (FNAC) in the diagnosis of metastatic cutaneous nodules. Materials and Methods: From 2015 to 2017, the department received 22,000 cases for FNAC. Among these cases, aspirations from the skin and subcutaneous region were performed on 6,083 cases. After excluding primary tumors of skin/subcutis, 25 cases on cytology were suggestive of metastasis. Clinicoradiological and histopathological profiles in these cases were reviewed. Results: Among these 25 patients, the male to female ratio was 1:1.09 (F, 12; M, 13) in the age group of 18–72 years. Most common primary malignancy in females was of breast and in males was gall bladder. The most common manifestation was a palpable skin nodule, with the abdominal wall being the predominant site. The most common diagnosis, on cytology, was metastatic adenocarcinoma. Conclusion: FNAC is a minimally invasive method, which aids in prompt detection and appropriate management of cases presenting with skin nodules and clinically unsuspected of malignancy. Whereas in known primary tumor, it indicates dismal prognosis by diagnosing CM; in cases with unknown primaries, cytomorphology in conjunction with clinicoradiological findings often gives a clue to the possible primary site.

Keywords: Cutaneous, fine needle aspiration cytology, metastasis, nodule

INTRODUCTION

Skin is the largest organ of the body and is a common host to infections and tumors. Most common tumors that involve the skin and subcutis are the primary dermatological cancers, namely, squamous cell carcinoma, basal cell carcinoma, and malignant melanoma. Metastasis to this site is however, a rare phenomenon and confers a diagnostic challenge as they masquerade the more common primary skin tumors. The incidence is <5% and increases with age. Fine needle aspiration cytology (FNAC) is a rapid, noninvasive technique that acts as a valuable tool that can be used for diagnosing such lesions. This study highlights the role of FNAC, its advantages and its limitations when dealing with such lesions.

MATERIALS AND METHODS

From 2015 to 2017, the department received 22,000 cases for FNAC. Among these cases, aspirations from the skin and subcutaneous region were performed on 6,083 cases (27.6%). After excluding primary tumors of skin/subcutis; 25 cases on cytology were suggestive of metastasis. Clinicoradiological findings were noted in each case. Cases of primary malignant tumors of the skin and recurrences were excluded from the study.

FNAC was performed by standard technique using 22-gauge needle and 10-ml disposable plastic syringe and multiple air dried and alcohol fixed smears were prepared from the aspirate and stained with May–Grünwald–Giemsa (MGG) and Papanicoloau (PAP) stain, respectively. Cell block was made wherever feasible. Special stains such as Mucicarmine, periodic acid Schiff (PAS), and relevant immunocytochemistry (ICC) was used whenever required. Flow cytometric analysis was done for cases suspected of lymphoma.

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RESULTS

Of 25 cases, M: F = 1.09:1 (13 males and 12 females), in the age range of 18–72 years were seen. Skin nodule was the most common presentation. A single nodule was observed in 84% of cases and more than one nodule was seen in 16% cases.

The most common primary site of metastasis in males was of gall bladder (30.7%) and in females was breast (41.6%). Most common metastatic site involved was abdomen and chest (32%). Although abdominal metastasis was most frequently associated with carcinoma gall bladder; one case each of intestinal cancer, kidney, hematolymphoid malignancy, and carcinoma cervix metastasizing to abdomen were also seen. Metastasis in chest was almost exclusively associated with carcinoma breast. Usually the site of metastasis was present in proximity to the tumor site; however, distant metastasis was also observed in three cases: carcinoma cervix metastasizing to arm, renal cell carcinoma metastasizing to shoulder, and testicular cancer metastasizing to back. The most common cytological diagnosis was adenocarcinoma (52%).

Although the primary tumor was known in 19 cases (76%), 6 cases (24%) presented with skin lesions as the first clinical manifestation [Tables 1 and 2]. In known cases, the cytomorphology of the metastatic lesion was compatible with its primary. However, in unknown cases, a range of suitable differential diagnosis based on the clinical history and cytomorphology was kept and the relevant radiological workup of the patient was advised [Figures 1-3]. Patients were reviewed on follow-up, when the radiological report was analyzed and a final cytological report was issued based on the entire workup.

Table 1: Summary of cases with known primary

| S No | Primary  | Age/sex | Site of metastasis | No. of lesions | Cytology diagnosis                      |
|------|----------|---------|--------------------|---------------|----------------------------------------|
| 1    | Breast   | 45/F    | Chest              | Single        | DC                                    |
| 2    | Oral cavity | 60/M  | Scalp              | Single        | SCC                                   |
| 3    | GB       | 38/M    | Abdomen            | Single        | PD AdenoCa (ICC: CK 7+)                |
| 4    | Lung     | 65/M    | Chest              | Single        | SCC                                   |
| 5    | LN       | 52/M    | Abdomen            | Single        | B-NHL (proven by flow cytometry)       |
| 6    | Cervix   | 60/F    | Abdomen            | Multiple      | SCC                                   |
| 7    | GB       | 70/M    | Abdomen            | Single        | PD AdenoCa (ICC: CK 7+)                |
| 8    | Intestine| 70/M    | Abdomen            | Single        | PD AdenoCa                            |
| 9    | LN       | 35/F    | Chest              | Single        | B-NHL (proven by flow cytometry)       |
| 10   | Cervix   | 35/F    | Upper limb         | Single        | SCC                                   |
| 11   | Breast   | 45/F    | Chest              | Single        | DC                                    |
| 12   | Kidney   | 60/M    | Scalp              | Single        | RCC (ICC: CK, vimentin, CD 10+)        |
| 13   | Breast   | 55/F    | Chest              | Single        | DC                                    |
| 14   | Thyroid  | 18/F    | Scalp              | Single        | FCT                                   |
| 15   | Breast   | 50/F    | Chest              | Multiple      | DC                                    |
| 16   | GB       | 70/M    | Abdomen            | Single        | PD AdenoCa (ICC: CK 7+)                |
| 17   | Bone     | 16/M    | Lower limb         | Single        | Osteosarcoma                          |
| 18   | Breast   | 45/F    | Chest              | Single        | DC                                    |
| 19   | Kidney   | 72/M    | Abdomen            | Single        | RCC (ICC: CK, Vimentin, CD 10+)        |

