Diagnostic value of cervical lymphadenopathy in the detection of underlying pulmonary diseases

Waleed M. Hussen[a], Ali Naif[b]

[a]Department of Thoracic and Vascular, College of Medicine, [b]Department of Thoracic and Cardio-Vascular, Bn Al-Bitar Hospital, Baghdad, Iraq

Correspondence to Prof. Dr. Waleed Mustafa Hussen, MBChB, MS, FIBMS (Th.C.V.S.), FACS, MRCS, FRCS (Glasgow), Chairman of the scientific council of Thoracic and Cardio-Vascular surgery, Iraqi board of medical specializations, Head of the Department of Thoracic and Vascular Surgery, Consultant Thoracic and Vascular Surgeon, College of Medicine, University of Baghdad. Medical City Teaching Hospital Baghdad, Iraq. Bab Almudham P.O.Box 61335. C.N 12114. Mob: 00964 7901327452; e-mail: dr_waleedmustafa@yahoo.com

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Background
Cervical lymphadenopathy is usually defined as cervical lymph nodal tissue measuring more than 1 cm in diameter, and can be caused by benign local or generalized infection, but occasionally, it might herald the presence of a more serious disorder such as malignancy. Cervical lymphadenopathy can be soft, firm, or stony hard according to the disease process by which they involved. Clinical examination, radiological studies, and biopsies can lead to a definitive diagnosis.
Aim
This work aimed to study in detail the results of cervical lymphadenopathy that was removed surgically, and its value in detecting pulmonary diseases (i.e. to analyze the pathological spectrum of variant benign or malignant diseases affecting the cervical lymph node).
Patients and methods
This was a prospective and retrospective study of 32 patients who presented with respiratory symptoms discovered during a physical examination to have cervical lymphadenopathy, were admitted, and were treated surgically at Al-Shaheed Ghazi El-Hareri Hospital of the Medical City Teaching Complex during the period from 1 July 2014 to 30 June 2015. Proper assessment of history and clinical examination, in addition to radiological studies and biopsy analysis, were performed to analyze the causes of cervical lymphadenopathy.
Results
Twenty-one of our patients were males; the remaining 11 patients were females. The youngest patient was a 10-year-old male and the oldest patient was a 50-year-old male. Fever was the most common presenting feature in 26 patients. All patients were referred for neck ultrasound to detect the size of the enlarged nodes; 23 patients had a lymph node diameter of more than 1 cm. Chest radiography was performed for all patients; it was found that 22 patients had central lesions (closed to the hilum). Computed tomography-chest showed pleural effusion in 18 patients, lung masses in 16 patients, and mediastinal masses in nine patients.
Conclusion
Cervical lymph node involvement has a major impact on the prognosis and treatment decision in patients with pulmonary malignancy.

Keywords:
cervical lymph nodes, cervical lymphadenopathy, excisional biopsy, lymph node enlargement

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Introduction

An enlarged cervical lymph node can have different pathology, may be a benign, or may denote an underlying malignant process. Lymph nodes are groups of specialized cells that represent a division of the defense system in the human body. The body has ~600 lymph nodes, and their locations are scattered around ports of entry as well as major vessels. The peripheral groups are those readily palpable by clinical examination, and routinely looked for, but only those in the submandibular, axillary, or inguinal regions may normally be palpable in healthy individuals [1].

The lymphoid organs contain lymphocytes and other cells that are responsible for the body's immunity. The bone marrow and thymus are called primary lymphoid organs because they are the sites for the generation of B lymphocytes and T lymphocytes. Lymph nodes, spleen, and mucosa-associated lymphoid tissue, including tonsils, the appendix, solitary lymphoid nodules, and Peyer patches of the ileum, are the secondary lymphoid organs. Lymph nodes are present throughout the body and distributed along the path of the lymphatic vessels. They are bean shaped and encapsulated. Lymph nodes act as filters for the lymph; histologically, a lymph node consists of a cortex, a para-cortex, and a medulla. The most

common cells in lymph nodes are lymphocytes, macrophages, plasma cells, follicular cells, and reticular cells [2].

The distribution of cervical lymph nodes is shown in Fig. 1 [3].

