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ORIGINAL ARTICLE

Pediatric neck masses: how clinical and radiological features can drive diagnosis

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Abstract

Pediatric neck masses are a common occurrence and often represent a diagnostic challenge. The primary aim of this retrospective study was to evaluate the clinical and radiological features of neck masses in children and how they can drive diagnosis. The secondary aim was to create a diagnostic algorithm based on clinical features. We evaluated 190 children with neck masses who needed hospitalization. Clinical data and imaging findings were collected. The patients were divided into six groups: congenital/developmental lesions, tumors, acute and subacute lymphadenopathies, chronic nonspecific lymphadenopathies, cat-scratch disease, and mycobacteriosis. Reactive lymphadenopathies were observed in the majority of cases (65.8%). Congenital/developmental cysts were present in 28.9%, while 5.3% had a tumor. A lower mean age was observed for acute/subacute lymphadenopathies and mycobacteriosis. Fever and a painful mass were typical of acute/subacute lymphadenopaties and cat-scratch disease. A hard and fixed mass was not only typical of tumors. Concerning imaging findings, multiple lymph nodes at the same level was mainly observed in mycobacteriosis, while bilateral lymph node enlargement and colliquation were present in lymphadenopathies.

Conclusion: A complete and adequate clinical assessment should be the basis for every diagnostic and therapeutic choice in children with neck masses.

What is Known:
- *Pediatric neck masses are a common occurrence and often represent a diagnostic challenge.*
- *Clinical features, serological exams and imaging findings should drive the physician to an appropriate diagnostic hypothesis.*

What is New:
- *A lower mean age was observed for acute/subacute lymphadenopathies and mycobacteriosis.*
- *A hard and fixed mass was not only typical of tumors.*
- *Multiple lymph nodes at the same level were mainly observed in mycobacteriosis, while bilateral lymph node enlargement and colliquation were present in nonspecific lymphadenopathies.*

Keywords Neck mass · Children · Cysts · Lymphadenopathy · Pediatric tumors · Cat-scratch disease

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Abbreviations

ANOVA	Analysis of variance
PFAPA	Periodic fever, aphthous stomatitis, pharyngitis, adenitis
SPSS	Statistical Package for Social Sciences

Introduction

Pediatric neck masses are a common occurrence and often represent a diagnostic challenge. Fortunately, 80 to 90% of pediatric neck masses is benign in nature, with the majority stemming from infectious sources. Other sources of pediatric neck masses include congenital malformations, benign neoplasms, and rarely malignancies [1]. A complete history and physical examination are essential when dealing with pediatric neck masses, in order to differentiate benign lesions from malignant tumors. An accurate diagnosis is essential for treatment planning as well as for prognosis of malignancies [2, 3].

Clinical features should drive the physician to an appropriate diagnostic hypothesis. An objective examination of ears, nose, oral cavity, and neck is mandatory. A flexible fiber optic endoscopy is useful to evaluate nasal cavities, pharynx, and larynx. The physician should also assess the presence of fever and/or other systemic symptoms/signs (lymphadenopathies, itch, weight loss, skin rash, night sweats). Then, serological exams and imaging can confirm or refute the diagnostic suspicion. First-level serological exams include blood count, reactive C protein, liver enzymes, Epstein–Barr virus antibodies, interferon-gamma release assay. An ultrasound examination of the neck is essential. When a diagnosis is not achieved, further analyses include serological evaluation for *Toxoplasma gondii*, *Bartonella henselae*, *Cytomegalovirus*, *Borrelia burgdorferi*, *Brucella* spp., and *Francisella tularensis*. The child should undergo an evaluation by an infectiologist and/or a medical oncologist. Computer tomography and/or magnetic resonance imaging are needed when ultrasound is not diriment, and they are mandatory when malignancy or neck abscesses are suspected [1].

In some cases, a complete physical and instrumental examination may not contribute to a definite diagnosis. In these cases, a fine needle aspiration cytology (FNAC) or a surgical excision of the mass is mandatory for diagnosis. According to definite diagnosis, an appropriate medical or surgical treatment should be performed [1].

The primary aim of this retrospective study was to evaluate the clinical and radiological features of neck masses in children and how they can drive diagnosis. The secondary aim was to create a diagnostic algorithm based on clinical features.

Materials and methods

In this retrospective study, 190 consecutive patients who presented at the Department of Pediatrics of our tertiary center between 2011 and 2016 and needed hospitalization were evaluated. Inclusion criteria were unilateral or bilateral neck masses; age < 16 years. The analysis was carried out sifting medical reports stored using the TrakCare software (InterSystem Corporation, Cambridge, MA). From each record, we collected information about age, sex, presence of fever and/or inflammation of the upper airways, clinical features of the mass (site, consistency, fixity, pain, hyperemic overlaying skin, presence of fistula), and imaging findings (maximum dimension, colliquation, presence of multiple unilateral, and/or bilateral lymphadenopathies). Informed consent was obtained. The study was in accordance with the Code of Ethics of the World Medical Association (Helsinki Declaration).

