Clinical approach to pediatric neck masses: Retrospective analysis of 98 cases

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ABSTRACT

OBJECTIVE: Pediatric neck masses (PNMs) are a frequently encountered problem in otorhinolaryngology practice. The clinical approach to cervical masses in childhood varies from that of adults. Due to differences among clinicians in the assessment of a PNM, studies investigating this subject are significant contributions to the literature. For this reason, a review was conducted of pediatric PNM cases with an open biopsy (incisional/excisional) and a histopathological diagnosis.

METHODS: The hospital records of 98 (34 girls, 64 boys) pediatric patients aged between 8.5 months and 16 years were reviewed. The history, physical examination findings, blood tests, medical treatments, imaging reports, and the pathology and/or microbiology results of the patients were recorded and evaluated. The cervical masses were categorized according to the etiology, imaging features, size, and location.

RESULTS: Surgical biopsy was planned due to the suspicion of malignancy, typical clinical presentation or location, or size greater than 20 mm despite antibiotherapy for 2 to 6 weeks. Excisional biopsy (91.8%) was the first choice for histopathological sampling. Infectious masses were observed most commonly, followed by congenital and neoplastic masses, at a rate of 49%, 27.6%, and 23.4%, respectively. Hodgkin lymphoma was the most frequent type of malignancy (39.1%). Thyroglossal and branchial cysts constituted 74.1% of congenital masses. Sixty-seven percent of all masses were solid, and the lateral levels of the neck were the most affected locations (44.9%).

CONCLUSION: In most cases, the diagnosis can be made with a detailed history and physical examination. In the presence of nonspecific findings, blood tests, imaging, and histopathological sampling are required. Ultrasound should be the first preference for imaging, and excisional biopsy is suggested rather than fine needle aspiration biopsy for histopathological sampling in pediatric neck masses.

Keywords: Children; Hodgkin lymphoma; lymphadenitis; lymphadenopathy; neck; thyroglossal cyst.

Pediatric neck masses (PNMs) are among the most frequently encountered problems in otorhinolaryngology practice. Traditionally, they are classified based on the etiology as infectious, congenital, or neoplastic. Most of the time, anamnesis and a physical examination suffice to establish the diagnosis, but when the diagnosis cannot be made, additional radiological, and histopathologi-

cal analyses are required. Total excision of the mass is often preferred in undiagnosed cases for both diagnostic and therapeutic purposes [1].

This retrospective study is a discussion of the etiology, location, size, histopathological, and radiological characteristics of 98 PNMs in the light of the literature data.

MATERIALS AND METHODS

The cases of 123 pediatric patients who were biopsied in the clinic between 2008 and 2016 were retrospectively reviewed. Twenty-five patients whose clinical findings and/or histopathology results were incomplete were excluded. A total of 98 patients (female: n=34, 34.7%; male: n=64, 65.3%) aged between 8.5 months and 16 years (median age: 9.3 years) were included in the study. Hospital files provided data of symptoms; examination findings; radiology, pathology and/or microbiology reports; operation notes; and blood analysis. Age; gender; location of the neck mass and its dimensions; ultrasonography (US), magnetic resonance imaging (MRI), and computed tomography (CT) scan characteristics; results of diagnostic fine-needle aspiration (FNAB); Tru-Cut (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), incisional, and excisional biopsies; pathology results; and, if available, microbiological examination results, were recorded.

The masses were divided into 3 groups: infectious, congenital, or neoplastic, and their histopathological subgroups. Neoplastic neck masses were classified as malignant or benign lesions. The PNMs were grouped separately based on the radiological dimensions as those with a diameter of ≥20 mm, <20 mm, ≥30 mm, and <30 mm, and were matched with malignant or benign characteristics. Structural characteristics of the masses were categorized as solid, cystic, or mixed, based on the radiological evaluation.

The masses were also classified using the histopathological diagnosis and the location as midline, lateral neck (levels 2,3,4), submandibular region, posterior cervical angle, postauricular, or suboccipital region.

Numerical data were expressed as arithmetic mean, range, and incidence rate among 100 people.

This retrospective study was approved by the Sisli Hamidiye Etfal Training and Research Hospital ethics committee. Verbal informed consent for participation in the study was obtained from the parents with available contact information in the hospital data system.

