

## CERVICAL LYMPHADENOPATHY: DIAGNOSTIC APPROACH

**Mohammad Ashfaq, Naseer Ahmad, Ihsan Ullah, Malik Javed Iqbal**

Department of Ear, Nose & Throat, Head & Neck Surgery,  
Postgraduate Medical Institute, Lady Reading Hospital, Peshawar

### ABSTRACT

**Objective:** To study the etiology of unexplained cervical lymphadenopathy of more than one month duration, not easily diagnosed on clinical ground or after simple investigations.

**Material and Methods:** This study was conducted at Postgraduate Medical Institute, Lady Reading Hospital, Peshawar from January 2003 to June 2004. A total of 100 patients with prolonged unexplained cervical lymphadenopathies were included in this study. All the patients were evaluated through detailed history and clinical examination. Beside these, laboratory, radiological, endoscopic examination, FNAC and histopathological studies were performed.

**Results:** Out of 100 cases, 54 (54%) were female and 46 (46%) male. Laboratory evidence revealed tuberculous lymphadenitis in 58 (58%) cases, metastatic lymph nodes in 18 (18%) cases, lymphoma in 18 (18%) cases, infectious mononucleosis in 3 (3%) cases and leukemias in 3 (3%) cases. Histopathology of the lymph nodes gave conclusive diagnosis with 100% sensitivity rate in cases of granulomatous lymphadenitis and lymphomas.

**Conclusion:** Tuberculous lymphadenitis (58%) represented the commonest infectious aetiology in present study and carcinoma is less common as compared to the western figures. It is advised that any treatment for cervical lymphadenopathy should be preceded by histological proof.

**Key Words:** Cervical Lymphadenopathy, Diagnosis, Histopathology, Tuberculosis, Malignancy.

### INTRODUCTION

Nodal cells proliferate in response to infection (specific and non-specific), infectious mononucleosis, toxoplasmosis, cytomegalovirus, brucellosis, fungi like histoplasmosis etc.<sup>1</sup> These infections usually develop over weeks and months often with minimal systemic complaints or findings. The glands tend to be firm with some degree of fixation and infection of overlying skin. Tuberculosis is now commonly seen in adult population within the posterior triangle. Atypical mycobacteria are commonly found in paediatric age group. Typical mycobacterial infection usually involves anterior triangle lymph nodes with browning skin in duration and pain. Typical tuberculosis lymphadenopathies often respond to anti-tuberculous medication. Atypical mycobacterial infection usually responds to surgical excision.

Lymphoma can occur in all age groups but is more common in paediatric and young adult group. Around 80% of children with Hodgkin's

disease have a neck mass.<sup>2</sup> Progressive enlargement of a lateral neck mass is often the only sign of disease in head and neck. Systemic signs of fever, hepatosplenomegaly and diffuse adenopathy should be sought. Mass often appears discrete, rubbery and non-tender. Lymphoma of head and neck presenting as a mass has often proven to be a challenging diagnosis when it can not be easily differentiated from carcinoma, it often leads to multiple biopsies and diagnostic delays.<sup>3</sup>

Fine needle aspiration biopsy (FNAB) is the first line diagnostic test. But still lymph node biopsy plays an important role in typing of lymphoma and helps in those cases which can not be diagnosed definitely by FNAC.<sup>4</sup> FNAC can also be performed in children. In a child younger than 2 years of age sedation is usually needed.<sup>5</sup> Cervical lymphadenopathy is the most common presentation for the Hodgkin's and non-Hodgkin's lymphoma.<sup>3</sup> Among primary care patients presenting with lymphadenopathy, the prevalence of malignancy

has been estimated to be as low as 1.1 percent. The critical challenge for the primary care physician is to identify which cases are secondary to malignancy or other serious conditions. Key risk factors for malignancy includes older age, firm and fixed lymph nodes.<sup>6</sup> The loss of normal intercellular adhesions is believed to be one of the earliest events in the process of metastases. Cadherins proteins that span the intercellular spaces between the two cells are found predominantly in the cells of epithelial origin. E Cadherin, a member of this family is a calcium dependent protein that maintains epithelial cell adhesion and polarity. Loss of E. Cadherin has been shown to occur early in epithelial carcinogenesis.<sup>7</sup> Connective tissue disorders like rheumatoid arthritis, systemic lupus erythematosus can cause nodal cell proliferation. Drugs like Phenytoin, Hydralazine and Allopurinol cause reactive hyperplasia. There is also hyperplasia in lipid storage diseases when cells are loaded with lipid material.

