

PROSPECTIVE DESCRIPTIVE STUDY OF NON-THYROIDAL NECK SWELLINGS IN WESTERN INDIAN POPULATION

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Background. *Nonthyroidal neck swellings are common and cause diagnostic challenges. This study highlights various diagnosis associated with non-thyroidal neck swellings and their management challenges.*

Objective. *This pilot study highlights the various diagnosis associated with nonthyroidal neck swellings and their management challenges. The clinical spectrum of two most common aetiology of nonthyroidal neck swelling: tubercular cervical lymphadenopathy and lymphomas, are also compared.*

Methods. *This prospective study was conducted in a tertiary care teaching hospital from 01 Jun 2018 to 31 Dec 2019. The first 100 nonthyroidal neck swellings presented to the surgical outpatient department were included and assessed clinically, radiologically and histopathologically. Comparison was carried out between the first two common diagnosis of tubercular cervical lymphadenitis and lymphoma. Continuous variables were analysed using Student's t-test and categorical data were analysed using the Chi square test. A statistical p value <0.05 was taken as significant.*

Results. *There were 73 lymph node swellings and 27 non-lymph node swellings in the study. The most common diagnosis was tubercular cervical lymphadenitis (n=38) and lymphoma (n=17). The mean volume of lymph nodes in the lymphoma group (38.72±22.12 cm³) was significantly bigger than in the tuberculosis group (9.44±5.99 cm³) P=0.00001. The mean age (33.81±11.8 years) of tubercular patients was significantly less than the lymphoma (52.38±25.3 years) with P=0.000167. The clinical diagnosis was nearly accurate in 85% of cases. However, in 15 cases clinical diagnosis was changed after fine needle aspiration cytology.*

Conclusions. *Ultrasonography and fine needle aspiration cytology are very useful adjunct in arriving at a definite diagnosis of a lymph node swelling in neck. Tubercular cervical lymphadenopathy and lymphoma were two major diagnosis. Tubercular cervical lymphadenopathy is significantly different from lymphomas in terms of early age of presentation and smaller size at the time of presentation.*

KEYWORDS: neck mass; cervical; lymphadenopathy; tubercular; lymphoma.

Introduction

Neck swellings are commonly seen in the general surgery outpatient departments. Cervical lymphadenopathy constitutes around half of these swellings. Thyroid swellings are the next common neck swelling which account for 32% of all neck mass [1]. Non thyroidal neck swellings are varied and sometimes cause diagnostic dilemma. There are many more diagnostic variants, emerging diseases and diagnostic surprises when managing nonthyroidal neck mass. This pilot study highlights various diagnosis associated with nonthyroidal neck swellings and their management challenges. This study also compares the clinical

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spectrum of two most common aetiology of nonthyroidal neck swelling: tubercular cervical lymphadenopathy and lymphomas.

Methods

This prospective study was conducted in a tertiary care teaching hospital in Western India from 01 Jun 2018 to 31 Dec 2019. The first 100 nonthyroidal neck swellings presented to the surgical outpatient department were included in the study. The exclusion criteria were symptom that lasted less than one week, thyroid swelling, known primary with lymph node metastasis and recurrent swelling of neck. All patients were scrutinised with detailed history and clinical examination in a well-lit room. All swellings were classified into a lymphnodal swelling and non-lymphnodal swelling. After

