Study of Multifactorial Origin and Clinical Presentation of Peripheral Lymphadenopathy and Recent Trends of Management

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Abstract
Background: Lymphadenopathy is a very common clinical manifestation of many diseases, defined as an abnormality in the size or character of the lymph nodes, caused by the invasion or propagation of either inflammatory cells or neoplastic cells. There are about 800-1000 lymph nodes in the body out of which 300 are present in the neck in about 25 nodal basins. Peripheral lymphadenopathy is quite common in our country and forms a quite big group of patients attending the surgery outdoors. Tuberculous lymphadenitis constitute a major health problem in our country. Also the metastatic lymphadenopathy is quite a common cause. A lymph node appears to be the most accessible and appropriate organ which could easily lend to cytology by needle aspiration and excisional biopsy and imprint smears.

Aims and Objective
Study the multifactorial origin of peripheral lymphadenopathy.
And detailed clinical study the distribution of secondary involvement of peripheral lymph nodes in relation to various malignancy. And to assess the role of aspiration biopsy/ cytology in diagnosing peripheral lymphadenopathy, along with recent trends of management in peripheral lymphadenopathy.

Material and Methods: The study is comprised of 150 cases suffering from peripheral lymphadenopathy due to various causes who attended surgery OPD/ Cancer OPD or were admitted in surgery/cancer wards during the period of Sep. 2011 to Feb. 2018. 100 cases were screened retrospectively from records (Sep. 2011 to Sep 2016). 50 cases from (Oct. 2016 to Feb. 2018) were screened by the author. Patients included in this study had clinically detectable cervical, axillary and inguinal lymphadenopathy. From each patient a thorough history was taken and underwent a thorough clinical examination and relevant investigations. Every patient was subjected to FNAC or Biopsy of the node or biopsy of primary site in cases of cancer of head and neck or breast or penile carcinoma.

Result: The study comprised of 150cases of various peripheral lymphadenopathies Patients were broadly classified into five groups. 1.Acute lymphadenitis (25) 2. Chronic Non specific lymphadenitis (10) 3.Tubercular lymphadenitis (95) 4. Lymphomas (8) 5. Secondaries (12) There were 82 male(54.66%)and 68 female(45.33 %) patients .most of patients of age group of 25-40 year
Majority were from rural area (57.33%). All patients have common complain of Swelling. Cervical lymphadenopathy is most commonly seen in peripheral lymphadenopathy. Most of the patients were case of Tuberculous lymphadenitis (63.33%) 9% patients has HIV infection. In 50% cases montoux test was positive. Most of patients were managed conservatively 99(66%).

Conclusion: Any lymph node enlargement exceeding 1.5 cm should be taken as presumptive evidence of abnormality. Aspiration biopsy provides a reliable, safe, rapid and economical method of investigating lymph node enlargements. The diagnosis of lymphomas was invariably suggested, but classification could not consistently be made. Primary lymph nodes disease is best diagnosed by incisional or excisional biopsy which details such as capsular invasion, architectural pattern and reaction of perinodal tissues can be studied carefully. In lymph nodes the presence of other than lymphoid tissue is evidence of a secondary or metastatic disease. FNAC is very reliable procedure to diagnose tubercular lymphadenitis. Epitheloid cells, multinucleated giant cells and caseation necrosis was confidently diagnosed. Proper history, careful clinical examination and FNAC of lymph nodes should reliably diagnose tubercular lymphadenitis. Montoux reaction might be used as an adjunct but it is not very specific, its role is diminished.

Keywords: Lymphadenopathy, FNAC, Biopsy.

Introduction

Lymphadenopathy is a very common clinical manifestation of many diseases, defined as an abnormality in the size or character of the lymph nodes, caused by the invasion or propagation of either inflammatory cells or neoplastic cells. There are about 800-1000 lymph nodes in the body out of which 300 are present in the neck in about 25 nodal basins. Relatively higher incidence of cervical lymphadenopathy has been attributed to rich lymphatic supply in the neck region. Peripheral lymphadenopathy is quite common in our country and forms a quite big group of patients attending the surgery outdoors.