According to guidelines [1], each patient underwent an appropriate diagnostic iter based on otorhinolaryngology/infectiology/oncology consultation, serological exams, imaging (ultrasound, computer tomography, and/or magnetic resonance), and biopsy when necessary. Definitive diagnosis was recorded. Basing on diagnosis, the patients were divided into six groups: congenital/developmental lesions (i.e., cysts, lymphangioma), tumors, acute and subacute lymphadenopathies (less than 2 weeks in duration and between 2 and 6 weeks in duration [4, 5]), chronic nonspecific lymphadenopathies (over 6 weeks in duration [4, 5]; no specific microbe isolated on culture test), cat-scratch disease (Bartonella henselae infection), mycobacteriosis. Thus, relationships between diagnosis and clinical features were analyzed in order to identify the clinical factors that can drive diagnosis. Basing on definite diagnosis, each patient underwent the appropriate medical and/or surgical treatment.

All statistical analyses were carried out using Statistical Package for Social Sciences (SPSS), version 17.0. A descriptive analysis of all data was performed, and they were reported as means or percentages and standard deviations. Two-tailed t test and the analysis of variance (ANOVA) were used to assess differences between groups in the mean of continuous variables. Furthermore, multiple comparison analysis was performed by adopting the Bonferroni method in order to have a stricter criterion on whether to accept an effect as significant. A multinomial regression analysis was used to assess the influence of clinical and radiological features on the final diagnosis. The chi-square test was used for categorical variables. A p value less than 0.05 was considered statistically significant.

Results

Between 2011 and 2016, 190 children (101 male, 89 female) with neck masses were hospitalized for diagnostic/prognostic challenges and/or for surgical treatment. Therefore, uncomplicated reactive lymphadenopathies concurrent to acute inflammation of the upper airways and/or PFAPA (periodic fever, aphthous stomatitis, pharyngitis, adenitis) syndrome are not present in our case series. Table 1 shows clinical features of patients and masses. Reactive lymphadenopathies were observed in the majority of cases (125 patients, 65.8%). Congenital/developmental lesions were present in 55 patients (28.9%), while 10 children had a tumor (5.3%). Patients with cat-scratch disease or mycobacteriosis were grouped apart from other reactive lymphadenopathies because of their peculiar clinical characteristics.

In the group of congenital/developmental anomalies, 32 children had a thyroglossal duct cyst, 12 had a branchial cyst (one patient with bilateral cysts), 9 had a micro or macrocystic lymphangioma, and 2 had a dermoid cyst. Five children with thyroglossal duct cysts and 5 with branchial cysts presented with an infected mass. In the group of neoplastic lesions, the following were observed: 6 lymphomas (3 Hodgkin diseases, 2 non-Hodgkin lymphomas, and one post-transplant lymphoproliferative disease), one neuroblastoma, one alveolar sarcoma, one congenital immature teratoma, one nodal metastasis from nasopharyngeal carcinoma. Acute and subacute

Table 1 Clinical and radiologic features of pediatric neck masses

	Congenital lesions	Tumors	Acute and subacute lymphadenopathies	Chronic nonspecific lymphadenopathies	Cat-scratch disease	Mycobacteriosis	*p* value[b]
	(55 patients)	(10 patients)	(65 patients)	(20 patients)	(6 patients)	(34 patients)	
Mean age (months)	63.17 ± 40.89	72.42 ± 66.09	47.85 ± 44.10	93.43 ± 48.22	84.17 ± 49.82	49.18 ± 35.92	0.001
Range (minimum–maximum)	(0–166)	(0–200)	(0–178)	(14–178)	(26–153)	(5–149)	
Mean time from onset (days)	66.39 ± 60.86	45.74 ± 37.63	5.88 ± 3.99	56.75 ± 23.07	21.67 ± 11.25	44.53 ± 27.21	< 0.001
Range (minimum–maximum)	(1–300)	(0[a]–120)	(1–30)	(45–90)	(10–40)	(20–120)	
Mean maximum dimension (cm)	2.67 ± 1.79	5.24 ± 2.61	3.01 ± 1.35	2.90 ± 0.64	3.70 ± 1.43	3.35 ± 1.72	< 0.001
Range (minimum–maximum)	(0.7–7)	(2–10)	(1.1–8)	(2–4)	(2–6.2)	(1.3–10)	
Site (*n*, %)							
Median (Ia-VI levels)	35 (64)	1 (10)	2 (3)	0 (0)	0 (0)	0 (0)	< 0.001
Parotid	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	
Sub/retromandibular (Ib–II levels)	0 (0)	1 (10)	29 (45)	8 (40)	2 (33)	20 (59)	
Lateral neck (III–IV–V levels)	20 (36)	8 (80)	34 (52)	12 (60)	4 (67)	12 (35)	
Total	55 (100)	10 (100)	65 (100)	20 (100)	6 (100)	34 (100)	
Fever (*n*, %)	8 (15)	1 (10)	39 (60)	4 (20)	3 (50)	5 (15)	0.026
Inflammation of the upper airways (*n*, %)	4 (7)	0 (0)	17 (26)	2 (10)	0 (0)	5 (15)	< 0.001
Painful mass (*n*, %)	19 (34)	2 (20)	57 (88)	11 (55)	6 (100)	19 (56)	< 0.001
Hard mass (*n*, %)	10 (18)	6 (60)	40 (62)	12 (60)	3 (50)	24 (71)	< 0.001
Fixed mass (*n*, %)	9 (16)	6 (60)	24 (37)	5 (25)	2 (33)	14 (41)	0.001
Hyperemic skin (*n*, %)	5 (9)	0 (0)	15 (23)	1 (5)	2 (33)	11 (32)	0.011
Imaging findings							
Multiple lymph nodes at the same level (*n*, %)	0 (0)	1 (10)	16 (25)	7 (35)	3 (50)	28 (82)	< 0.001
Bilateral node enlargement (*n*, %)	11 (20)	2 (20)	38 (58)	14 (70)	4 (37)	15 (44)	< 0.001
Colliquation in the mass (*n*, %)	0 (0)	1 (10)	39 (60)	12 (60)	5 (83)	29 (85)	< 0.001

