http:// ijp.mums.ac.ir
Review Article (Pages: 1005-1014)

Pediatric Neck Mass

*Guilherme Machado de Carvalho[1], Milena Silva de Lavor[1], Jeniffer Cristina Kozechen Rickli[2], Tammy Fumiko Messias Takara[2], Alexandre Caixeta Guimarães[1], Agrício Nubiato Crespo[1]

[1]Otolaryngologist, Department of Otolaryngology, Head and Neck, Clinicas Hospital, School of Medical Sciences, State University of Campinas, Brazil.
[2]Medical Doctor FCMSCSP (São Paulo –SP) /FURB (Blumenau – SC), Brazil.

Abstract

Introduction

Neck masses include a wide variety of diagnostic possibilities, with more than 60 etiologies that depend on clinical aspects such as age, location and time of disease progression. The interview and physical examination guide research that cross the neck masses in pediatric patients in 3 groups: infectious / inflammatory, and neoplastic embryonic remnants. The aim of this study was to present a protocol for evaluation of neck masses in the pediatric age group, based on a review of literature on the subject and experience of this service.

Materials and Methods

Survey of literature data from PubMed / Medline, Google Scholar and Scopus Database without language restriction, since 1980 sources, with the MeSH term "Pediatric neck mass".

Results

Prepared flowchart guidelines to be followed according with diagnostic suspicions. Patients were divided into 3 groups according to the initial clinical manifestations and according to etiological hypotheses formulated recommend evaluations protocols.

Conclusion

The standardization of the evaluation of neck masses in children proves valuable and can help in the differential diagnosis of different etiologies involved.

Key-Words: Etiology, Neck mass, Pediatric neck mass.

Corresponding Author:

Guilherme Carvalho, MD, Department of Otolaryngology, Head and Neck, Clinicas Hospital, School of Medical Sciences, State University of Campinas, Brazil.

Email: guimachadocarvalho@gmail.com

Received date: Aug 2, 2015 Accepted date: Aug 22, 2015

1-Introduction

Cervical mass as a main complaint is quite common in medical practice and can become a diagnostic challenge due to lots of conditions that have this signal as the main manifestation. A detailed history and physical examination are essential to guide the investigation, namely: patient age, location in the neck, time course of the disease and the characteristics of the mass on palpation (1-3).

Regarding etiology, cervical masses can be didactically classified into three groups: inflammatory or infectious, abnormal embryonic development and neoplastic(4). The distribution of patients in all three groups varies according to the age group. Benign diseases prevalent in the pediatric population, the most frequent causes the reaction to infections of the upper airways (1,5,6) lymphadenitis. However, alarm bells should be investigated to exclude neoplastic causes, whereas 5% of malignant tumors in childhood are located in the head and neck region(4).

The presence of associated systemic symptoms such as fever, weight loss, night sweats, pallor and poor general condition, should alert the clinician or specialist for a thorough investigation (2, 3, 4).

Attention should be paid to physical examination characteristics of the cervical mass as well as its location in the neck, since this information give strong evidence both for diagnosis and for prognosis (1, 6). Didactically, cervical tumors can be classified according to their location in the neck in midline lesions, lateral line and posterior triangle. The midline tumors usually present as changes in embryonic development, and the thyroglossal duct cysts, the dermoid cyst, the plunging ranula and teratoma prime examples (1, 2, 7). Importantly, the physical examination of thyroglossal duct cysts mobility of the lesion with swallowing or protrusion of the tongue, which can differentiate it from the dermoid cyst (1, 2).

The plunging ranula is a characteristic lesion in the mouth floor, this may be the only finding associated, without presenting submental component (8). The teratoma may be present both in the midline and in the lateral line and its development begins in the embryonic period, characterized as cervical mass of (9) neonatal period.

