Clinical Features and Management of Oral Nonodontogenic Masses in Children

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Research Article

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Abstract

**Background:** There are numerous clinical reports of oral tumors in children. However, the clinical features and management of oral nonodontogenic masses in children were rare reported. The aim of this article is to present a large series of oral nonodontogenic masses in children, analyzing the clinical characteristics of such masses and reviewing the relevant procedures for treatment.

**Methods:** We conducted an observational retrospective study, reviewing medical records of 171 patients who were treated for oral nonodontogenic masses between 2014 and 2019 at the Department of Pediatric Surgery, Children's Hospital of Nanjing Medical University. Data collected included age, gender, site, pathologic diagnosis and treatment strategy.

**Results:** All patients were hospitalized in our department. Of the 171 cases, all of them were benign, however, only 1 case diagnosed as inflammatory myofibroblastic tumor showed a malignant process. The most frequent type was hemangioma (63.7%), followed by lymphangioma (16.4%), ranula (7.6%). The most common location of oral masses in the buccal mucosa. The second common location was in tongue. 16 cases of hemangioma were located in two or more sites in cavity. And 29 patients (26.6%) of hemangioma and 11 patients (39.3%) lymphangioma of were found other extraoral lesions. With regard to some cases of hemangioma, the other patients commonly undergone surgical resections or sclerotherapy. The follow-up period ranged from 1 to 5 years. The recurrence rate of hemangioma and lymphangioma were 8.3%, 17.9%, respectively.

**Conclusion:** Most of oral nonodontogenic masses are benign, few oral masses are malignant or mimic a malignant process. Surgical resections are the most common treatment with excellent success.

Background

There are numerous clinical reports of oral tumors in children [1]. However, the clinical features and management of oral nonodontogenic masses in children were rare reported. The Although many oral masses in children represent benign processes, a small but significant portion may be associated with impending serious events, underlying respiratory obstruction, even malignancy[2, 3]. Furthermore, the signs and symptoms of oral nonodontogenic masses in childhood can change with aging[4]. These differences should be recognized by physicians involved in the care of children. Hence, familiarity with the clinical features and further workup of common oral nonodontogenic masses may facilitate the broad differential diagnosis and the choice of effective therapeutic approach. The purpose of this study is to analyze the clinical characteristics, treatment and outcome of oral nonodontogenic masses. Acute and chronic inflammatory processes are not addressed.

Methods

A retrospective observational study was performed, reviewing the medical records of patients who were diagnosed with oral nonodontogenic masses at the Department of Pediatric Surgery, Children's Hospital
of Nanjing Medical University, during a 5-year period from January 2014 to January 2019. Some cases meanwhile presenting extraoral similar or same lesions were also included, unless the oral mass was not the primary diagnosis or interventions were not taken for oral masses. Data collected included age of present, gender, site, symptom, pathologic diagnosis and treatment strategy. Incomplete clinical data reports with a doubtful or controversial diagnosis and odontogenic mass were excluded from the study. All case records were reevaluated to classify the lesions according to accepted clinical diagnostic criteria. A total of 171 infants and children were enrolled. The lesion site was divided into for anatomic regions: palate, buccal mucosa, tongue (including the basement of mouth), and lip. Besides, multiple intraoral and extraoral sites were included. This study was reviewed and approved by the Ethics Committee at Children's Hospital of Nanjing Medical University. All procedures were performed in accordance with relevant guidelines.