RESULTS

A total of 98 pediatric patients (female: n=34, 34.7%; male: n=64, 65.3%) aged between 8.5 months and 16 years (mean age: 9.3 years) were included in the study. Eighty-two (83.7%) patients were presented at the outpatient ear, nose, and throat (ENT) clinic, while the remaining 16 (16.3%) patients were referred by polyclinics of children's health and diseases or other external centers for further examination or biopsy.

A radiological examination was requested for 26 (26.5%) patients because of asymptomatic clinical infection, strong suspicion of malignancy, or typical location or presentation of the mass (midline mass, existence of a fistula opening) without prior administration of antibiotherapy. Seventy-two (73.5%) patients, an infectious etiology was suggested, had received antibiotherapy for minimum 2 weeks before radiological examination. Most frequently amoxicillin+clavulanate, ampicillin+sulbactam combinations, and cephalosporin were preferred. Radiological examination was requested due to a lack of significant improvement in the size of the mass despite antibiotherapy, as detected on physical examination, suspicion of malignancy, or family concern.

Imaging

As an imaging modality, US was preferred in 89 (90.8%) patients. In 6 (6.7%) patients, CT and/or MRI was performed for further examination. For 9 (9.2%) patients, no radiological examination was requested.

The size, structural characteristics (solid, cystic, or mixed), and malignant/benign histopathology of the mass lesions are presented in Table 1. In all,

TABLE 1. Classification of the pediatric neck masses according to size and structural characteristics observed with imaging modalities and the rate of malignancy

Size (mm)	n (%)	Malignant n (%)	Benign n (%)	Solid n (%)	Cystic n (%)	Mixed n (%)
≥20	68 (69.4)	13 (19.1)	55 (80.9)	52 (76.5)	13 (19.1)	3 (4.4)
<20	30 (30.6)	2 (6.7)	28 (93.3)	14 (46.7)	14 (46.7)	2 (6.6)
≥30	33 (33.7)	9 (27.3)	24 (72.7)	25(75.7)	6 (18.2)	2 (6.1)
<30	65 (66.3)	6 (9.2)	59 (90.8)	41 (63.1)	21(32.3)	3 (4.6)
Total		15	83	66	27	5

27 cystic lesions were benign, and 14 (21.2%) of 66 solid masses and 1 (20%) of 5 mixed mass lesions had malignant characteristics. In addition, 6.7% of mass lesions with a diameter <20 mm, and 19.1 % of the mass lesions with a diameter of ≥20 mm had malignant characteristics. Malignancy was also detected in 9.2% and 27.3% of the lesions with a diameter of <30 mm and ≥30 mm, respectively. Of the solid mass lesions with a diameter of ≥30 mm, 36% demonstrated malignant characteristics.

Diagnostic interventions

FNAB was performed in 5 (5.1%) of 98 patients, and 3 of them also underwent an excisional biopsy as a result of the failure to diagnose these patients using above-mentioned diagnostic methods. Eight (8.1%) patients were diagnosed using an incisional biopsy, while in 90 (91.8%) patients, diagnosis was based on the results of an excisional biopsy.

Histopathology

In this study, PNMs were classified based on the results of a biopsy (Table 2). Most were infectious (n=48; 49%), followed by congenital (n=27; 27.6%), and neoplastic (n=23; 23.4%) masses. The intragroup prevalence rates are presented in Table 2 with the histopathological diagnoses. Among infectious mass lesions, 75% were reactive lymphadenopathy, among congenital masses, 48.2% were a thyroglossal cyst, and among neoplastic mass lesions, 39.1% were Hodgkin lymphoma. Eighty

percent of all malignant mass lesions were lymphoma.

Five (45.5%) of 11 neck masses were diagnosed as tuberculous, and 2 (18.2%) as toxoplasma lymphadenitis. The etiology of 4 (36.4%) cases could not be determined.

Location

The location of the neck masses of the study patients can be seen in Table 3. PMNs were most often (21.4%) observed in the lateral aspects of the neck (levels 2,3, and 4), followed by the midline and submandibular regions (level 1B) (16.3% and 14.3%, respectively).