Causes of cervical lymphadenopathy

The causes of lymphadenopathy are essentially because of either an immune response to infective agents or inflammatory cells in infections. Moreover, it may occur because of infiltration of neoplastic cells. Alternatively, primary neoplastic proliferation of lymphocytes may be the underlying pathology of lymphadenopathy [1]. The causes may be bacterial such as streptococcal pharyngitis, diphtheria, and brucellosis, viral such as mumps, HIV, and herpes simplex, or mycobacterial such as tuberculosis, fungal such as histoplasmosis, protozoal infections such as leishmaniasis, neoplastic such as lymphoma, leukemia, and squamous cell cancer of the head and neck or metastatic, or lymphoproliferative disorders such as autoimmune lymphoproliferative diseases, connective tissue diseases such as SLE, immunological such as drug reaction, and miscellaneous such as sarcoidosis.

Clinical features of abnormal lymph node enlargement

Abnormal lymph node enlargement tends to commonly result from infection/immune response, cancer, and less commonly because of infiltration of macrophages filled with metabolite deposits (e.g. storage disorders). Infected lymph nodes tend to be firm, tender, enlarged, and warm. Inflammation can spread to the overlying skin, causing it to appear reddened. Lymph nodes harboring malignant disease tend to be firm, nontender, matted, and fixed, and increase in size over time.

Nodes are generally considered to be normal if they are up to 1 cm in diameter; however, some authors suggest that epitrochlear nodes larger than 0.5 cm or inguinal nodes larger than 1.5 cm should be considered abnormal [4,5].

In children, lymph nodes larger than 2 cm in diameter (along with an abnormal chest radiograph and the absence of ear, nose, and throat symptoms) were predictive of granulomatous diseases (i.e. tuberculosis, cat-scratch disease, or Sarcoidois) or cancer (predominantly lymphomas) [6].

An increase in nodal size on serial examinations is significant. Hence, nodes that continue to grow in size are important and those that regress in size tend to be more reassuring when a lymph node rapidly increases in size, its capsule stretches, and causes pain. Pain is usually the result of an inflammatory process or suppuration, but pain may also result from hemorrhage into the necrotic center of a malignant node. Stony-hard nodes are typically a sign of cancer, usually metastatic.

Very firm, rubbery nodes suggest lymphoma. Softer nodes are the result of infections or inflammatory conditions. Suppurant nodes may be fluctuant. A group of nodes that feels connected and seems to move as a unit is considered to be 'matted.' Nodes that are matted can be either benign (e.g. tuberculosis, sarcoidosis, or lymphogranuloma venereum) or malignant (e.g. metastatic carcinoma or lymphomas). Constitutional symptoms such as fever, weight loss, fatigue, or night sweats could suggest disorders such as tuberculosis, lymphoma, collagen vascular diseases, unrecognized infection, or malignancy.