Results

A total of 171 cases met our inclusion criteria and selected in our study. There were 74 male and 97 female patients. The male: female ratio was 1: 1.3. The gender distribution was outlined in Table 1. All patients had a mean age of 2.9 ± 3.2 years, with a range of 0–14 years. The peak prevalence of oral masses was in patients of 1-3 years, followed by 0-12 months. More than 90% (154) patients were under 7 years. [Table 2]
| Diagnosis                             | Male | Female | M/F Rate | Total (%) |
|---------------------------------------|------|--------|----------|-----------|
| Vascular anomalies                    | 142  | 83     |          | 109(63.7) |
| Hemangioma                            | 40   | 69     | 1 : 1.7  | 109(63.7) |
| Lymphangioma                          | 17   | 11     | 1.5 : 1  | 28(16.4)  |
| Mixed vascular malformation           | 3    | 2      | 1.5 : 1  | 5(2.9)    |
| Cystic masses                         |      |        |          | 18(10.5)  |
| Ranula                                | 8    | 5      | 1.6 : 1  | 13(7.6)   |
| Mucocele                              | 2    | 3      | 1 : 1.5  | 5(2.9)    |
| Other benign tumors                   |      |        |          | 11(6.4)   |
| Teratoma                              | 2    | 3      | 1 : 1.5  | 5(2.6)    |
| Hamartoma                             | 0    | 2      | 0 : 2    | 2(1.2)    |
| Neurofibroma                          | 1    | 1      | 1 : 1    | 2(1.2)    |
| Papilloma                             | 1    | 0      | 1 : 0    | 1(0.6)    |
| Inflammatory myofibroblastic tumor    | 1    | 0      | 1 : 0    | 1(0.6)    |
| **Total**                             | 74   | 97     | 1 : 1.3  | 171(100)  |
Table 2 Age distribution of oral nonodontogenic masses in children

| Age                  | 0-12 months | 1-3 years | 4-7 years | 8-11 years | 12-14 years | Mean year |
|----------------------|-------------|-----------|-----------|------------|-------------|-----------|
| Vascular anomalies   |             |           |           |            |             |           |
| Hemangiom            | 41          | 44        | 13        | 4          | 7           | 2.8       |
| Lymphangioma         | 6           | 11        | 7         | 4          | 0           | 3.6       |
| Mixed vascular       | 1           | 2         | 1         | 1          | 0           | 4.1       |
| malformation         |             |           |           |            |             |           |
| Cystic masses        |             |           |           |            |             |           |
| Ranula               | 8           | 1         | 3         | 1          | 0           | 2.5       |
| Mucocele             | 1           | 2         | 2         | 0          | 0           | 3.6       |
| Other benign tumors  |             |           |           |            |             |           |
| Teratoma             | 2           | 1         | 2         | 0          | 0           | 2.6       |
| Hamartoma            | 2           | 0         | 0         | 0          | 0           | 0.4       |
| Neurofibroma         | 0           | 1         | 1         | 0          | 0           | 3         |
| Papilloma            | 0           | 0         | 1         | 0          | 0           | 5         |
| Inflammatory myofibroblastic | 0     | 1         | 0         | 0          | 0           | 2         |
| Total (%)            | 61(35.7)    | 63(36.8)  | 30(17.5)  | 10(5.8)    | 7(4.1)      | 2.9       |

Types of masses

All of the oral masses were benign, only one case diagnosed with inflammatory myofibroblastic tumor (IMT) presented a malignant process in clinical and radiological behavior. In all nonodontogenic masses, the highest proportion was the vascular anomalies (142 cases, 83.0%) and followed by cystic masses (8 cases, 10.5%). Among the vascular anomalies, hemangiomas were the most frequent lesions (109 cases, 63.7%), lymphangiomas (28 cases, 16.4%) and mixed vascular malformations (5 cases, 2.9%) were the next. The most common of cystic masses in oral patients was ranula (13 cases, 7.3%); second most common was mucocele (5 cases, 2.9%). The other benign oral masses were teratomas, hamartomas, neurofibromas and IMT. Among them, the only one oral mass with a malignant process was IMT. The data mentioned above was noted in Table 1.

Sites

Table 3 showed site distribution of nonodontogenic masses in oral cavity in children. The oral nonodontogenic masses were found most commonly in the tongue (76 cases, 44.4%) and buccal mucosa (40 cases, 23.4%) and less commonly in the lip (4 cases, 2.3%) and palate (6 cases, 3.5%) which
showed in Table 2. However, some cases were showing a multi-site trend. Among them, the masses of 16 patients were found in multiple intraoral sites, meanwhile there were 29 cases detected with intraoral and extraoral masses. Furthermore, the multi-site trend only occurred in hemangiomas, and the ratio was 41.3% (45 cases).