[a] 0 refers to congenital teratoma

[b] The *p* values refer to ANOVA test among groups. Statistically significant *p* values of post hoc tests between pairs of groups are highlighted in Fig. 1

lymphadenopathies included viral and bacterial adenitis (e.g., infectious mononucleosis, staphylococcal, or streptococcal adenitis with or without colliquation/abscess). No diagnosis of Kawasaki disease was set. Chronic nonspecific lymphadenopathies included adenitis with negative culture test; in three cases, a granulomatous adenitis was observed. In the group with mycobacteriosis, one children had an infection from Mycobacterium tuberculosis, while 33 had an adenitis from atypical mycobacteria. Six patients had a cat-scratch disease.

Figure 1 highlights mean age, mean time from onset, and mean maximum dimension for every group. Figure 2 shows

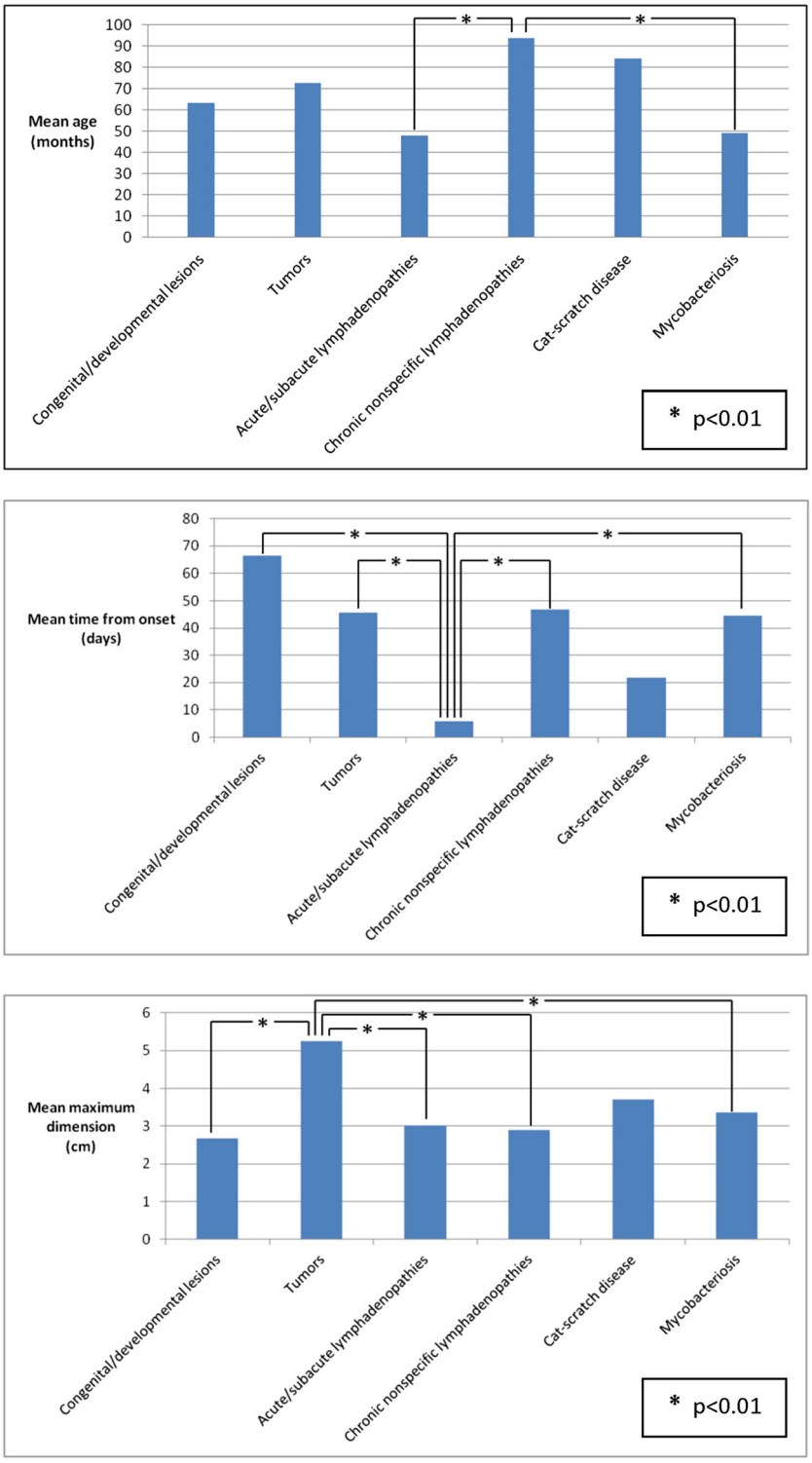

Fig. 1 Mean age, mean time from onset, and mean maximum dimension for each group

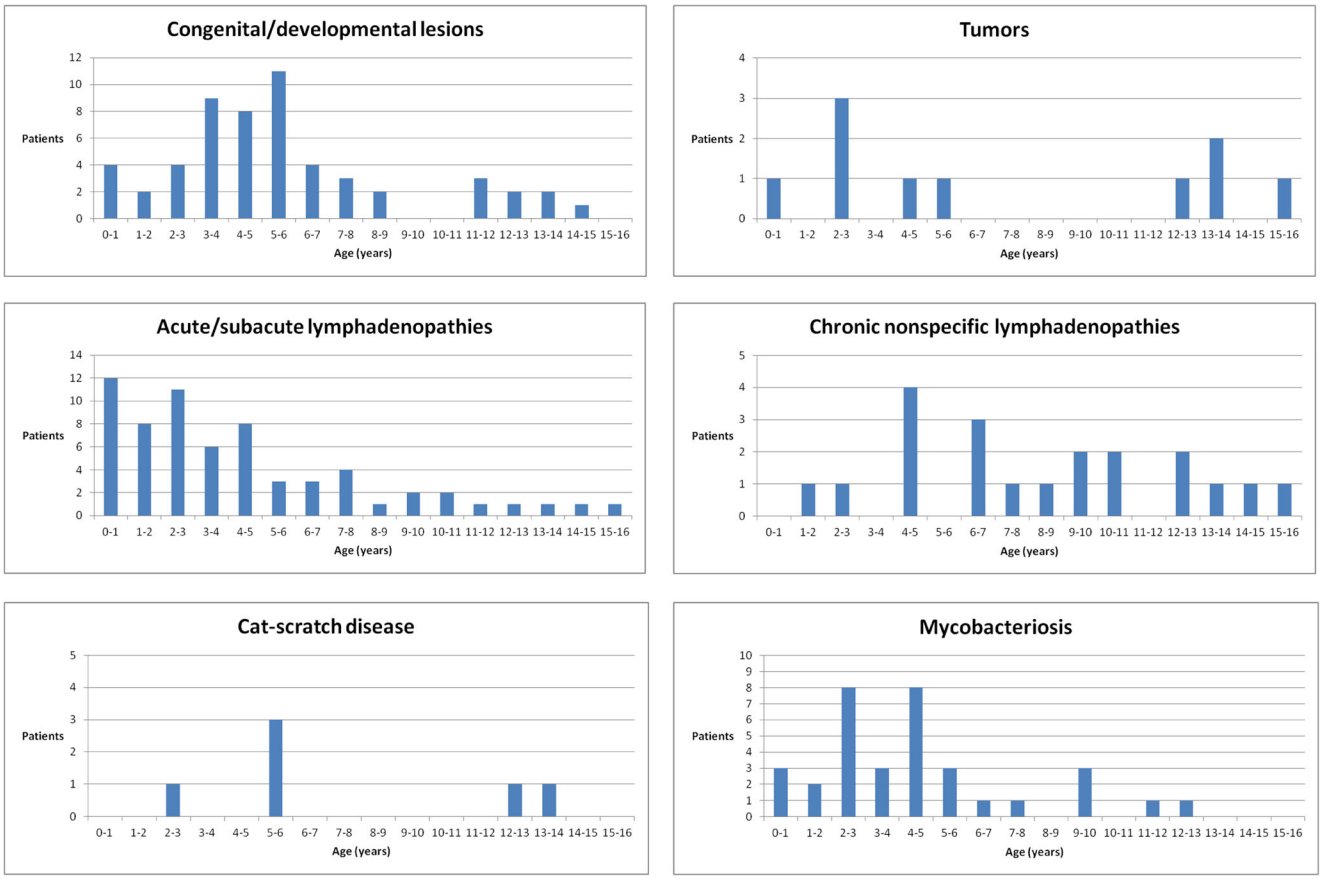

Fig. 2 Age distribution for each group

the age distribution for every group. A lower mean age was observed for acute/subacute lymphadenopathies and mycobacteriosis ($p = 0.001$). A clear bimodal distribution of age was seen in children with tumors (it peaked at 2 and 13 years). An higher time from onset was observed in the group with congenital/developmental lesions ($p < 0.001$). Children with tumors or mycobacteriosis had a time from onset similar to those with chronic nonspecific lymphadenopaties ($p > 0.05$). The statistically significant difference in time