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The Spectrum of Histological Findings in Oral Biopsies

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Abstract

Aim
To undertake a retrospective analysis of the use of a diagnostic pathology service, to determine the source of oral biopsies submitted for histological analysis, and to examine the range and frequencies of histologically diagnosed oral lesions in an Irish population.
Methods
A retrospective analysis was carried out on all oral biopsies submitted for histological analysis to an oral and maxillofacial diagnostic pathology service from June to December 2015.
Results
In total 724 oral biopsies were submitted. The majority of diagnoses were benign (80.3%) and the remaining diagnoses were made up of malignancies (6.7%) and potentially malignant disorders (PMDs), histologically characterised by epithelial dysplasia (13%). Less than 1% of biopsies were submitted from general dentists in primary care.
Conclusion
This study showed that oral biopsies are not submitted from the primary care setting, but rather from hospital-based specialist units or referral-based specialist practitioners. There was a broad range of histological diagnoses, the majority of which were benign.

Introduction

The histological analysis of a tissue biopsy is considered the gold standard in the diagnosis of oral lesions.[1-2] Clinicians rely on the histological analysis of incisional biopsies to assist them in making an accurate diagnosis and thus plan the patient's treatment.[3] They also rely on the histological analysis of excisional biopsies to confirm the diagnosis of a presumed benign lesion (e.g. fibroepithelial polyp, squamous papilloma).[3-4]

The American Academy of Oral and Maxillofacial Pathology recommends that "all abnormal tissue be submitted promptly for microscopic evaluation and analysis".[1] Dentists in primary care tend to submit very few biopsies to diagnostic pathology

services.[5-7] However, in addition to dental professionals, oral soft tissue disease may present to medical professionals in primary care.[8-9] This study looks at the source of oral biopsies submitted to a diagnostic pathology service in Ireland.

This is also the first study to examine the range and frequencies of histologically diagnosed oral lesions in Ireland. Outside of Ireland, a number of studies have documented the range and frequencies of histologically diagnosed oral lesions over a given time period in other populations.[10-15] The smaller studies include 357 cases over five years,[10] 400 cases over one year,[11] 562 cases over 15 years,[12] and 616 cases over six years.[13] Two larger studies carried out in the United States and the United Kingdom analyzed 15,783 cases over 18.5 years and 44,007 cases over 30 years respectively.[14-15]

The objective of this study was to undertake a retrospective analysis of the use of diagnostic pathology service, to determine the source of the oral biopsies submitted for histological analysis, and to examine the range and frequencies of histologically diagnosed oral lesions in an Irish population.

Materials and Methods

A waiver of ethical approval was granted by the St. James Hospital Research Ethics Committee.
The oral and maxillofacial diagnostic pathology service of the Dublin Dental University Hospital (DDUH) is based in St. James's Hospital Dublin. All tissue biopsies submitted to the lab are entered on the Telepath Laboratory Information Management System. For each biopsy, the Telepath system utilizes the internationally recognized SNOMED codes: a T code to denote the anatomical site and an M code to denote the diagnosis. In this study, an electronic search was conducted of the Telepath Laboratory Information System from June to December 2015 for all biopsies with the following T codes: maxilla, mandible, gingiva, tongue, palate, buccal mucosa, floor of mouth, oral mucosa, alveolar ridge, salivary gland and tooth. The diagnostic report was reviewed for each biopsy, which provided information about the patient (age, sex), the biopsy (anatomical site, diagnosis) and the referring clinician (specialty, source location). This study is part of a larger research project focused oral health, so biopsies from extra-oral head and neck sites such as lip, skin, ear, nasopharynx, oropharynx, hypopharynx, larynx, lymph nodes, paranasal sinuses and nasal cavity were excluded.

Results

During the six-month period, 724 oral biopsies were submitted to the diagnostic pathology service. The 724 biopsies were representative of 724 separate oral lesions from 700 patients, as 24 patients underwent two biopsies from different oral sites. Of these 700 patients, 324 were male and 376 were female (M:F = 0.86:1).

The majority of patients were aged between 30 and 60 years (51.1%), with those patients older than 60 years and younger than 30 years accounting for 34.6% and 14.3% respectively. Details of the referring clinician for each biopsy were recorded so that the source location could be identified. The biopsies were submitted from a range of sources, which were grouped into three categories: the DDUH, dentally-trained private practitioners (PP) and general hospitals (GH).

The DDUH submitted 291 (40.2%) biopsies during the study period, of which 280 (96.2%) were submitted from oral and maxillofacial surgery and oral medicine clinics. The remaining biopsies were submitted from restorative dentistry (3.1%) and paediatric dentistry (0.7%) clinics.