DC: Ductal carcinoma, AdenoCa: Adenocarcinoma, SCC: Squamous cell carcinoma, PD: Poorly differentiated, GB: Gall bladder, NHL: Non-Hodgkin’s lymphoma, FCT: Follicular carcinoma thyroid, RCC: Renal cell carcinoma

Figure 1: (a) Computed tomography (CT) scan revealed ill-marginated mass measuring 7 × 5 × 4.5 cm in cervix involving lower half of uterus, upper vagina, rectum, and bladder. (b) Section from cervical punch biopsy revealing features of large cell keratinizing squamous cell carcinoma (H & E x 100). (c) Clinical picture: tender, erythematous, focally ulcerated nodule in right arm measuring 2 × 2 cm in size. (d) FNAC smear reveal malignant squamous cells with inky blue cytoplasm lying in small cluster in a necrotic background (Giemsa stain x 400). Inset shows similar cells in (Papanicolaou stain x 100)
Dermatological involvement from any malignancy indicates a dismal prognosis and is often considered to be harbinger of an end stage disease. Though Spencer et al. reported a higher incidence of 9–10% in their autopsy study on patients with internal malignancies, the extensive review of the literature published from 2007 to 2017 indicate an incidence of 0.8–5% in these cases. The current study was done on 25 patients and showed an incidence of 0.4%.

Cutaneous metastasis (CM) occurs in both genders with a slight predilection in males as seen in the current study with M:F ratio of 1.09:1. Though the phenomenon is noticed among children also; majority of the cases occur in the adult age group after fifth decade of life. In the present study, 44% of the cases were above 50 years of age.

**DISCUSSION**

Clinically, CM has variable manifestations and can occur as nodule, telangiectatic lesion, plaque like lesion or large cystic lesions. The lesion can be solitary or multiple. Most of the studies reveal nodule as the predominant presentation. The present study had 100% of the cases presenting as single or multiple nodule. This can be explained by the fact that nodular lesions are most amenable to FNAC and therefore referred for the procedure that acts as a useful technique in identifying these cases, hence, often obviating the need for surgical biopsies. Positive malignant cells on cytology, in cases with known primary, often indicate either failure of therapy/recurrence or development of secondary malignancies.

Extensive literature search reveals breast and lung as the most common primary site in the females and males, respectively. However, in the present study though breast was the most common primary site in females; gall bladder was the most common primary site in the males. The most common site of metastasis in the current study was abdomen and chest wall that is in concordance with the
The site of metastasis is usually present in proximity to the tumor site. Though the factors governing the mode of spread in these lesions are poorly understood, the most popular theory suggests the role of lymphatics. Most of the lesions seen in the current study were present adjacent to the primary site.

Distant metastasis was noted in three cases in the current study: carcinoma cervix metastasizing to arm, renal cell carcinoma metastasizing to shoulder, and testicular cancer metastasizing to back. Though occasional cases have been reported with remote site metastasis; the phenomenon remains unusual and is likely due to hematogenous spread of these tumors.

Cutaneous involvement by hematological malignancies is a rare event and has occasionally been reported in the literature. Though rare, it was observed in three cases in the current series with occurrence of metastasis in limbs and abdomen. Two cases of non-Hodgkin’s lymphoma and one of chloroma were also reported. All the cases were further verified by flow cytometric analysis.

Thick cases with known primary are easy to diagnose, cases with unsuspected primary impose diagnostic challenge and masquerade primary skin adnexal tumors. Eccrine sweat gland tumors often show tubular differentiation, squamoid as well as clear cell change and can be confused with duct carcinoma of breast or renal cell carcinoma. Demonstration of presence of glycogen in renal cells using PAS along with diastase sensitivity helps in distinction of the site of origin. Primary versus metastatic adenocarcinomas can be distinguished based on morphological clues like presence of extracellular pools of mucin, signet cell morphology, three dimensional papillae that often points toward metastatic etiology. Special stains such as alcin blue at pH 2.5 can distinguish among sulfated mucins present in adenoid cystic carcinoma and adenoid basal cell carcinoma of lacrimal and salivary glands from nonsulfated mucins present in gastrointestinal tract, breast, and lung.

Therefore, cytomorphology in conjunction with ancillary techniques like special stains, ICC, cell blocks, and flow cytometry can often give clue to the possible primary site in cases with unknown primary, substantially reducing the time and money spent on investigations. In the current series, six cases of unknown primary were encountered; diagnosis was successfully made in all of them after the radiological workup based on clinical and cytomorphological features.

Treatment of CM is essentially palliative and includes surgery, radiotherapy, and chemotherapy singly or in various combinations. Overall, CM is a sign of preterminal disease and indicate dismal prognosis with a mean survival rate of 3 months.

**CONCLUSION**

To conclude, FNAC is a minimally invasive procedure that can be used for ascertaining the nature of skin lesions. The procedure can be effectively used as a replacement for punch/trucut biopsies and as a follow-up modality in known cancer patients. In cases with occult primary, cytomorphology can provide invaluable clue to the possible primary sites and aid in early detection of primary.

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**Conflicts of interest**

There are no conflicts of interest.

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