from onset between acute/subacute and chronic lymphadenopathies is due to their definition. Mean time from onset in cat-scratch disease ranged from 10 to 40 days; thus, it could be an acute, subacute, or chronic lymphadenopathy. Concerning maximum dimension, the bigger lesions were neoplastic ones ($p < 0.001$). However, the range of maximum dimension was overlapping among the groups.

Regarding anatomical site, the median masses (levels Ia and VI sec. Robbins) were usually congenital/developmental anomalies, such as thyroglossal duct cysts or dermoid cysts. Sub/retromandibular masses (levels Ib and II sec. Robbins) were generally acute or chronic lymphadenopathies, including atypical mycobacteriosis. Masses from all the groups were present at levels III, IV, and V sec. Robbins. However, the majority of the neoplastic lesions were found at these levels.

A statistically significant difference among groups was observed for all the clinical features analyzed (Table 1). Fever and a painful mass were typical of acute/subacute lymphadenopathies and cat-scratch disease, but they were not present in all the cases. Inflammation of the upper airways was seen in 26% of acute/subacute lymphadenopathies, while it was rare in the other conditions. Hyperemic overlying skin was observed in some cases of infectious disease, included infected cysts. A fistula was present in two cases of branchial cysts and six cases of reactive lymphadenopathies (4 acute and 2 chronic with atypical mycobacteriosis). An hard and fixed mass was not only typical of tumor and tumor-like lesions.