The side lesions include a wide variety of diseases, including the three major etiological groups defined above. We highlight the branchial anomalies, especially the second and fourth arches, benign tumors such as schwannoma, paraganglioma and major salivary glands, vascular causes such as jugular ectasia and lymphangioma, and to a lesser extent the malignant tumors, such as lymphoma and (6, 7, 10) neuroblastoma.

The posterior triangle may have lesions that are characteristically of infectious origin, preferably toxoplasmosis, rubella, roseola infantum, dermatophytosis or acute HIV infection. However, the presence of lymphadenopathy in this region should draw attention to neoplastic diseases, being the preferential localization of non-Hodgkin lymphoma in the head and neck (11).

Characteristics of the lesion on palpation are suggestive of etiological groups considered, and the coalescent and fixed to typical deep layers of malignancy lesions, whereas cystic lesions and inflammatory signs are typically inflammatory (1, 4, 12, 13). The presence of lymphadenopathy may occur in 38-42% of healthy children. The abnormal mass or any palpable cervical lymph node in the newborn, regardless of size (1, 4). Between 6 months and 12 years old, are considered abnormal greater or equal to 1 cm and masses over 12 years, when greater than or equal to 3 inches. Faced with adenopathies of inflammatory or

infectious cause, lesions tend to regression within 12 weeks. In case of persistence or progression of the condition, should be considered in chronic granulomatous disease (1, 2, 6).

Among the uncommon causes of cervical lymphadenopathy in children there are the atypical mycobacteriosis, cat scratch disease, histiocytosis, Kawasaki disease, drug reactions (isoniazid, phenytoin, allopurinol), storage diseases and Autoimmune lymphoproliferative syndrome (ALPS) (4,14-17).

This syndrome (ALPS) is a recently described genetic disorder in lymphocyte apoptosis, resulting in an accumulation of lymphocytes and consequently generalized lymphadenopathy and splenomegaly in childhood. The importance of early diagnosis is at increased risk of B-cell lymphoma associated with the syndrome, in addition to immune destruction leading primary immunodeficiency (5, 18, 19).

This work aims to develop a protocol for evaluation of neck masses in childhood, based on the main differential diagnoses present in this age group discussed in the literature.

2-Materials and Methods

Performed the literature search for articles published from 1980, indexed in PubMed / Medline, Google scholar and Scopus Database, without restriction on language of publication, with the Mesh Term "Pediatric neck mass".

A proposal flowchart for evaluation of patients with cervical mass in childhood was drafted by two authors. The work was in accordance with the guidelines of the Institutional Review Board.

3-Results

671 articles were found with MesH *pediatric neck mass*. Stratification of these types of articles was as follows: 259 were case reports, review articles were 71 (with 51 of these revisions were associated with case series and 6 of those were specific for diagnosis of diseases with cervical masses), 44 were of the clinical trial *(clinical trial)*, 15 were randomized controlled trials and 13 were systematic reviews. There was no meta-analyzes, classic articles, *guidelines* (there was an effusive about chronic otitis media, addressing the lymph node as a further aspect) or consensus (Figure.1).

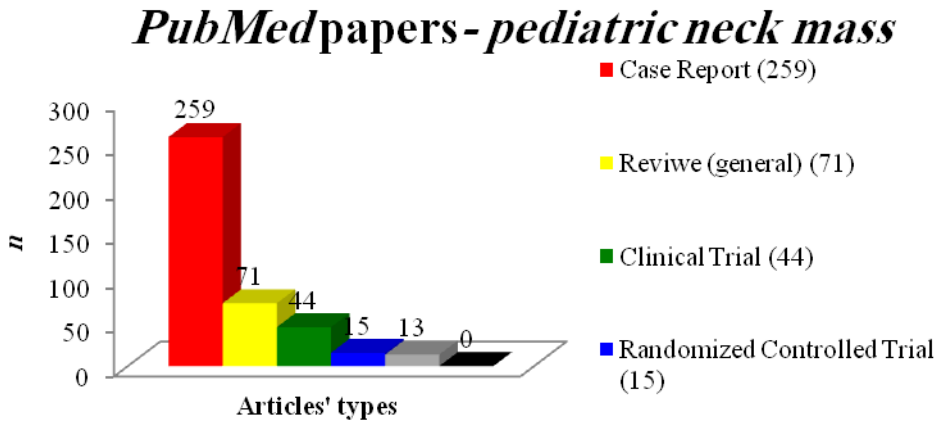

Fig. 1: Laminates types of articles found in the search term pediatric neck mass in PubMed (total of 671 articles).