DISCUSSION

Neck masses are among the most frequently encountered problems in the practice of pediatric otorhinolaryngology. Though most have an infectious or congenital etiology, it is mandatory to exclude malignancies in the differential diagnosis because 12% of all malignant masses in children has been detected in the head and neck region [2]. Most PMNs are asymptomatic. They are typically detected by the parents or the patients, or incidentally during routine physical examinations [3]. In symptomatic masses, the spectrum of symptoms reported is quite extensive. A detailed anamnesis and physical examination play an important role in narrowing the differential diagnosis. However, because there are few guidelines available concerning taking a thorough medical

TABLE 2. Classification of the pediatric neck masses, the intragroup histopathological diagnosis, and prevalence

	n (%)	Malignant n (%)	Benign n (%)
Congenital	27 (27.6)		
Thyroglossal cyst	13 (48.2)		
Cystic hygroma	1 (3.7)		
Hemangioma	2 (7.4)		
Ranula	1 (3.7)		
Branchial cyst	7 (25.9)		
Ectopic thyroid	1 (3.7)		
Ectopic thymus	1 (3.7)		
Epidermoid cyst	1 (3.7)		
Infectious	48 (49)		
Reactive adenopathy	36 (75)		
Granulomatous lymphadenitis	11 (22.9)	5 tbc, 2 toxo, 4 Ø	
Chronic sialadenitis	1 (2.1)		
Neoplastic	23 (23.4)	15 (65.2)	8 (34.8)
Hodgkin	9 (39.1)	m	
Non-Hodgkin	3 (13)	m	
Rhabdomyosarcoma	1 (4.4)	m	
Thyroid papillary carcinoma	1 (4.4)	m	
Mucoepidermoid carcinoma	1 (4.4)	m	
Pleomorphic adenoma	1 (4.4)		B
Lipoblastoma	1 (4.4)		B
Castleman disease	1 (4.4)		B
Fibrolipoma	1 (4.4)		B
Pilomatrixoma	2 (8.6)		B
Schwannoma	1 (4.4)		B
Fibroepithelial polyp	1 (4.4)		B

Ø: indeterminate etiology; b: Benign; m: Malignant; tbc: Tuberculosis; toxo: Toxoplasmosis.

history, what to look for in the physical and radiological examination of the mass, duration of medical treatment, antibiotics to be used, and the selection of masses that require histopathological analysis, clinicians are forced to make decisions based on their own experience and accumulation of knowledge. The addition of further studies of PNMs to the literature will contribute to a consensus approach to these masses.

To this end, the data of a total 98 pediatric patients who had undergone a surgical biopsy (incisional/excisional) of a neck mass and had a histopathologi-

cal diagnosis were retrospectively examined. Male dominancy of nearly 2:1 was observed in the study population. The first presentation of 83.7% of the patients was to the ENT clinic, while 16.3% were referred by clinics of children's health and diseases or family medicine specialists for surgical resection or histopathological verification.

In the evaluation of PMNs, a detailed anamnesis and physical examination are essential. The onset of the manifestations of the mass; its location and growth pattern; palpation characteristics; the presence of pain, hyperemia, fever, weight loss, or night

TABLE 3. Location of the pediatric neck masses and the histopathological diagnosis

Histological diagnosis	Midline	Submandibular	Lateral (2,3,4)	Posterior cervical	Parotid lodge	Postauricular	Suboccipital
n (%)	17 (17.3)	12 (12.2)	44 (44.9)	13 (13.3)	3 (3.1)	1 (1.1)	1 (1.1)
Thyroglossal	13						
Ectopic thymus	1						
Ectopic thyroid	1						
Dermoid cyst	1						
Ranula	1						
Hemangioma		1	1				
Hygroma		1					
Reactive adenitis		6	24	6			
Granulomatous lymphadenitis		1	6	4			
Chronic sialadenitis		1					
Hodgkin		1	8	1			
Non-Hodgkin		1		1	1		
RMS							1
MEC					1		
Papillary carcinoma			1				
Pleomorphic adenoma						1	
Lipoblastoma							
Castleman disease			1				
Fibrolipoma			1				
Schwannoma			1				
Pilomatrixoma				1		1	
Fibroepithelial polyp			1				

MEC: Mucoepidermoid carcinoma; RMS: Rhabdomyosarcoma.

sweats; and any travel that may be relevant are important etiological factors that should be considered in the differential diagnosis. Assessments of whole blood cell count (WBC), C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) have been recommended in the exclusion of infectious masses, and measurement and control of lactate dehydrogenase (LDH) and uric acid have been recommended in cases suggestive of lymphoproliferative disease [4]. In this study group, WBC, CRP, and ESR levels were frequently requested in the monitoring and evaluation of the treatment response of masses with a presumptive infectious etiology. However, it was observed that in the initial diagnosis of lymphoproliferative disease, LDH and uric acid measurements were not included in the routine procedure, and histopathological sampling was preferred.