Concerning imaging findings, multiple lymph nodes at the same level was mainly observed in mycobacteriosis. Bilateral lymph node enlargement was seen in 70% of chronic lymphadenopathies and in 58% of acute/subacute ones. Colliquation in the mass was mainly observed in infectious adenitis, both acute and chronic ($p < 0.001$). Some cases can be seen in Figs. 3 and 4.

The multinomial regression analysis did not show any statistical significance. Therefore, no clinical or radiological feature can predict alone the final diagnosis.

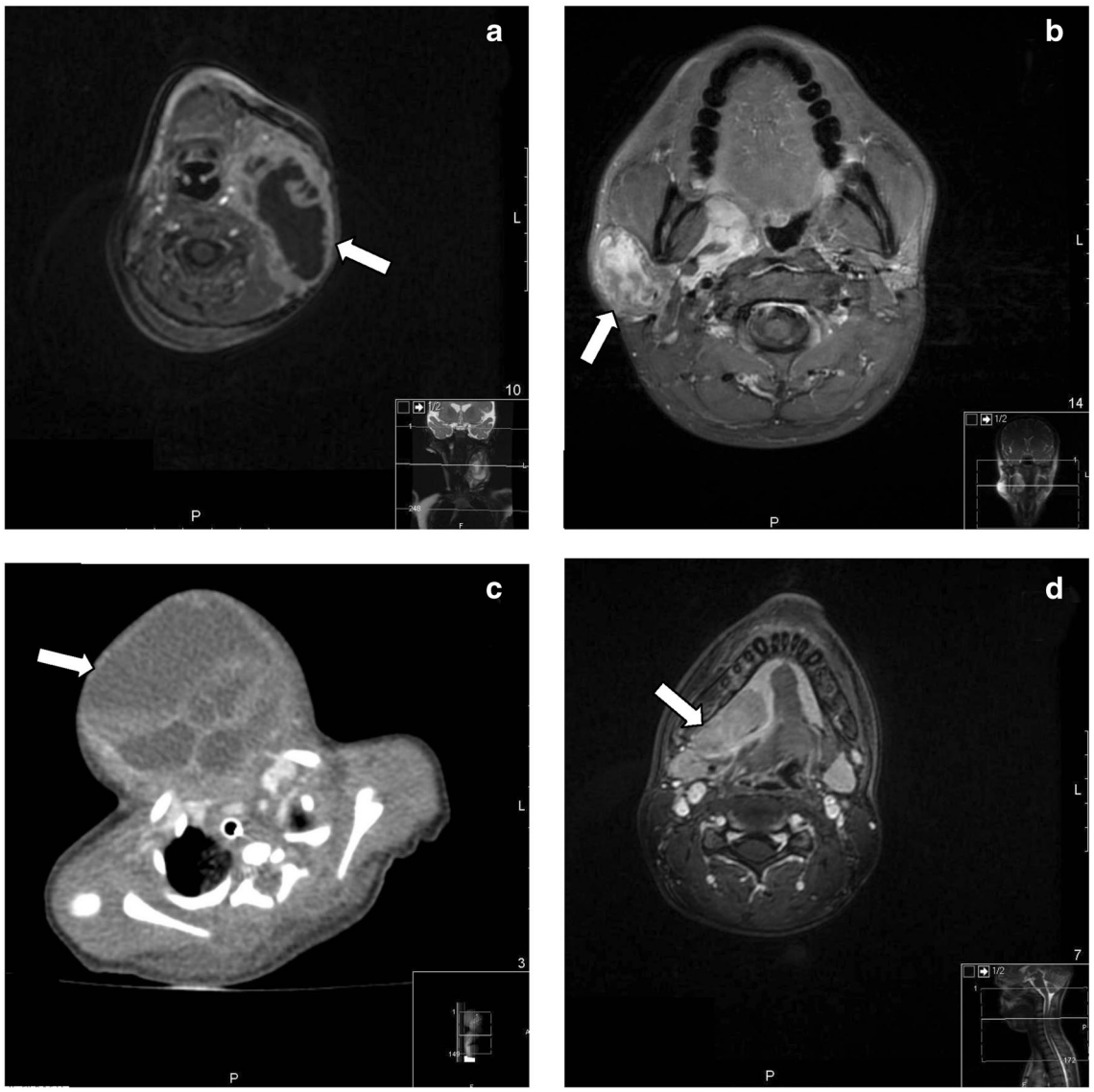

Fig. 3 Imaging findings from children with neck masses (white arrows): congenital/developmental lesions and tumors. **a** T1-weighted MRI: left-sided branchial cyst of the third arch (maximum dimension 60 mm) in a 5-month-old female. **b** T1-weighted MRI: right-sided lymphangioma (maximum dimension 29 mm) in a 15-year-old male. **c** CT: right-sided congenital immature teratoma (maximum dimension 65 mm) in a newborn female. **d** T1-weighted MRI: right-sided submandibular alveolar sarcoma (maximum dimension 38 mm) in a 13-year-old male. MRI magnetic resonance imaging, CT computed tomography

Discussion

Pediatric neck masses could present diagnostic challenge, because of the variety of possible etiologies, ranging from congenital anomalies to malignancies. Serological exams and imaging, such as ultrasound, computed tomography, and magnetic resonance, help the physician in the diagnosis [1]. A thorough history and physical examination are necessary to generate the best diagnostic hypothesis and drive the choice of appropriate serological and imaging examinations. Nevertheless, Gov-Ari et al. showed that pre- and post-operative diagnoses not always matched. The highest percentage of cases with correct pre-operative diagnosis, based on clinical and radiological findings, was seen with congenital masses (75% of cases), followed by benign tumors (73% of cases) [6].