### Table 3 Site distribution of oral nonodontogenic masses in children

| Location                              | Buccal mucosa | Tongue | Lip | Palate | Multiple intra-oral | Multiple extra-oral |
|---------------------------------------|---------------|--------|-----|--------|--------------------|--------------------|
| Vascular anomalies                    |               |        |     |        |                    |                    |
| Hemangioma                            | 33            | 26     | 3   | 2      | 16                 | 29                 |
| Lymphangioma                          | 6             | 22     | 0   | 0      | 0                  | 0                  |
| Mixed vascular malformation           | 0             | 5      | 0   | 0      | 0                  | 0                  |
| Cystic masses                          |               |        |     |        |                    |                    |
| Ranula                                | 0             | 13     | 0   | 0      | 0                  | 0                  |
| Mucocele                              | 1             | 3      | 1   | 0      | 0                  | 0                  |
| Other benign tumors                    |               |        |     |        |                    |                    |
| Teratoma                              | 0             | 1      | 0   | 4      | 0                  | 0                  |
| Hamartoma                             | 0             | 2      | 0   | 0      | 0                  | 0                  |
| Neurofibroma                          | 0             | 2      | 0   | 0      | 0                  | 0                  |
| Papilloma                             | 0             | 1      | 0   | 0      | 0                  | 0                  |
| Inflammatory myofibroblastic tumor    | 0             | 1      | 0   | 0      | 0                  | 0                  |
| Total (%)                             | 40(23.4)      | 76(44.7)| 4(2.3)| 6(3.5) | 16(9.4)            | 29(17.0)           |

**Clinical feature, treatment and prognosis**

Most oral masses were found accidently by patients. Mucosal hemangiomas in oral cavity often showed a raised red lesion with rubbery on palpation, whereas submucosal hemangiomas appear blue or purple. Mucosal lesions of lymphangioma appeared as small and cystic with a salmon roe appearance. Some other cases of oral nonodontogenic masses were admitted to hospital with dyspnea or mass ulceration. A few patients could coexist with congenital abnormalities, such as cleft palate, mandibular retraction.

Except vascular anomalies, most masses in oral site were resected. The patients with vascular masses were accepted the individualized treatment programs: surgical excision or cautery, repeated injection of sclerosing agents, oral drugs and combination therapy. 20 hemangiomas patients were received
propranolol and regular monitoring blood sugar. It could be significantly reduction in size and color changes in children treated with propranolol. Surgical excision (22 cases; 7 cases), injection of sclerosing agents (31 cases; 4 cases) and combination therapy (36 cases; 17 cases) have all been used in the management of large oral cavity hemangiomas or lymphangiomas, respectively. The follow up was 1-5 years. Recurrence of vascular anomalies occurred in 15 cases—9 hemangiomas (8.3%), 5 lymphangiomas (17.9%), and 1 mixed vascular malformation.

Cystic masses including ranulas and mucoceles were enucleated and recurrence was not observed in any of these cases. Enucleation was performed in 5 teratomas, 2 hamartomas, 2 neurofibromas and 1 papilloma displayed in Table 1. Among them, only one patient of teratoma diagnosed with cleft palate at the same time and occurred recurrence; further recurrence has not been found more than 1 year after resection, it needed longer time follow-up to observe whether it would recur again. The patient with cleft palate was accepted the two-stage cleft palate repair operation.

For IMT occurred in tongue, the patient underwent two surgical partial excisions and one complete surgical excision in the age of 1 year and 5 months, 1 year and 8 months and 2 years and 5 months, respectively. "Borderline" lesions of IMT are not clearly malignant, but are treated as a low-grade malignant tumor. The patient accepted regular target drugs to delay the progression and decrease the recurrent rate. No recurrence has been observed at the time of writing this article for 1 year after the last surgery.

**Discussion**

The patients of odontogenic masses would see a stomatologist or otorhinolaryngologist, thus the odontogenic masses were not discussed here. The fact that most of the cases were benign is consistent with our study, which was in common with that found in the previous studies[5]. The vascular anomalies were the greatest occurrence in children aged under 14 years, which was similar to those of the previous reports in the United States[2]. Some experts believed that the vascular anomalies and hamartoma might be developmental malformations rather than neoplasms[6], if this hypothesis were to be accepted, except for cyst, tumors included 5 teratomas, 2 hamartomas, 2 neurofibroma, 1 papilloma and 1 IMT, with an incidence of 6.4% (11 cases) in our study [Table 1]. Tumors would be less prevalent in oral nonodontogenic masses in children[7]. The tongue was the most common site, meanwhile, some cases of hemangiomas appeared multiple-site lesions not only intraoral but all body locations.