In 72 (73.5%) of 98 patients included in the study, antibiotics were used before a radiological examination. Most commonly, amoxicillin+clavulonate, ampicillin+sulbactam, and cephalosporin were preferred. The duration of medical treatment varied. The clinician-directed longevity of antibiotherapy ranged between 2 and 6 weeks (min-max). The cases in which the disease did not regress (<2cm) despite medical treatment as assessed in a physical examination subsequently underwent a radiological

examination. In a study by Jeremy et al. [5] on the duration of medical treatment, the authors first recommended oral antibiotherapy in cases demonstrating infectious symptoms, and if disease regression is observed within 2 to 3 days, continuation of oral antibiotherapy for a total of 10 days was suggested. If regression was not observed, then a request for imaging modalities was advised to eliminate the possibility of abscess formation.

In our study, the clinician requested a radiological examination without prescribing antibiotherapy in in 26 (26.5%) cases with an initial diagnosis of congenital malformation or a strong suspicion of malignancy. Nine (9.2%) patients did not undergo any radiological examination, and the decision for an excisional biopsy was presumably made with reference to examination findings and anamnesis. Seven (77.8%) of these 9 patients were discovered to have reactive hyperplasia, 1 (11.1%) had non-Hodgkin lymphoma, and 1 (11.1%) had a fibroepithelial polyp. Therefore, in patients for whom radiological tests were not requested, examination findings and medical history were inadequate to establish the diagnosis. Within this context, the role of imaging in the decision to perform an excisional biopsy should be investigated. In this study, US was preferred as an imaging modality in 79.6% of the patients. US has been preferred in the investigation of PNMs because of its noninvasiveness, easy availability, cost-effectiveness, non-exposure to radioactivity, and the fact that there is no need for anesthesia. US has 95% sensitivity and 83% 83% specificity in the differentiation between neoplastic and reactive lymph nodes [6]. In this study, the primary sonographic findings that affected the decision-making process for surgical excision in 78 patients were; [i] loss of ovoid structure in lymph nodes, [ii] conglomeration, [iii] fading or non-visualization of hilar echogenicity, [iv] pure cystic lesions, [v] necrotic, degenerated lymphadenopathies, [vi] intralesional punctate or coarse calcific foci, [vii] cystic lesions with septations, [viii] cortical thickening and irregular contours of the mass, and [ix] mass diameter >20 mm. Although rarely requested, CT imaging is preferred in the evaluation of the relationship of the lesion to bony structures and in staging, while MRI is preferred in the evaluation of the mass

to deep, complex cervical spaces (parapharyngeal, retropharyngeal regions) and neurovascular or vital structures. Both CT and MRI require sedation or general anesthesia, especially in small children and infants. Furthermore, the ionized radiation emitted by CT limits its field of application. In our study, these 2 imaging modalities were requested in 6.7% of the patients, in addition to US.

As seen in Table 1, malignancy was observed in 6.7% of the masses with a diameter <20 mm, and in 19.1% of the masses with a diameter >20 mm. The prevalence of malignancy was 9.2% in mass lesions with a diameter <30 mm, while its prevalence increased up to 27.3% in mass lesions with a diameter >30 mm. The prevalence of malignancy rose to 36% in solid lesions with a diameter >30 mm. Therefore, malignancy should be ruled out in the differential diagnosis of mass lesions with a diameter of ≥30 mm. Up to 6 years of age, acute leukemia, neuroblastoma, rhabdomyosarcoma, and non-Hodgkin lymphoma are the most frequent causes of malignancy. Hodgkin lymphoma and non-Hodgkin lymphoma are seen between 7 and 13 years of age with a comparable incidence rate, while rhabdomyosarcoma and thyroid cancers are relatively rare. From the age of 13, Hodgkin lymphoma is the most prevelant malignancy in adolescent children [7]. In our study, the most frequently seen neoplastic disease was Hodgkin lymphoma (39.1%) (9/23), and the median age at diagnosis was 10.8 years (range: 4-16 years). Among all neck masses, malignancy was detected in 15.3% (15/98) of the cases studies, which was consistent with the literature data [8].

