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ORIGINAL ARTICLE

Ralf-Bodo Tröbs · Elinor Mader · Thomas Friedrich
Joachim Bennek

Oral tumors and tumor-like lesions in infants and children

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Abstract The aim of this retrospective study was to survey the spectrum of oral tumors and tumor-like lesions treated in a pediatric surgical unit. The clinical features and treatment outcome are presented, and guidelines for management discussed. Long-term follow-up was carried out both by re-examination and by means of a questionnaire. A total of 95 patients were encountered over a 30-year period. The age at presentation ranged from 1 day to 16 years, and the male to female ratio was 0.7:1. The lesions were located predominantly on the lips (22%), tongue (21%), and cheek (19%). Patients were divided into five groups based on histological diagnosis. Benign lesions accounted for 83 (87%) of the cases. Of these, 41 (43%) were benign tumors, the most common of which were the hemangiomas (17 cases). Hamartomas accounted for a further 22 benign lesions (23%), among which 12 were lymphangiomas. Furthermore, we saw 14 cases (15%) of mucoceles, ranula and dysontogenetic cysts, and a further 6 cases (6%) were classed as miscellaneous lesions. Simple surgical resection was successful in treating most benign lesions, with occasional re-excision being necessary in lymphangiomas. The long-term effects of treatment include reduction of the red volume of the lips, scarring following resection of parotid hemangiomas, a forked tongue after wedged resection, and partial facial nerve palsy. The group of 12 (13%) malignant tumors consisted of 5 rhabdomyosarcomas, 2 fibrosarcomas, 2 carcinomas of the parotid, 1 osteosarcoma, and 2 metastases. A multimodal approach was used in patients with rhabdomyosarcomas, while fibrosarcomas and parotid carcinomas were normally treated by surgical excision. Six of 12 patients with malignant tumors were alive after a median follow-up of 20.5 years. Re-examination of the malignant tumor group revealed scarring, impaired growth and function of the maxilla associated with local irradiation, and an external salivary fistula. In conclusion, while most oral and maxillofacial tumors of children are benign, malignant tumors of soft tissue, salivary glands and bones must be taken into account. There are specific aspects related to certain developmental and biological characteristics that make a mainly conservative approach preferable in these children.

Keywords Oral cavity · Oral tumor · Hamartoma · Cyst · Infancy · Childhood

R.-B. Tröbs (✉) · E. Mader · J. Bennek
Klinik und Poliklinik für Kinderchirurgie,
Universitätsklinikum Leipzig AöR,
Oststrasse 21–25, 04317 Leipzig, Germany
E-mail: trob@medizin.uni-leipzig.de
Tel.: +49-341-9726400
Fax: +49-341-9726409

T. Friedrich
Institut für Pathologie,
Universitätsklinikum Leipzig AöR,
04317 Leipzig, Germany

Introduction

Pediatric surgeons, oral surgeons, dentists and pediatricians are faced with a spectrum of different tumors and tumor-like lesions of the oral cavity in infants and children. For accurate counseling of such patients it is clearly necessary to make informed judgments concerning the probability of diagnosis based on data concerning occurrence, expected biological behavior and prognosis. Despite numerous case reports, the currently available information on treatment methods and long-term results for oral and maxillofacial tumors in children is largely incomplete. Of nine comprehensive papers on this topic published since 1963 [1, 3, 16, 17, 20, 28, 30, 33, 35], the vast majority consider oral lesions in children from the point of view of oral surgeons or pathologists. From these studies it is clear that oral lesions in children are commonly benign. However, long-term results are only occasionally reported. The aim of our investigation was to conduct a survey from the pediatric surgical point of view, considering the complete spectrum of oral and perioral lesions treated in a pediatric surgical unit, with

the main emphasis on treatment, treatment results and long-term outcome.

Materials and methods

In a retrospective study, we identified 95 infants, children and adolescents who received operative treatment in our institution between 1970 and 1999. The inclusion criteria were based on anatomical definition of lesions of the tongue, cheek, lips, alveolar ridges, hard and soft palate, oral mucosa, and of the glands with ducts opening into the cavity [10]. Odontogenic tumors, abscess formations and lesions managed non-operatively were excluded.

