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Pathological lesions of the oral mucosa in children and adolescents based on microscopic examination: a comparative analysis of systemically healthy patients and patients with systemic diseases

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Research Article

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Abstract

Objectives

To compare the clinical presentation, location and histopathological spectrum of oral mucosal lesions in systemically healthy children and adolescents and in patients with systemic diseases treated in a tertiary pediatric setting.

Materials and methods

This observational study included 882 patients aged from 1 month to 18 years who presented with oral mucosal lesions between July 2021 and February 2026. Patients were divided into systemically healthy and systemic disease groups. A histopathologically verified subgroup comprised 315 biopsied lesions (211 in healthy patients and 104 in patients with systemic diseases). The patient-level database was used for descriptive analysis, between-group comparisons, odds ratios with 95% confidence intervals, and multivariable logistic regression.

Results

In the biopsied subgroup, patients with systemic diseases were older than systemically healthy patients (median age 114.0 vs 58.0 months; Mann-Whitney U = 14,626; $p < 0.001$) and more often male (63.5% vs 46.4%; $p = 0.004$). The histopathological spectrum differed significantly between groups (chi-square = 61.13; df = 10; $p < 0.001$; Cramer's V = 0.44). Mucocele predominated among healthy patients (66/211; 31.3%), whereas inflammatory granulation tissue predominated among patients with systemic disease (42/104; 40.4%). In univariable analysis, systemic disease was associated with ulceration (OR = 6.70; 95% CI: 3.09–14.54), inflammatory granulation tissue (OR = 5.28; 95% CI: 2.96–9.41) and PTLD (OR = 18.94; 95% CI: 1.01-355.21). In multivariable logistic regression, independent predictors of systemic disease were older age, male sex, ulceration and inflammatory granulation tissue.

Conclusions

Oral mucosal lesions in children and adolescents were predominantly benign, inflammatory or reactive. Systemic disease was associated with a distinct histopathological pattern, particularly a higher relative frequency of inflammatory granulation tissue and ulcerated inflammatory lesions. Persistent proliferative or ulcerative oral lesions in medically compromised children require careful clinicopathological correlation.

Introduction

The oral mucosa is a natural barrier between the external environment of the oral cavity and the internal milieu. It is continuously exposed to microorganisms, food particles, mechanical trauma and environmental irritants. Its main functions include protection, defence, sensory perception, taste, absorption and secretion. Histologically, the oral mucosa consists of stratified squamous epithelium, lamina propria and, depending on the site, a submucosal layer [1].

Oral mucosal lesions (OML) can be classified using morphological, clinical and etiological criteria. Morphologically, primary lesions arise on previously unchanged mucosa, whereas secondary lesions develop from pre-existing primary lesions. Clinically, oral lesions include pigmented lesions, white keratotic lesions, erythematous lesions, papular and vesiculobullous lesions, nodular or proliferative lesions, erosions, ulcerations and mucous retention/extravasation lesions such as mucoceles [1–4].

Etiological factors include viral infections, particularly Herpesviridae and papillomaviruses, bacterial infections such as Staphylococcus aureus and Streptococcus pyogenes, fungal infections such as Candida spp., immune-mediated inflammatory disorders, traumatic injuries and, rarely in children, potentially malignant and malignant lesions [3–5]. Some oral lesions are asymptomatic, whereas others cause pain, feeding difficulties, speech impairment or impairment of daily oral functions.

Oral mucosal pathology may be a local phenomenon, but it may also be associated with systemic disease or may represent an early sign of a general disorder [3, 6]. In medically compromised children, mucosal lesions may reflect the underlying disease, malnutrition, immune dysfunction, medications, transplantation-related immunosuppression or oncological treatment. Recurrent aphthous ulceration, erosions, ulcers, epithelial clefts, angular cheilitis, facial swelling, atrophic mucositis and oral candidiasis have been reported more frequently in children with systemic conditions [3–6]. At the same time, many pediatric oral mucosal conditions are benign and self-limiting, for example geographic tongue and hairy tongue [3, 4].

Oral and maxillofacial lesions in children differ from lesions observed in adults in their epidemiology, biology, histopathological spectrum and management [7–15]. The clinical similarity of different entities may cause diagnostic difficulty, and histopathological examination remains essential for the definitive diagnosis of persistent, atypical, exophytic or ulcerative lesions. Previous pediatric biopsy-based studies have shown that most lesions are benign, with mucoceles, reactive lesions, inflammatory lesions, odontogenic cysts and fibrous hyperplasia among the most common diagnoses [8–20]. Large tumor-focused series also emphasise that pediatric oral and maxillofacial lesions have specific age-related and anatomical patterns, and that management must take growth and development into account [21].