In the PP category, there were 284 biopsies (39.2%) submitted by 35 dentally-trained private practitioners: 13 periodontists, 12 oral surgeons, four oral and maxillofacial surgeons, three endodontists and three general dentists. The five practitioners who submitted the highest number of biopsies were oral surgeons and accounted for 172 (60.6%) biopsies from this category. The GH category consisted of 13 hospitals that referred biopsies for histological analysis. Of the 149 (20.6%) biopsies, 111 (74.5%) were submitted from St. James's Hospital, the majority of which were from oral and maxillofacial surgery clinics (65.8%). The remainder of biopsies in this category were submitted from ear, nose and throat (ENT) clinics (30.6%) and the emergency department (3.6%). The other 38 biopsies were submitted from 23 oral and maxillofacial surgeons, five periodontists and three ENT surgeons from the 12 other hospital sites. There were seven biopsies submitted from seven histopathologists for second opinion. Among the 724 biopsies, there were 79 diagnoses,

which were grouped into 10 diagnostic categories. Jones and Franklin's 2006 publication was used to categorise the various diagnoses under the appropriate headings.[15] The five most common diagnostic categories (mucosal pathology, odontogenic cysts, benign tumours, malignant tumours and periodontal pathology) accounted for 85.8% of the overall total. Table 1 shows how the five most common diagnoses (fibroepithelial hyperplasia, epithelial dysplasia, lichen planus/ lichenoid reaction, squamous papilloma and squamous cell carcinoma) accounted for almost half of the biopsies submitted (49.8%). In addition, among the five most common diagnoses, the number of biopsies as submitted from each source category is also shown (Table 1).

Table 1:
(i) Oral biopsy diagnostic categories; the number (N) of diagnoses in each category, and the corresponding proportion of the overall total (%T).
(ii) The five most common diagnoses overall; the corresponding numbers (N) and proportions (%C) as submitted from each source category.

(i) Diagnostic Category	N	%T
Mucosal Pathology	353	48.9
Odontogenic Cysts	90	12.4
Benign Tumours	83	11.5
Malignant Tumours	48	6.7
Periodontal Pathology	46	6.3
Miscellaneous Pathology	36	4.9
Bone Pathology	22	3.0
Dental Pathology	21	2.9
Salivary Gland Pathology	18	2.5
Non-Odontogenic Cysts	7	0.9
Total	724	100

	DDUH		*PP*		*GH*	
(ii) Diagnosis	N	(%C)	N	(%C)	N	(%C)
Fibroepithelial Hyperplasia	40	(38.8)	50	(48.6)	13	(12.6)
Epithelial Dysplasia	59	(62.8)	17	(18.1)	18	(19.1)
Lichen Planus /Lichenoid Reaction	26	(33.8)	46	(59.7)	5	(6.5)
Squamous Papilloma	14	(31.1)	24	(53.3)	7	(15.6)
Squamous Cell Carcinoma	10	(24.4)	0	(0)	31	(75.6)

Mucosal pathology, which consisted of 16 diagnoses, comprised 48.9% of all diagnoses and represented the three most common diagnoses overall. Fibroepithelial hyperplasia, also described as a fibroepithelial polyp, was the most common diagnosis and represented 14.2% of all biopsies. Fibrous epulis, a fibroepithelial overgrowth on the gingiva, is recorded in the category of "periodontal pathology".[15] Epithelial dysplasia and lichen planus/ lichenoid reaction were the second and third most common diagnoses overall and represented 13% and 10.7% of all biopsies respectively. Hyperkeratosis (No Dysplasia) was the fourth most common diagnosis in this category and represented 4.1% of the overall total (Table 2).

Table 2:
Mucosal pathology diagnoses, the overall number of each diagnoses (N), the corresponding proportions of the mucosal pathology category (%C) and of the overall total (%T)

Diagnosis	N	%C	%T
Fibroepithelial Hyperplasia	103	31.3	14.2
Epithelial Dysplasia	94	28.6	13.0
Lichen Planus/ Lichenoid Reaction	77	23.4	10.7
Hyperkeratosis (No Dysplasia)	30	9.1	4.1
Mucosal Inflammation (Non-Specific)	19	5.5	2.6
Ulceration (Non-Specific)	9	2.7	1.2
Amalgam Tattoo	5	1.4	0.7
Melanotic Macule	2	0.6	0.3
Mucous Membrane Pemphigoid	2	0.6	0.3
Discoid Lupus Erythematosus	2	0.6	0.3
Geographic Tongue	2	0.6	0.3
Verruciform Xanthoma	2	0.6	0.3
Denture Granuloma	2	0.6	0.3
Smoker's Melanosis	1	0.3	0.1
Pyostomatitis Vegetans	1	0.3	0.1
Eosinophilic Ulcer	1	0.3	0.1
Pemphigus Vulgaris	1	0.3	0.1
Total	353	100	48.9

