Cytopathological Spectrum of Lesions in the Axilla - A Population Based Study from a Tertiary Care Centre in North-East India

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ABSTRACT

BACKGROUND

The axilla is a triangular space between the lateral wall of thorax and the upper part of arm. The component of axilla can give rise to different diseases ranging from developmental and reactive to neoplastic. Various mesenchymal tissues present in the axilla can give rise to different lesions. Fine needle aspiration cytology (FNAC) is a safe, quick, easy, and a cheap diagnostic tool to decipher the benign or the malignant nature of the swelling. Imaging techniques and FNAC, both used individually or coupled, improve the accuracy of diagnosis and help in avoiding unnecessary invasive procedures. The most common lymph node lesion in axilla is benign reactive lymph node hyperplasia. It is caused by inflammation of the lymph nodes or the adjacent organs, such as the breast or lung.

METHODS

The present study is a retrospective review of swellings aspirated from axillary region. FNAC was performed following strict aseptic precautions. Inadequate aspirates were excluded from the study. The aspirated sample was blown on clean glass slides and smears were made using squash preparation. Smears were fixed using air dried and alcohol fixation method. Smears were stained with Giemsa stain, and the alcohol - fixed smears were stained with haematoxylin and eosin and Papanicolaou stains. Cytological smears were evaluated for adequacy, cellularity, type of cells, arrangement of cells and nuclear as well as cytoplasmic features.

RESULTS

A total of 191 axillary swelling were aspirated during the study period. Out of which 148 (77.5 %) cases were females and 43 (22.5 %) cases were males. Most common lesion was lipoma followed by axillary tail of breast.

CONCLUSIONS

Various pathological processes may affect the axilla. There is overlap in the imaging findings of these diseases. FNAC is a diagnostic tool which is required for conformation of diagnosis of axillary lesions.

KEYWORDS

Axillary Swelling, Fine Needle Aspiration, Lipoma

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BACKGROUND

The component of axilla can give rise to different diseases ranging from developmental and reactive to neoplastic. These diseases can arise de novo as primary lesions or be secondary diseases from distant sites. The often encountered congenital lesions are the aberrant breast tissues which are also subject to same disorders of the breast such as mastitis, lactational changes, phyllodes tumour, fibrocystic changes, fibroadenoma, and cancers located at usual anatomical sites.[1] The axilla is a triangular space between the lateral wall of thorax and the upper part of arm. The contents of the axilla include the axillary artery and vein and their branches, branches of the intercoastal nerve, lymph nodes, fat, fibrous tissue and vestigial breast glandular tissue. Various mesenchymal tissues present in the axilla can give rise to different lesions.[2] Soft tissue tumours in the axilla are lipoma, schwannoma, and dermatofibroma including their malignant counterparts. Other reported diseases are skin adnexal tumours.[1]

Accessory breast occur in 0.4 – 6 % of women. They may present as asymptomatic mass or cause pain, restriction of arm movement, cosmetic problems or anxiety. Commonly accessory breasts are bilateral. Most of the ridge undergoes regression except on the anterior thorax where breast develop. If this regression does not occur and ridge persists, supernumerary nipples or breasts develop along milk line. Accessory breast tissue usually becomes noticeable after hormonal stimulation usually after puberty, pregnancy or lactation. They can undergo monthly premenstrual changes such as tenderness, swelling and irritation from clothes. There have been reports of fibroadenoma and even cancer developing in the accessory breasts.[3]

Lymphadenopathy accounts for > 80 % of axillary masses. Axillary lymph nodes can be divided into three levels based on their relationship with the pectoralis minor muscle. Level 1 lie inferolateral, level 2 lie posterior and level 3 lie superomedial to the muscle.[4] The most common lymph node lesion in axilla is benign reactive lymph node hyperplasia. It is caused by inflammation of the lymph nodes or the adjacent organs, such as the breast or lung. Collagen vascular disorders, including rheumatoid arthritis, psoriasis, scleroderma, and systemic lupus erythematous, also cause nodal hyperplasia. Unlike malignant lymphadenopathy, which usually has circumscribed borders, tuberculous lymphadenitis commonly has ragged indistinct borders because of peri adenitis and surrounding soft tissue oedema. Matting of lymph node is a common feature of tuberculosis. Fine needle aspiration biopsy (FNAB) is a less invasive and more practical diagnostic technique than excisional biopsy, especially in tuberculosis-endemic countries, but it has wide range of sensitivities. Combination with tuberculin skin test enhances the sensitivity of FNAB.[2]