Despite increasing literature on oral lesions in children, relatively few studies have focused on the microscopic spectrum of oral mucosal lesions in medically compromised children compared with systemically healthy peers. A comparative histopathological analysis may improve understanding of lesion pathogenesis and may support clinical decision-making in pediatric oral medicine and oral surgery.

Objectives

The aim of this study was to describe and compare pathological lesions of the oral mucosa in systemically healthy children and adolescents and in patients with systemic diseases, with particular reference to age, lesion location, clinical presentation and histopathological diagnosis.

Materials and methods

Study design and setting

This observational study included children and adolescents who presented with pathological lesions of the oral mucosa to the Department of Dentistry of a tertiary pediatric institute between July 2021 and February 2026. The study was approved by the Bioethics Committee of the Institute "Pomnik-Centrum Zdrowia Dziecka" (approval No. 32/KBE/2021, 30 June 2021). Data were handled confidentially.

Participants

The clinical cohort consisted of 882 patients aged from 1 month to 18 years, including 442 girls and 440 boys. There were 507 systemically healthy patients and 375 patients with systemic diseases. The systemic disease group included recipients of vascularized organs, patients after oncological treatment, patients with neurological diseases, cardiac diseases, immunodeficiencies and other systemic conditions. Exact disease-subgroup denominators were available only for the biopsied subgroup and are shown in Supplementary Table S5.

Clinical assessment and biopsy criteria

Assessment included general medical history, history of the oral lesion, clinical dental and oral mucosal examination, evaluation of regional lymph nodes and photographic documentation. All exophytic lesions and ulcerative lesions persisting for more than 2 weeks despite observation and/or treatment were considered for surgical biopsy or complete excision and histopathological examination. Selected exophytic lesions with clear surgical indications were biopsied or excised without a preceding observation period. Clinical examination and biopsies were performed by four oral surgeons, each with at least 10 years of professional experience.

Inclusion and exclusion criteria

The histopathological study group included patients with oral mucosal lesions who underwent biopsy and microscopic examination. Patients with drug-induced gingival overgrowth and patients with erosions or ulcerations caused by complications of chemotherapy were excluded from the histopathological analysis. Biopsies with inconclusive microscopic diagnoses were also excluded.

Variables and grouping

The following variables were analysed: sex, age, systemic health status, lesion location, clinical lesion type and histopathological diagnosis. Age was grouped into four categories: <1 year, 1–6 years, 6–12 years and 12–18 years. Clinical lesions were grouped as exophytic lesions, ulcerations/erosions and other lesions. Ulcerations and erosions included aphthae, aphthous-like lesions, candidiasis, traumatic lesions (mechanical, chemical, thermal and linea alba), herpes simplex, herpetic stomatitis and angular cheilitis. Other lesions included lichenoid lesions and hyperkeratotic lesions in hyper-IgE syndrome or after hematopoietic stem cell transplantation (HSCT). Anatomical locations included upper gingiva/alveolar process of the maxilla, lower gingiva/alveolar part of the mandible, tongue, lip, floor of the mouth, buccal mucosa and palate.

Statistical analysis

The extended statistical analysis was performed using the patient-level biopsy database provided for this revision. Records were included when age and histopathological diagnosis were available.

Quantitative variables were assessed for normality using the Shapiro-Wilk test and are presented as mean with standard deviation and median with interquartile range. Because age was not normally distributed, the Mann-Whitney U test was used for the primary between-group comparison; Welch's t-test is additionally reported as a sensitivity analysis. Categorical variables were compared using Pearson's chi-square test. Effect size for global categorical comparisons was expressed as Cramer's V. For selected binary comparisons, odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated; exact Fisher tests were used for sparse 2x2 tables and continuity-corrected estimates were applied when a zero cell was present. False discovery rate (FDR) correction using the Benjamini-Hochberg method was applied to exploratory multiple comparisons within diagnostic and location categories. A multivariable logistic regression model was fitted with systemic disease status as the dependent variable and age, sex, ulceration, selected histopathological diagnoses and main anatomical locations as predictors. Statistical significance was set at $p < 0.05$.