The prevalence of congenital/developmental lesions in children varies between 26 and 56%, of inflammatory masses between 32 and 48%, and of benign or malignant tumors between 9 and 15%, in different case series [2, 6–8]. In our study, congenital/developmental anomalies were 28.9%, inflammatory lesions 65.8%, and tumors 5.3%. As a tertiary center, complicated or atypical lymphadenopathies were sent to our divisions. Maybe this was the reason of the higher prevalence of inflammatory lesions in our case series, compared to literature.

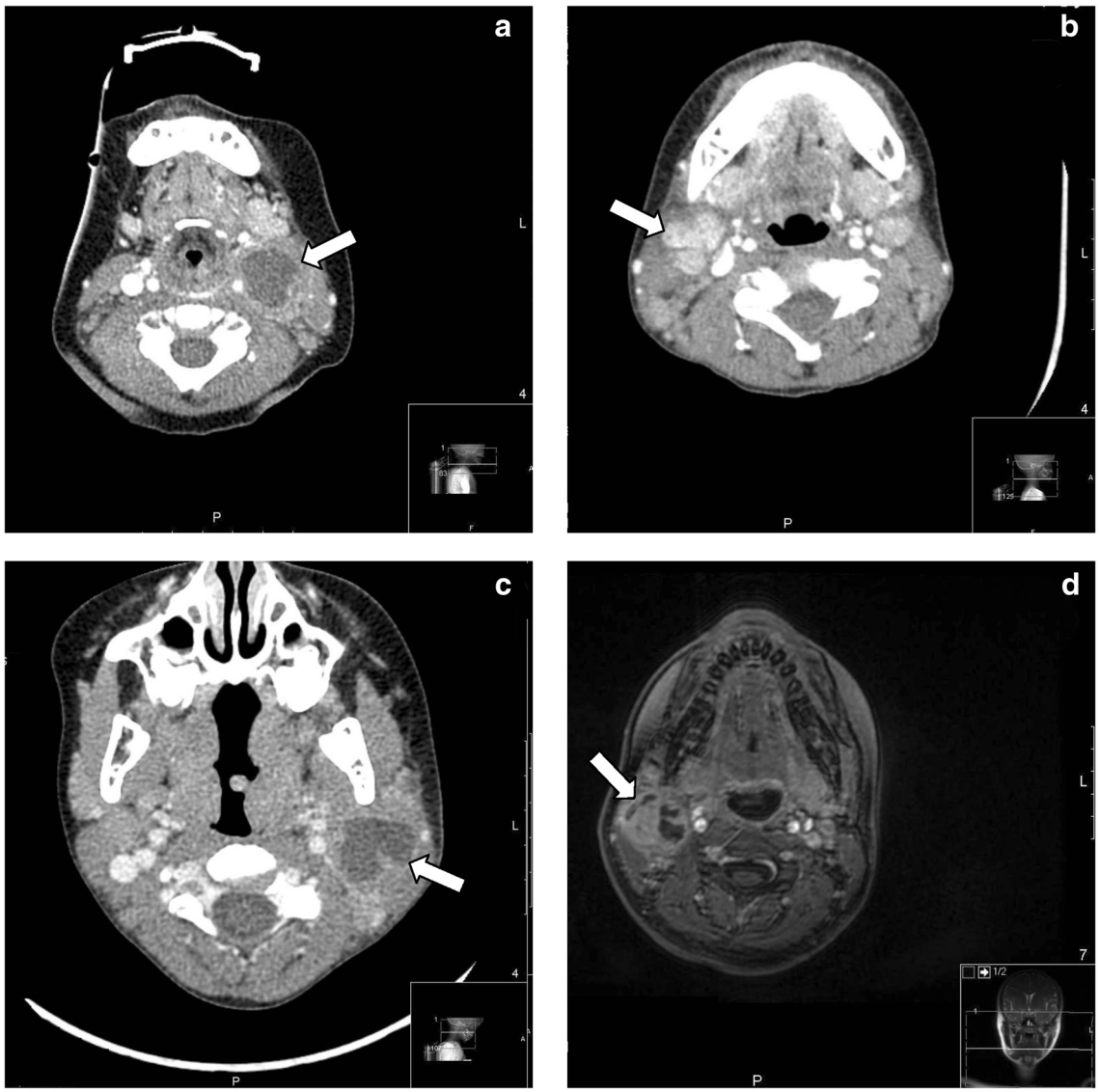

Fig. 4 Imaging findings from children with neck masses (white arrows): acute and chronic lymphadenopathies. **a** CT: left-sided acute lymphadenopathy with colliquation (neck abscess) (maximum dimension 35 mm) in a 4-year-old male. **b** CT: right-sided chronic nonspecific lymphadenopathies without colliquation (maximum dimension 25 mm) in a 5-year-old male. **c** CT: left-sided mass with colliquation due to cat-scratch disease (maximum dimension 28 mm) in a 6-year-old female. **d** T1-weighted MRI: right-sided mycobacteriosis with partial colliquation of multiple lymphadenopathies of neck level II (maximum dimension 47 mm) in a 12-year-old female. MRI magnetic resonance imaging, CT computed tomography