Diagnoses were based on the results of pathohistological investigations, and for the purposes of this study patients were divided into 5 groups based on histological diagnosis and biological behavior: genuine benign tumors, hamartomas and tumor-like lesions, epithelial lined cysts, miscellaneous lesions, and malignant tumors.

In all cases, the clinical records were re-examined together with the pathohistological reports. The clinical appearance was analyzed according to age, sex, site, relapse, and survival. Pathohistological specimens were re-evaluated in 15 selected cases, leading in one case to revision of the original diagnosis of infantile fibrosarcoma to one of myofibroma of the cheek.

Follow-up information covering a period of 1–26 years post treatment was obtained from 72 patients by clinical examination, by an evaluative questionnaire regarding long-term effects or by telephone interviews.

Results

The age at presentation ranged from the day of birth to 16 years 10 months. The median age at diagnosis was 2.3 years. Seventy-one infants and children in the first 6 years of life accounted for the majority (75%) of patients. The male to female ratio was 0.7:1 (39 boys and 56 girls).

The evaluation revealed 83 (87%) benign and 12 (13%) malignant lesions. At the time of reevaluation the majority of patients were alive and well. However, a total of 8 patients had died and in 6 cases the death was tumor associated.

The lesions were predominantly located on the lips ($n=21$, 22%), tongue ($n=20$, 21%), cheek ($n=18$, 19%), floor of the mouth ($n=12$, 13%), and major salivary glands ($n=12$, 13%). Less common were lesions on the alveolar ridge ($n=5$, 5%), maxilla ($n=4$, 4%), and palate ($n=3$, 3%).

Types and sites of tumors

Genuine benign tumors Forty-one benign lesions were considered to be genuine tumors (Table. 1); 36 of these were of mesenchymal, 5 of epithelial (papilloma of the tongue, pleomorphic adenoma) origin. Tumors of vascular origin were predominant, with the majority being hemangiomas. Connective tissue tumors were diagnosed in 6 cases. Congenital epulis (syn. congenital granular cell tumor) was observed in 4 infants, and occasional lipomatous, myogenous and neurogenic tumors were also recorded. (Hamartomas and tumor-like lesions are listed in Table. 2.) The most common hamartomas were lymphangiomas, hemangiolymphangiomas, and venous malformations (cavernous hemangioma). Eosinophilic granuloma (Langerhans' cell histiocytosis) was diagnosed in 2 cases. The group of miscellaneous lesions included cases of inflammatory and infectious processes. The group of cysts (Table. 3) included retention cysts of the small salivary glands, ranulas and dysontogenetic cysts of the tongue lined with respiratory epithelium. In addition, we handled a thyreoglossal duct cyst of the tongue and a large submandibular gastrogenic cyst involving the floor of the mouth. The group of *malignant tumors* comprised 9 tumors of mesenchymal and 3 tumors of epithelial origin. Soft tissue sarcomas occurred in 7 children. One patient with retinoblastoma developed an osteosarcoma of the maxillary bone at the

Table 1 Type and site of benign tumors ($n=41$). *P* Parotid gland, *S* submandibular gland

Tumor	Number	Lips	Palate	Cheek	Floor	Tongue	Alveolar ridge	Major salivary glands
Hemangioma	17	9	0	1	-	2	1	4 (P)
Hemangioendothelioma	1	-	-	-	-	1	-	-
Hemangiopericytoma	1	-	-	1	-	-	-	-
Fibroepithelioma	3	-	-	-	-	3	-	-
Fibroma	2	-	1	-	-	1	-	-
Musculoaponeurotic fibromatosis	1	-	-	-	1	-	-	-
Myofibroma	1	-	-	1	-	-	-	-
Rhabdomyoma	1	-	-	-	-	1	-	-
Lipoma	2	-	-	1	-	1	-	-
Fibrolipoma	1	-	1	-	-	-	-	-
Neurinoma	1	-	-	-	1	-	-	-
Neurofibroma	1	-	-	1	-	-	-	-
Papilloma	3	-	-	-	-	3	-	-
Pleomorphic adenoma	2	-	-	-	-	-	-	2 (P, S)
Congenital granular cell tumor	4	-	-	-	-	-	4	-