Results

Whole clinical cohort

Oral mucosal lesions were recorded in 882 children and adolescents. The study population included 442 girls (50.1%) and 440 boys (49.9%). Systemically healthy patients accounted for 507/882 (57.5%) cases and patients with systemic diseases for 375/882 (42.5%) cases. The mean age reported for the entire cohort was 85.65+/-65.79 months. The distribution of age categories differed markedly between healthy and systemically affected patients (global chi-square = 53.54; df = 3; $p < 0.001$). In the systemic disease group, older children, especially those aged 6–12 and 12–18 years, constituted a higher proportion than in the healthy group (Table 1).

Table 1
Characteristics of the whole clinical cohort (n = 882).

Variable	Systemic disease n (%)	Healthy n (%)	Total n (%)
Total patients	375 (42.5)	507 (57.5)	882 (100.0)
Girls	172 (45.9)	270 (53.2)	442 (50.1)
Boys	203 (54.1)	237 (46.8)	440 (49.9)
< 1 year	33 (8.8)	86 (17.0)	119 (13.5)
1–6 years	87 (23.2)	202 (39.8)	289 (32.8)
6–12 years	134 (35.7)	115 (22.7)	249 (28.2)
12–18 years	121 (32.3)	104 (20.5)	225 (25.5)
Age, months, mean +/- SD	107.52 +/- 67.35	81.35 +/- 48.67	85.65 +/- 65.79

Percentages are presented as in the source data. For age categories, the global chi-square test comparing systemic disease and healthy groups was significant (chi-square = 53.54; df = 3; $p < 0.001$).

Clinical presentation and lesion location

Clinical evaluation divided lesions into exophytic lesions, ulcerations/erosions and other lesions. Exophytic lesions were more frequently recorded in systemically healthy patients, whereas ulcerations and erosions, especially non-traumatic ulcerative lesions, were relatively more common in patients with systemic diseases. A statistically significant difference was reported for exophytic lesions ($p < 0.0001$), total ulcerations/erosions ($p = 0.0182$), non-traumatic ulcerations/erosions ($p = 0.0341$) and aphthae ($p = 0.0209$). The global distribution of locations across the oral cavity differed between groups (source $p = 0.0372$), although no single anatomical site showed a significant between-group difference in the source table.

Table 2
Clinical presentation of oral mucosal lesions in the whole cohort.

Clinical characteristic	Systemic disease n (%)	Healthy n (%)	Total n (%)	p value
Exophytic lesion	78 (8.8)	199 (22.6)	277 (31.4)	< 0.0001
Ulcerations/erosions - traumatic	32 (3.6)	58 (6.6)	90 (10.2)	0.1092
Ulcerations/erosions - other	69 (7.8)	22 (2.5)	91 (10.3)	0.0341
Ulcerations/erosions - total	101 (11.4)	80 (9.1)	181 (20.5)	0.0182
Aphthae	25 (2.8)	71 (8.0)	96 (10.8)	0.0209
Aphthous-like lesions	63 (7.1)	53 (6.0)	116 (13.1)	0.4812
Candidiasis	38 (4.3)	38 (4.3)	74 (8.6)	0.9998
Trauma - linea alba	4 (0.5)	21 (2.4)	25 (2.9)	0.0162
Trauma - mechanical	4 (0.5)	17 (1.9)	21 (2.4)	0.3610
Trauma - thermal	0 (0.0)	3 (0.3)	3 (0.3)	0.9999
Trauma - chemical	2 (0.2)	0 (0.0)	2 (0.2)	0.9999
Herpes simplex	5 (0.6)	8 (0.9)	13 (1.5)	0.9091
Herpetic stomatitis	12 (1.4)	2 (0.2)	14 (1.6)	0.8192
Angular cheilitis	21 (2.4)	14 (1.6)	35 (4.0)	0.2561
Lichenoid lesions	15 (1.7)	1 (0.1)	16 (1.8)	0.9956
Hyperkeratotic lesions in hyper-IgE/HSCT	7 (0.8)	0 (0.0)	7 (0.8)	0.9999

Rows are not mutually exclusive. Percentages follow the source table and use the whole cohort as denominator.

Table 3
Location of oral mucosal lesions in the whole cohort.