Chronologically, we can see that 24% of these articles were published before 2000, 42% between 2000 and 2010 and 34% from 2010 until 2014. Among the specific diseases, there was the cat scratch disease, which mainly affects the pediatric age group. 1,963 articles on the subject (general survey, not only in the head and neck) were found, 580 of these published in the last 10 years. Most of the articles found was published in English (1,380 articles); on the type of study 795 reported cases and 253 review articles were found.

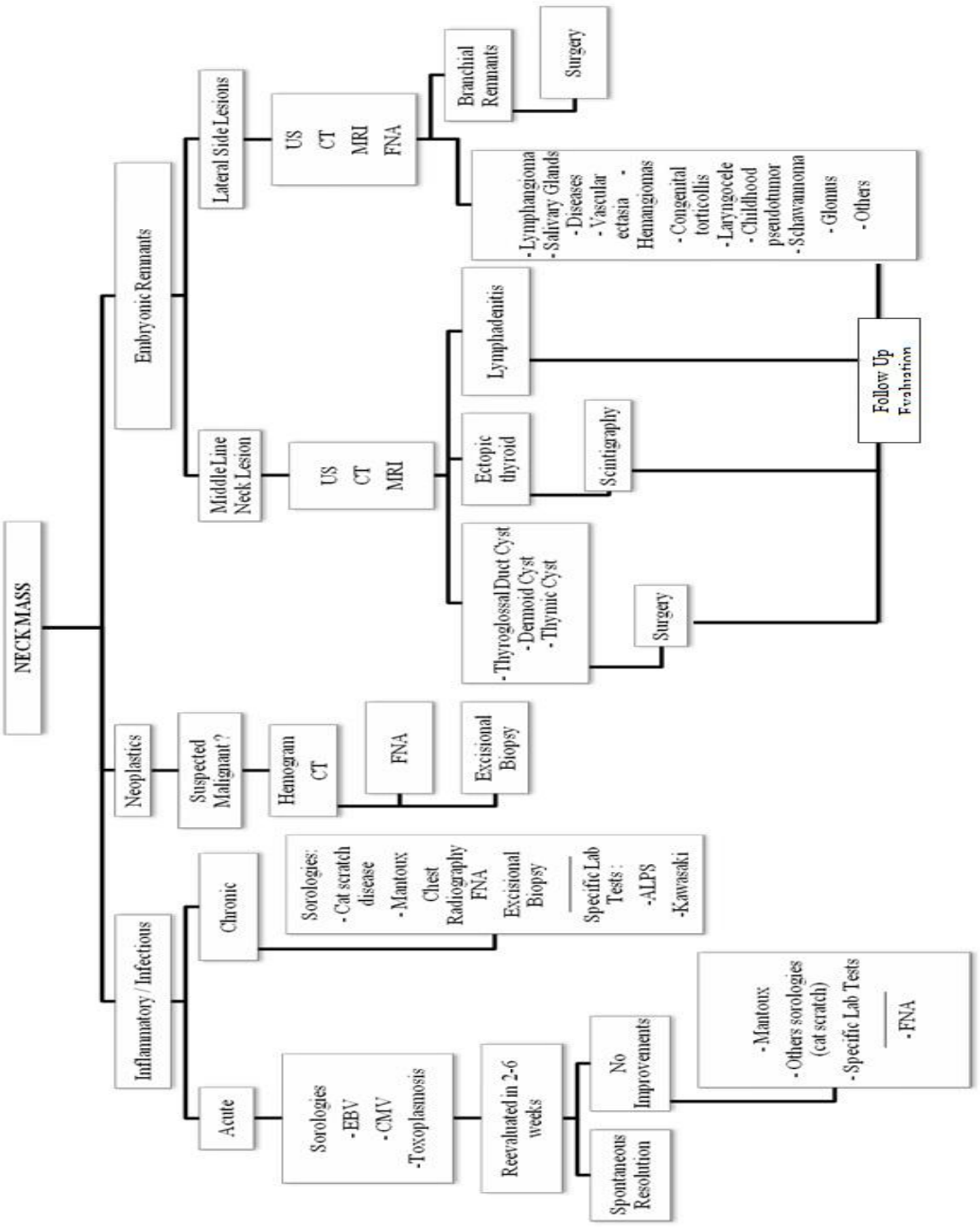

Fig.2: Flowchart of the schematic model for the evaluation of patients with cervical mass in childhood.

3-1:About Flowchart:

The initial assessment is to categorize the patient into a large dostrês groups: infectious / inflammatory, neoplastic and embryonic remnants (these being further divided between the midline and lateral line) according to the initial clinical manifestations (Figure.1).