In 400 children (0–12 years of age) with neck masses in India, Showkat et al. observed an inflammatory lesion in 48% of patients and congenital/developmental malformations in 26%. Among inflammatory lesions, reactive lymphadenopathies were the commonest (16%), followed by tubercular lymphadenitis (11.5%), while congenital/and developmental malformations were mainly hemangiomas (12%) and thyroglossal duct cysts (6.5%). Benign neoplastic lesions were seen in 7% of cases and malignant lesions in 2% [7]. In an American case series of surgically treated pediatric neck masses by Gov-Ari et al., congenital anomalies were present in 38.8% of children, reactive lymphadenopathies in 34.5%, and tumors in 12.8% [6]. Among Chinese children, Shengwei et al. demonstrated that the prevalence of congenital anomalies and inflammatory lesions was 56.4% and 32.1%, respectively. Tumors were observed in 11.5% of the cases [8]. A slightly higher percentage of neoplastic masses (14.9%) was seen by Lucumay et al. in Tanzania. Moreover, they observed that 38.5% and 43.9% of children had congenital and inflammatory lesions, respectively [2].

In our study, thyroglossal duct cyst represented the main finding among congenital/developmental anomalies (58%). Lymphomas were the most observed neoplastic lesion (60%). Among lymphadenopathies, acute lesions were prominent (52% of all the cases of lymphadenopathies). The literature reports that acute bilateral cervical lymphadenitis is usually

caused by a viral upper respiratory tract infection or streptococcal pharyngitis, while acute unilateral cervical lymphadenitis is caused by streptococcal or staphylococcal infection in 40 to 80% of cases [4]. The most common causes of subacute or chronic cervical lymphadenitis are reported to be cat-scratch disease, mycobacterial infection, and toxoplasmosis [4].

Mean age for tumors and congenital/developmental anomalies were similar to those reported in other studies [6]. A lower mean age was observed for acute/subacute lymphadenopathies and mycobacteriosis. However, since the range of age was overlapping among the groups, the age was not the most important factor to drive diagnosis. The same concept can be applied to maximum dimension. A less strict reasoning may be performed for the anatomical site of the mass. In particular, median masses were usually congenital/developmental anomalies, as similarly reported in literature [7, 9]. A lower percentage of neoplastic masses can be found at levels Ib and II sec. Robbins, compared to levels III, IV, and V, similar to other studies [4]. Nevertheless, anatomical site cannot drive diagnosis much more, especially for masses of the lateral neck.

Although some clinical features are generally considered specific for the different etiologies, they have not been systematically analyzed in literature. For example, a painless hard fixed mass is generally associated to a neoplastic lesion, while a painful tender mass is considered an inflammatory lesion [4, 10]. However, these associations are not always valid. A statistically significant difference was observed for all the clinical features analyzed (consistency, fixity, pain, hyperemic overlaying skin, presence of fistula, fever, and/or inflammation of the upper airways). Nevertheless, clinical features were not present in all the cases and were not typical of one or a few aetiologies. Fever and inflammation of the upper airways were mainly present in acute/subacute lymphadenopathies, but also in infected congenital/developmental anomalies. They are rarely observed in tumors (10% of cases). It is important to consider systemic symptoms, other than fever, such as generalized itching, weight loss, and/or night sweats (lymphomas B symptoms), especially when a tumor is suspected. Moreover, it is important to examine other groups of lymph nodes to determine whether the lymphadenopathy is localized or generalized. Similarly to fever, hyperemic overlaying skin is mainly observed in acute/subacute lymphadenopathies and infected congenital/developmental anomalies. In contrast to what is generally believed, a hard fixed mass is not only associated to a neoplastic lesion, but may be observed also in 25–41% of chronic nonspecific lymphadenopathies and mycobacteriosis, and in 60% of acute/subacute lymphadenopathies. In some cases of acute lymphadenopathies, a hard consistency is followed by colliquation of the central zone of the mass (abscess) with evolution to a tender consistency. The reduced motility of reactive lymphadenopathies is due to inflammation of the surrounding tissues, as it can be observed during surgical treatment. Except for the higher percentage of pain and sub/retromandibular localization, clinical features of mycobacteriosis (hard fixed mass) are quite similar to neoplastic lesions. Although cat-scratch disease could have an acute,

