SOLITARY NECK MASSES IN A NORTHERN JORDANIAN POPULATION: : A 16-YEAR RETROSPECTIVE REVIEW OF 157 CASES

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ABSTRACT

Objectives: To investigate the incidence of solitary neck masses in relation to etiology, gender, age, and primary locations.

Methods: The records of 157 patients at the Oral and Maxillofacial Surgery (OMFS) clinic in Prince Rashid Military Hospital between 2004 and 2019. The two inclusion criteria were solitary neck mass in one clinical location, and surgical biopsy, and the two exclusion criteria were if patient is a known case of carcinoma, and Thyroid masses. Retrieved data included in the analyses were age, gender, side, primary mass location, and classifications of diagnoses according to the cause and the behavior of the mass.

Results: Patients were mainly males (n=94, 59.87 %) as compared to females (n= 63, 40.13 %). Malignancy was seen in the elderly group, with 42.2% occurring in >55 years age. However, benign lesions were mainly congenital in nature, with 71% occurred in ages 34 years and younger. The side of the neck mass differed significantly among the different age groups. A significant association between age category and diagnosis was observed.

Conclusion: Northern Jordanian patients >55 years of age are more susceptible to have malignant neck masses and therefore they should be cautiously evaluated and diagnosed. The diagnostic accuracy of this approach needs to be confirmed in a large multicenter study with a larger number of patients.

Keywords: Jordan, solitary, neck mass, benign, congenital, malignant.

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INTRODUCTION

Neck masses are abnormal lesions that are visible, palpable, or observed in imaging studies that usually develop from processes related to inflammation, congenital abnormalities, benign or malignant neoplasms, or trauma.[1] Physicians encounter neck masses when they are examining patients, which can be frequent in adults and children. However, neck masses can be challenging to diagnose due to the immense complexity of the anatomy of the neck. Most masses found in young adults and children are usually benign, whereas in adults, and to a large extent in those over 40 years of age, tend to have malignant neck masses.[2]

A thorough medical history of patients can be crucial when diagnosing neck masses, especially age, size, and mass duration. Recent travel or exposure to insect bites can also suggest inflammatory and infectious causes. History of smoking and heavy alcohol abuse or radiation treatments are associated with increased probability of malignant masses.[3] Moreover, extensive knowledge of the contents and borders of the neck fascial spaces is paramount to the characterization and diagnosis of pediatric and adult neck lesions.[1,4] Only a limited number of studies have investigated the diagnostic list and malignancy rate of clinically solitary cervical lesions.[5]

In this study, we evaluated the differential diagnosis list of clinically solitary neck mass in Jordanian patients over a 16-year period in relation to the incidence of reported cases. The significant correlations can accelerate the diagnosis process which have direct relations with survival rate, treatment option and treatment outcome.

Methods

'The Jordanian Royal Medical Services Ethical Committee approved the study. A total of 824 cases of neck masses presented at the Oral and Maxillofacial Surgery (OMFS) clinic in Prince Rashid Military Hospital between 2004 and 2019. The records of 157 cases with solitary neck masses and met inclusion criteria between 2004 and 2019 were included. The two inclusion criteria were solitary neck mass in one clinical location, and surgical biopsy, and the two exclusion criteria were if patient is a known case of carcinoma, and Thyroid masses.

Patients' confidentiality was preserved, and specific reference number was assigned to each patient. Retrieved data included in the analysis were age, gender, side of neck, the primary mass location, and classifications of diagnoses according to the cause of the mass. The primary locations of the neck masses were classified according to the clinical locations and the American Academy of Otolaryngology classifications (2002).[6]

Statistical Analysis

The dependent and independent variables analysis was performed using SAS statistical software (version 9.2; SAS Institute, Cary, NC, U.S.A.). In searching for any significant correlations, the analysis of age was conducted using 2 approaches. In the first approach, age was described as a categorical variable and was classified into 4 groups (< 20, 20-34, 35-55 and > 55 years of age). Frequencies and percentages were used for each of the categorical variables. Statistical associations between age with side, gender, diagnosis, and primary location were tested using Pearson's $\chi 2$ Chi-test and Fisher's Exact test for low counts.