Squamous papilloma (6.2%) and squamous cell carcinoma (5.7%) were the most common diagnoses in the benign and malignant tumour categories respectively and were the fourth and fifth most common diagnoses overall. Benign tumours accounted for 83 (11.5%) biopsies and malignant tumours accounted for 48 (6.7%) biopsies. Of the 10 diagnostic categories, benign tumours had the broadest range of diagnoses with 17 in total (Table 3). Odontogenic tumours accounted for 14.5% of all benign tumours, of which ameloblastoma was the most common type. Squamous cell carcinoma accounted for the vast majority of malignant biopsies (85.4%), and cumulatively lymphomas (Diffuse Large B Cell Lymphoma and Follicular Lymphoma) accounted for just over 10% of malignant biopsies (Table 3).

Table 3:
(i) Benign and (ii) malignant tumour diagnoses, the overall number of each diagnoses (N), the corresponding proportions of the category (%C) and of the overall total (%T)

(i) Benign Tumour Diagnoses	N	%C	%T
Squamous Papilloma	45	54.2	6.2
Haemangioma	7	8.4	1.0
Fibroma	7	8.4	1.0
Ameloblastoma	5	6.0	0.7
Pleomorphic Adenoma	3	3.6	0.4
Calcifying Cystic Odontogenic Tumour	2	2.4	0.3
Odontome	2	2.4	0.3
Lipoma	2	2.4	0.3
Osteoma	2	2.4	0.3
Angiomyoma	1	1.2	0.1
Plexiform Schwannoma	1	1.2	0.1
Neurofibroma	1	1.2	0.1
Lymphangioma	1	1.2	0.1
Neurilemmoma	1	1.2	0.1
Adenomatoid Odontogenic Tumour	1	1.2	0.1
Ameloblastic Fibroma	1	1.2	0.1
Calcifying Epithelial Odontogenic Tumour	1	1.2	0.1
Total	83	100	11.5
(ii) Malignant Tumour Diagnoses	N	%C	%T
Squamous Cell Carcinoma	41	85.4	5.7
Diffuse Large B Cell Lymphoma	4	8.4	0.6
Mucoepidermoid Carcinoma	2	4.2	0.3
Follicular Lymphoma	1	2	0.1
Total	48	100	6.7

Table 4 shows the four most common diagnoses within other diagnostic categories. Odontogenic cysts, both inflammatory and developmental, represented 12.4% of all diagnoses and were present in almost equal proportions. Inflammatory odontogenic cysts, in the form of radicular, paradental and residual cysts, accounted for 6.4% of biopsies. Developmental odontogenic cysts, in the form of dentigerous cysts, odontogenic keratocysts and gingival cysts, accounted for 6% of biopsies. The most commonly diagnosed cyst was the radicular cyst, which represented 5% of cases, and was the sixth most common diagnosis overall. Odontogenic keratocysts and dentigerous cysts accounted for 2% and 3.9% of the overall total. Non-odontogenic cysts accounted for less than 1% of all biopsies (Table 4). Periodontal, bone and dental pathology combined represented 12.2% of biopsies submitted. Neoplastic and non-neoplastic salivary gland disease represented 3.2% of all diagnoses. Mucoceles (mucous extravasation cysts and mucous retention cysts) represented over half of the salivary gland disease diagnosed (1.8%), and neoplastic salivary gland disease (pleomorphic adenoma and mucoepidermoid carcinoma) accounted for almost 1% of all diagnoses.