Table 2 Hamartoma and tumor-like lesions ($n=22$), miscellaneous lesions (*; $n=6$). *S* submandibular gland, *G* salivary gland

Lesion	Number	Lips	Palate	Cheek	Floor	Tongue	Major salivary glands
Lymphangioma	12	1	-	8	2	1	-
Hemangiolymphangioma	4	1	-	-	1	-	2 (P)
Venous malformation	4	2	-	1	-	1	-
Eosinophilic granuloma	2	1	1	-	-	-	-
Buccal fat hyperplasia*	1	-	-	1	-	-	-
Pyogenic granuloma*	1	-	-	-	-	1	-
Sclerosing sialoadenitis*	2	-	-	-	-	-	2 (S, G)
Common warts*	1	1	-	-	-	-	-
Caseous tuberculosis*	1	-	-	1	-	-	-

Table 3 Cysts of the salivary gland duct, dysontogenetic cysts ($n=14$)

Lesion	Number	Lips	Palate	Cheek	Floor	Tongue	Major salivary glands
Ranula	4	-	-	-	4	-	-
Retention cysts of small glands	6	3	-	-	1	2	-
Dysontogenetic cysts	2	-	-	-	-	2	-
Thyreoglossal duct cyst	1	-	-	-	-	1	-
Gastrogenic cyst	1	-	-	-	1	-	-

age of 11 years. A metastatic tumor of the lip was the first sign of a disseminated stage IV-S neuroblastoma in a 6-month-old girl. The malignant tumors of epithelial origin exclusively affected the parotid gland.

Treatment and long-term results

Therapeutic strategies were modified to keep pace with developments in the field over the 30-year period covered by this study. With the exception of hemangiomas, small resectable soft tissue tumors were generally excised.

Benign lesions Treatment modalities for hemangiomas (including cavernous forms) consisted of excision ($n=9$), electrocoagulation with a needle ($n=4$), oral administration of prednisone ($n=3$), laser treatment ($n=2$), local irradiation ($n=1$), and observation ($n=2$). One child experienced an incomplete facial nerve palsy immediately after resection of a hemangioma of the parotid. Long-term follow-up data are available for 18 patients originally diagnosed with hemangioma/hemolymphangioma. In two of these cases re-excision of residual vascular malformations of the lower lip was necessary. Four female hemangioma patients complained of cosmetic impairment due to reduction of the red volume and/or recurrent swelling of the lips. Four patients reported extended scars after excision of parotid hemangiomas and one reported malposition of the permanent teeth. One woman suffered from severe psychological problems caused by a forked tongue after wedged resection of a cavernous hemangioma. However, she refused corrective surgical treatment. In one patient, a fibrous remnant at the base of the tongue is present 18 years after resection of a hemangioendothelioma. Lymphangiomas were excised in 11 of 12 patients, with re-excision being necessary after relapse or incomplete removal in 5 patients. With the exception of delayed dentition in one girl, none of the four infants with congenital granular cell tumors developed any sequel. Repeated recurrence of a neurofibroma involving parts of left face in a 15-year-old boy led to subsequent surgical interventions by a plastic surgeon. No recurrence of the papillomas was observed. The two patients with pleomorphic adenoma were cured by resection of the involved salivary gland (follow-up 3 years and 24 years). After excision of fibroepitheliomas, fibromas and fibrolipomas, children generally had a favorable outcome. Twelve of 14 cystic lesions (ranulae, mucoceles, and dysontogenetic cysts) were excised completely, while a marsupialization was performed in 2 children with ranula. Following excision, recurrent cysts were observed in two cases.

