Section: Pathology

Research

CLINICAL STUDY AND MANAGEMANT OF CERVICAL LYMPHADENOPATHY

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Abstract

Background: Cervical lymphadenopathy is a common presentation in the course of a number of diseases. This condition is generally not a disease by itself; rather, it may be a symptom of many possible underlying problems. The diseases can be Neoplastic or inflammatory, and include lymphoma, metastatic carcinoma, granulomatous disease, infectious diseases, tuberculosis, etc. since cervical lymphadenopathy is not a manifestation of a single disease, diagnosis becomes very difficult and moreover, it requires a strong knowledge about the differential diagnosis of cervical lymphadenopathy. Most patients can be diagnosed on the basis of a careful history and physical examination. This study is presents a methodical clinical approach and the treatment to patients presenting with cervical lymphadenopathy Objectives: Our aim of study was to study the etiology of cervical lymphadenopathy and to study clinical presentation and clinical course and management of cervical lymphadenopathy. **Materials and Methods:** The study was conducted in TRR Institute of Medical Sciences, Patancheru, A detail clinical history taken, clinical examination of the patient carried out. Patients were selected randomly and 66 cases were personally studied. All patients underwent fine FNAC and blood examination as routine. Radiological examination of chest was carried out to find out association of primary lesion in the lung. **Result:** The maximum incidence was found to be of tuberculosis, which was 63.63%, next was secondaries 13.63%, reactive lymphadenitis 12.12 Hogdkin's 4.54%, Non Hodgkin's lymphoma 1.51%. The maximum incidence of tuberculosis was found to be between the ages of 11-30 years i.e., 56%. In secondaries, maximum incidence was found to be >60 years. Digastric group was found to be affected in maximum cases (42%). The presenting complaint was swelling (79%), consistency was firm (62%) and matting was found in 29% of the cases. Tuberculosis which was detected in 42 patients, were given ATT for 6 months. Symptoms had decreased and general health improved. Two patients of secondaries were operated and one underwent chemotherapy. Patients of Hodgkin's lymphoma and non Hodgkin's lymphoma were treated with chemotherapy and improved. **Conclusion:** Of the 66 cases studied, tuberculosis had the maximum incidence (63.63%), followed by metastatic diseases of lymph nodes (13.63%). Between 11-30 years, tuberculosis had the maximum incidence and > 40 years metastatic disease had the maximum followed by Hodgkin's disease. All the patients had cervical lymphadenopathy (100%) and 50% had history of pain and fever (36%). They were put on antitubercular drugs for 6 months, recovery was 100%. The cheapest and the most reliable method of diagnosis was fine needle aspiration cytology. In investigations, FNAC was found to be accurate with 90% accuracy for the diagnosis of tuberculosis, metastatic and Hodgkin's. In metastatic lymph node, method of diagnosis was fine needle aspiration cytology and we treated 1 patient with chemotherapy and 2 patients were operated.