Aim of this work was to study the etiology of unexplained lymph adenopathy, of more than one month duration that can not be easily diagnosed on clinical grounds or after simple investigations.

## MATERIAL AND METHODS

This study included 100 cases suffering from unexplained persistent cervical lymphadenopathies. All the patients were managed in the department of Otolaryngology, head & neck surgery lady Reading Hospital, Peshawar. This study was carried out from January 2003 to June 2004. Data was collected via a proforma especially designed for this purpose.

### Inclusion criteria:

1. History of unexplained cervical lymphadenopathy of more than one month duration.
2. History of non-responsive neck lymphadenopathy to antibiotic therapy.
3. Failure to reach the proper diagnosis after thorough clinical examination and simple routine investigations like complete blood picture, tuberculin test and x-ray chest.

### Patients were subjected to:

1. Complete history
2. Thorough clinical examination including ear, nose throat examination. Examination of head & neck and local examination of lymph nodes. Examination of lymph nodes included site size, shape, mobility, number, consistency, whether matted or discrete, translucency and auscultation.

3. X-ray lateral view neck in extension for diagnosis of primary malignancy. X-ray lateral view nasopharynx and x-ray sinuses.
4. CT scan neck, ultrasound of neck and abdomen..
5. Serological examination was performed for the diagnosis of infections mononucleosis.
6. Culture of the aspirate for microorganisms
7. FNAC of lymph node.
8. Selected patients underwent the examination of upper aerodigestive tract. This included examination of nasopharynx under anesthesia, direct laryngoscopy, bronchoscopy, esophagoscopy.
9. Proof biopsies performed in those cases where no primary malignancy was found but FNAC report was metastatic carcinoma.
10. Lymph node biopsy was performed in all the patients except those who were suspected to have nodal metastases. It was performed mostly under local anesthesia.
11. Special investigations like pus examination for AFB and bone marrow aspiration were performed when ever required.

## RESULTS

In our study, out of 100 cases studied, 54 (54%) were female and 46 (46%) male. Male to female ratio was 1:1.7. Majority of the patients were between 20-30 years. The study revealed that the majority of the cases (58%) proved to be tuberculous lymphadenitis. Others included metastatic lymph nodes in 18 (18%) cases, lymphoma in 18 (18%) cases, infectious mononucleosis in 3 (3%) cases and leukemias in 3 (3%) cases (Table No. 1). Among the lymphomas, 12 (12%) patients were of Hodgkin lymphoma and 6 (6%) patients were of non-Hodgkin's type.

Among tuberculous lymphadenitis group, 38 (65.5%) were female and 20 were male (34.5%). Majority of the patients were between 20-

## ETIOLOGY OF CERVICAL LYMPHADENOPATHIES

Disease	No of Patients	Percentage
T.B Lymph Adenitis	58	58%
Nodal Metastasis	18	18%
Hodgkin lymphoma	12	12%
Non-Hodgkin lymphoma	6	6%
Infectious mononucleosis	3	3%
Leukemia	3	3%

Table 1

## DISTRIBUTION OF PRIMARY MALIGNANCY

Primary Growth	No. of patients n=18	Percentage
Carcinoma Nasopharynx	7	38.9%
Carcinoma Hypopharynx	4	22.2%
Carcinoma Larynx	3	16.6%
Carcinoma tongue	2	11.1%
Carcinoma maxilla	1	5.6%
Oesophagus	1	5.6%