Metastatic disease represents the most common cause of lymphadenopathy. Lymph node metastases may develop from primary malignancies originating from the breast, lung, head and neck, stomach, ovary or ipsilateral arm. Extra nodal extension of tumour denoting extracapsular growth of tumour cells, and spread into the extra - nodal axillary fat is prognostically significant.[4]

Breast cancer is one of the most common cancers in women in India and is a leading cause for mortality and morbidity. Axillary lymph node staging is the most important prognostic indicator of outcome in patients with breast cancer. Ultrasound guided fine needle aspiration (FNA) is a quick non morbid method of staging disease in the axilla. A positive ultrasound - guided FNA result obviates sentinel lymphadenectomy, allowing the patient to proceed directly to axillary lymph node dissection or neoadjuvant chemotherapy.[5] Axillary lymphadenopathy occurs in approximately 30 % and is the initial manifestation of lymphoma in 9 % of cases. Non - Hodgkin's lymphoma more commonly affect the axilla. Size cannot be used to accurately predict the benign versus malignant status of an axillary lymph node, a short axis diameter of > 10 mm has high specificity for malignant involvement. Haemangiomas are common benign endothelial tumours. They may contain non vascular elements including fat, smooth muscle, fibrous tissue, bone, hemosiderin and thrombus and present most commonly in young patients. Lipomas are common benign tumours composed of adipocytes and present as well circumscribed masses of fat divided into lobules by thin connective tissue septa. Blood vessels or muscle fibres may be prominent. They usually arise in the superficial sub - cutaneous tissue but can rarely occur in deeper tissues, or infiltrate through muscle.[4]

Fine needle aspiration cytology (FNAC) is a safe, quick, easy, and a cheap diagnostic tool to decipher the benign or the malignant nature of the swelling. It involves random sampling of the cells using a needle, from the potentially pathological swelling. It is also a less invasive and less traumatic procedure. It is of utmost importance for the clinician to examine and palpate the axillary masses. Various studies have shown that imaging techniques and FNAC, both used individually or coupled, improve the accuracy of diagnosis and help in avoiding unnecessary invasive procedures.[6]

Objectives

- To document the spectrum of lesions encountered in the axillary area
- Value of FNAC to decipher the nature of these lesions

METHODS

The present study is a retrospective review of swellings aspirated from axillary region over a period of two years from January 1, 2018 to December 31, 2019. FNAC was performed following strict aseptic precautions. Inadequate aspirates were excluded from the study. Patients attending cytology outpatient department (OPD) with axillary swelling were the study population. Consent was obtained from each patient before the procedure.

Procedure

The size of the axillary swelling being aspirated was noted. A 22 / 23 gauge needle attached to 20 ml syringe mounted

on Cameco handle was used for obtaining the material. The needle was inserted into the swelling and full suction pressure was applied. The needle was moved briskly in different directions in the swelling till sufficient material was visualized in the stem of the needle. The negative pressure of the syringe was released, and the needle was taken out. The aspirated sample was blown on clean glass slides and smears were made using squash preparation. Smears were fixed using air dried and alcohol fixation method. Smears were stained with Giemsa stain, and the alcohol-fixed smears were stained with haematoxylin and eosin and Papanicolaou stains. Few of the smears were heat fixed and stained with Ziehl Neelsen (ZN) stain. All cytological smears were evaluated for adequacy, cellularity, type of cells, arrangement of cells and nuclear as well as cytoplasmic features. Background was evaluated in all smears for any specific findings like necrosis or presence of mucin.

Statistical Analysis

The result was collected and analysed on SPSS version 21 and percentages were calculated.