In the clinical assessment is essential and very important to detail the age of onset, duration, location and characteristics of palpation. One should also remember to pay attention to a history of infections, contact with animals / cats and risk factors for *Tuberculosis* (TB) and HIV.

A further review of all possible etiologies, is through laboratory tests (blood count, serology, specific tests, focus for infectious / inflammatory), pathology [biopsy and *Fine needle aspiration* (FNA]; neoplastic focus) and imaging [ultrasound, *Computerized tomography* (CT) and resonance, focus to embryonic remnants].

3-2: Age and etiology:

We can see from the chart below the distribution of etiologies according to patient age. Inflammatory/infectious diseases are much more prevalent in the early years of life, as well as neoplastic are more common after the fifth decade of life (Figure. 3)(20).

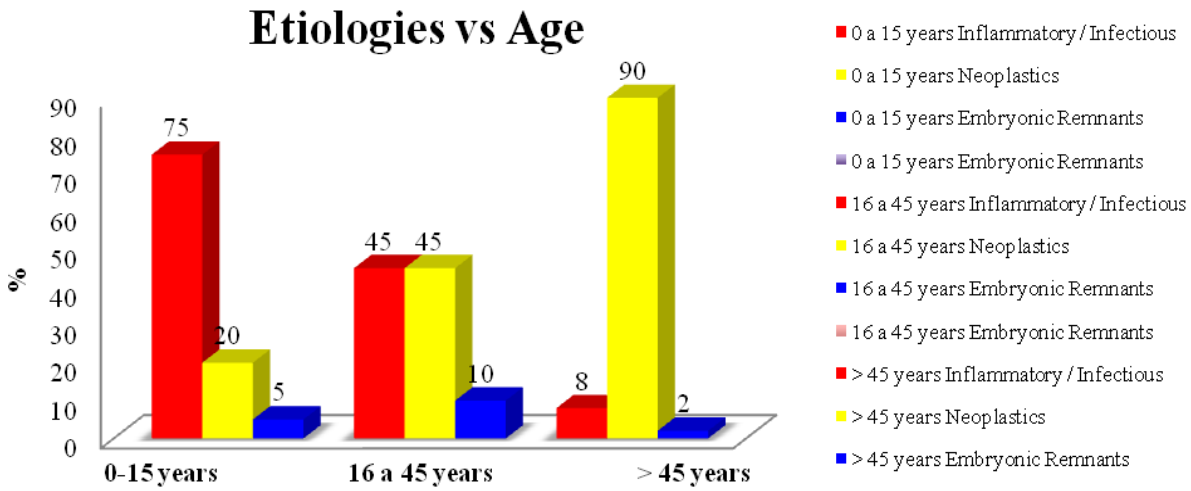

Figure 3: Relation of the etiology of cervical masses according to age.