The location of the mass provides many diagnostic clues. A midline location is a typical feature of thyroglossal and dermoid cysts. Branchial cysts and vascular/lymphatic malformations are more frequently seen on the lateral side of the neck. The incidence of malignancy was higher in masses localized posterior to the sternocleidomastoid muscle (SCM) when compared with the anterior aspect of the SCM [9]. The location and subtypes of the PNMs studied are provided in Table 3. The most frequent were lateral neck masses (21.4%) (levels 2, 3 and 4), followed by midline (16.3%), submandibular (14.3%) (level 1B), and posterior cervical (12.2%) (level 5) localizations.

Malignancy was most often observed (60%; 9/15) in the lateral neck.

In 75% (n=36) of infectious neck masses, reactive lymphoid hyperplasia was detected. Normal and reactive lymph nodes appear as hyperechogenic, oval masses on US [10]. The upper limit for the axial diameter of nodes is 9 mm in the subdigastric and submandibular regions, and it is 8 mm for other cervical nodes [11]. In this study, surgical sampling was performed for sonographically benign lymph nodes with a diameter ≥20 mm despite medical treatment. Concern of the family was also influential in the decision to perform a biopsy. Granulomatous lymphadenitis was detected in 11 (22.9%) infectious mass lesions. These patients received the diagnosis of tuberculosis lymphadenitis (n=5; 45.5%) and toxoplasmosis (n=2; 18.2%), while in 4 (36.3%) patients, no diagnosis could be determined. If empirical antibiotherapy is not effective and the suspicion of infection still persists , the patient should be evaluated for tuberculous lymphadenitis [12]. The most frequently seen pediatric extrapulmonary tuberculosis is cervical lymphadenitis [13]. In the differential diagnosis of cases with fistulization to the skin, chronic course, unresponsiveness to antibiotherapy, and tuberculin skin test positivity in addition to sonographically detected hypoechoic, round mass lesions without the echogenic hilus associated with intranodal cystic necrosis, tuberculous lymphadenitis should be considered [14].

Histological sampling can be performed via FNAB or Tru-Cut or open biopsy. According to a study performed by Huyett et al. [15], FNAB did not diagnose 8.9% of pediatric neck masses, and general anesthesia and sedation are required in 73% of the patients. In the same study, the sensitivity and specificity of FNAB were reported as 93.5% and 64.3%, respectively. Though FNAB can identify atypical cells, it cannot identify subtypes of lymphoma. Furthermore, a cytopathologist may not be available. FNAB is not preferred as the first-line alternative out of concern for false negativity, and because it cannot provide sufficient tissue for histopathological typing in the presence of lymphoma [16, 17]. In this study, 5.1% (n=5) of the patients underwent FNAB. The histopathological examination of FNAB speci-

mens established the diagnosis of thyroid papillary carcinoma in 1 case, and mucoepidermoid carcinoma in another patient. Three undiagnosed patients underwent an excisional biopsy. In recent years, the frequency of Tru-Cut biopsies performed with the guidance of US and CT has gradually increased [18]. Open biopsies are preferred in cases where another form of biopsy cannot provide an adequate amount of tissue or when surgery offers an additional treatment advantage. However, it is noteworthy that since the tissue-healing time is longer after an open biopsy when compared with a needle biopsy, in cases of malignancy, initiation of treatment may be delayed. [19, 20]. In cases with suspected tuberculous lymphadenitis, instead of FNAB, total excision of the mass with its capsule decreases the risk of postprocedural fistula formation [19, 20].

The most marked limitation of this study is its retrospective design. Decisions regarding hematological analysis, choice of antibiotherapy and duration, preferred imaging modality, and surgical biopsy were made by more than 1 physician. The preoperative clinical evaluation of the patients was based on the collaborative approach of ENT specialists, pediatricians, and family medicine specialists.

CONCLUSION

In most cases of PNM, diagnosis is made based on a detailed anamnesis and the findings of the physical examination. Most masses are easily identified due to a typical anamnesis and clinical presentation of the patient. Diagnosis is harder to make in the presence of nonspecific findings. If radiological examination is required, US should be the first choice. If malignancy is suspected, an excisional biopsy is recommended, in that it provides more detailed diagnostic information than FNAB, and allows for typing of the mass.

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