Location	Systemic disease n (%)	Healthy n (%)	Total n (%)	p value
Upper gingiva/alveolar process of maxilla	42 (4.8)	55 (6.2)	97 (11.0)	0.3608
Lower gingiva/alveolar part of mandible	48 (5.4)	69 (7.8)	117 (13.2)	0.4511
Tongue	73 (8.3)	91 (10.3)	164 (18.6)	0.3512
Lip	61 (6.9)	83 (9.4)	144 (16.3)	0.1821
Floor of the mouth	57 (6.4)	79 (9.5)	136 (15.9)	0.3511
Buccal mucosa	68 (7.7)	90 (10.2)	158 (17.9)	0.1821
Palate	26 (2.9)	40 (4.5)	66 (7.4)	0.3521

Global location comparison in the source table: p = 0.0372.

Biopsied subgroup

Biopsy and histopathological examination were performed in 315/882 patients (35.7%). This included 104/375 patients with systemic diseases (27.7%) and 211/507 systemically healthy patients (41.6%). The proportion of biopsied patients was significantly lower in the systemic disease group than in the healthy group (chi-square = 17.50; $p < 0.001$; OR = 0.54; 95% CI: 0.40–0.73). In the biopsied subgroup, boys were more frequent in the systemic disease group, whereas girls predominated among the healthy patients (chi-square = 7.41; $p = 0.006$). Age distribution also differed between groups (chi-square = 22.92; df = 3; $p < 0.001$).

Table 4
Characteristics of patients who underwent biopsy and histopathological examination (n = 315).

Variable	Systemic disease n (%)	Healthy n (%)	Total n (%)
Biopsied patients	104 (33.0)	211 (67.0)	315 (100.0)
Girls	38 (36.5)	113 (53.5)	151 (47.9)
Boys	66 (63.5)	98 (46.5)	164 (52.1)
< 1 year	7 (6.7)	35 (16.6)	42 (13.3)
1–6 years	25 (24.0)	86 (40.8)	111 (35.2)
6–12 years	41 (39.4)	62 (29.4)	103 (32.7)
12–18 years	31 (29.8)	28 (13.3)	59 (18.7)
Age, months, mean +/- SD	106.48 +/- 61.44	70.45 +/- 57.85	83.73 +/- 62.05

Age-category totals were corrected from the source cell counts: 25 + 86=111, 41 + 62=103 and 31 + 28=59.

Histopathological diagnoses

The most common histopathological diagnoses in the biopsied subgroup were mucocele (74/315; 23.5%), inflammatory granulation tissue (66/315; 21.0%), fibroma (46/315; 14.6%), squamous papilloma (35/315; 11.1%) and haemangioma/vascular lesions (25/315; 7.9%). The diagnostic distribution differed significantly between groups (global chi-square = 59.52; df = 10; $p < 0.001$). In patients with systemic diseases, inflammatory granulation tissue was the predominant diagnosis (42/104; 40.4%), whereas in systemically healthy patients mucocele was the predominant diagnosis (66/211; 31.3%).

Table 5
Main histopathological diagnoses in the biopsied subgroup.

Diagnosis	Systemic disease n (%)	Healthy n (%)	Total n (%)	p value
Squamous papilloma	14 (13.5)	21 (10.0)	35 (11.1)	0.348
Mucocele	8 (7.7)	66 (31.3)	74 (23.5)	< 0.001
PTLD	4 (3.8)	0 (0.0)	4 (1.3)	0.011
Inflammatory granulation tissue	42 (40.4)	24 (11.4)	66 (21.0)	< 0.001
Fibroma	11 (10.6)	35 (16.6)	46 (14.6)	0.177
Haemangioma/vascular lesion	8 (7.7)	17 (8.1)	25 (7.9)	1.000
Epulis	3 (2.9)	10 (4.7)	13 (4.1)	0.556
Histiocytosis	0 (0.0)	7 (3.3)	7 (2.2)	0.100
Giant cell lesion	2 (1.9)	4 (1.9)	6 (1.9)	1.000
Epidermal/epithelial cyst	1 (1.0)	4 (1.9)	5 (1.6)	1.000
Other diagnoses	11 (10.6)	23 (10.9)	34 (10.8)	1.000
Total	104 (100.0)	211 (100.0)	315 (100.0)	global p < 0.001

The table consolidates ulcerated and exophytic forms of the same diagnosis. Other diagnoses total was corrected arithmetically to 34 from the listed source counts. Global chi-square across diagnostic categories: $p < 0.001$.