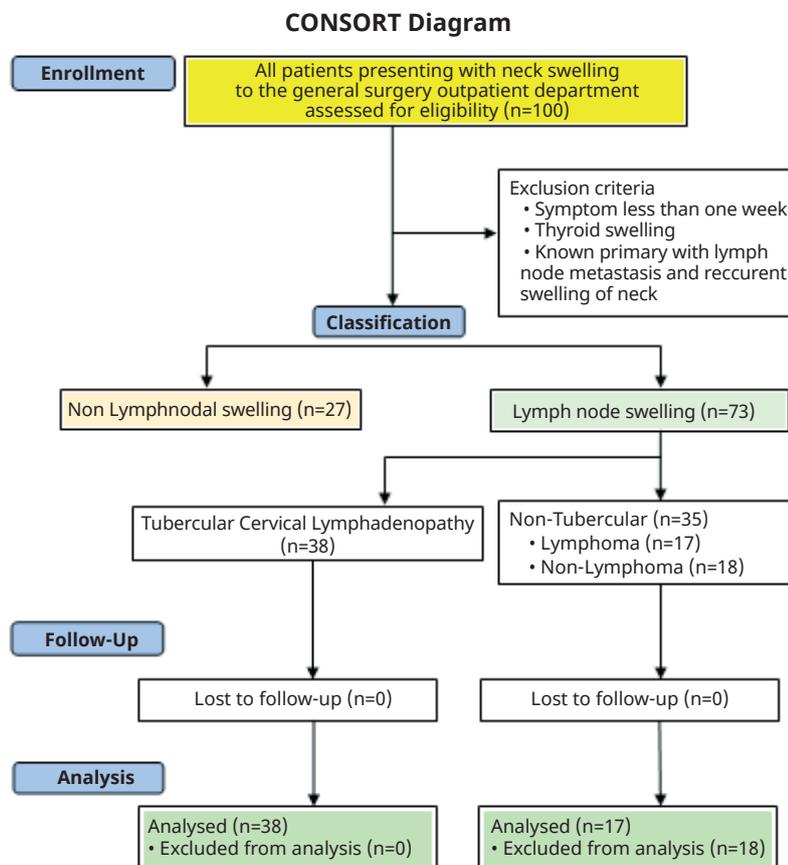
clinical examination all patients with lymph node swelling underwent haematological examination for complete hemogram and base line biochemistry tests. Three sputum samples, two early morning and one routine was sent for Acid Fast Bacilli as per recommendations. Further tests and management were based on the hospital protocol as summarised in the consort diagram.

Radiological examination included ultrasonography for neck and chest radiogram posteroanterior view. All ultrasonography was performed in the dept of radiology by consultant radiologists in a Siemens 4D Ultrasound machine using multi frequency linear array probe. Chest X-ray was performed according to the standard protocol for posteroanterior view. All chest X-rays were studied for presence of tuberculosis and malignancies. All patients underwent fine needle aspiration cytology (FNAC) either free hand or USG guided for histopathological diagnosis. FNAC was performed under aseptic condition using a 23-gauge needle fitted to 10 ml disposable syringe attached to a plunger. If the FNAC findings were inconclusive, an excision biopsy was contemplated. All non-lymph node swellings also underwent surgical excision and specimen were

sent for histopathology. A final diagnosis was made with histopathological examination of the excision biopsy or of the specimen in all 100 cases. No immunohistochemical studies were carried out. Comparison was also carried out between the clinical and final histopathological diagnosis. Computed tomography and magnetic resonance imaging were done in selected cases, in our study only for 16 cases, where the ultrasound and FNAC were inconclusive or additional information was required.

Benign cases were managed medically or surgically depending upon aetiology but for malignant lesions, if primary - detected definitive treatment was carried out with radical excision and appropriate neck dissection. However, in cases of unknown primary, options of chemotherapy/radiotherapy/surgery were explored based on a case to case basis and existing protocols of the hospital.

Statistical analysis was completed using IBM SPSS Version 26. For data with normal distribution the Levene's test of equity of variance was performed. Means of continuous variables were analysed using the Student's t-test for statistical significance. Categorical data were analysed using the Chi square test. A statistical p value < 0.05 was taken as significant.



Results

A total of first 100 cases of nonthyroidal neck swellings were included in this study. There were 61 men (61%) and 39 women (39%). The mean age was 39.14 ± 16.9 (range 1-76 years). The majority of the patients were in the third and fourth decade of life (47%). Duration of the swelling was variable with 68% cases having a short duration of one to six weeks and 32% cases with swelling more than 6 weeks. Most of the patients (42%) presented in first two weeks of swelling onset and had reactive lymphadenopathy managed with antibiotics.