INTRODUCTION

Cervical lymphadenopathy is a common presentation in the course of a number of diseases. This condition is generally not a disease by itself; rather, it may be a symptom of many possible. Underlying problems. The diseases can be Neoplastic or inflammatory, and include lymphoma, metastatic carcinoma, infectious diseases, tuberculosis, etc. Since cervical lymphadenopathy is not a manifestation of a single disease, diagnosis becomes very difficult and moreover, it requires a strong knowledge about the differential diagnosis of cervical lymphadenopathy. Most patients can be diagnosed on the basis of a careful history and physical examination. This study is presents a methodical clinical approach and the treatment to patients presenting with cervical lymphadenopathy Lymph nodes which are interposed throughout the course of collecting lymphatic channels, vary from a millimeter to a centimeter or more in size. They act as filtering mechanism within the host that restricts propagating malignant cells and resists spread of infection. There are about 800 lymph nodes in the body of which 300 are in the neck. For a surgeon lymph node is an index of spread of infection and malignancy. Cases of lymphadenopathy are common in our country. There are many causes of enlargement of lymph nodes. Lymph node biopsies are the only certain means of establishing the diagnosis. The microscopic interpretation of abnormal lymphnode is extremely difficult. More errors are made on the lymph node than any other organ in the body.[1] Of the many causes for cervical lymphadenitis, tuberculosis is still a common cause for lymphadenitis. In generalized lymphadenopathy, the most likely diagnoses are probably tuberculosis and Hodgkin's disease. Even though the problem is practically eradicated in Western countries it is still prevalent in India. Lymph node tuberculosis is a disease of great antiquity. It is commonest of extra/pulmonary tuberculosis and is probably the commonest cause of chronic lymphadenitis in children. Even after the advent of effective chemotherapy for tuberculosis, it still poses considerable problems in diagnosis and management. The diseases even present as painless lymphadenopathy of superficial lymph nodes of insidious onset.[2] Head and neck cancers account for 2.8% of all newly discovered cancers. Metastatic carcinoma within cervical lymph nodes with an unknown primary tumour site accounts for 3% to 5% of all head and neck cancers. The control of such regional metastatic disease constitutes a significant part of the process of treating head and neck cancer. The presence of an enlarged node proven histologically positive for metastasis is an ominous findings and as a general rule decreases the 5/year survival rate by at least 50%. When nodal involvement becomes multiple extends low in neck, no patient gets cured regardless of the treatment given the primary site of carcinoma is known, focused therapy to the primary site and cervical lymphadenopathy can be given. Without this knowledge clinician are obligated to treat the entire pharyngeal axis and larynx to cover the possible origins of the metastatic carcinoma. The occult primary treatment regimen results in a significant increase in morbidity to the patient. Proper understanding of the anatomy and detection of cervical metastatic disease is crucial to this process.

Objectives of the Study

To study the various clinical presentation of cervical lymphadenopathy

To study the clinical course and management of cervical lymphadenopathy.

MATERIALS AND METHODS

The clinical material consists of patient randomly selected with history of cervical lymphadenopathy, who came to surgical OPD & patients admitted in the IPD at TRR Institute of Medical Sciences, Patancheru. Patients were selected randomly and 66 cases were personally studied by me in present series. The majority of patients were from Hyderabad City and from neighboring villages.

A detailed case history taking, clinical examination of the patient and investigation were carried out according to the proforma given. In local examination, importance was given to the site, size, laterality, number, matted/discrete, secondary changes, level of the cervical lymph nodes and involvement of other (inguinal/axillary) lymph nodes. Systemic examination also carried out. An attempt was made to find out the primary tumour in cases of lymph nodes suspicious as secondaries in neck. After making a clinical diagnosis further investigations were carried out to confirm the diagnosis. Routine investigations included haematological and radiological. FNAC was put in the front line for diagnosing and to get a cytological diagnosis at hand. Lymph node biopsy was carried out meticulously, it was studied grossly, and sent to pathologist for expert opinion. Further tests were carried out on the basis of histopathological diagnosis (for example, secondaries in the neck). ENT opinion, contrast radiological investigations, endoscopy carried out in relevant cases. Medical treatment was employed predominantly for conditions like tubercular lymphadenitis, infective lymph node swellings. Cases requiring surgical management were operated accordingly and patients requiring radiotherapy, chemotherapy and expert oncologic surgeries, patients were referred to MNJ Cancer Institute of Hyderabad. All patients were asked to attend the surgical OPD for follow/up after discharge. Necessary advice was given.

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RESULTS

In the present series 66 cases were evaluated for cervical lymph node enlargement. All cases were taken for Fine Needle Aspiration Cytology (FNAC), but in 6 cases FNAC was inconclusive. Excisional biopsy was performed in all 54 cases and these cases were analyzed in detail. In the present study it was observed that maximum numbers of cases were in the age group of 21/30 years (24 cases, 36.37%). Next commonest age group involved was between 31/40 years (19 cases, 28.78%), thus the third and fourth decade constituting 43 of the 100 cases (65.15%). Out of the 66 cases studied 35 cases were males and 31 cases females and the male to female ratio was 1.13:1. 10 cases (15.15%) cases were in the age group of 11/20 years and 4 cases were in the age group of 41/50 years. Only 4 cases were found to be above 60 years. Lowest age recorded was 12 years of age and highest 65 years of age. Out of these 66 cases, 46 cases (70%) were confirmed as tubercular, 7 cases (10%) as reactive lymphadenitis, 7 cases (10%) as chronic non/specific lymphadenitis, 5 cases (8%) as secondaries and 1 case (2%) as lymphoma. Thus among the lesions affecting neck lymph nodes tubercular etiology was the most common. The causes of cervical lymphadenopathy were broadly classified as neoplastic(13Cases) and non/neoplastic lesions(53Cases).