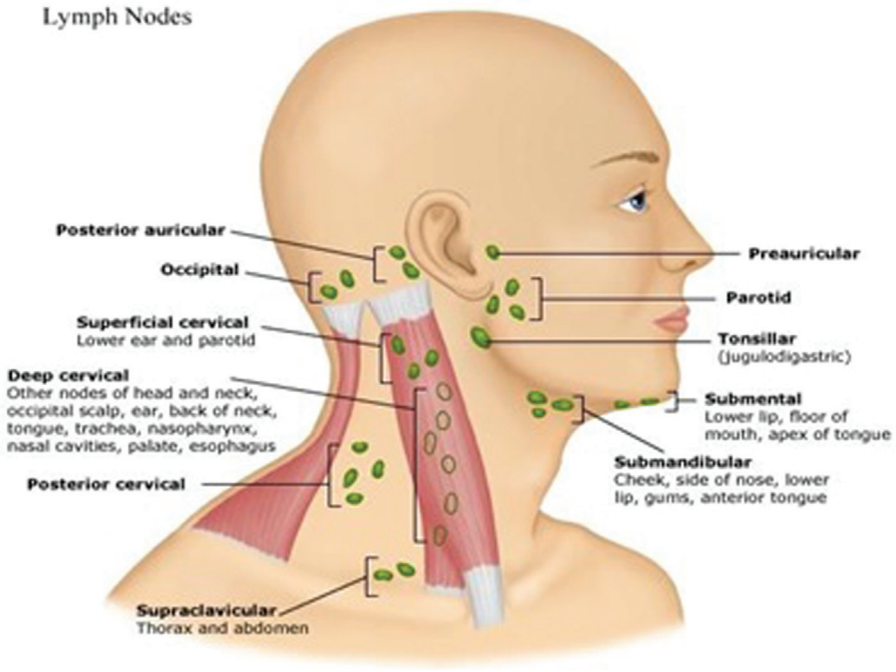
Diagnosis

Ultrasound is a useful imaging modality in the assessment of cervical lymph nodes. Useful features include size, shape, and status of echogenic hilum, micronodular appearance, intranodal necrosis, and calcification. Adjacent soft tissue edema and matting are particularly useful to identify tuberculosis. It can be combined with fine-needle aspiration cytology in which a sample of cells from the lymph node is aspirated using a needle and examined under the microscope. Ultrasound is a useful imaging modality in the evaluation of cervical lymphadenopathy because of its high sensitivity (98%) and specificity (95%) when combined with fine-needle aspiration cytology [7].

Computed tomographic scans can detect the presence of enlarged cervical lymph nodes with a short-axis diameter of 5 mm or greater [8].

Excisional biopsy remains the diagnostic procedure of choice in the delivery of timely and appropriate medical care to patients presenting with lymphadenopathy. It can be done under local or general anesthesia. Lymph nodes should ideally be completely excised rather than incised to avoid contaminating the neck with cancer cells of an unsuspected cervical metastasis. Such a biopsy can lead to certain complications that include bleeding, infection, lymph leakage, and seromas. Bleeding at a biopsy site can be controlled usually with direct pressure. Infection at a biopsy site will appear 5–10 days postoperatively, and may require opening of the wound to drain the infection. Seromas or lymphatic leaks resolve with aspiration of

Figure 1



Lymph nodes of the head and neck and their drainage areas [3].

seromas and the application of pressure dressings, but may require repeated treatments [9].

Patients and methods

This is a prospective (21 patients) and retrospective (11 patients) study of 32 patients presenting with respiratory symptoms discovered during physical examination to have cervical lymphadenopathy and were thus admitted and treated surgically in the thoracic surgery department at Al-Shaheed Ghazi El-Hareri hospital of the medical city teaching complex during the period from 1 July 2014 to 30 June 2015.

Study design

Data of the patients were collected from patients' records and surgeon notes, and then analyzed in terms of their age, sex, presenting features, characteristics of the lymph nodes, imaging study (chest radiography, computed tomographic-findings, and ultrasound), examination, and procedures performed such as bronchoscopy, chest tube thoracostomy insertion, incisional, or excisional biopsy. Surgery was performed under general anesthesia or local anesthesia (for patients in whom general anesthesia is not suitable or for children) and after opening the skin, subcutaneous tissue, splitting of the platysma muscle, and investing layer of deep cervical fascia, lymph node either totally removed or pieces of it, if it is attached or adherent to major vessel. Also, the obtained histopathological reports and any associated morbidity and mortality, and their follow-up were studied.

Results

Twenty-one (65.6%) of our patients were male and the remaining 11 (34.4%) patients were female. The youngest patient was a 10-year-old male and the oldest patient was a 50-year-old male. The mean age of the patients was 37 years.

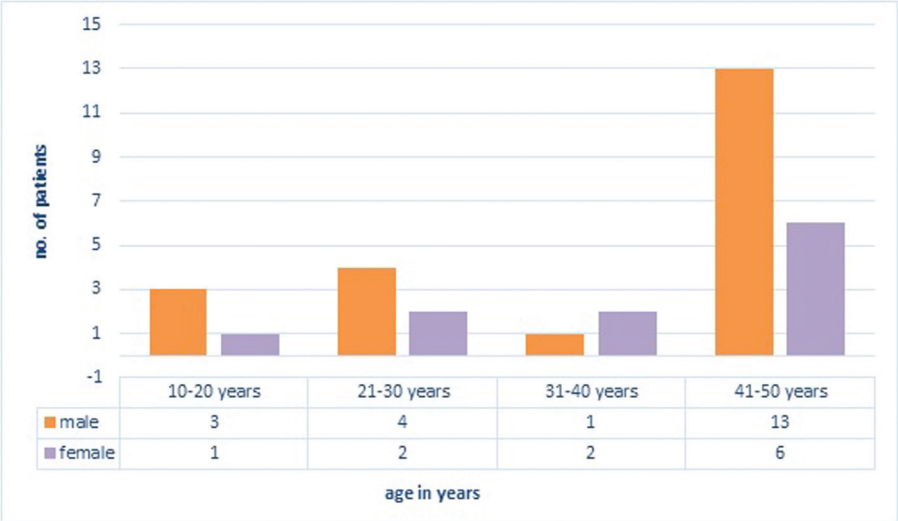
The distribution of the patients in terms of their age and sex is shown in Fig. 2.