The commonest associated symptom was fever of low grade (42%), non-productive cough (18%) and weight loss (14%). A typical evening rise of temperature was evidenced in 26% of cases. Brief spell of fever at the onset was reported in 14% cases. Only five cases presented with specific complaint of loss of appetite, in rest of the cases it was either associated with fatigue, night sweats or dysphagia. The rest 46% of patients had no associated symptoms. The majority of swellings were unilateral 56%, and 44% were bilateral. Only 22% cases presented with a solitary swelling, and 78% cases – with multiple swellings. The majority of swellings (47%) were in range of 1-3 cm (60%). There were 24 cases of swelling size of 3-5 cm and 29 cases with swelling of more than 5 cm.

In our study, 73% were lymph node swelling and 27% were non-lymph node swelling. The majority of the lymphnodal swelling were clinically and histopathologically diagnosed to be benign. There were more cases of cervical

tubercular lymphadenitis (n=38) compared to non-tubercular cervical lymphadenitis (n=35). It is pertinent to mention that the incidence of tuberculosis infection in this part of the country is 210 per one lakh population. The commonest non-tubercular cervical lymphadenitis were lymphoma (n=17) followed by reactive lymphadenopathy (n=8), carcinoma of unknown primary (n=4), HIV associated lymphadenopathy (n=4) and one patient each of Kikuchi Fujimoto disease and cat scratch disease (Fig. 1-3). The incidence of lymphoma in this part of the country is 2.5 per 100000 population.

The mean volume of lymph nodes in the lymphoma group ($38.72 \pm 22.12 \text{cm}^3$) was significantly bigger in the tuberculosis group ($9.44 \pm 5.99 \text{cm}^3$) with $P=0.00001$. It was also seen that the mean age (33.81 ± 11.8 years) of tubercular patients was significantly lower than the lymphoma (52.38 ± 25.3 years) with $P=0.000167$. There was no statistical significance in any other parameter among these groups (Table 1).

The clinical diagnosis was nearly accurate in 85% of cases. However, in 15 cases the clinical diagnosis was changed after FNAC and a new pathology was discovered that changed the complete line of management. They were six cases of tubercular lymphadenitis, three cases of metastatic lymphadenopathy, and one case each of lymphangioma, neurofibroma, carotid body tumour, adenoid cystic carcinoma and inflamed branchial cyst.

There were 27 non-lymph node swellings and they were lipoma (n=6), sebaceous cyst (n=6), salivary gland tumour (n=6), branchial



Fig. 1. A – cervical tubercular lymphadenopathy Level 5; B – cystic hygroma; C – metastatic carcinoma mass in neck; D – dermoid neck; E – cold abscess; F – Kikuchi Fujimoto disease.

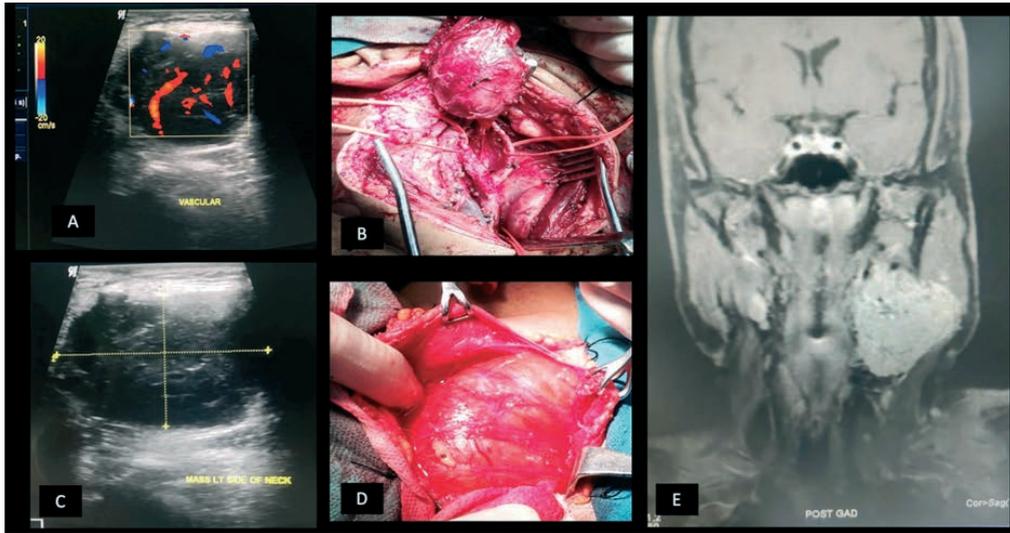


Fig. 2. Investigation and operative pictures: A - vascular doppler neck mass - carotid body tumour; B - intra-operative image of carotid body tumour; C - ultrasonography neck showing cystic hygroma; D - intra-operative image of neck nymphangioma; E - MRI right sided carotid body tumour.