**Vascular anomalies**

Hemangiomas are benign vascular tumors common in childhood, affecting 5% of all infants [8, 9]. However, few large series of oral hemangiomas were reported in the literatures[10]. In this study we present 109 cases, representing one of the largest series in children to date, although it was not discussed alone. The literature showed it was a female-dominated disease. In this study females were predominant, 69 girls and 40 boys showed in Table 1. This finding is similar to that of other reports[11, 12]. In difference with other authors that lip was the most site of oral hemangiomas[13, 14], in this study the
most common location was the buccal mucosa, tongue is the second. Under 3 years and 7 years in Table 2, the ratio of oral hemangiomas were 80.0% and 89.9%, respectively, which is higher than other literature reports[15]. Table 1 indicated that 41.3% oral hemangiomas could be detected similar lesions in multiple intraoral (16 cases) and extraoral regions (29 cases), the most common extraoral site was head and neck. Some reports indicated that multiple infantile hemangiomas in children were associated with hepatic hemangioma[16]. However, it’s still controversial for universal screening hepatic hemangioma in multiple hemangiomas. Because of hemangiomas spontaneous regression[17], conservative observation is usually recommended, these cases were disposed in outpatient department and not included in our study. Aggressive treatment is warranted when complications arise from uncontrolled hemorrhage, pain, ulceration, infection, or airway obstruction[18]. There were many forms of therapies in dealing with hemangiomas, such as oral medication, surgical removal, sclerotherapy and laser surgery. Oral propranolol usually is the first-line management in oral hemangiomas after clinical evaluation[18]. Sometimes single therapy could not achieve a satisfactory result or after failure of a single treatment, repeated treatment with same method or multimodality therapy may be a better choice with less recurrence. Although using a variety of therapy strategies, there were about 8.3% (9/109) patients recurrent during 1-5 years follow-up in present cases.

Lymphatic malformations (LMs), otherwise known as lymphangiomas or macrocystic LMs (formerly cystic hygromas), involve the presence of low-flow vascular anomalies caused by defective embryologic development[19]. Lymphangiomas were rare, benign, congenital malformation of unknown cause originates from lymph vessels. Mucosal lesions appear as small and cystic with a salmon roe appearance. Lymphangiomas is most commonly located on the head and neck region, with an incidence of 50-70%[20]. it is more common in males by a ratio of 1.5 to 1 in Table 1 in our study. In contrast to hemangiomas, spontaneous regression is not seen. Intraoral lymphangiomas occur more frequently on the dorsum of tongue, which is consistent with previous reports[20]. Surgical excision is the treatment of choice. Besides, sclerosing treatment, oral medicines (sirolimus) and laser surgery are alternative methods. A fraction of the complicated cases which were thought partial surgical resection still need following combination therapy. Local oral recurrence occurred in 17.9% (5/28) of patients.

Mix vascular malformations were not common seen in oral cavity, only accounting for 3.5% (5/142) of vascular anomalies. The most frequent clinical type was mixed venous-lymphatic malformation. Its clinical and imaging features were similar to venous malformation and that must careful be distinguished by postoperative pathology.

Cystic masses

Cystic masses included 13 ranulas and 5 mucoceles, as a rate of 10.5% (18/171) in oral nonodontogenic masses in children [Table 1]. Cysts and pseudocysts of the minor salivary glands are considered the most prevalent cysts of the oral cavity[21]. The obstruction of the duct of a salivary gland may lead to an enlarging mass within the floor of the mouth. The gold standard procedure is the as advocated by Pandit and Park[22] suggested that complete excision of the lesion along with excision of the sublingual gland
is the best choice for minimizing recurrence. However it followed a wide range of complications, including injury the lingual nerve, damage to submandibular duct, bleeding/hematoma, lead to a recurrent plunging ranula, scarring, and restricted mobility of the tongue, et al[23]. Surgery to conserve the sublingual gland often following high a high recurrence rate. Operative approaches remain disputed. Given the early age children in our department, simple cyst excision was performed. No recurrence was observed in any patients, it could be to do with a small number of cases and rather short-term following up.