Tuberculous lymphadenitis constitute a major health problem in our country. Also the metastatic lymphadenopathy is quite a common cause. But many other diseases also present as peripheral lymphadenopathy. Lymphadenopathy is classically described as a node larger than 1 cm.

Breast adenocarcinoma often metastasizes initially to the anterior and central apical group of nodes which can be palpable before the discovery of primary tumour. Hodgkin’s and Non-Hodgkin’s lymphomas manifest solely or initially in the axillary nodes. Antecubital or epitrochlear lymphadenopathy can suggest lymphomas of upper extremity, which first metastasizes to the ipsilateral regional lymph nodes. Review of literature reveals various methods that have from time to time been devised for a rapid diagnosis especially of those tumours and lesions which do not shed cells spontaneously for examination. The effort has been to obtain a film preparation, which would show clearly, the structural details of the individual cells and fragments of tissues for cytologic interpretation. The films have been prepared either from the materials obtained through fine needle aspirations or scrapped from the freshly out surfaces of tissues and of impressions made by merely pressing the freshly out surfaces of lesions on to clean glass slides. Enlarged lymph nodes often pose a diagnostic problem in the outpatient’s clinic of a hospital. A lymph node appears to be the most accessible and appropriate organ which could easily lend to cytology by needle aspiration and excisional biopsy and imprint smears.

Historical Background

Grey and Grey, in 1904 were the first to perform the aspiration biopsy of the lymphnodes in order to isolate the etiologic agent of trypanosomias. They however, did not offer any comments on the importance of the cellular study of lymphnodes. Guthrie in 1981 was the first to adapt systematically the technique of gland puncture as a cytodiagnostic measure, but gave little information on his findings. Lymphadenopathy is a normal finding or one that requires further study, up to and including biopsy. Soft, flat, submandibular nodes (<1 cm) are often
Palpable in healthy children and young adults, and healthy adults may have palpable inguinal nodes of up to 2 cm, which are considered normal. Further evaluation of these normal nodes is not warranted. In contrast, if the physician believes the node(s) to be abnormal, then pursuit of a more precise diagnosis is needed.

The site of localized or regional adenopathy may provide a useful clue about the cause. The chief malignant causes include metastatic cancer from head and neck, breast, lung, and thyroid primaries. Enlargement of supraclavicular and scalene nodes is always abnormal. Virchow's node is an enlarged left supraclavicular node infiltrated with metastatic cancer from a gastrointestinal primary. Metastases to supraclavicular nodes also occur from lung, breast, testis, or ovarian cancers.

Axillary adenopathy is usually due to injuries or localized infections of the ipsilateral upper extremity. Malignant causes include melanoma or lymphoma and, in women, breast cancer. Inguinal lymphadenopathy is usually secondary to infections or trauma of the lower extremities and may accompany sexually transmitted diseases such as lymphogranuloma venereum, primary syphilis, genital herpes, or chancroid.

These nodes may also be involved by lymphomas and metastatic cancer from primary lesions of the rectum, genitalia, or lower extremities (melanoma).

The size and texture of the lymph node(s) and the presence of pain are useful parameters in evaluating a patient with lymphadenopathy. Nodes <1.0 cm² in area (1.0 cm x 1.0 cm or less) are almost always secondary to benign, nonspecific reactive causes.

Patients with node(s) 1.0 cm² should be observed after excluding infectious mononucleosis and/or toxoplasmosis unless there are symptoms and signs of an underlying systemic illness.

The texture of lymph nodes may be described as soft, firm, rubbery, hard, discrete, matted, tender, movable, or fixed. Tenderness is found when the capsule is stretched during rapid enlargement, usually secondary to an inflammatory process.