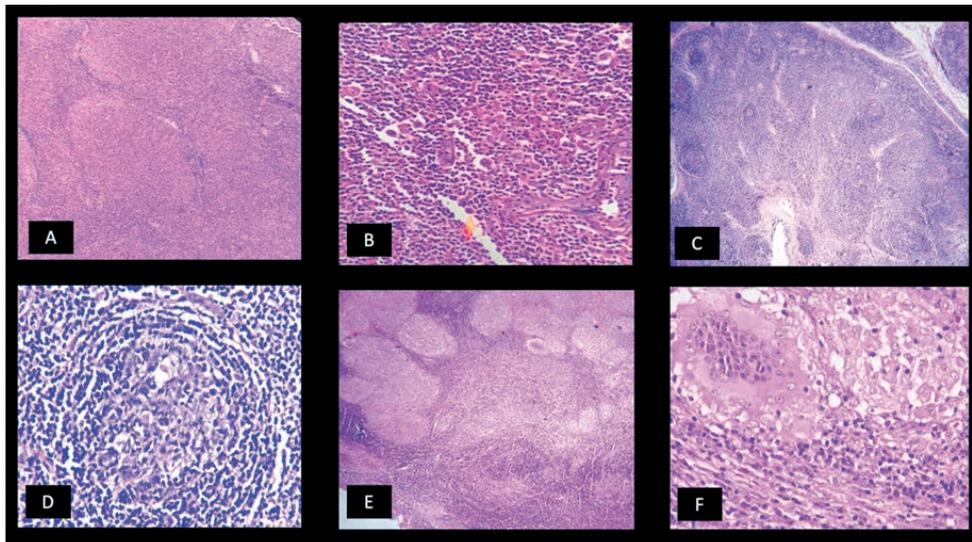


Fig. 3. Histopathological findings: A - follicular lymphoma (40x); B - Hodgkin's lymphoma (400x); C - reactive lymphadenitis (40x); D - reactive lymphadenitis (400x); E - necrotising granuloma (40x); F - necrotising granuloma (400x).

Table 1. Comparison of tubercular cervical lymphadenopathy and lymphoma presenting as a neck mass

Variable		Tubercular lymphadenitis (n=38)	Lymphoma (n=17)	P-value
Sex	Male	22	12	
	Female	16	5	
Age (Years)	Mean (SD)	33.81 (11.18)	52.38 (25.28)	0.000167
Duration of symptoms (weeks)	Mean (SD)	4.28 (3.69)	3.83 (2.45)	0.318085
Mean Size (cm ³)	Mean	9.44 (5.99)	38.72 (22.12)	<0.00001
Associated symptoms	Fever	19	9	0.9654
	Weight Loss	11	5	0.972046

cyst (n=2), cystic hygroma (n=3), carotid body tumour (n=1), parathyroid adenoma (n=1), adenocystic carcinoma (n=1), lymphangioma (n=1).

Discussion

Thyromegaly is a major diagnosis in neck swelling and accounts for only 20-30 % of all neck swellings. The other neck masses are non-thyroidal in origin. More than 50% of the neck swellings revealed in the general population originate from the cervical lymph nodes. Commonly tuberculosis and malignancies present as cervical lymphadenopathy. Other considerations are infections, lymphoma, leukaemia, and metastatic swellings. Neck swelling in younger age group tend to be more benign and are congenital, infectious or benign neoplasms. However, the chances of malignant swelling in neck increases to a greater extent after 40 years of age [2]. This correlates with our findings.