RESULTS

A total of 191 axillary swelling were aspirated during the study period, out of which 148 (77.5 %) cases were females and 43 (22.5 %) cases were males, with a male : female ratio around 1:3. Most common axillary lesion in paediatric age group was reactive hyperplasia of lymph node.

Age Group in Years	No of Cases	Percentage
1 - 10	17	8.9
11 - 20	25	13.1
21 - 30	43	22.5
31 - 40	43	22.5
41 - 50	34	17.8
51 - 60	15	7.9
61 - 70	9	4.7
71 - 80	5	2.6
Total	**191**	**100.0**

Table 1. Number of Cases in Each Age Group (N = 191)

As shown in table 1, of 191 cases around 45 % of cases were from twenty one to forty years age group

Lesions	No of Cases
Lipoma	48 (25 %)
Axillary tail	46 (24 %)
Acute suppurative lymphadenopathy	39 (20.4 %)
Non-specific reactive lymphadenitis (NSRL)	21 (11 %)
Epidermal inclusion cyst (EIC)	11 (5.8 %)
Malignant lesions	10 (5.2 %)
Tubercular lymphadenitis	7 (3.7 %)
Fibroadenoma of ectopic breast	7 (3.7 %)
Vascular lesions (VL)	2 (1 %)

Table 2. Distribution of Various Lesions in the Axilla (N = 191)

As shown in table 2, of 191 cases 25 % of axillary swelling were lipoma, the smears showed sheets and clusters of benign mature adipocytes along with fibrous stromal fragments and 24 % of cases were reported as axillary tail of breast, were the smears showed presence of benign ductal epithelial cells arranged in monolayered sheets of variable shapes and sizes along with overriding myoepithelial cells. Acute suppurative lymphadenopathy constitutes around 20.4 %, plenty of neutrophils along with macrophages (both intact and degenerated) were seen against necrotic background in the smear. Occasional tangible body macrophages were also seen along with degenerated lymphoid cells.

As shown in table 3, the most common lesion in paediatric age group was NSRL constituted 9 (4.7 %) cases, the smears showed the presence of polymorphous population of lymphoid cells at various stages of maturation comprising of predominantly small lymphocytes with a variable number of centrocytes, and also tangible body macrophages with occasional cases showing variable amounts of plasma cells. There was no evidence of granulomas or any atypical cells in these smears. Of seven tubercular lymphadenitis cases 3 (1.5 %) cases were reported in 21 - 30 years age group. The smears showed abundant caseous necrosis along with polymorphous population of lymphoid cells.

Occasional multinucleated giant cells of Langhan's type were also seen. ZN stain revealed the presence of acid - fast bacilli. Malignant lesions in the axillary region were reported in the older age group, of 10 (5 %) cases 5 (2.5 %) cases were reported in 41 - 50 years age group

	Lesions								
Age Group in Years	Axillary Tail	Lipoma	Acute Suppurative Lymphadenopathy	NSRL	EIC	Malignancy	Tubercular Lymphadenitis	VL	Fibroadenoma of Ectopic Breast
1 - 10	0	0	5	9	0	0	2	1	0
11 - 20	7	5	7	2	2	0	0	1	1
21 - 30	15	12	9	1	3	0	3	0	0
31 - 40	11	13	10	3	1	1	1	0	3
41 - 50	8	11	5	0	1	5	1	0	3
51 - 60	2	3	2	4	2	2	0	0	0
61 - 70	2	3	1	1	1	1	0	0	0
71 - 80	1	1	0	1	1	1	0	0	0

Table 3. Age Wise Distribution of Cases (N = 191)

As shown in table 4 out of 10 (5 %) malignant cases 6 (3 %) cases were reported in females and 4 (2 %) cases were reported in males. Of two cases of metastatic poorly differentiated carcinoma, each case was reported in both males and females. The smears showed disseminated population of poorly differentiated malignant cells. Individual cells were highly pleomorphic with high nuclear : cytoplasmic ratio, moderate to abundant cytoplasm, round to oval nuclei with irregular margins and coarse clumped chromatin with occasional nucleoli.