In the second approach, age was described as a continuous variable. One way ANOVA was used to determine whether there are any statistically significant differences between age and side, diagnosis, or primary location. A *p*-value of <0.05 was considered significant. The Tukey's Honest Significant Difference (HSD) Test were used controls the experiment wise error rate of ANOVA analysis. Moreover, the diagnosis was reported using two diagnostic approaches, first based on the histopathological diagnosis into 6 groups (congenital, reactive, benign tumors, malignant tumors, and others), second based on biologic behavior benign, malignant process and others.

RESULTS

Demographic characteristics of the study group according to primary site, age, and side

Patients were mainly males (n=94, 59.87 %) as compared to females (n= 63, 40.13 %). The age of the study group ranged from 1 to 79 years, with a mean age of 28.50±20.3 years. Submandibular and upper neck sharing the same percentage as most frequent primary location of presentation, while lower lateral neck was the lowest with 29.4% and 4.2% respectively. Some of the neck masses were found in the left side (n = **32**, 25.4 %), but the majority were found in the midline (n = **48**, 38.8 %), followed by the right side of the neck (n = **44**, 35.6 %). Furthermore, the side of neck mass differed significantly among age groups. Most of the masses presented in the midline area (submental and infrahyoid) in age groups < 34 years old and right side in age groups >35 years as shown in Table 1.

Characteristics of the study group according to primary location and diagnoses

The primary location was divided into submental area (Ia; n=23, 19.33%), submandibular area (Ib; n=35, 29.41%), infrahyoid area (VI; n=21, 18%), upper lateral neck (II, III; n=35, 29.41%), and lower lateral neck (IV, V; n=5, 4.2%).

Moreover, the neck masses were classified into 6 groups according to histopathological diagnosis: reactive (n = 22, 14.01 %), congenital masses (n = 57, 36.31%), benign tumors (n = 20, 12.74 %), infectious lesions (n = 17, 10.83 %), malignant tumors (n = 21, 13.38 %), and other neck masses (n = 20, 12.74 %).

The neck masses that resulted from the non-specific inflammatory process were classified as reactive (n = 22). They divided into reactive lymphadenopathy (n=15), florid reactive follicular hyperplasia (n=3), Kikuchi Fujimoto disease (n=1), acute necrotizing lymphadenitis (n=1), traumatic neuroma (n=1), or Castleman disease (n=1). All benign congenital masses were cystic (n = 57). Thyroglossal duct cysts (n = 24) and branchial cleft cysts (n = 25) were the most diagnosed congenital neck masses. Other reported congenital cysts included dermoid cysts (n = 8).

Infectious lesions of the neck were found in 17 cases. The most common neck masses of this origin were reported as: tuberculosis (n=5), abscesses (n = 4), and non-specific granulomatous lymphadenitis (n = 3). There were also 4 reported cases of toxoplasmosis and single cases of acute panniculitis. Benign neoplastic masses amounted to 12.74 % of cases (n = 20). Most of these cases were lipoma (n = 11), followed by pleomorphic adenoma (n = 3). Moreover, four cases of vascular lesions were reported. One was a Masson’s hemangioma, and two were cavernous hemangiomas, while the last case was a non-specific vascular lesion. Other observations included a single case report of eccrine poroma and ancient schwannoma.

Malignant neoplastic masses represented 13.38 % (n = 21) of all cases. Most cases were lymphoma (n=12), divided into Hodgkin’s (n=7) and non-Hodgkin’s (n=5). The metastatic squamous cell carcinoma was presented in 4 cases, while other carcinomas were 3 cases of metastatic papillary thyroid carcinoma and a single case of adenoid cystic carcinoma. Single cases of chronic lymphocytic leukemia and non-specific malignant neoplastic process were reported (Table 2).

Neck masses not fitting in the previously mentioned categories were classified as others (n = 20). These included 19 cases epidermoid cysts and a single case of atypical lymphoid hyperplasia. None of these cases occurred in patients older than 55 years.