Table 1: Showing histopathological diagnosis in the study

Histopathological diagnosis	Number of cases	Percentage
Tubercularlymphadenitis	42	63.63
Chronic nonspecific lymphadenitis	3	4.54
Reactive lymphadenitis	8	12.12
Secondaries	9	13.63
Hodgkin's lymphoma	3	4.54
NonHodgkin's lymphoma	1	1.51
Total	66	100

Among the neoplastic causes, secondaries had the maximum number of cases (9 cases) followed by lymphoma (4 case).The constitutional symptoms considered are fever, malaise, weight loss, loss of appetite, difficulty in swallowing, change of voice and cough. Presence of any of the symptom or symptoms was considered as positive for constitutional symptoms. In the present study, majority of cases of tubercular lymphadenitis and malignant secondary in neck did not have constitutional symptoms. 18 cases (42.87%) out of 42 cases of tubercular etiology showed presence, while 3 cases (33.33%) out of 9 cases of secondaries in neck showed presence of symptoms. In comparison 8 cases out of 11 cases (72.72%) of reactive/chronic non/specific lymphadenitis showed presence of symptoms. Half the patients of lymphomas were positive for symptoms.

Table 2: Showing incidence of presenting symptoms

Presenting symptoms	No of cases	Percentage
Neck swelling	52	78.78
Fever	28	42.42
Change of voice	3	4.54
Cough	9	13.36
Malaise	12	18.18
Difficulty in swallowing	2	3.03
Loss of appetite	7	10.06
Loss of weight	15	22.72

In the present series neck swelling was the most common symptom, seen in 78.78% of cases, followed by fever in 42.42 % and malaise in 18.18% of the cases.

Table 3: Showing history of contact with tuberculosis in tubercular lymphadenitis cases

Contact with tuberculosis	Number of cases	Percentage
Positive	7	16.66
Negative	35	83.34
Total	42	100

Only few cases with tubercular lymphadenitis had a positive history of contact with tuberculosis. It was observed that on 7 cases (16.66%) out of 42 cases had a positive history.

Table 4: Showing site distribution of TB cervical lymphadenitis & lymphomas

	Number of cases (with percentage)	
	Tubercular lymphadenitis	Lymphomas
Level 2 (upper jugular group)	10(23.8%)	0
Level 3 (middle jugular group)	3(7.1%)	0
Level 4 (lower jugular group)	2(2.8%)	0
Level 5 (posterior triangle group)	14(33.33%)	0

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Level 6 (anterior compartment group)	1(2.4%)	0
More than one site in neck	11(21.2%)	4(100%)
Total	42	4

The neck lymph nodes were classified as levels and the involvement was studied for each category. Only tubercular and lymphomas are considered here. In the present series, it was observed that posterior triangle group was the commonest to get involved in tuberculosis (33.33%) followed by upper deep jugular group (23.8%). Levels 1, 3 and 4 were equally involved. About 30% cases had more than one site involvement.In comparison all 4 cases of lymphomas had more than one site involvement.

Table 5: Showing size of lymph nodes in tubercular cervical lymphadenitis

Size in cm in biggest diameter (of largest nodeif multiple)	Number of cases	Percentage
< 4	36	85.71
≥ 4	6	14.29
Total	42	100

It was observed that the majority of nodes affected in tuberculosis (78.4%) were less than 4 cm in size. The remaining (21.6%) were equal or more than 4 cm.Unilateral involvement of lymph nodes was observed to be more common. It was seen in 34 cases out of total 42 cases (81%). The remaining (19%) cases had bilateral involvement. In this study, tuberculosis had multiple node involvement in 26 cases (61.9%) while 16 cases (38.1%) showed single node involvement. Again in reactive lymphadentis 5 cases (62.5%) showed multiple node involvement as compared to 3 cases (37.5%) with single node. In chronic non/specific lymphadenitis 66.66% single nodal involvement observed. In malignant secondaries, 77.78% multiple nodal involvement was seen. In lymphomas, multiple lymph nodes were involved exclusively. body.condaries, 77.78% multiple nodal involvement was seen. In lymphomas, multiple lymph nodes were involved exclusively.Matting of lymph nodes was observed in 12 of the 42 cases (28. 58%).Tuberculous lymphadenitis presented more commonly as discrete lymph nodes which was present in 30 of the 42 cases (71.42%).