Oral mucocele is the most common benign minor salivary gland lesion. The mechanism is that trauma to the excretory duct of the gland, mucoproteins leak into the surrounding tissues leading mucus retention in local tissues[24]. Clinical features included single or multiple, translucent, ill-defined nodules, ranging from the normal colour of the oral mucosa to deep blue. They represent the 17th most common lesion of the oral cavity[25]. The lower lip was the most common site for mucocele and no sex preference in previous reports[25, 26]. Only one of five cases occurred in the lower lip in our study. Complete resection is the first choice of traditional treatments. Microwave, sclerotherapy or laser treatments were alternative techniques[25, 26]. Mucocele has a lower recurrence rate and fewer complications than ranulas.

Other benign tumors

Teratoma

Teratoma is a congenital malformation, accounting for 3% of all childhood tumors[27]. It arising from the oral cavity is extremely rare in the newborn and 2.6% (5/171) of oral teratomas present in oral nonodontogenic masses [Table 1]. They can arise in the base of cranium and have associated craniofacial anomalies including cleft palate, cystic hygroma and other multifocal teratomas[28]. Small tumors can be discovered by accident, some cases were followed by feeding difficulties, partial oral teratomas can cause seriously airway obstruction, even resulting in asphyxia at birth. Congenital teratomas can be detected by the prenatal ultrasound diagnosis in early pregnancy and further MRI examination in the later stages of pregnancy[29]. Other cases were diagnosed by clinical characteristics and imaging expression at birth. Early diagnosis and complete tumor resection are the only means to achieve good survival in children with oral teratomas[29]. Some reports indicated that the risk of malignant transformation up to 90% in the patients of failing to diagnose or treat head and neck teratomas when they grew up[28]. However giant oral teratomas might not be resected completely to prevent serious craniofacial defect and dysfunction. Palliative surgeries were taken and have high risk of recurrence. Alpha-fetoprotein (AFP) is a good marker of malignant transformation and as a screening tool for postoperative follow up[30]. Developing better treatments for these patients is needed in the future.

Hamartoma

Hamartoma is a benign pseudoneoplastic malformation mainly composed of an abnormal arrangement of tissues, such as fat, nerves, and blood vessels[31]. However, smooth muscle predominant (leiomyomatous) hamartomas are rare. The first case in the tongue was reported in 1945 by Stamm and
Tauber[32]. Two cases reported in this paper were both leiomyomatous hamartomas. Most of the oral hamartomas occurred at the tongue[33]. At least 50% leiomyomatous hamartoma were known to be present at birth and the most common age of diagnosis was under 12months[34]. The mass of oral hemartoma mostly are asymptomatic. Other masses affecting the tongue that should be considered in the differential diagnosis include thyroglossal duct cyst, lingual thyroid, choristoma, and congenital dermoid cysts. The definitive diagnosis was the postoperative pathological examination. It is generally agreed that complete resection of the tumor is the most effective treatment with better prognosis, and no cases with follow-up data available had tumor recurrence in literature reports, as well as our work.

Neurofibroma

Neurofibroma is an uncommon benign tumour of the oral cavity originating from the nerve sheath, commonly can be found in patients with neurofibromatosis type-1 (NF-1), with an incidence of 72%[35]. Oral cavity involvement by a solitary and peripheral plexiform neurofibroma in patients with no other signs of neurofibromatosis is uncommon[36]. NF-1 is an autosomal dominant and multisystem genetic disorders, known as Recklinghausen syndrome, nearly 50% of NF-1 have a positive family history[37]. It is the most common type of neurofibromatosis which affects approximately 1 in 3500 people and can be seen in 90% of all cases[38]. The oral clinical presentation includes gingival enlargement and pigmentation, dental abnormalities, dental caries, neoplastic lesions and osseous lesions. The tongue is the most commonly affected region of oral neurofibroma[39]. In our study, the symptom of two cases were oral neoplastic lesion of NF-1 patients, both located in tongue, and only one patient’s mother has similar clinical features. Besides oral manifestations, light brown pigmentation spots on the skin and multiple small tumors surround the nerves in other parts of the body. Surgical excision represents the treatment of choice for oral neurofibroma. Although mostly benign, malignant transformation of neurofibromas could be found in some certain NF-1 patients.