Table 2

30 years of age. Most of the patients with nodal metastasis were above 50 years of age. There were 12 male and 6 female in this group. Their distribution of primary malignancy is shown in table No.2. Among the seven patients with carcinoma nasopharynx, 4 patients presented with mobile unilateral metastatic (N1) glands. Two patients were having N2 mobile bilateral metastatic glands. In all the cases upper deep cervical glands were involved. One patient presented with unilateral fixed glands (N3). In all the seven patients, consistency of glands was firm to hard. In 4 patients, cervical metastasis were because of carcinoma hypopharynx. Three patients were having carcinoma of pyriform fossa while in one it was post cricoid growth. In 3 patients nodes were of stage N2 while in one patient it was N3. In two patients upper deep cervical (level II) nodes, while in remaining two patients middle deep cervical (level III) nodes were involved. In three patients nodes were of firm consistency while hard in one patient.

Three patients had supraglottic carcinoma larynx and has had upper deep cervical glands involved. In two cases nodes were of N1 stage while in one case of N2. In patients with carcinoma tongue, carcinoma maxilla and carcinoma esophagus unilateral gland enlargement was found.

Among the 18 patients with lymphoma, 12 (66.6%) were of Hodgkin's and 6 (33.3%) were of non-Hodgkin's type. There were 9 males and 3 females with Hodgkin's lymphoma. Majority of the patients were of the age group of 20-30 years. Histology report in 8 patients was nodular sclerosis, 3 patients mixed cellularity and in one patient lymphocyte depletion type. Three patients were diagnosed as leukemia, two were males and one was female. All the patients were having acute lymphocytic leukemia and they were young. Mean age was 19 years. Three patients were having infectious mononucleosis. Two were male and one was female. Mean age was 22 years. Maximum number of patients i.e. 40 (40%) were from Peshawar followed by Charsadda i.e. 18 (18%), Mardan i.e. 10 (10%). Remaining patients came

from rest of the province. Most of the patients (65%) belonged to poor socioeconomic group. Majority of them were having infections lymphadenopathies. In this study 71 (71%) of the patients were Pakistani and 29 (29%) were Afghan refugees.

## DISCUSSION

Cervical lymphadenopathy is a common clinical problem that confronts all specialties. Usually lymphadenopathy cannot be easily diagnosed on clinical grounds or by routine laboratory investigations and a series of specific investigations may be required to reach a definite diagnosis. In some instances even after exhaustive investigations including lymph node biopsy 30-53% of cases cannot be definitely diagnosed.

Tuberculous lymphadenitis (58%) represented the commonest infectious aetiology of lymphadenitis in the present study like that of a Abdel-Wahab MF et al.<sup>8</sup> It is the commonest form of extra pulmonary tuberculosis.<sup>9</sup> Mycobacterium tuberculosis predominates as a cause of cervical lymphadenitis in adults.<sup>10</sup> Clinical examination of the lymph nodes did not provide distinctive criteria characteristic of tuberculous lymphadenitis except matting and non tenderness.<sup>11</sup> The same finding was also observed in some cases of non-Hodgkin's lymphoma. Anemia (32%) usually normochromic and normocytic, lymphocytosis (46%), raised ESR (68%) and strongly positive tuberculin test (73%) were suggestive of tuberculous infection. Any group of cervical lymph nodes can be infected but in our study upper deep cervical group was mostly involved. None of our cases had tuberculous focus on x-ray chest in contrast to study performed by Alleva M et al.<sup>12</sup>