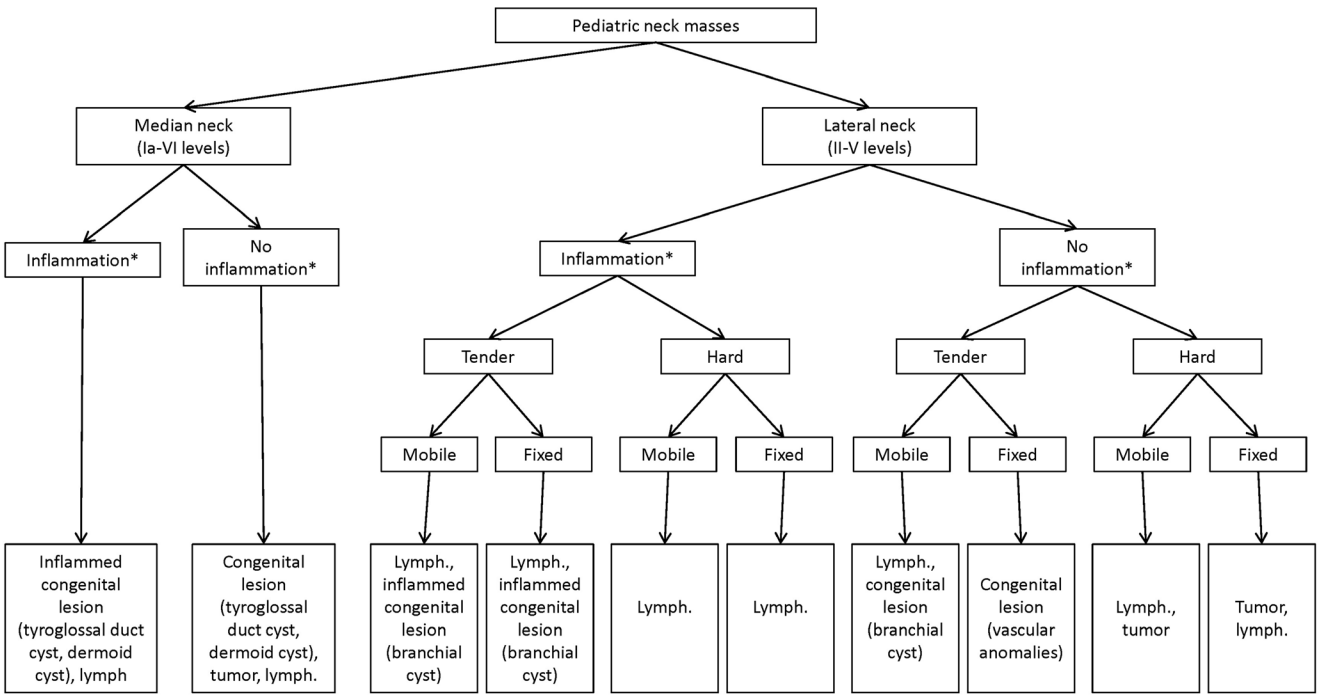

Fig. 5 Clinically based diagnostic algorithm that highlights the most probable diagnoses. It is important to remember that they are not the only possible diagnoses. Lymph. = lymphadenopathy (acute, subacute, or chronic); asterisks indicate systemic and/or local signs of inflammation (fever, pain, hyperemic overlaying skin)

subacute, or chronic onset, it has clinical features similar to acute lymphadenopathies (fever, painful mass). Mycobacteriosis is usually a chronic lymphadenopathies (over 6 weeks in duration), but sometimes, it can be classified among subacute lymphadenopathies (between 2 and 6 weeks in duration).

The clinical presentation should drive the physician to choose the appropriate serological and radiological exams. First-level serological exams and neck ultrasound should be always performed when a neck mass did not solve after an appropriate medical therapy (e.g., antibiotics). Further analyses should be taken into account if a definite diagnosis was not achieved. In particular, computer tomography and/or magnetic resonance imaging are necessary when malignancy or neck abscess is suspected. An abscess should be suspected in case of a tender/fluctuating mass with pain and fever. Hard and fixed masses without local or systemic signs of inflammation may be tumors. Further imaging, other than ultrasound, is also important when serological exams indicate mycobacteriosis. In the last case, imaging is useful for surgical treatment. A biopsy is mandatory for persistent masses that were resistant to medical therapy, and in every case of suspicion of malignancy.

Imaging findings represent an important tool in driving the diagnosis [11]. Besides the imaging features of the primary lesion, the presence of multiple lymphadenopathies at the same or other levels could be useful in the diagnostic reasoning. In particular, multiple lymphadenopathies at the same level with a less common bilateral node enlargement may suggest mycobacteriosis. On the other hand, bilateral node enlargement without multiple lymphadenopathies at the same level is more typical of chronic nonspecific lymphadenopathies. Colliquation in the mass is almost exclusively present in reactive lymphadenopathies.

No clinical or radiological feature can predict alone the final diagnosis. Basing on literature and our data, Fig. 5 shows an algorithm that may help the physician to achieve the most realistic diagnostic hypothesis from clinical features. However, it highlights only the most probable diagnoses. As widely discussed, although some clinical features are more typical for an etiology, they are not strictly specific for it and a thorough history and physical examination are necessary to generate the best diagnostic hypothesis and drive the choice of the appropriate medical and/or surgical treatment.

Our algorithm could help the physician toward the most appropriate serological and imaging studies for every patient. The definite diagnosis has to be achieved with appropriate imaging and/or biopsy [12–14]. In particular, when a neck mass does not respond to medical treatment, surgical removal is mandatory.

In conclusion, a complete and adequate clinical assessment should be the basis for every diagnostic and therapeutic choice in children with neck masses.

Authors' contributions Giuseppe Riva: data collection and analysis and writing of the manuscript. Matteo Sensini: data collection and analysis. Federica Peradotto: data collection and analysis. Carlo Scolfaro: review of the manuscript. Gianpaolo Di Rosa: review of the manuscript. Paolo Tavormina: review of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

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