Von Haller in 1743 was the first to describe a non-thyroidal swelling of the neck which later was known as carotid body tumour [3]. Von Mikulicz-Radecki, in 1888, reported a patient who experienced bilateral, painless, symmetrical swelling involving lacrimal, submandibular and parotid gland. This disease was later termed as Mikulicz disease [4]. Martin in 1957 published his classic work "Surgery of Head and Neck Tumors" which first gave a varied and detailed description of neck masses [5]. There are other rare cases of non-thyroidal neck swellings described in medical literature. Recently Kikuchi Fujimoto disease is an emerging cause of necrotizing cervical lymph node mass revealed particularly in the Asians. The disease is very much amenable to management with steroids [6]. Kawasaki disease is another uncommon cause of cervical lymphadenopathy but can deteriorate to multiorgan failure in a short span of time [7]. In 2021, Kesavan et al. described two unusual cases of neck swelling. First was a case of achalasia cardia reported as neck swelling in a 75-year-old man [8]. Abuzayad et al. described a swelling in the region of carotid in a 15-year-old girl, which was later diagnosed as Castleman disease [9].

Sometimes the neck masses may not be of any pathological significance. These lesions called pseudo lesions may be due to normal variant anatomy, atypical location of organ of other location and foreign bodies due to iatrogenic causes or self-introduction [10]. Cervical ectopic thymus is one of the common such pseudo lesion and is widely reported [11].

Many studies were conducted in regards to evaluation of neck swellings but the diagnostic accuracy of clinical examination was purely discussed. In our study we were accurate by 85% in correctly diagnosing the cause for nonthyroidal neck swellings. However, the physical examination frequently requires to be supplemented by proper investigation to improve the diagnostic accuracy. The two important investigations that help to diagnose neck swellings are ultrasound and FNAC.

Ultrasound has been found to be a reliable and sensitive diagnostic tool in diagnosis of soft tissue cysts, vascular neoplasms, deep neck abscesses, palatal tumours, salivary gland diseases, fractures of facial bone, solid and cystic lesions of the jaws, temporomandibular joint pathology, head and neck cancer and nodal metastases. The recent Indian study conducted in 2011 by Chandak et al. pointed out that the diagnostic accuracy of clinical examination of 85.7% in diagnosis of neck swellings, while ultrasonography of neck had a sensitivity and accuracy of 98.5% [12]. In another study regarding the ultrasonographic evaluation of cervical lymphadenopathy, the most significant distinguishing feature is strong internal echoes seen in 84% of tubercular lymph nodes. This finding is found in only 11% of metastatic nodes and absent in lymphomatous nodes [13]. The other findings such as irregular margins, hypoechoic centre, fusion tendency, peripheral halo and absent hilus are helpful in differentiating reactive from diseased nodes but show considerable overlap in the 3 groups of tubercular, metastatic and lymphoma lymph nodes. However, ultrasound for neck masses is a valuable diagnostic tool, its accuracy depends on the characteristics of the ultrasound probe and the experience of the radiologist [14].

This vulnerability was overcome by higher modes of radiological diagnostic procedures. The capabilities of CT scan to distinguish between soft tissue structures coupled with the added advantage of utilizing intravascular contrast, particularly suits the examination of neck disorders. With improved equipment permitting thinner sections and shorter exposure times, applications in head and neck diagnosis are increased. CT is used in the evaluation of salivary gland enlargements, staging of known tumours and evaluation of a variety of neck swellings. In some cases, CT alone may be the only imaging procedure necessary, while in other situations, CT may comprise an important portion of comprehensive imaging evalua-

tion [15]. Important anatomic variants are pointed out so the surgeon can avoid potential intraoperative complications. Secondly, nodal staging can be assessed in an effort to increase the number of abnormal nodes detected by physical examination and more importantly to precisely define their location by a standard classification system that can be understood and consistently applied by the radiologist, surgeon, radiation oncologist and pathologist. Although secondary to the previously described tasks, CT scan imaging frequently enables saving the patient unnecessary risk and shortening the time to diagnosis and ultimate treatment [16].