Papilloma

Oral squamous papilloma is a benign tumor whose pathogenesis has been associated with human papillomavirus (HPV) usually HPV-6 or HPV-11[40]. The lesions are low proportion in oral benign neoplasms, occupying 22%[41]. The lesion can occur in any site of oral cavity. The most prevalent site was the tongue and the palate, with an incidence of 34%[41, 42]. They appear clinically as asymptomatic and often found by accident. The typical clinical manifestations were an exophytic growth, with a rough surface that appears a cauliflower-like and, usually white but sometimes pink and/or red in color. The frequently occurrence of oral squamous papilloma is adults aged between 30 and 40, predominate in female (75%)[43]. It accounts for 8% of all tumor in children[42]. The correct diagnosis depends on clinical features and histopathology. An alternative means of treating oral squamous papilloma is surgical removal including electrocautery, cryosurgery, laser ablation and intratumoral injection. Solitary papilloma has a relatively low rate of recurrence while a high rate in multiple ones. Oral squamous papilloma caused by HPV may evolve cancration.

Inflammatory Myofibroblastic tumor (IMT)
IMT as a rare mesenchymal tumor composed of myofibroblast differentiated spindle cells and contain inflammatory cells, plasma cells, and/or lymphocytes[44]. It can occur at any age, but common in children and young adults. It shows a high predilection in the lung, however, it has been found anywhere in the body. Head and neck region accounts for 14-18% of extrapulmonary sites of IMT[45]. Oral IMTs are extremely rare and the sites of involvement in oral nonodontogenic IMTs include the buccal mucosa, tongue, hard palate and floor of the mouth. World Health organization (WHO) defined IMTs as tumors of intermediate biological potential associating with a tendency of recurrence and metastasis[44]. The exact etiology and pathogenesis of IMT is unknown. Researchers and social scientists believe that it represents an extravagant immune host reaction to microorganisms, surgery, trauma, tissue damage, foreign bodies or even radiotherapy[46]. The ALK gene is thought to be participated in the pathogenesis of IMT[47]. It has no specific clinical manifestation. Radiographical depiction can be found the presence of bone absorption or destruction when the lesion involves in certain skeleton and easily misdiagnosed as sarcoma. Moreover, the atypical histologic appearance is much confusing that sometimes overwhelms pathologists. The pathological character shows numerous plasma cells, spindle cells, lymphocytes and myoblastic cells. The treatment of the tumor depends on operation, corticosteroid therapy, chemotherapy, radiotherapy and a combination therapy[48]. Complete surgical excision and/or corticosteroid combination is a non-controversial way to treat oral IMTs. There are 80 % cases respond to corticosteroid treatment. However, the remaining cases are no respond to corticosteroid because of few inflammatory cells in tumor tissues[49]. Oral IMTs usually run a more favorable clinical course and respond well to the treatment with no reported recurrence. However, in the present case of our department, having underwent the first surgical excision of oral IMT, the patient received the second and third surgical removal and chemotherapy during 3 months, 9 months after first surgery, respectively. No recurrence was observed in one-year follow up.

Conclusion

We show that the clinical features and managements of oral nonodontogenic masses in children in our department. Most of them are benign, few oral masses are malignant or mimic a malignant process, such as IMT. Surgical resections are the most common treatment with excellent success.

Abbreviations

IMT: inflammatory myofibroblastic tumor

LM: Lymphatic malformations

NF-1: neurofibromatosis type-1

Declarations

Ethics approval and consent to participate (informed consent)
This study was reviewed and approved by the Ethics Committee at Children’s Hospital of Nanjing Medical University and informed consent was obtained from their parents in all children patients.

**Consent for publication**

Not applicable

**Availability of data and materials**

The datasets analysed during the current study available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

Hao Zhang conceived, collected the data and co-wrote the article. Qiongqiong Zhou co-wrote the article. Weiming Shen guided the article. All authors read and approved the final manuscript.

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