Tuberculosis is more common in developing countries like Pakistan as compared to developed countries.<sup>13</sup> In our province tuberculous infection is very common because of poor hygiene conditions, poverty, over crowding, and especially because of immigration of infected Afghan refugees to this part of country. Eight patients out of 58 (13.7%) presented with discharging sinuses. In an another study conducted by Afridi SP et al<sup>14</sup> this incidence was 21.5%. Pus was sent for AFB but in non of the patients it was positive. Biopsy of the discharging sinus proved to be tuberculous lymphadenitis. Eighteen (18%) of the cases were diagnosed as metastatic nodes. It is almost the same as compared to other local studies which reported an incidence of 16%.<sup>13</sup> In all these patients endoscopic examination and CT scan was done to find the site and extent of primary tumour. It is debatable whether CT or MRI is more accurate for determining if lymph nodes contain metastases but neither is highly accurate.<sup>15</sup> It has

been suggested that ultrasound is better than CT for determining if a lymph node harbors metastases. Size of the lymph node is an important criterion. Presence of normal hilar echogenicity and a normal hilar pattern of blood flow suggest a benign lymph node. Metastatic lymph nodes can lose both the normal hilar architecture and blood flow.<sup>16</sup>

Positron Emission Tomography uses metabolic activity to evaluate for metastatic lymph nodes. PET scans usually include the entire body and so may detect metastases even distant from neck.<sup>17,18</sup> Some studies have found PET helpful for staging head and neck cancers.<sup>19</sup> Whereas other find it of no benefit relative to CT, MRI or ultrasound.<sup>20,21</sup> Lymphoma represented 18% of the cases of lymphadenopathy in the present study. These include 12 cases of Hodgkin's lymphoma (12%) and 6 cases of non-Hodgkin lymphoma (6%). Incidence was more as compared to study of Abdullah P et al who reported an incidence of 5.8% of lymphoma cases.<sup>4</sup> In a study conducted by Khan JA et al<sup>23</sup> incidence for non-Hodgkin's lymphoma was 7.3% and for Hodgkin's it was 4.6%. Al-Sohaibeni<sup>24</sup> and Hooper AA<sup>25</sup> show a high incidence of malignant lymphomas ranging from 42% to 53%. Mediastinal lymphadenopathy was detected in 5 cases. Abdominal lymph nodes were enlarged in 3 cases (as detected by abdominal ultrasonography). Clinical examination of lymphomatous nodes revealed that they were larger in size than infectious ones and usually form bulky masses, matted, immobile and adherent to the surrounding structures. There was no correlation between the size of node and pathological entity. Javaid M et al had diagnosed lymphoma in 4.76% cases on FNAC.<sup>26</sup>

Laboratory investigations in Hodgkin's disease revealed anemia in 3 (25%) patients, normal white blood count in 9 (75%) cases, thrombocytopenia in 1 (8.3%) case, ESR above 100 mm in 11 (91.61%) cases and negative tuberculin test in all the cases. In non-Hodgkin's lymphoma, anemia was found in 2 (33.31%) cases, and normal blood count in 1 (16.6%) case, thrombocytopenia in 1 (16.21%) patient, ESR above 100mm in 5 (83.3%) cases and negative tuberculin test in 5 (83.31%) cases. Histologically, lymph node showed reactive hyperplasia in case of infectious mononucleosis. Blood picture in infectious mononucleosis showed relative lymphocytosis in 2 (66.61%) cases and monocytosis in 1 (33.33%) case, total white blood cells were within normal limits in 100% cases. Three percent cases were diagnosed as leukemias. All the 3 cases were having acute lymphocytic leukemia. Blood picture revealed raised total white count in all cases. Blood film showed blast cells

and other primitive cells in all cases. Diagnosis was conformed by bone marrow examination.

## CONCLUSION

We conclude that tuberculosis is the most common cause of cervical lymphadenopathy. Incidence of both primary and metastatic carcinoma is less common as compared to the western figures. It is advised that any treatment for cervical lymphadenopathy should be preceded by histological proof. This could prevent delay in the treatment of serious malignant disorders, avoid unnecessary antituberculous treatment in patients with benign reactive lymphadenopathy and prevent delay of antituberculous treatment in tuberculous patients with atypical clinical presentation.

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**Address for Correspondence:****Dr Mohammad Ashfaq**

Department of Ear, Nose & Throat;  
 Head & Neck Surgery,  
 Postgraduate Medical Institute,  
 Lady Reading Hospital,  
 Peshawar.