Malignant tumors (Table. 4). Six of 12 patients with malignant tumors were alive and free of disease at the time of our investigation (median follow-up 20.5 years). In four children (fibrosarcoma, carcinoma of the parotid) the tumors were excised without any adjuvant treatment. A multimodal approach including surgery (biopsy or excision), antineoplastic chemotherapy and/or radiation was used for eight patients with malignant mesenchymal tumors. Four patients (rhabdomyosarcoma, fibrosarcoma, osteogenic sarcoma) had received local irradiation with doses of 22 to 50 Gy. Physical reexamination of three of these patients 10, 11, and 18 years after radiation treatment revealed mild scars in two cases, while the third one suffered from impaired

Table 4 Malignant tumors: appearance, therapy and outcome ($n=12$). *ACT-D* – actinomycin-D, *ADM* – adriamycin, *Cyclo* – cyclophosphamide, *ETO* – etoposide, *IFO* – iphosphamide, *VCR* – vincristine; *EFS* – event-free survival, *DOD* – died of disease

Case no., sex, year	Age (years)	Site	Histology	Surgery	Chemotherapy	Radiation	Survival	Problems, Ddifficulties, Sside effects	Follow-up
1, M, 1970	3	Maxilla	RMS embryonal	Biopsy	Cyclo	No	DOD, 9 days	Progression	DOD
2, M, 1980	4	Cheek	RMS	Biopsy	VCR, Cyclo, ACT-D, ADM	45 Gy	EFS, >19 years	Hypoplasia of maxilla, lockjaw	EFS, >10 years
3, M, 1981	2	Maxilla	RMS embryonal	Excision	VCR, Cyclo, ACT-D, ADM	22.5 Gy	EFS, >21 years	No impairment	EFS, >10 years
4, M, 1987	4 mo	Lower lip	RMS undifferentiated	Excision	VCR, Cyclo, ADM	No	Died, 15 days	Acute liver failure	Died
5, F, 1994	16	Maxilla	RMS embryonal	Biopsy	ETO, VCR, ACT-D, IFO, ADM	Yes	DOD, 2 years 10 months	Progression	DOD
6, F, 1978	6 mo	Cheek	Infantile fibrosarcoma	Excision	No	No	EFS, >21 years	No	EFS, >21 years
7, F, 1980	10	Lower lip	Fibrosarcoma	Excision, re-excision	No	Brachytherapy, 50 Gy	EFS, >11 years	No	EFS, >11 years
8, M, 1982	12	Maxilla	Osteosarcoma	Excision, re-excision	Yes	50.6 Gy	DOD, 10 years 10 months	No	DOD
9, M	14	Parotid	Adenoid-cystic carcinoma	Excision, neck- dissection	No	No	>26 years	Local relapse	Survival, >27 years
10, F	9	Parotid	Mucoepidermoid carcinoma	Excision	No	No	EFS, >14 years	No	EFS
11, F		Parotid	Metastasis of lymphoepithelial carcinoma	Excision	No	No	DOD, 6 months	Progression	DOD
12, F, 1970	6 mo	Upper lip	Metastasis of neuroblastoma	Excision	Cyclo	No	DOD, 4 months	Relapse and progression	DOD

growth of the maxillary bone, an asymmetric face, partial lockjaw, and a lack of dentition involving three teeth. Two of the three patients with malignant tumors of the parotid survived for more than 20 years after surgery. One of them had a local relapse which was successfully treated by re-excision. At re-examination, one patient presented a small external salivary fistula below the zygomatic bone. A total of five children died due to tumor progression, while one infant with a rhabdomyosarcoma of the lower lip developed a liver failure induced by the antineoplastic chemotherapy.