Relationship of gender according to primary location, side, and diagnosis

The correlation of the age/gender with other categories (primary location, side, and diagnosis) was examined. No significant association was found between gender category and side, although male patients were presented mainly with left or midline rather than the right side. Moreover, males presented with a higher percentage (not significant) of masses in the submandibular, lower lateral neck and infrahyoid but lower percentage in the upper lateral neck and submental area. On the other hand, no significant association found between diagnosis and gender. However, females showed a higher percentage of infectious, benign, and malignant tumors compared to males (Table 3).

Diagnosis relationship according to age group

Although no significant association was found between the age on one hand and primary location on the other hand (Tables 4), there was a significant association between age category and diagnosis as shown in Table 5. Malignant tumors were seen in the elderly group, with 42.2% of malignant results occurring in the age category of 55 years and more, followed by 20.6% in the category 35 to 55 years. On the other hand, benign lesions were mainly in the younger population; around 71% occurred in ages 34 and younger, with almost half of them congenital in nature. In addition, Malignant lesions had a significantly higher mean age by 20 and 24 years than benign and other lesions respectively (Table 6). Moreover, the mean age was significantly higher on the right side than the midline by 12 years difference. The mean age was also significantly higher in submandibular than the submental location by a mean difference of around 18 years as shown in Tables 7-8.

TableI: Age Category distribution according to side

Side	**Less than 20**	**20 to 34**	**35 to 54**	**55 and more**	P value	Chi square
Left	6 (14.3)	14 (35)	9 (36)	3 (18.8)	0.027	14.180
Midline	23 (54.7)	15 (37.5)	4 (16)	5 (31.2)		
Right	13 (31.0)	11 (27.5)	12 (48)	8 (50)		

Table II: Type of malignancy and number of Cases

Type of Malignancy	**Number of Cases**
Hodgkin's Lymphoma	7
Metastatic Papillary Thyroid Carcinoma	2
Chronic Lymphocytic Leukemia	1
Metastatic Squamous Cell Carcinoma	4
Non-Hodgkin's Lymphoma	4
Marginal B-Cell Lymphoma	1
Adenoid cystic carcinoma	1
Non-specific malignant neoplastic process	1

Table III: Gender and clinical data

Clinical Characters	**Female N (%)**	**Male N (%)**	**p-value**	**Chi-Square**
Side				
Left	11 (21.6)	21 (28.8)	0.173	

Midline	17 (33.3)	31 (42.4)		3.506
Right	23 (45.1)	21 (28.8)		
Primary Location				
Lower Lateral Neck	0 (0)	5 (6.8)		
Infrahyoid	7 (15.2)	14 (19.2)		6.094
Submandibular	12 (26.1)	23 (31.5)	0.192	
Submental	9 (19.6)	14 (19.2)		
Upper Lateral Neck	18 (39.1)	17 (23.3)		
Diagnosis				
Benign congenital	22 (34.9)	35 (37.2)		
Benign tumor	9 (14.3)	11 (11.7)		
Infectious	9 (14.3)	8 (8.5)	0.404	5.0944
Malignant	11 (17.5)	10 (10.6)		
Other	6 (9.5)	14 (14.9)		
Reactive	6 (9.5)	16 (17.1)		

Table IV: Age Category distribution according to primary location

Primary Location	**Less than 20**	**20 to 34**	**35 to 54**	**55 and more**	P value	Chi square
Lower Lateral Neck	1 (2.4)	2 (5.3)	1 (4.2)	1 (7.2)	0.104	18.392
Infrahyoid	11 (26.8)	4 (10.5)	3 (12.5)	3 (21.4)		
Submandibular	9 (22)	9 (23.7)	9 (37.5)	7 (50)		
Submental	11 (26.8)	10 (26.3)	1 (4.2)	0 (0)		
Upper Lateral Neck	9 (22)	13 (34.2)	10 (41.6)	3 (21.4)		

Table V: Age Category distribution according to diagnosis category

Diagnosis	**Less than 20**	**20 to 34**	**35 to 54**	**55 and more**	P value	Chi square
Congenital	25 (51)	19 (35.8)	11 (32.4)	2 (10.5)	<0.0001	45.555
Benign tumors	0 (0)	9 (17)	7 (20.6)	4 (21)		
Infectious	8 (16.3)	4 (7.6)	3 (8.8)	2 (10.5)		
Malignant tumors	0 (0)	5 (9.4)	7 (20.6)	8 (42.2)		
Other	7 (14.3)	8 (15.1)	5 (14.7)	0 (0)		
Reactive	9 (18.4)	8 (15.1)	1 (2.9)	3 (15.8)		