Table 6: Showing adherent/non7adherent lymph nodes in cervical lymph node lesions

	Number of cases	Percentage
Adherent	10 Secondaries–6 Tubercular–3 NHL–1	15.15
Non7adherent	56	84.85
Total	66	100

Out of the 66 cases studied only 10 cases (15.15%) presented with adherent nodes of which 6 were due to malignant secondaries, 3 tubercular adenitis and 1 non/Hodgkin's lymphoma.In the present study, it was observed that 24 (57.15%) cases had caseation in the lymph nodes. The remaining 18 (42.85%) cases had non/caseated nodes.

Table 7: Showing involvement of other lymph nodes (in addition to cervical lymph nodes) in cervical lymphadenopathy

Lymph node group	Tubercular		Reactive and CNSL		Lymphomas	
		%	No. of Cases	%	No. of Cases	%
Cervical + Axillary only	1	2.4	0	/	1	25
Cervical + Inguinal Only	0	/	0	/	1	25
Cervical + Axillary + Inguinal (Generalised)	0	/	0		2	50
Total	1		0		4	

It was observed that 1 (2%) case had axillary lymph node involvement, in total 12 (2.4%) cases of tubercular cervical lymphadenitis had lymph nodes elsewhere in the 1 cases (25%) of lymphomas had axillary lymph nodes enlarged while 1 (25%) case presented with inguinal lymph node enlargement in addition to cervical lymphadenopathy. 2 cases (50%) had generalised nodal involvement.

Table 8: Showing chest X7ray positivity in tubercular cervical lymphadenitis

Chest X7ray	Number of cases	Percentage
Positive	9	21.42
Negative	33	78.58
Total	42	100

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Only 9 (21.42%) cases had a positive chest X/ray in tubercular lymphadenitis while 33 (78.58%) cases were negative.

Table 9: Showing main types of lymphomas

Typesoflymphoma	Numberofcases	Percentage
Hodgkin'slymphoma	3	75
Non7Hodgkin'slymphoma	1	25
Total	4	100

Of the 4 cases of histpathologically confirmed lymphomas, 1 (25%) were Non/ Hodgkin's variety and 3 (75%) were Hodgkin's.

Table 10: Showing sensitivity and specificity of FNAC in Tuberculous cervical lymphadenitis

Sl.No.	ByFNAC	Numberofcases
1	Truepositive	36
2	Falsepositive	0
3	Falsenegative	6
4	Truenegative	24
	Total	66

True positiveSensitivity =x 100 True positive + False negative

True negativeSpecificity = x 100 True negative + False positive

Sensitivity = 86% Specificity = 100%

Out of the 42 histopathologically confirmed cases of TB cervical lymphadenitis, a diagnosis of tuberculosis was made in 36 cases by FNAC. There were no False Positive cases on FNAC. 24 cases were true negative for tuberculosis. The sensitivity and specificity of FNAC for diagnosing tuberculous lymphadenitis is therefore 86% and 100% respectively.

Table 11: Showing sensitivity and specificity of FNAC in diagnosing chronic non7 specific lymphadenitis

Sl.No.	By FNAC	Number of cases
1	True positive	3
2	False positive	3
3	False negative	1
4	True negative	58

Sensitivity = 75% Specificity = 95%

Table 12: Showing sensitivity and specificity of FNAC in diagnosing secondaries in cervical lymph nodes

Sl.No.	By FNAC	Number of cases
1	True positive	9
2	False positive	0
3	False negative	0
4	True negative	57
	Total	66

Sensitivity = 100% Specificity = 100%

Table 13: Showing sensitivity and specificity of FNAC in diagnosing lymphomas in cervical lymph nodes

Sl. No.	By FNAC	Number of cases
1	True positive	4
2	False positive	0
3	False negative	0
4	True negative	62
	Total	66

Sensitivity = 100% Specificity = 100%

Table 13: Showing haemoglobin levels of patients involved in the study

Hb level (g%)	Number of cases	Percentage
<10	30	45.45
≥ 10	36	54.55
Total	66	100

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36 cases (45.45%) of the 100 cases studied had a haemoglobin level of < 10 g% while 36 (54.55%) cases had a haemoglobin of ≥ 10 g%. 25(59.53%) cases of the 42 cases of tubercular lymphadenitis had an ESR of ≥ 20 mm/hr.