Some malignant diseases such as acute leukemia may produce rapid enlargement and pain in the nodes. Nodes involved by lymphoma tend to be large, discrete, symmetric, rubbery, firm, mobile, and non-tender. Nodes containing metastatic cancer are often hard, non-tender, and nonmobile because of fixation to surrounding tissues. The coexistence of splenomegaly in the patient with lymphadenopathy implies a systemic illness such as infectious mononucleosis, lymphoma, acute or chronic leukemia, SLE, sarcoidosis, toxoplasmosis, cat-scratch disease, or other less common hematologic disorders. The patient's story should provide helpful clues about the underlying systemic illness.

In the young, mediastinal adenopathy is associated with infectious mononucleosis and sarcoidosis. In endemic regions, histoplasmosis can cause unilateral paratracheal lymph node involvement that mimics lymphoma.

Tuberculosis can also cause unilateral adenopathy. In older patients, the differential diagnosis includes primary lung cancer (especially among smokers), lymphomas, metastatic carcinoma (usually lung), tuberculosis, fungal infection, and sarcoidosis.
Figure 1 Lymph nodes of the head and neck, and the regions that they drain.

Figure 2 Axillary lymphatics and the structures that they drain.

Figure 3 Inguinal lymphatics and the structures that they drain.
Nodal Character and Size
Lymph nodes that are hard and painless have increased significance for malignant or granulomatous disease and typically merit further investigation.
Two series, reported maximum diameters of more than 2 cm and 1.5 cm, respectively, as an appropriate starting point for high suspicion of malignant or granulomatous disease. Increasing size and persistence over time are of greater concern for malignancy than a specific level of nodal enlargement.

Peripheral Lymphadenopathy

Material and Methods
The study is comprised of 150 cases suffering from peripheral lymphadenopathy due to various causes who attended surgery OPD/ Cancer OPD or were admitted in surgery/cancer wards during the period of (Sep. 2011 to Feb. 2018). 100 cases were screened retrospectively from records (Sep. 2011 to Sep. 2016). 50 cases from Oct. 2016 to Feb. 2018 were screened by the author.
Patients included in this study had clinically detectable cervical, axillary and inguinal lymphadenopathy. From each patient a thorough
history was taken and underwent a thorough clinical examination and relevant investigations. Every patient was subjected to FNAC or Biopsy of the node or biopsy of primary site in cases of cancer of head and neck or breast or penile carcinoma.

Result
The study comprised of 150 cases of various peripheral lymphadenopathies. Patients were broadly classified into five groups. 1. Acute lymphadenitis (25) 2. Chronic Non specific lymphadenitis (10) 3. Tubercular lymphadenitis (95) 4. Lymphomas (8) 5. Secondaries (12).

There were 82 male (54.66%) and 68 female (45.33%) patients. Most of patients of age group of 25-40 year (56.6%). Majority were from rural area (57.33%). All patients had common complain of Swelling. Cervical lymphadenopathy is most commonly seen in peripheral lymphadenopathy. Most of the patients were case of Tuberculous lymphadenitis (63.33% of total patients), most of the patients were cachectic and poorly nourished but healthy patients were also seen. Most of the patients were between the age of 25 to 40 years of age (56.6%) and a definitive male preponderance was noticed. Most of the patients belong to rural area (57%). Patients with secondary malignant disease of the lymph nodes presented with poor general health.

Discussion
The present study was carried out in GMH & SGM Hospital Rewa over 150 subjects with clinically detectable peripheral lymphadenopathy from Sep 2011 to Feb 2018. From each subject a good history was taken and thorough clinical examination was done. The nodes were subjected to FNAC/FNAB or Biopsy if required.

History
As in all conditions a proper history is one of the very important first step towards unearthing the cause of peripheral lymphadenopathy. Similarly in our country where tuberculosis is so rampant a good history will go long way to prevent unnecessary investigation to diagnose TB lymphadenitis. Although a classic history of evening rise of temperature, cough with hemoptysis, chest pain might not always be available. In such cases, past, family or socioeconomic history might play an important role.