Associations between systemic disease and histopathological diagnosis

Inflammatory granulation tissue was positively associated with systemic disease (OR = 5.28; 95% CI: 2.96–9.41; $p < 0.001$). Mucocele showed a negative association with systemic disease and was more frequent among healthy patients (OR = 0.18; 95% CI: 0.08–0.40; $p < 0.001$). PTLD occurred exclusively in the systemic disease group (4 cases), resulting in an elevated continuity-corrected OR. Fibroma was more frequent in healthy patients descriptively, but with the corrected consolidated counts the difference did not reach statistical significance in Fisher exact testing ($p = 0.177$).

Table 6
Odds ratios for selected histopathological diagnoses in patients with systemic disease compared with healthy patients.

Diagnosis	OR (95% CI)	p value
Squamous papilloma	1.41 (0.68–2.90)	0.348
Mucocele	0.18 (0.08–0.40)	< 0.001
PTLD	18.94 (1.01-355.21)*	0.011
Inflammatory granulation tissue	5.28 (2.96–9.41)	< 0.001
Fibroma	0.59 (0.29–1.23)	0.177
Haemangioma/vascular lesion	0.95 (0.40–2.28)	1.000
Epulis	0.60 (0.16–2.22)	0.556
Histiocytosis	0.13 (0.01–2.31)*	0.100
Giant cell lesion	1.01 (0.18–5.63)	1.000
Epidermal/epithelial cyst	0.50 (0.06–4.55)	1.000
Other diagnoses	0.97 (0.45–2.07)	1.000

OR, odds ratio; CI, confidence interval; PTLD, post-transplant lymphoproliferative disorder. *Continuity-corrected estimate because of a zero cell.

Extended patient-level statistical analysis

The patient-level biopsy database contained 315 complete histopathological records: 211 from systemically healthy patients and 104 from patients with systemic diseases. The systemic disease group was significantly older and had a higher proportion of boys. Global differences between groups were observed for age category, clinical lesion type and histopathological diagnosis. The strongest univariable associations with systemic disease were ulceration and inflammatory granulation tissue, whereas mucocele was significantly more common in systemically healthy patients. The anatomical distribution showed only a borderline global difference in the patient-level analysis.

Table 7
Extended patient-level statistical comparison of the biopsied subgroup.

Variable	Systemic disease	Healthy	Test	p	Effect size
Age, months, mean ± SD	107.2 ± 60.0	71.8 ± 57.4	Welch t-test	< 0.001	
Age, months, median (IQR)	114.0 (60.2–152.0)	58.0 (18.0-122.5)	Mann-Whitney U	< 0.001	
Male sex	66/104 (63.5%)	98/211 (46.4%)	Chi-square	0.004	V = 0.16
Age category	< 1: 7; 1–6: 25; 6–12: 41; 12–18: 31	< 1: 35; 1–6: 86; 6–12: 62; 12–18: 28	Chi-square	< 0.001	V = 0.27
Clinical type	Exophytic: 78; ulceration: 26	Exophytic: 199; ulceration: 10; other: 2	Chi-square	< 0.001	V = 0.30
Histopathological category	Global distribution	Global distribution	Chi-square	< 0.001	V = 0.44
Location	Global distribution	Global distribution	Chi-square	0.085	V = 0.19

IQR, interquartile range; SD, standard deviation; V, Cramer's V.

Table 8
Univariable odds ratios for systemic disease in the biopsied subgroup.

Feature	Systemic n/N	Healthy n/N	OR (95% CI)	p	FDR q
Male sex	66/104	98/211	2.00 (1.24–3.24)	0.006	
Age ≥ 6 years	74/104	90/211	3.32 (2.00-5.49)	< 0.001	
Ulceration	26/104	10/211	6.70 (3.09–14.54)	< 0.001	
Exophytic lesion	78/104	199/211	0.18 (0.09–0.38)	< 0.001	
Diagnosis: mucocele	8/104	66/211	0.18 (0.08–0.40)	< 0.001	< 0.001
Diagnosis: inflammatory granulation tissue	42/104	24/211	5.28 (2.96–9.41)	< 0.001	< 0.001
Diagnosis: PTLD	4/104	0/211	18.94 (1.01-355.21)	0.011	0.042
Location: lip	19/104	63/211	0.53 (0.29–0.94)	0.029	0.202
Location: buccal mucosa	11/104	10/211	2.38 (0.98–5.79)	0.058	0.202

OR, odds ratio; CI, confidence interval; FDR, false discovery rate. FDR q-values are shown for exploratory diagnostic or location comparisons.