Fine needle aspiration cytology (FNAC) is the most important step in the management of neck lumps. It is easy to perform and also relatively cheap. FNAC has high sensitivity (94.6%), specificity (97.9%), accuracy (96.7%), and both positive predictive (95.9%) and negative predictive (97.2%) value in the diagnosis of neck masses [17]. FNAC also serves as an excellent preliminary screening procedure. FNAC can be performed free-hand or ultrasound-guided to increase confidence of diagnosis if the lesion is impalpable. FNAC has excellent patient compliance, is simple and quick to perform in the outpatient department and can be readily repeated. Studies reveal the burden of tubercular lymphadenitis to be significant in most developing countries [18]. FNAC is deemed as frontline investigation with further investigations based on FNAC result. However, histopathological examination is still the most dependable diagnostic tool. Surgical intervention is definitely required in many cases, though most of the cases are medically curable [19]. Out of 100 cases 36 (36%) had tubercular lymphadenitis. The high percentage of tubercular lymphadenopathy in the Indian subcontinent setting is mirrored by similar findings by Fatima et al in Pakistan where the incidence of tubercular lymphadenopathy of 52.7% [20]. FNAC was a prime diagnostic tool in establishing the diagnosis in this study. A total of 95 patients were subjected to FNAC excluding cases of cystic hygroma, lymphangioma and carotid body tumour. Of the 95 neck swellings, FNAC was accurate in 81 cases, inconclusive in 11 cases and disparate with the final diagnosis in 3 cases. Thus, in 85.26% the FNAC diagnosis correlated with the final histopathological diagnosis. This is similar to the findings by Pandey et al., who reviewed the role of FNAC in 395 patients [21]. In our study FNAC

has been accurate in 94% for diagnosis of tuberculosis. Das et al. has shown in their series of 180 cases an accuracy of 84.4% for detection of tuberculosis [22]. In our study, a total of 72% of neck swellings were found to be of lymph nodal in origin. This is similar to the findings by Jasani et al., which found the prevalence of lymph nodal swellings to be 69% in a series of 450 patients, who underwent FNAC [23].

In our study, 4 patients were finally diagnosed with metastatic lymphadenopathy labelled as carcinoma of unknown primary source (CUPS). The success rate of diagnosis of metastatic carcinoma by FNAC was 100 percent in this study. These findings are similar to the study published by Narang et al., where the success rate of diagnosing metastatic carcinoma by FNAC was 100% [24]. There were total of 17 cases of lymphoma in this series, comprising of 14 non-Hodgkin's (14%) and 3 Hodgkin's lymphoma (3%). This is similar to the findings in the British study by Smith et al., where 11 cases of lymphoma were reported in a series of 100 cases [25]. There were 10 cases of non-specific adenitis in our series, constituting 19.6% of lymph node swellings that was similar to the 2007 study by Song et al., showing the prevalence of non-specific adenitis to be 22.4% in 147 patients with lymph node swellings [26].

In our series 8% of the neck swellings were diagnosed to be lipomas. Similar incidence was seen in a series of 109 patients where four fifth of lipomas are 1.0-5.0 cm in maximum dimension [27]. In our series 4 lipomas were approximately 3 cm in size and 2 were 4-5 cm in size. There were two cases of cystic hygroma in our study, constituting 1.8% of benign tumour of the neck. Both were located in the posterior triangle. This is similar to the finding in the older study which showed one case of cystic hygroma in 100 consecutive cases. There were two cases of branchial cyst in the same study. Both swellings were in right lateral position. This conforms to previous published series by Liston et al., where it is mainly either on right or on left side. It rarely occupies the midline position [28]. Our study reported a total of 6 cases of salivary gland tumour. In our study there was one case of chronic sialadenitis of sub mandibular gland. This is consistent with the findings of Hag et al., where less than 5% cases of sialadenitis were detected in 225 neck swellings [29].

Conclusion

Non thyroidal neck swellings are commoner diagnosis than goitre. Most of the time diagno-

sis can be correctly established after a thorough history and clinical examination. The ultrasonographic and fine needle aspiration cytology are very useful adjunct in arriving at a definite diagnosis. Tubercular cervical lymphadenopathy and lymphoma were two major diagnosis constituting more than 50% of nonthyroidal neck swellings. Tubercular cervical lymphadenopathy was found to be significantly different from lymphomas in terms of mean age and the mean size of swelling.