Secondary carcinoma of lymph nodes is very common in the elderly. Many times patients presents with only cervical or inguinal or axillary lymphadenopathy and the primary tumour is unknown. Here history will suggest you the line of investigation and the site of primary tumour.

Clinical Evaluation
Including 150 cases in the study and evaluating many more gives an idea that lymph node enlargement exceeding 1.5 cm should be given as presumptive evidence of abnormality. But the location of the node, its consistency, and the site and the character of possible primary lesion has a bearing on whether or not a node is investigated.

In cases of tubercular lymphadenopathy (63.33% of total patients), most of the patients were cachectic and poorly nourished but healthy patients were also seen. Most of the patients were between the age of 25 to 40 years of age (56.6%) and a definitive male preponderance was noticed. Most of the patients belong to rural area (57%). Patients with secondary malignant disease of the lymph nodes presented with poor general health.

FNAC
The main features in aspiration cytology noted were epitheloid cells in tubercular lymphadenitis; increased cellularity in chronic non specific lymphadenitis, mainly of large lymphocyte, histiocytes and polymorphonuclear cells. Hypercellularity, mitotic cells, equal admixture of lymphoblasts and lymphocytes with increase in reticular cells in lymphomas. Secondaries of malignancies showed typical cells depending on the primary.

In our study the FNAC sensitivity for tubercular lymphadenitis was 93.75% and for secondaries was 91.67%. The results were comparable to previous studies Sarda A K in his study of 359 patients with cervical lymphadenopathy showed that the sensitivity of malignancy was 100% and in tuberculosis the sensitivity was 96%. (J Assoc. Physicians India, 1990 March 38:3).
Another study in Calcutta where 108 cases of cervical lymphadenopathy were studied by FNAC, the sensitivity for tubercular lymphadenitis was 84.4% and for metastatic carcinoma was 89%.

HsuC and Leung (1990) in their study of 1484 Chinese patients with FNAC showed the sensitivity of 95% for metastatic carcinoma and 76.9% for tubercular lymphadenitis.

Dandapat and Mishra (1990) in their 192 patients with peripheral lymphadenopathy and found the sensitivity of FNAC to be 83% for tubercular lymphadenitis.

Lou SK and Wei (1990) in their study of 1349 FNABs from the head and neck region showed the sensitivity of FNAC to be 77% in tubercular lymphadenitis and a specificity of 93%.

Yadav and Goel in their study of 50 cases of cervical lymphadenopathy showed an overall sensitivity of 89.8%.

In our study the FNAC sensitivity for lymphomas was 77.7%, which is comparable with the study of Lasseke et al 1946 studied 25 aspiration biopsies of Hodgkin’s disease the sensitivity was 56% while in Maurice Morrison study it was 83%.

**Biopsy**

Excisional biopsy in this study was used in most of the cases of tubercular lymphadenitis, non specific lymphadenitis, lymphomas and metastatic deposits. And was considered the gold standard against which all comparisons are made.

Coincident observations regarding tuberculin reaction and HIV positivity in patients need also be mentioned.

**Conclusion**

Any lymph node enlargement exceeding 1.5 cm should be taken as presumptive evidence of abnormality. Aspiration biopsy provides a reliable, safe, rapid and economical method of investigating lymph node enlargements, The diagnosis of lymphomas was invariably suggested, but classification could not consistently be made. Primary lymph nodes disease is best diagnosed by incisional or excisional biopsy in which details such as capsular invasion, architectural pattern and reaction of perinodal tissues can be studied carefully. In lymph nodes the presence of other than lymphoid tissue is evidence of a secondary or metastatic disease .FNAC is very reliable procedure to diagnose tubercular lymphadenitis. Epitheloid cells, multinucleated giant cells and caseation necrosis was confidently diagnosed. Proper history, careful clinical examination and FNAC of lymph nodes should reliably diagnose tubercular lymphadenitis. Montoux reaction might be used as an adjunct but it is not very specific, its role is diminished.

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