3-3: Inflammatory / Infectious:

The presence of an inflammatory mass with signs of local heat, redness and pain on palpation associated with a history of fever or infection of the upper airways points to infectious or inflammatory causes. In these cases, the clinical history should be directed to research the etiologic agent, evaluating contact with patients with tuberculosis bacillus, contact with animals, especially cats, and presence of risk factors for HIV infection. The duration of lesions also indicate possible causal agents because of some chronic diseases. For lesions with acute, must be requested serology all major congenital infections, said Toxoplasmosis, rubella, cytomegalovirus, herpes simplex and syphilis (TORCH), and the *Epstein-Baar virus*. Lack of improvement in 2 to 6 weeks indicates the presence of chronic

infections requiring serology for unusual diseases like cat scratch, tuberculin skin test, specific test for ALPS and Kawasaki disease or a fine needle aspiration cytology (FNA). The most common inflammatory / infectious causes are described in (Table. 1). Lymphadenitis is the main reaction in this group. There is still the cause of related storage diseases (genetic) as Gaucher disease, Niewann-Pick, Pompe and other remember.

Table 1: Most frequent causes among inflammatory / infectious diseases.

Viral	Bacterial	Farasitic	Fungal	Autoimmune
Reactive lymphadenitis	Reactive lymphadenitis	Toxoplasmosis	Coccidioido mycosis	ALPS
IVAS	Purulent lymphadenitis	Blastomycosis	Tinea	SLE
Mononucleosis	Abscesses	Leishmaniasis	Other	JAR
CMV	Tuberculosis	Other		Sarcoidosis
HIV	Mycobacteriosis			Kawasaki disease
Herpes virus	Bartolenoses *			Drugs reactions**
Rubella	Dental causes			Other
Measles	Leptospirosis			
Other	Other			

Note: SLE (Systemic Lupus Erythematosus); JRA (Juvenile Rheumatoid Arthritis); * Cat Scratch Disease *(Bartonella henselae)* ** Phenytoin, allopurinol, isoniazid.

3-4: Neoplastics:

FNA should be sought on suspicion of malignancy and diagnostic confirmation when this is not possible by imaging. Recent studies indicate FNA as a safe, minimally invasive and with good accuracy in the diagnosis of cystic and solid lesions in children without the need for sedation or general anesthesia in most cases method.

Children who initially present with solid, coalescing neck masses, quick installation, located in the posterior triangle and associated with systemic disorders such as fever, weight loss, and arthralgias should call attention to the diagnosis of neoplastic diseases. In these cases, CT should be the test of choice in additional evaluation and histopathological analysis is imperative.

If FNA is not sufficient in diagnosis of lesion, excisional biopsy should be performed, especially in cases of lymphoproliferative disorders, in which the FNA may not be sufficient for diagnosis. The incisional biopsy is a diagnostic option for larger lesions, however this should be avoided due to the risk of postoperative fistula.

In the presence of suspected malignancy, general tests should be requested, namely: blood count, to aid diagnosis of hematological malignancies and chest radiography, useful for evaluation of lymphomas and granulomatous diseases. The most common malignant causes are listed in (Table.2).

Table 2: Most frequent causes among neoplastic diseases.

Neoplastic causes	
Leukemias	Raddomiossarcoma
Non-Hodgkin's lymphoma	Neuroblastoma
Lymphoma Hodgikn	Histiocytosis
Other	

3-5: Embryonic Remnants:

Lesions arising from changes in embryonic development are characteristically cystic aspect palpation and located generally on the side lines and middle neck. Ultrasonography (USG) is a useful

test in differentiating solid and cystic tumors with accuracy between 90 and 95%, and should be the first imaging examination to be told, especially the ease of performance in children (30). The most common causes are listed in (Table.3).