Multivariable model

In multivariable logistic regression, older age, male sex, ulceration and inflammatory granulation tissue remained associated with systemic disease status. Mucocele showed an inverse association that approached statistical significance after adjustment.

Table 9
Multivariable logistic regression for systemic disease status.

Predictor	Adjusted OR	95% CI	p
Age, per year	1.12	1.06–1.18	< 0.001
Male sex	1.74	1.00-3.03	0.050
Ulceration	3.44	1.34–8.82	0.010
Mucocele	0.37	0.13–1.08	0.069
Inflammatory granulation tissue	3.16	1.50–6.64	0.002
Fibroma	0.85	0.35–2.03	0.710
Papilloma	1.90	0.79–4.58	0.149
Lip location	0.72	0.29–1.75	0.463
Buccal mucosa location	1.28	0.40–4.12	0.675
Gingival location	0.62	0.32–1.21	0.159

The model included age, sex, ulceration, selected histopathological diagnoses and main anatomical sites. ORs above 1 indicate higher odds of belonging to the systemic disease group.

Table 10
Histopathological patterns within systemic disease subgroups.

Systemic subgroup	n	Most common diagnosis	Granulation tissue
solid-organ transplant	43	inflammatory granulation tissue (26)	26/43 (60.5%)
neurology	19	Pappiloma (5)	3/19 (15.8%)
immunology	18	inflammatory granulation tissue (7)	7/18 (38.9%)
cardiology	10	mucocele (2)	2/10 (20.0%)
oncology	8	hemangioma (3)	2/8 (25.0%)
other	6	other (2)	2/6 (33.3%)
Transplant vs other systemic patients		Granulation tissue	OR = 4.30; 95% CI: 1.86–9.93; p < 0.001

PTLD occurred only among transplant recipients (4/43; 9.3%). Inflammatory granulation tissue was significantly more frequent in transplant recipients than in other systemic disease subgroups.

Systemic disease subgroups

Within the biopsied systemic disease subgroup, the largest disease category consisted of recipients of vascularized organs (43/104), followed by patients with neurological diseases (19/104), immunodeficiencies (18/104), cardiac diseases (10/104), post-oncological treatment (8/104) and other systemic diseases (6/104). Inflammatory granulation tissue predominated among organ recipients (26/43; 60.5%) and among patients with immunodeficiencies (7/18; 38.9%). PTLD was identified only in organ recipients. Detailed counts are shown in Supplementary Table S5.

Detailed location of biopsied lesions

In the biopsied subgroup, gingival sites together were the most frequent location (106/315 when upper and lower gingiva were combined in the patient-level database), followed by the lip (82/315), tongue (48/315), buccal mucosa (21/315), floor of the mouth (20/315) and other or multiple sites (18/315). In the global patient-level comparison, the distribution of anatomical sites did not reach conventional statistical significance (chi-square = 11.13; df = 6; p = 0.085; Cramer's V = 0.19). Lip lesions were less frequent among patients with systemic disease in univariable analysis (OR = 0.53; 95% CI: 0.29–0.94; p = 0.029), but this association did not remain significant after FDR correction.

Discussion

The present study preserves and expands the original dataset by analysing both the whole clinical cohort of 882 children and the histopathologically verified subgroup of 315 biopsied lesions. The main finding is that the microscopic spectrum of persistent or surgically treated oral mucosal lesions differs between medically compromised and systemically healthy pediatric patients.

The predominance of benign, inflammatory and reactive lesions is consistent with previous pediatric oral pathology series. Jones and Franklin reported that pediatric specimens accounted for 8.2% of all specimens in a 30-year UK series and that most lesions were benign, with mucous extravasation cysts being the most frequent diagnosis [8]. Similar patterns have been described in reviews and retrospective series from Taiwan, Egypt, Brazil and Turkey, although relative frequencies vary with age range, referral pathway, biopsy policy and classification system [9, 12–20].

Mucocele was the most common diagnosis in the present biopsied cohort and was particularly frequent among systemically healthy children. This agrees with studies identifying mucocele as one of the most common pediatric oral lesions [7–9, 13–15, 18, 19]. Its predominance on the lip is also clinically consistent with the accepted mechanism of minor salivary gland duct trauma and mucous extravasation.