Treatment

In the present study all the 42 cases proved as tubercular were treated with DOTS as per the RNTCP guidelines from the RNTCP centre at our hospital. As per the WHO guidelines, tubercular lymphadenitis comes under category/III for which the treatment regimen is as follows:Intensive phase / 2 months Isoniazid, Rifampicin and Pyrazinamide – (HRZ)3 Continuation phase – 4-month Isoniazid and Rifampicin – 4(HR)3 of the 42 tubercular cases, 3 cases had active pulmonary lesion (new sputum positive) and as per WHO guidelines comes under category/I. These patients were treated with 2(HRZE)3 + 4(HR)3 regimen. The patients who presented with abscess were drained surgically and those presented with sinus underwent excision of sinus in addition to chemotherapy.Out of the 66 patients 4 cases did not come for regular follow/up. 0f the 62 cases who came for follow/up regularly, 49 cases the nodes resolved uneventfully. In the remaining 13 cases, 4 cases developed fresh nodes which later resolved on continuing the treatment. 2 cases developed abscess which was evacuated. At the end of therapy, 4 cases (8.9%) had residual lymph nodes. All these cases were lost to follow/up after completion of 6 months' chemotherapy. The initial treatment for the 11 cases diagnosed as reactive and chronic non/specific lymphadenitis commenced with antibiotics which are active against gram positive bacteria. In the present study, a 10/15 days' course of penicillin group or macrolide group of antibiotics was prescribed and the clinical course observed. Those presenting with suppurative lymphadenitis underwent incision & drainage (4 cases). Appropriate cultures were obtained. In 1 case no response was seen and the node was excised under local anaesthesia. Of the 9 cases diagnosed as malignant secondaries in cervical lymph nodes, 2 cases had primary in the larynx, 1 each from Papillary Ca thyroid, Sq cell carcinoma Lower Lip, Carcinoma tongue, Carcinoma Pyriform fossa, Carcinoma Stomach (Stage IV, inoperable) and remaining 2 had an unknown primary. One case with primary in the larynx had a massive (>6) bilateral nodes (fixed), was inoperable. The other case of primary in larynx had a unilateral 2/3cm muntiple adherent nodes underwent MRND with appropriate surgery for the primany lesion. The cases diagnosed with primary in the Thyroid and Lip were operated upon at our hospital, both underwent Selective neck dissections with appropriate surgery for the primary Tumour. Remaining cases were referred to MNJ Cancer Institute,for Radiotherapy, Chemotherapy & Radical Surgery. All the 3 patients were followed up during the study period. And two patients who had inoperable Carcinoma Larynx and stage IV Carcinoma Stomach expired during the follow/up period. 3 cases of lymphomas were referred to medical Oncology deptartment, MNJ Cancer Institute.

DISCUSSION

In the present study, out of 66 cases of cervical lymphadenopathy, 53 were non/ neoplastic lesions (80.3%) and 13 (19.7%) were neoplastic lesions. These are incidence of non/neoplastic and neoplastic lesions was 90.6% and 9.4% respectively. In the present series, tuberculosis accounted for 63.63% of cases, 12.12% turned out to be chronic non/specific lymphadenitis and 4.54% reactive lymphadenitis. Among the neoplastic lesions, malgnant secondaries accounted for 13.36% and Hodgkin's lymphomas for 4.54% each, while non/ Hodgkin's lymphoma comprised the remaining 1.51%. Similar observations were made by Watt B et al.[3] who studied 94 cases, of which tuberculosis was confirmed in 63.8% cases. The findings observed by Jindal N. et al., Nataraj G. et al., Guo B et al.[4] are also comparable with the present study. The lower incidence of tuberculosis in study by Vasan RS et al.[5] is probably because the patients were from non/prevalent areas. In the study by Jha B.C. et al., the commonest age group involved was 11/20 years, while study by Sahana SN et al.[6] had 72% cases in the age group of 11/30 years, which is comparable with the present study. The study by Kim L.H. et al. comparable with present study, as it had maximum number of cases between 20/50 years of age. Of the 66 cases, 35 cases were males 31 females. The sex ratio in the present study was 1.13:1 (M: F). Most of the studies show female predilection. Few studies like Purohit. S. D. et al. and Tripathy. S. N. et al. are comparable with this study. In the present study, only 42.8% of the cases with tuberculosis had constitutional symptoms. Similarly, only 33.33% of cases with malignant secondaries had symptoms. In comparison 72.7% & 50% presented with symptoms in reactive/nonspecific lymphadenitis and lymphomas respectively. Similar observations were made by JHA B. C et al and Jindal N. et al.[7]In the present study, the Memorial Sloan/Kettering Hospital classification of neck lymph nodes from level 1 through level 7 was utilized. It was observed that in tuberculosis, the level 5 (posterior triangle group) was most commonly affected (33.3%) followed by level 2 (upper jugular group) at 23.8%. About 11 cases (21.2%) had more than one site involved in the neck. In contrast, all cases (100%) of lymphoma had more than one site involvement. In the Jha B.C. et al. series, upper deep jugular group was the most commonly involved. In Richard S Snell et al.[8]79 study posterior triangle was the commonest at 51% (comparable to the present study). In the Manolidis S. study anterior triangle (excluding submandibular) was the most commonly involved (35.1%), similar percentage had