Fever was the most common presenting feature in 26 (81%) patients, and 24 (75%) patients presented with neck swelling. The distribution of clinical features is shown in Table 1.

The characteristics of the examined lymph nodes were not documented in detail in the patients reports; however, in 26 (81.25%) of the patients examined, the nodes were matted together, whereas in six (18.75%) patients, the lymph nodes were mobile and discrete. Also, 31.25% of the patients had painful lymph nodes.

All patients were referred for neck ultrasound to detect the size of the enlarged nodes; 23 (71.8%) patients had a lymph node diameter of more than 1 cm, and the rest

Figure 2



Age and sex distributions.

Table 1 Clinical features

Clinical feature	*n* (%)
Neck swelling	24 (75)
Hoarseness of voice	13 (40.6)
Chest pain	8 (25)
Cough	16 (50)
Fever	26 (81)
Loss of weight	20 (62)
Loss of appetite	24 (75)
Night sweating	13 (40.6)
Painful lymph node	10 (31.25)

of the patients were had enlarged lymph nodes less than 1 cm in size.

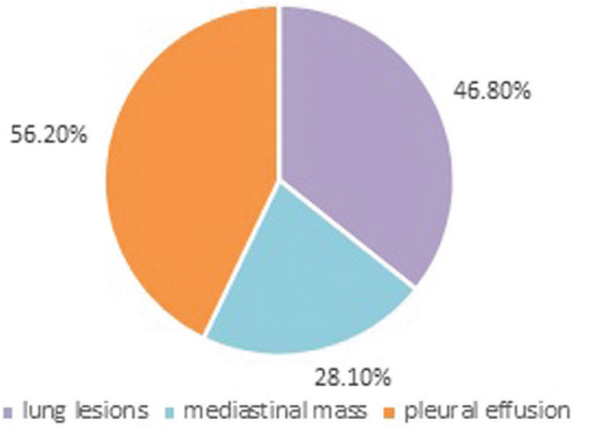
The posterior lymph node group and the right supraclavicular group were the most common sites for lymph node enlargement: 75 and 50% (24 vs. 16 patients, respectively). In 25% of the patients, both groups were involved.

In addition, splenomegaly was found during clinical examination in 10% of the patients.

All of our patients had significant findings in their chest radiography: either central lesions (closed to hilum), which were present in 22 (69%) patients, or peripheral lesions, which were found in 10 (31%) patients, and pleural effusion, which was found in 11 (34.3%) patients.

Computed tomography-chest was performed for all patients: pleural effusion was found in 18 (56.2%) patients, parenchymal lung masses in 15 (46.8%) patients, and mediastinal masses in nine (28.1%) patients as shown in Fig. 3.

Figure 3



Computed tomography-chest findings.

In 21 (65.6%) patients, surgery was performed under general anesthesia and in the remaining 11 patients (34.4%) patients, surgery was performed under local anesthesia.

The obtained histopathological reports of the removed specimen are shown in Table 2, which shows that 19 (59.3%) patients had metastatic adenocarcinoma of primary pulmonary origin.

Three of our patients had venous bleeding, which was controlled immediately by pressure or by suturing with proline 0/4. The rest of our patients went uneventful course, with no mortality. The results of the

Table 2 Results of biopsy

Results of biopsy	*n* (%)
Adenocarcinoma	19 (59.3)
Tuberculosis	6 (18.57)
Lymphoma	4 (12.5)
Reactive hyperplasia	3 (9.3)

histopathological reports obtained and their percent are shown in Table 2.

The patients with metastatic adenocarcinoma were referred to the oncologist for further treatment, as they are beyond surgery. Patients with positive biopsy for tuberculosis were referred to the tuberculosis center. The patients diagnosed with lymphoma were referred to a hematologist. The remaining patients were administered supportive and symptomatic treatment.

Discussion

Cervical lymphadenopathy is not uncommonly discovered during routine examination for patients referred or admitted to our thoracic and vascular department of Al-Shaheed Ghazi El-Hareri hospital with the complaint of respiratory symptoms, with a suspicion of underlying infection or malignancy that necessitates some surgical procedures such as tube thoracostomy or bronchoscopy.