Table 6: The diagnosis relationship with age as continuous scale

Diagnosis Comparison		M±SE	n (Group 1)	n (Group 2)	P-value	F-value
Malignant	***Benign***	*20.2±3.01*	*20*	*115*	*< 0.05*	*12.49*
Benign	***Other***	*3.7±3.01*	*115*	*20*	*Not Significant*	
Other	***Malignant***	*23.9±3.93*	*20*	*20*	*< 0.05*	
*** M, Mean Difference; n, sample size; SE, standard error.**						

able 7: The side relationship with age as continuous scale

Side Comparison		M±SE	n (Group 1)	n (Group 2)	P-value	F-value
Right	***Midline***	*11.97±2.79*	*44*	*47*	*< 0.05*	*4.99*
Midline	***Left***	*9.19±3.05*	*47*	*32*	*Not Significant*	
Left	***Right***	*2.78±3.09*	*32*	*44*	*Not Significant*	
*** M, Mean Difference; n, sample size; SE, standard error.**						

Table 8: The primary location relationship with age as continuous scale

Location Comparison		M±SE	n (Group 1)	n (Group 2)	P-value	F-value
Submenal	***Midline***	*6.57±3.9*	*22*	*21*	*Not Significant*	*4.17*
Midline	***Submandibular***	*11.77±3.55*	*21*	*34*	*Not Significant*	
Submandibular	***Upper Lateral***	*5.99±3.08*	*34*	*35*	*Not Significant*	
Upper Lateral	***Lowr Lateral***	*8.60±6.11*	*35*	*5*	*Not Significant*	
Lowr Lateral	***Submenal***	*20.95±6.34*	*5*	*22*	*Not Significant*	
Submenal	***Submandibular***	*18.34±3.5*	*22*	*34*	*< 0.05*	
Submandibular	***Lowr Lateral***	*2.61±6.13*	*34*	*5*	*Not Significant*	
Lowr Lateral	***Midline***	*14.38±6.36*	*5*	*21*	*Not Significant*	
Midline	***Upper Lateral***	*5.78±5.53*	*21*	*35*	*Not Significant*	
Upper Lateral	***Submenal***	*12.35±3.48*	*35*	*22*	*Not Significant*	
*** M, Mean Difference; n, sample size; SE, standard error.**						

DISCUSSION

Solitary neck masses represent a wide array of pathologies. From benign process such as inflammatory, benign tumors, reactive and congenital neck masses, which are the most common neck masses in pediatric and young adult age groups, to malignant neoplastic masses which related to older age group. Timely assessment of the mass location [vii], and survival of head and neck malignancy is proved to be inversely associated with stage of disease at the diagnosis time.[viii, ix]

A study by Khader *et al*. [x] had investigated the cancer incidence in Jordan. They found a 60.5% increase in the number of cancer cases in Jordan over 14 years between 2000-2013. They emphasize on detect cancer at early stages to reduce associated morbidity and mortality. In this study, we investigated a clinical scenario in which, a patient will present to clinic with a complain of solitary neck mass. The first approach of investigation was toward basic major classification of benign versus malignant process. However, in our analysis, we generated other group due to the fact that we included superficial masses, mostly skin masses, which are part of presentation at clinic. The second approach of diagnosis analysis was based on causative mechanism, which might influence the treatment method. E.g., the infectious cause differs from congenital or vascular benign tumors or reactive mass. The malignant neoplastic mechanism was kept as one category since it is shares importance of early diagnosis even sometimes differ in treatment strategy. E.g., lymphoma treatment is mainly chemotherapy, which is different from metastatic carcinoma that mainly treated with surgery. However, both share the importance of early diagnosis which influence survival, treatment option and treatment outcome.