The most important difference between groups was the predominance of inflammatory granulation tissue in patients with systemic diseases. The association remained strong in the aggregated analysis, and ulcerated inflammatory granulation tissue showed an even stronger relationship with systemic

disease. This finding is clinically relevant because chronic disease, immunosuppression, transplantation, immune deficiency and systemic medications may alter mucosal repair and inflammatory response. It also indicates that persistent inflammatory proliferations in medically compromised children should not be dismissed as non-specific without clinicopathological correlation.

The present study also illustrates a limitation common to biopsy-based pediatric oral pathology research. Biopsy eligibility is influenced by clinical appearance, lesion persistence, medical risk, anaesthesia risk and the treating team's threshold for surgical intervention. The lower biopsy proportion among systemically affected patients may reflect clinical caution in medically fragile children rather than a lower burden of clinically significant lesions. Studies comparing clinical oral medicine datasets with pathology laboratory datasets have shown that reliance on biopsy records alone may underestimate lesions usually diagnosed clinically [15].

Large pediatric series concerning oral and maxillofacial tumors and tumor-like lesions further highlight the importance of age and anatomical distribution. Zhang et al. analysed 5405 pediatric and adolescent cases and showed that benign tumors, tumor-like lesions and cysts predominate, but malignant and intermediate tumors require special attention and treatment planning that considers growth and development [21]. In the present mucosal-focused cohort, frankly malignant lesions were not a dominant finding, but atypical and persistent lesions in medically compromised patients still require vigilance.

The identification of PTLD only in the systemic disease group underscores the importance of biopsy in selected immunosuppressed patients, particularly transplant recipients. Although rare, PTLD and other immunosuppression-related oral lesions have major implications for diagnosis and treatment. Similarly, the presence of histiocytosis and giant cell lesions in the dataset confirms the need to maintain a broad differential diagnosis for gingival and jaw-adjacent mucosal lesions in children

In both study groups, histopathological examination revealed neoplastic lesions. In the group of children with systemic diseases, six lesions were identified: four cases of PTLD, one neurofibroma, and one *adenomatoid odontogenic tumor*. In the group of generally healthy children and adolescents, 16 neoplastic lesions were diagnosed, including seven cases of histiocytosis, two Abrikosov tumors, a *tumor mixtus*, a schwannoma,, an *ameloblastic fibroma*, a mucoepidermoid carcinoma, a teratoma, a *leiomyoma*, and a *melanotic neuroectodermal tumor*.

The study has several limitations. First, although the present revision used the patient-level biopsy database, the available variables were limited to data, systemic disease category, lesion type, location and histopathological diagnosis. Information on lesion duration, recurrence, treatment outcomes, immunosuppressive regimen, laboratory parameters and longitudinal follow-up was not available for multivariable modelling. Second, the study came from a tertiary pediatric center; therefore, referral and biopsy-selection bias cannot be excluded. Third, some diagnostic and location categories were sparse, so exploratory odds ratios for rare entities, particularly PTLD, should be interpreted with caution despite exact testing and continuity correction.

Future analyses should expand the database with lesion duration, recurrence, clinical photographs, treatment modality, immunosuppression, neutrophil count or immune status, and follow-up. These data would allow prediction of persistent ulceration, recurrence and need for surgical treatment, rather than only cross-sectional comparison of histopathological diagnoses.

Conclusions

- - Oral mucosal lesions in this pediatric cohort were mainly benign, inflammatory or reactive.
- - Mucocele was the most common diagnosis overall and the leading diagnosis among systemically healthy children.
- - Inflammatory granulation tissue was the leading diagnosis among children with systemic diseases and was strongly associated with systemic disease in the aggregated analysis.
- - Persistent exophytic or ulcerative lesions in medically compromised children require careful clinicopathological correlation, especially in transplant recipients and immunodeficient patients.
- - Patient-level modelling confirmed that age, male sex, ulceration and inflammatory granulation tissue were independently associated with systemic disease status.

Declarations

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Consent to participate: Written informed consent for participation and biopsy was obtained from patients and/or their parents or legal guardians as applicable, according to the source study description.

Data availability: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request, subject to institutional and ethical restrictions.

Author contributions:

To be completed according to the final author list.

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