Discussion

Here we report our experience with a number of children encountered and treated over a 30-year period. As previous studies have demonstrated, the vast majority of oral lesions in infants and children is of mesenchymal nature, and is benign in character, ranging from 84% to 99% of cases (Table 5). However, malignant tumors clearly should be taken into account regardless of age. In general, mesenchymal tumors are predominant while tumors of epithelial origin occur only rarely. The rate of odontogenic tumors varies between 1.9% and 33.7% [3, 17, 20, 28, 30, 33, 35]. These patients are commonly treated by oral surgeons and dentists and, with the exception of infants with congenital granular cell tumor, are excluded from our analysis. In contrast to the female predominance reported here, a male predominance is reported in three of five studies [1, 20, 35] while the remaining two authors report equally distributed genders. However, since both congenital granular cell tumors and vascular tumors in children are known to show clear female predominance [6, 27], the relatively large number of vascular lesions which were considered here, together with the cases of granular cell tumors, may be responsible for the predominance of girls in our series. Our observations concerning site distribution are consistent with the literature [29, 33], and with the predominant occurrence of oral lesions at mechanically stressed regions like the lips, tongue, buccal mucosa, and cheeks. Despite the prevalence of reactive lesions, dysontogenetic cysts, inflammatory lesions and benign tumors in this patient group, the incidence of malignant tumors should not be underestimated. The 13% incidence of malignancy observed in our study lies at the upper end of the range of 1–16% reported for other European and North American studies, while the exceedingly high rate of 40% malignant tumors in Nigerian children [1] is attributable to the high prevalence of Burkitt's lymphoma in this population. Our malignancy rate is probably biased upwards on the one hand by exclusion of the large number of benign odontogenic tumors, and on the other hand by the inclusion of lesions of the large salivary glands. Within the parotid gland hemangioma, lymphangioma and pleomorphic adenoma are common lesions [22, 28]. It is remarkable that carcinomas accounted for 3 of the 12 lesions affecting the parotid gland in our series. Considering the 35–46% incidence of malignant parotid tumors in children, all parotid lesions should be suspected of being malignant until proven otherwise [18, 21, 22, 28]. Previous studies have reported lymphomas and soft tissue sarcomas to be the most common malignant oral tumors in children [16, 17, 29, 33, 35], and it remains unclear why lymphomas were not observed in our investigation.

The prognosis for circumscript oral lesions is generally excellent, and complete resection should be the goal when treating a child with an oral tumor. However, the maintenance of normal orofacial growth and function must also be taken into account [33]. A transoral route for resection is preferable in order to avoid scars and subsequent cosmetic problems.

A spectrum of embryonal tumors occurs exclusively during infancy and childhood. Congenital granular cell tumor (epulis) is a benign tumor of the gingiva that originates from the alveolar ridge. Clinically, it appears as a round or ovoid, sessile and pedunculated swelling, usually arising from the upper jaw. Treatment consists of simple excision, recurrence has not been reported and prognosis is excellent [14, 27, 34]. Spontaneous involution has been described in isolated cases [8].

The retrospective nature of our study made it difficult to distinguish between hemangiomas and venous malformations. The completely different biological behavior

Table 5 Surveys on oral lesions in children (*ND*- no data, *NOD* – non-odontogenic, *OD* – odontogenic tumors included).

Author	No. of patients	Age (years)	Male:female ratio	Lesions studied	Benign (%)	Malignant (%)	Odonto-genic (%)	Mucocele, cysts (%)
Jones 1965	161	0–15	ND	NOD	92.5	7.5	0	0
Bhaskar 1963	293	0–14	0.9 :1	OD	91	9	15	
Skinner et al. 1986	1525	1–19	ND	OD	99.9	0.1	19	21.7
Keszler et al. 1990	1289	0–15	ND	OD	84	16	5	25.4
Arotiba 1996	174	0–15	1.4:1	ND	59.8	40.2	18.4	ND
Sato et al. 1997	250	4 mo –15	ND	OD	93	7	31.6	0
Tanaka et al. 1999	105	6 mo –15	1:1	OD	97.1	2.9	26.7	0
Ulmansky et al. 1999	966	0–15	1.25:1	OD	98.1	1.9	1.9	Included
Maaita 2000	172	6 mo –18	1.5:1	OD	91	9	33.7	0
Present study	95	0–16	0.7:1	NOD	87	13	4.2	14.7

of these conditions demands different therapeutic strategies. Hemangioma is reported to be one of the most common non-odontogenic oral tumors [16, 29, 33]. It is characterized by a high endothelial proliferation rate and invasive growth during the first year of life [25]. Proliferating hemangiomas may impair vital structures and functions due to compression, ulceration, pain or bleeding. Modern therapy concepts prefer early local laser and cryotherapy as well as systemic corticosteroid or α-interferon therapy for refractory, fast growing or systemic forms [36]. In contrast, cavernous hemangioma is considered to be a vascular malformation (hamartoma) [25]. It does not proliferate and grows proportionately with the infant [25]. Epidemiological investigations have shown a high prevalence of vascular borderline tumors such as hemangioendothelioma and hemangiopericytoma in the head and neck region [4]. Wide local excision is the recommended treatment [11], although postoperative chemotherapy may be required for hemangiopericytoma [2, 24].