Sex	Non - Hodgkin Lymphoma	Metastatic Adenocarcinoma	Metastatic Mucinous Carcinoma	Metastatic Poorly Differentiated Carcinoma
Male	2 (1 %)	1 (0.5 %)	-	1 (0.5 %)
Female	1 (0.5 %)	2 (1 %)	2 (1 %)	1 (0.5 %)

Table 4. Sex Wise Distribution of Malignant Lesions (n=10)

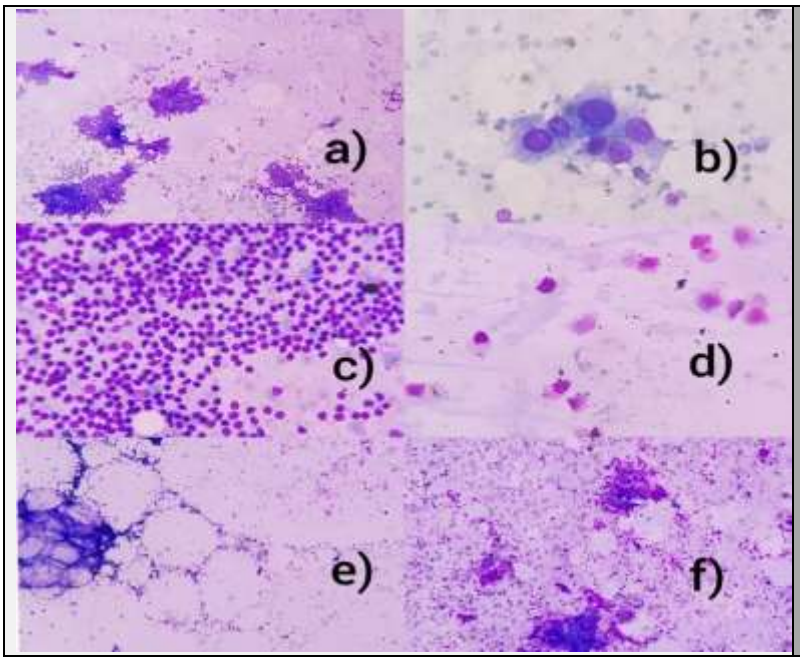

Figure 2. Photomicrograph of a) Fibroadenoma Showing Cohesive Clusters of Benign Ductal Epithelial Cells in a Papillaroid Pattern Mixed with Myoepithelial Cells Numerous Naked Bipolar Cells in the Background [Giemsa, 100X], b) Metastatic Undifferentiated Carcinoma Showing Clusters of Malignant Cells having Pleomorphic Hyperchromatic Nuclei with Cytoplasmic Vacuolation [Giemsa, 400X], c) NSRL Showing Heterogenous Population of Lymphoid Cells with Pred. of Mature Small Lymphocytes [Giemsa, 100X], d) EIC Showing Numerous Mature Anucleate Squames [Giemsa, 100X], e) Lipoma Showing Fat Tangles in an Oily Background [Giemsa, 100X], f) Tubercular Lymphadenitis Showing Clusters of Epithelioid Cells with Caseous Necrosis [Giemsa, 100X]

DISCUSSION

The axilla is pyramid - shaped. It comprises a truncated apex, a concave base and four walls (anterior, posterior, medial and lateral). The lymph nodes are 20 - 30 in number. These are the anterior, posterior, lateral, central, and the apical groups. The anterior group receives lymph from the major part of the breast, whereas the posterior group receives lymph from the axillary tail of the breast. The apical group receives lymph from the upper part of the breast.[7]

In this study lipoma was the most common cytological diagnosis followed by axillary tail of breast, whereas in the study conducted by Dey A et al[6] reactive lymphadenitis was the most common cytological diagnosis. Lipomas are benign fatty tumours and may occur in any location. Three cytomorphological patters of lymphadenopathy were seen in this study, viz. reactive pattern, tubercular and acute suppurative, whereas in the study conducted by Dey A et al[6] four cytomorphological patters were seen, apart from these three patterns granulomatous pattern was noted in there study. Second most common lesion encountered in this study was axillary tail of breast accounting for 24 % which is similar to the study conducted by Bello U et al,[1] whereas the percentage of case is relatively lower around 13.6 % compared to the current study. The percentage of neoplastic lesions encountered in the current study is around 57 % which is in concordance to the study conducted by Bello U et al[1] and Andrade et al,[8] in whose study around 52.5 % of cases were neoplastic.