However, computed tomography (CT) remains the best test in the evaluation of neck masses due to the precision in tumor location and better assessment of vascular lesions with the use of contrast, and allows differentiation between cystic and solid lesions and assist in planning Surgical.

As disadvantages, introduced the use of contrast, limiting the evaluation in allergic children or renal disease, the presence of radiation and the need for sedation in young children. Magnetic resonance imaging (MRI) provides almost the same information in the evaluation of cervical lesions compared to CT, with higher cost. However, this can be considered examination for the evaluation of vascular lesions and high neck masses or base of the skull, where this artifact in CT makes assessment difficult.

Other imaging tests may also be required in specific cases, such as scintigraphy in suspected ectopic thyroid, the main cause of hypothyroidism in children

Table 3: Frequent Causes from the embryonic remnants

Causes - Embryonic Remnants		
Lesion at Middle Line	Thyroglossal Duct Cyst	Thymic Cyst
	Dermoid Cyst	Ranula (susternal)
	Lymphadenopathy	Teratoma
	Ectopic thyroid	Other
Lesion at Lateral Side (Line)	Branchial remnants	Laryngocele
	Salivary Glands Diseases	Childhood pseudotumor
	Lymphangioma	Schawannoma
	Vascular / jugular ectasia	Glomus
	Congenital torticollis	other

Discussion

The differential diagnosis of neck masses is of utmost importance in medical practice due to its high prevalence and large amount of diagnostic possibilities involved, making it sometimes a challenge even for the expert (1, 2, 11).

In children, especially, early diagnosis is essential for the identification and treatment planning of neoplastic lesions, determining the prognosis of these patients (1, 4, 21). However, in this study it was observed that most cases of cervical masses in children under 15 years old are sourced from inflammatory and infectious diseases, and neoplastic causes account for only 5% of cases (4).

Only between infectious and inflammatory, prevalent in the pediatric population, there are more than 60 causes diagnostic possibilities; this way, the history and physical examination play a key role in the diagnostic and research direction in the request for supplementary examinations (22).

Among the causes just discussed, the cat scratch disease gains importance due to the preferential involvement of patients below 20 years of age and progressive increase in incidence in recent years, especially in tropical countries. This is a benign disease, associated with a history of contact with animals, especially the cat, and that leads to chronic lymphadenopathy (19, 23-25).

The study also showed that there are still a few cases reported in Brazil, which should not be attributed to low incidence, but the lack of resources required for the diagnosis, since serology is not very specific and the Polymerase chain reaction (PCR) is considered the gold standard, even little is available in our country (19, 23-25).

In this study few studies on the evaluation of neck masses in children, probably due to the heterogeneity of the group of

diseases that cause these injuries as the main manifestation, making it difficult to standardize protocols were found. Moreover, the majority of studies appear as case reports, whose evaluation is usually based on the experience of each service, leaving few studies meta-analysis and consensus.

A major goal of systematizing the evaluation of neck masses in the pediatric population is the early diagnosis of malignancies, especially lymphoma.

Prevalence study involving diagnosis of lymphoma in children indicate the presence of cervical lymph nodes as the initial signal in most of the surveyed population, with the most common histological type was found non-Hodgkin lymphoma cell B. The diagnosis should be based on clinical history and physical examination, avoiding excess complementary examinations often not tolerated in this age group (21, 22, 26, 27).

A biopsy is essential for definitive diagnosis and should be sought in cases of persistent lesions and suspicious, preferring to FNA. Recent studies highlight the importance of this technique in the early diagnosis of pediatric neck masses due to high accuracy, safety, easy access, low complication rate and tolerability (2, 28-31).

Regarding excisional biopsy can affirm that it is necessary in the histological diagnosis of some types of lymphoma and may not be completely replaced by FNA in some cases (32).

The identification and differentiation of neck masses in the pediatric population becomes important since the presence of such lesions entails great anxiety of parents and around a pediatric malignancy.