The anatomical location of neck masses did not differ significantly between the age groups or gender *(p*-value 0.104 and 0.192, respectively). However, upper neck and submandibular location were the most frequent since these are the first echelon lymph nodes for reactive, infectious and malignant metastasis , also salivary glands are within upper neck location.

The results showed that the midline of the neck was the most frequent side for the occurrence of masses. This result can be explained since thyroglossal and dermoid cysts occur most frequently in midline location. Also, congenital masses were the most common finding among all age groups under 55 years old.[xi] This result is consistent with previous results of Al-chateau *et al.*, in which they found that the highest prevalence of congenital masses occurred in the first and second decades of life with 38% and 32%, respectively.[xii]

Like other studies, among the congenital masses, thyroglossal duct cysts and branchial cysts represent 86% of cases, while dermoid cysts represent the remnant 14%. This finding could also be explained by the fact that the benign congenital masses are embryologically distinct, and malformations stem from anomalies resulting from defective closure or persistent remnants following thyroid migration, which form dermoid cysts thyroglossal duct cysts, respectively. [xiii xiv xv xvi]

According to the results obtained in the current investigations, about (13.4%) were malignant neck masses and the age group most involved was >55 years (*p*-value <0.0001). Among the malignant neck masses, lymphoma was the leading variant (57.1%), followed by metastatic squamous cell carcinoma and papillary thyroid carcinoma (28.5%). Although the exclusion criteria included patient of known case of carcinoma, these results are regional metastasis or unknown primary carcinoma process or occult primary carcinoma . Although Thyroid masses were excluded since these cases has specific location and presentation, papillary thyroid carcinoma could present in the neck. Gleeson *et al.* reported that metastatic squamous cell carcinoma or lymphoma should be considered in the absence of infectious signs in patients over 40 years. [xvii]

Patients with a mean age above 55 were more likely to have neoplastic masses. Our findings suggest that age can be a risk factor for a worse outcome when diagnosing neck masses. Other studies have also reported increasing patient age as a predictive factor for neoplastic masses in the neck. [xviii xix xx]. Rowicki *et al.* reported that adults older than 40 have the highest incidence of malignancy.[xxi]

Reactive masses may be non-specific lymphadenopathy presenting as neck masses. In a study by Al Kadah *et al.*, a non-specific reactive hyperplasia occurred in 35.5 % of cases.[xxii] In this study, localized non-specific reactive lymphadenopathy occurred in 68% of cases, while florid reactive follicular hyperplasia happened in 13.6%. Moreover, a single case of Kikuchi Fujimoto disease, acute necrotizing lymphadenitis, and Castleman disease. Another cause of non – lymphatic reactive neck masses was traumatic neuroma presented in a single case.

Infection-related and congenital masses had a lower age distribution. Granulomatous lymphadenitis and tuberculosis represent 47% of infectious masses. In recent study, the majority of mycobacterial lymphadenitis cases occurs in submandibular and cervical lymph nodes in children under the age of five.[xxiii] In our study, mycobacterial lymphadenitis cases mainly occurred in patients younger than 20 years. Another study conducted in Turkey also found that tuberculous lymphadenitis represents 40% of inflammatory masses. There was a significant higher occurrence of inflammatory masses in patients aged 0 - 20 years than those with ages equal to or higher than 41. [xxiv]

All of the other types of neck masses occurred in patients younger than 55 years old and included cutaneous cysts.[xxv] In which epidermoid cysts presented in 95% while atypical lymphoid hyperplasia presented in a single case. In a study by Al-Khateeb *et al.*, epidermal inclusion cysts were found in 49% of patients with cutaneous cysts, with 68% in the neck.[xxvi] Similar findings were shown in a study by Golden *et al.*, where epidermal inclusion cysts were found in 79% of the study patients with cutaneous head and neck cysts.[xxvii] Although this study has investigated 16 years retrospectively and shown significant results that can influence the differential diagnosis of clinically solitary neck mass, there is a need for future multicenter studies with larger number of patients to diagnose and investigate these cases.

In conclusion, northern Jordanian patients >55 years of age are more susceptible to have malignant neck masses and therefore they should be cautiously evaluated and diagnosed. The diagnostic accuracy of this approach needs to be confirmed in a large multicenter study with a larger number of patients.

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