Limitations

The limitations of this study were: a) single centre observation b) small duration of study c) hospital-based study. The advantages of this study were the prospective data collection and adequate sample size. As this is a pilot study a multicentre prospective study with more

participants is recommended based on this study design.

Conflict of Interests

Authors declare no conflict of interest.

Author's Contributions

Jafar Husain, S. Rajagopalan, Vipin Venugopal Nair, R. Nagamahendran, Pawan Sharma, Pankaj P. Rao – conceptualization, methodology; *Jafar Husain, S. Rajagopalan, Vipin Venugopal Nair, R. Nagamahendran, Pawan Sharma, Nilanjan Roy* – investigation, data curation, formal analysis; *Jafar Husain, Vipin Venugopal Pawan Sharma, Pankaj P. Rao* – writing – original draft; *Rajagopalan, Vipin Venugopal Nair, R. Nagamahendran, Pawan Sharma, Nilanjan Roy, Pankaj P. Rao* – writing – reviewing and editing.

ПРОСПЕКТИВНЕ ОПИСОВЕ ДОСЛІДЖЕННЯ НЕТИРЕОЇДНИХ НАБРЯКІВ ШИЇ У НАСЕЛЕННЯ ЗАХІДНОЇ ІНДІЇ

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Вступ. Нетиреоїдні набряки шиї є поширеним явищем і викликають труднощі у діагностиці. У цьому дослідженні висвітлюються різні діагнози, пов'язані з нетиреоїдними набряками шиї, і проблеми з їх лікуванням.

Мета. Це пілотне дослідження висвітлює різні діагнози, пов'язані з нетиреоїдними набряками шиї, і проблеми з їх лікуванням. У цьому дослідженні також порівнюється клінічний спектр двох найпоширеніших етіологій нетиреоїдного набряку шиї – туберкульозної шийної лімфаденопатії та лімфом.

Методи. Дане проспективне дослідження проводилося у навчальній лікарні третинного рівня з 01 червня 2018 р. по 31 грудня 2019 р. Перші 100 нетиреоїдних набряків шиї, представлених до хірургічного амбулаторного відділення, були оцінені клінічно, радіологічно та гістопатологічно. Проведено порівняння перших двох поширених діагнозів туберкульозного шийного лімфаденіту та лімфоми. Безперервні змінні аналізувалися за допомогою t-критерію Стьюдента, а категоричні дані аналізувалися за допомогою критерію хі-квадрат. Статистичне значення $p < 0,05$ вважалося значущим.

Результати. У дослідженні було виявлено 73 випадків збільшень лімфатичних вузлів і 27 набряків не пов'язаних із лімфатичними вузлами. Найбільш частим діагнозом був туберкульозний шийний лімфаденіт ($n=38$) та лімфома ($n=17$). Середній об'єм лімфатичних вузлів у групі лімфоми ($38,72 \pm 22,12 \text{ см}^3$) був статистично більшим у порівнянні з об'ємом лімфовузлів у групі туберкульозу ($9,44 \pm 5,99 \text{ см}^3$) $P=0,00001$. Середній вік хворих на туберкульоз був $33,81 \pm 11,8$ років, порівняно з віком пацієнтів з лімфомою $52,38 \pm 25,3$ років ($P=0,000167$). Клінічний діагноз був точним у 85% випадків. Однак у 15 випадках клінічний діагноз був змінений після тонкоголкової аспіраційної цитології.

Висновки. Ультразвукове дослідження та тонкоголкова аспіраційна цитологія є дуже корисним допоміжним засобом для встановлення точного діагнозу збільшень лімфовузлів на шиї. Туберкульозна шийна лімфаденопатія та лімфома були двома основними діагнозами. Туберкульозна шийна лімфаденопатія суттєво відрізняється від лімфом раннім віком появи та меншими розмірами на момент появи.

КЛЮЧОВІ СЛОВА: пухлини шиї; шийний; лімфаденопатія; туберкульозний; лімфома.

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