Lymphangiomas are benign hamartomatous lesions or malformations of lymphatic vessels with a marked predilection for the craniofacial and cervical region [13, 15]. As we observed, the tendency to infiltrate and surround neurovascular structures and adjacent tissues makes resection challenging and often incomplete [9, 19]. The reported complication rates following operative intervention range from 19% to 33% [15]. Laser photocoagulation or local instillation of sclerosing agents has been reported as a useful alternative to surgical resection in controlling lymphangiomas [13, 23, 36].

Cysts have previously been reported to account for one fifth to one fourth of oral lesions [17, 30]. Among these, the ranulas are congenital epithelial lined retention cysts of the floor of the mouth, usually resulting from obstruction of the ducts of the submaxillary, sublingual or perhaps other minor salivary glands [7]. In contrast, the mucous extravasation pseudocyst arises as a result of trauma to the sublingual duct. Reactive mucoceles commonly occur in females, with the lower lip being the most common site [30]. We performed simple marsupialization of 2 ranulas with success. To prevent relapse, excision of the cyst, possibly including the adherent sublingual salivary gland has been recommended [7, 19]. Small oral mucosal cysts situated either palatal or at the alveolar ridges are common in newborns and will disappear untreated [12].

Embryonal rhabdomyosarcoma is the most common malignant soft tissue tumor of the head and neck region in children [5, 26]. In the majority of oral and maxillofacial manifestations it is not possible to achieve complete resection with tumor-free margins. The use of a multimodal therapy including pre- and postoperative chemotherapy, and preoperative radiation therapy if necessary has improved survival rates [5, 26]. For the most part, mutilating resections are not included in the multimodal approach. Furthermore, the long-term morbidity associated with ionizing radiation in children demands that there be strong indications for radiation therapy to be undertaken. The major side effects of local irradiation depend on the age of the patient and the administered dose. They include impairment of the normal growth and development of oral structures and impaired dentition (micrognathia, microdontia, hypoplastic enamel, underdeveloped roots resulting in delayed or premature exfoliation of the primary and secondary teeth) [26]. The occurrence of infantile fibrosarcoma is not uncommon in the oral region [3, 20, 32]. If possible, wide local excision without sacrificing any significant function should be the preferred form of treatment [24, 32]. Carcinomas of the maxillofacial and oral region in children may occur within the mouth or nasopharynx, or may arise from the major salivary glands. Any suspicion of malignancy has to be taken as an indication for biopsy. The treatment of salivary gland carcinoma is total parotidectomy, involving resection of the portion of the parotid superficial and deep to the facial nerve, or subtotal parotidectomy (superficial parotid lobectomy), which involves resection only of that portion of the parotid that is superficial to the facial nerve [21, 28, 31]. A modified neck dissection is indicated in cases of lymph node infiltration. Multimodal treatment has been employed with variable results [21, 31]. Overall, the 5-year survival in children with mucoepidermoid and acinic cell carcinomas is greater than 90% [24]. In establishing a differential diagnosis, it is important to consider both pleomorphic adenoma (as the most frequently encountered benign epithelial tumor in childhood) and chronic sclerosing sialoadenitis [16, 19]. In the surgical treatment of pleomorphic adenoma, superficial lobectomy or total parotidectomy for a deep lobe tumor is required in order to prevent local relapse [19]. As reported here, the long-term consequences of parotidectomy can include facial nerve palsy, scar formation and external salivary fistula formation. The very rare lymphoepithelial carcinoma (Schmincke tumor) of the parotid arises from epithelium overlying the lymphoid tissue of the nasopharynx (nasopharyngeal carcinoma) and responds well to radiotherapy and chemotherapy [24].

In conclusion, most oral and maxillofacial tumors in children are benign, and simple surgical excision via an intraoral approach is adequate in the majority of cases. For differential diagnosis, sarcomas of bone and soft tissue as well as carcinomas of the salivary glands have to be taken into account. There are specific aspects related to certain developmental and biological characteristics that make a more conservative approach preferable in the management of childhood disease.

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