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multiplesite involvement. Posterior triangle (including supraclavicular) came next with 9.1% (again, comparable with present study). In the Jha B. C. et al study, multiple matted nodes were seen in 23 patients out of 60(38.3%), single discrete nodes were seen in 18 patients (30%). Discharging sinus and abscesses were uncommon. In the Baskota et al series, 83% cases had unilateral involvement of neck with single group only at 68%. In the agarwal P. et al study, single group involvement of neck was seen in 48.6% cases. In the Dworski I. study, unilateral involvement was seen in 87%. The present study had unilateral involvement in 81% cases with discrete nodes in 19% cases (comparable with above studies).Caseation was seen in 28.57% of tubercular cases in the present study comparable with Bedi R.S. study (39%). Chest X/ray positivity was seen in 21.5% cases of present study (comparable with Paneker C et al.[9] series where 28.3% had positivity, and Jha B.C. et al. series with 16%). In the present study Non/Hodgkin's lesion:Hodgkin's lesion ratio is 1:3. While findings by Peh S.C. and Shamine et al. had a ratio of 9:1. Raymond Alexandrian study had a ratio of 5.02:1.The commonest site of primary in a case of malignant secondary was lungs and pancreas in the studies by Linderman et al. and Osama Lipscomb et al.[10] In the present study it was larynx and thyroid. In the study by Osama Gaber et al., it was possible to establish primary in 86.7% whereas in the present study it was only 77.77%, this was because of limited resources available in the hospital. The study by Farhi DC et al.[11] reported a sensitivity of 92.8% in diagnosing tubercular lymphadenitis. The study by Chao S.S., Loh K.S. et al. showed sensitivity of 88% and specificity of 96% for thesame. Similarly, Ilkay Kazak, et al.[12] reported a sensitivity of 83% for tuberculosis. Dasgupta A. et al.[12] reported a sensitivity of 84.4% for tuberculosis and 89% for malignant secondary deposits. In a larger series of 444 cases, Tarshis et al.[13]83 reported 100% sensitivity in diagnosing tubercular and pyogenic lymphadenitis, and also Hodgkin's disease, 98% for metastatic deposits; 97% for chronic non/specific lymphadenitis; 92% for Non/Hodgkin's lymphomas. After studying 2216 cases, Les White et al.[14] noted sensitivity and specificity of 84% and 95% respectively for tubercular lymphadenitis; 97% and 99% for metastatic deposits; 80% and 98% for Hodgkin's disease; 81% % and 96% for Non/Hodgkin's lymphomas Elizabeth Grabb Breen.[15] Comparable observations were made in the present study.

CONCLUSION

Tuberculosis is an important disease, one of the commonest disease affecting lymph nodes, it is curable with antituberculous drugs if administered as per the accepted regimen.Clinical symptoms in cervical lymphadenopathy has limited significance and clinical behaviour can be highly variable. Dependence on clinical evidence alone would lead to erroneous diagnosis in a considerable number of cases.Most of the diseases are medically curable with limited role for surgery in non/ neoplastic lesions.Cervical lymphadenopathy is an important disease, commonly come across, and always calls for meticulous attention, analysis and treatment.

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