Conclusion

Infectious and inflammatory diseases are the leading causes of neck masses in the pediatric age group. However, the presence of neoplastic disease in the pediatric population, especially lymphoma, can manifest mimicking benign diseases, which should draw attention to the warning signs. Our protocol aims to guide this research, avoiding delays in diagnosis and initiation of treatment.

Conflict of Interest: Nothing to declare.

Fomentation: Nothing to declare.

References

1. Bull P, Cavinatto JN. Head and Neck Tumors in Children. In: Sih T, Chinski A, Eavey R, Godinho R. VII Manual of Pediatric Otorhinolaryngology, IAPO. 7th ed. Sao Paulo: Life & Consciousness, 2008: 106-112.
2. Crespo AN, Meléndez A, J Montovani, Cavinatto JN, VO Son. Cervical adenopathy. In: Sih T, Chinski A, Eavey R, Godinho R. IV Manual of Pediatric Otorhinolaryngology, IAPO. 4th ed. Sao Paulo: Editora Graphics and Lis; 2006. Pp. 93-101.
3. Goins MR , MS Beasley . Pediatric neck masses. Oral Maxillofacial Surg Clin North Am 2012; 24 (3) :457-68.
4. Gosche JR, Vick L. Acute, subacute, and chronic cervical lymphadenitis in Children. Semin Pediatr Surg 2006; 15(2): 99-106.
5. Prathima S, Suresh TN, Harendra Kumar ML, Krishnappa J. Fine Needle Aspiration Cytology in Pediatric Age Group with Special Reference to Pediatric Tumors: A Retrospective Study Evaluating Efficacy and Its Diagnostic Role. Ann Med Health Sci Res 2014;4 (1): 44-7.
6. Thorell EA, Chesney PJ. Cervical Lymphadenitis and Neck Infections. In: Kliegman RM, Jenson HB, Behrman RE, Stanton BF, Nelson WE. Nelson Treaty of Pediatrics. 18th ed. Rio de Janeiro: Elsevier; 2009. Pp. 143-55.
7. Sills RH. The Spleen and Lymph Nodes. In: MacMillan, JAR; Feigin, RD; Angelis

CD; Jones MD. Oski's Pediatrics: Principles and Practice. 4th ed.