No cases of congenital lesions were encountered in the current study, whereas Ali G et al[9] reported two cases of axillary cystic hygroma in adult while Manikoth P et al[10] reported an axillary cystic hygroma diagnosed in utero. Most cases of cystic hygroma (80 %) occur in the neck, usually in the posterior cervical triangle, less frequently other sites can be affected including the axilla, superior mediastinum, mesentery, retroperitoneal region, pelvis and lower limbs. Cystic hygroma may be associated with some congenital syndromes and anomalies like Turner syndrome, Noonan syndrome, trisomy, cardiac anomalies, and foetal hydrops.[11]

Tuberculous lymphadenitis usually is the most common form of extra pulmonary tuberculosis and arises as a result of lymphatic spread from a primary focus.[12] Granulomata are recognized cytologically by observing cohesive clusters of histiocytes of epithelioid type with or without multinucleated giant cells. A dirty necrotic background if present would suggest caseation and possibly tuberculosis.[13] Granulomatous inflammation in lymph nodes may be encountered in various non - neoplastic and neoplastic conditions. Neoplastic causes can be Hodgkin disease, non - Hodgkin lymphoma, and metastatic carcinomas.[14] Sen et al[15] in their study have given the spectrum of cytomorphological pattern than can be seen in tubercular lymphadenitis.

They further stressed that unless AFB is demonstrated, diagnosis of tuberculosis is difficult in cases when smears are richly cellular with an occasional cluster of epithelioid cell and absence of necrosis. In such cases, other granulomatous conditions need to be taken into consideration. Das et al[16] also suggested the importance of AFB demonstration in smears where only necrotic material was seen in FNAC smears. Around 4 % cases of fibroadenoma was reported in the study conducted by Dey A et al,[6] which is similar to the current study. Fibroadenoma, though relatively frequent and the most common benign neoplasm of the breast, are rarely found in the axillary ectopic breast tissue with few reported cases so far.[17]

Fibroadenoma show a bimodal cell population, with smears being more cellular. The triad of cellular smears with bimodal cell population, many bare bipolar nuclei lying singly and fibro myxoid stromal fragments in the background points towards a diagnosis of fibroadenoma.[18] Around 5.8 % cases of EIC were encountered in the current study. Various complications may arise in cases of epidermal cysts like rupture and development of squamous cell carcinoma. Rupture of epidermal cysts may result in foreign body giant

cell reaction, granulomatous reaction or formation of abscesses.[19] Dey A et al[6] reported around 4 % cases of EIC in their study.

The metastatic enlargement of axillary nodes may be the first sign of clinically occult carcinoma of the breast. This particular presentation of the disease occurs in approximately 1 % of all breast cancers.[20] In the current study 2 (1 %) cases of metastatic adenocarcinoma, 2 (1 %) cases of metastatic mucinous carcinoma and 1 (0.5 %) case of metastatic undifferentiated carcinoma were reported in females whose primary was not known during the study period. The mean age of the patients presenting with metastatic poorly differentiated carcinoma in the current study is around 55 years, which has similar findings to the study conducted by Pentheroudakis et al[19] and Dey A et al.[6] Metastasis of poorly differentiated malignancy to axillary lymph node is associated with unfavourable outcome.

CONCLUSIONS

Various pathological processes may affect the axilla. There is overlap in the imaging findings of these diseases. FNAC is a diagnostic tool which is required for conformation of diagnosis of axillary lesions. FNAC is a safe, easy and cheap diagnostic tool to decipher benign or the malignant nature of the swelling. It is a rapid, outpatient based and accurate procedure in the hands of experienced pathologists.

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