In the present study, males were affected more than females: 65.6 versus 34.4% respectively; this was comparable with the results of Mohan *et al.* [10] they demonstrated their results as 71.5, (28.4% to male versus female respectively.

Age is an important factor because it enables prediction of the likelihood of the presence of a benign versus a malignant process. In our study, lymphadenopathy was present because of a malignant process mostly in patients in the age group of 40–50 years, whereas the other nonmalignant causes of enlarged cervical lymph nodes were present in patients younger than 40 years of age; this is in agreement with the results of Hines *et al.* [11], who showed that in patients younger than 30 years of age, lymph node enlargement is because of benign underlying processes in ~80% of the cases, whereas in individuals older than 50 years of age, it is because of a malignant process in ~60% of the cases.

Usually, pain is the result of an inflammatory process or suppurations of the lymph node, and can be explained by stretching of the lymph node capsule as a result of a rapid increase in size [12]. The three (9.3%) patients with reactive hyperplasia had painful nodes. Nevertheless, pain may also result from bleeding into a necrotic center of a malignant node [13]. About seven patients with malignant lymph nodes, were painful, due to direct invasion of the skin. Therefore, it should be stressed that the history of painful lymphadenopathy is commonly reassuring, but this does not always necessarily suggest a benign cause.

The size of the node can be considered a significant factor. Normal nodes are generally less than or up to 1 cm in diameter. However, in one series of 213 adults with unexplained lymphadenopathy, no patient with a lymph node smaller than 1 cm had malignancy compared with 8 and 38% of those with nodes 1–2.25 cm and more than 2.25 cm in size, respectively [12,14]. This is in agreement with our results; all of the nodes of malignant enlargement were more than 1 cm in size.

Right supraclavicular lymph node enlargement is associated with malignancy in the mediastinum, lungs, or esophagus. The posterior cervical lymphadenopathy also carries a much higher risk for malignancy than anterior cervical lymphadenopathy [1,15]. This is in agreement with the results of our study, which showed that all of the enlarged nodes because of metastatic adenocarcinoma and lymphoma had posterior cervical lymphadenopathy, and 16 (50%) patients with metastatic adenocarcinoma had right supraclavicular lymphadenopathy.

In terms of the consistency of the lymph node, our results showed that 81.2% were hard and matted, and 18.8% were soft and mobile. These results are comparable with the epidemiological data of the lymph node, which showed that soft and fluctuant nodes are usually the result of infection or reactive hyperplasia. Firm nodes suggest lymphoma and metastatic nodes are usually stony hard. Matting of the nodes can occur in tuberculosis, lymphoma, or metastatic carcinoma [1,12].

Splenomegaly or hepatomegaly can occur concomitantly with lymphadenopathy in case of lymphoma; this can be the cause of splenomegaly that was present in 10% of our cases; all of them were because of lymphoma.

Chest radiography and computed tomographic scan (most accurate) are essential investigations in the evaluation of chronic localized and generalized lymphadenopathy, and may indicate mediastinal

widening because of lymphadenopathy from lymphoma, and up to two third of patients who have mediastinal lymphoma may show mediastinal widening on the chest radiography [2]. This is in agreement with our study, which shows that 22 (69%) patients had lesions closed to the hilum in chest radiography.

The presence of malignancy, which is the most serious cause of lymphadenopathy, is quite low among the generalized population with lymphadenopathy (as low as 1.1% or even lower) [1,2,11]. This is not in agreement with our study (adenocarcinoma 59.3%), but it must be stated that our study was carried out in a tertiary specialized center; hence, most of the cases were referred from other hospitals because of a high suspicion of a malignant process. Therefore, the increased percentage of malignancy discovered on biopsy results is expected. This explanation can be reinforced by a statistical study carried out by Lee *et al.* [16] that shows that lymph nodes biopsy has indicated malignancy in as many as 40–60% of cases in a referred center.

Three of the patients developed bleeding during surgery and were treated by pressing or suturing of the injured vessel, and all the patients had smooth postoperative period. The reported complications of surgery in patients with cervical lymphadenopathy that have been reported by us have not been reported in any other study.

Conclusion

Cervical lymph node involvement has a major impact on the prognosis and treatment decision in patients with pulmonary malignancy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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