8. O'Connor R , McGurk M . plunging ranula The: diagnostic difficulties and a less invasive approach to treatment. Int J Oral Maxillofac Surg 2013; 42 (11): 1469-74.
9. Padilla Iserte P , Sanroma Pérez , Folch B Ferri . Ultrasound evaluation of congenital cervical teratoma and therapeutic management (ex utero intrapartum treatment). Case Rep Obstet Gynecol 2012; 597489:1-4.
10. Benazzou S , Boulaadas M , Essakalli L. Cervicofacial lymphatic malformations pediatric Giant. Craniofac J Surg 2013; 24 (4): 1307-9.
11. Stokken J , Manz RM. The Flagg , Kate Gowans L , S Anne . Synchronous occurrence of nasopharyngeal carcinoma and Hodgkin lymphoma. Int J Pediatr Otorhinolaryngol 2014; 78 (1): 154-56.
12. Dulin MF, Kennard TP, Leach L, Williams R. Management of Cervical Lymphadenitis in Children. Am Fam Physician 2008;78(9):1097-98.
13. Cengiz K, Kumral TL, Yıldırım G. Diagno sis of Pediatric Recurrent Nasopharynx Carcinoma after adenoidectomy. Case Rep Otolaryngol 2013; 653963:1-3.
14. Kushwaha R , Ahluwalia C , Sipayya V . Diagnosis of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) by fine needle aspiration cytology. J Cytol 2009; 26 (2): 83-5.
15. Chang LY, Lu CY, Shao PL, Lee PI, Lin MT, Fan TY , et al. Viral infections associated with Kawasaki disease. J Med Assoc Formos 2014; 113 (3): 148-54.
16. Kanegaye JT, Van Cott E, Tremoulet AH, Salgado A, Shimizu C, Kruk P, et al. Lymph-node-first presentation of Kawasaki disease Compared with bacterial adenitis cervical and typical Kawasaki disease. J Pediatr 2013; 162 (6): 1259-63, 1263.e1-2.
17. Chomel BB, Kasten RW. Bartonellosis, an Increasingly Recognized zoonosis. J Appl Microbiol 2010; 109(3): 743-50.
18. JB Oliveira, Bleesing JJ, Dianzani U, Fleisher TA, Jaffe SE, Lenardo MJ, et al. Revised Diagnostic Criteria and classification for the autoimmune lymphoproliferative syndrome (ALPS): report from the 2009 NIH International Workshop. Blood 2010; 116(14): 35 - 40.
19. Carhiters HA. Cat-scratch disease: An overview based on a study of 1,200 patients. Am J Dis Child 1985; 139(11):1124-33.
20. Crespo AN, Vaz RM. Benign cervical tumors. In: Neto CS, Mello JRJ, Martins RHG, Costa SS. Otolaryngology and Facial Surgery. Sao Paulo: 2nd ed. Roca; 2011: 69 (IV): 796-806.
21. Nolder AR . Paediatric cervical lymphadenopathy: when to biopsy? Curr Opin Otolaryngol Head Neck Surg 2013; 21 (6): 567-70.
22. Lee J , Fernandes R. Neck masses: evaluation and diagnostic approach. Oral Maxillofac Surg Clin North Am 2008; 20 (3): 321-37.
23. Dean RL , Eisenbeis JF . Neck abscess secondary to cat-scratch disease. Ear Nose Throat J 2004; 83 (11): 781-83.
24. Szaleniec J, Oleś K, Składzień J, Strek P. Cat scratch disease -. an underestimated diagnosis. Otolaryngol Pol 2009; 63(3): 271-3.
25. Dong RP , Seeger LL , Yao L . Uncomplicated cat-scratch disease: findings at CT, MR imaging, and radiography. Radiology 1995;195(3):837-39.
26. Celenk F , Baysal E, Aytac I, Durucu C, Sari I, Mumbuc S, Kanlikama M. Incidence and predictors of malignancy in children with persistent cervical lymphadenopathy.Int J Pediatr Otorhinolaryngol 2013; 77 (12): 2004-7.
27. Rajasekaran K , P Krakovitz . Enlarged neck lymph nodes in children. Pediatr Clin North Am 2013; 60 (4): 923-36.
28. Showkat AS, Lateef M, Wani AA, Lone AS, Singh K, Yousuf I. Clinicopathological profile of cervicofacial masses in pediatric

patients. Indian J Otolaryngol Head Neck Surg 2009; 61(2): 141-46.

29. Alam K, Khan R, Jain A, Maheshwari V, Agrawal S, Chana RS, Harris SH. The value of fine-needle cytology in the evaluation of pediatric head and neck tumors aspiration. Int J Pediatr Otorhinolaryngol 2009; 73(7): 923-27.

30. Collins B , Stoner JA , Digoy GP . Benefits of ultrasound vs. computed tomography in the diagnosis of pediatric lateral neck abscesses. Int J Pediatr Otorhinolaryngol 2014; 78 (3): 423-26.

31. Fong Y, Lin YC, Wu CY, Wang HM, Lin LL, Chou HL, et al. The anti-proliferative and apoptotic effects of sirtinol, a sirtuin inhibitor on human lung cancer cells by modulating Akt/β-catenin-Foxo3A axis. ScientificWorldJournal. 2014 (in press).

32. Crespo AN, Silva RC, Meléndez A, Cavinatto JN. Differential Diagnosis of Cervical Masses in Children. In: Sih T, Chinski A, Eavey R, Godinho R. V Manual of Pediatric Otorhinolaryngology, IAPO. 4th ed. Sao Paulo: Lis Graphics and Publishing, 2006: 115-121.