Table 4: Four most common diagnoses within diagnostic categories, the overall number of each diagnoses (N), the corresponding proportions of the category (%C) and of the overall total (%T)			
Diagnosis	N	%C	%T
Odontogenic Cysts			
Radicular Cyst	36	40	5
Dentigerous Cyst	28	31.1	3.9
Odontogenic Keratocyst	15	16.7	2
Paradental Cyst	8	8.8	1.1
Periodontal Pathology			
Epulides	32	70	4.4
Chronic Periodontitis	6	13	0.8
Peripheral Giant Cell Granuloma	5	10.9	0.7
Pyogenic Granuloma	2	2.8	0.3
Miscellaneous Pathology			
Non-Diagnostic	15	36.6	2
Granulation Tissue	7	17.1	1
Scar Tissue	5	12.2	0.7
Amalgam Tattoo	5	12.2	0.7
Bone Pathology			
Sequestrum	11	50	1.5
Osteomyelitis	3	13.6	0.4
Fibro-osseous lesion	3	13.6	0.4
Osteonecrosis	3	13.6	0.4
Dental Pathology			
Periapical Granuloma	13	62	1.8
Dental Follicle – Normal	5	24	0.7
Idiopathic Cervical Resorption	1	4.7	0.1
Segmental Odontomaxillary Dysplasia	1	4.7	0.1
Salivary Gland Pathology			
Mucous Extravasation Cyst	8	44.4	1.1
Mucous Retention Cyst	5	27.8	0.7
Lymphocytic Sialadenitis	2	11.1	0.3
Chronic Sialadenitis	1	5.6	0.1
Non-odontogenic Cysts			
Nasopalatine Cyst	4	57.1	0.6
Solitary Bone Cyst	1	14.3	0.1
Epithelial Inclusion Cyst	1	14.3	0.1
Lymphoepithelial Cyst	1	14.3	0.1

Discussion

A high volume of oral biopsies was submitted to this diagnostic pathology service within the six-month study period when compared with other published studies.[10-13] The results showed that the majority of diagnoses were benign (80.3%) and the remaining diagnoses were made up of malignancies (6.7%) and epithelial dysplasia (13%). Epithelial dysplasia is a histological diagnosis best described as the combination of architectural and cytological abnormalities that indicate a potential for malignant transformation.[2] Epithelial dysplasia is histologically characteristic of potentially malignant

disorders (PMDs), which are usually described clinically as white, red/white or red mucosal lesions. PMDs are at risk of progressing to oral cancer in an unpredictable manner, so although not a malignancy, epithelial dysplasia is not classified as a benign diagnosis in these results.[16] Despite the broad range of diagnoses, the five most common account for almost half of all biopsies (49.8%). Fibroepithelial hyperplasia (in the form of a fibroepithelial polyp) is the most common diagnosis overall, which is the same as that found in two larger studies that similarly looked at the range and frequencies of histologically diagnosed oral lesions.[14-15] There was a higher frequency of epithelial dysplasia reported in these results by comparison to other studies. [14-15] However, other than epithelial dysplasia, the frequencies of other common diagnoses such as radicular cysts, epulides and hyperkeratosis (no dysplasia) were also similar to those found in these larger studies.[14-15]

Oral biopsies are submitted to diagnostic pathology services by a wide range of practitioners, usually by dentists who have undergone some form of advanced or specialist training, and not typically by general dentists in primary care.[5-7] This could be considered as somewhat surprising as dentists are likely to possess the necessary skills to perform simple incisional or excisional biopsies, and may be as capable of doing so as their hospital-based colleagues.[5,17] In this study, 284 biopsies were submitted by dentally-trained private practitioners, only three of which were submitted by general dentists. This accounted for only 0.4% of all biopsies submitted, which is a much lower percentage than similar studies [5,7] Jones and Franklin reported that 12.5% of biopsies were submitted by general dentists.[5] Wan and Savage reported that 10.9% of biopsies were submitted by general dentists.[7] The remaining 281 biopsies (98.9%) from the same source category were submitted by 32 referral-based specialist practitioners. These 32 practitioners submitted a high proportion of biopsies that were diagnosed as fibroepithelial polyps (48.6%) and squamous papilloma's (53.3%), which may suggest that even in the case of patients with benign-looking oral lesions, general dentists tend to consider an oral biopsy to be a more advanced or specialist procedure.[18]

The biopsy process is indeed more complex than simply removing the abnormal tissue and submitting it to a diagnostic pathology service. The decision to biopsy also requires the interpretation of the results and the initiation of the appropriate management.[19] Even in the case of receiving a benign diagnosis, such as the various different types of benign tumours diagnosed in this study (Table 3), general dentists may not feel comfortable explaining this type of diagnosis and its potential sequelae to a patient in the primary care setting.[4] The results show that there were 77 cases of lichen planus/lichenoid reaction diagnosed, in addition to other diagnoses such as mucous membrane pemphigoid and discoid lupus erythematosus, all of which may require further treatment and subsequent monitoring.[5] It is therefore important to know when to refer a patient to a specialist unit, where the expertise, support and resources are concentrated to provide the highest level of care. [5-6] This type of approach would be particularly important for suspicious-looking oral lesions.[20] In this study,100% of squamous cell carcinomas and 81.9% of PMDs were diagnosed from biopsies submitted by hospital-based specialist units (Table 1). In theory, it is possible that these patients may have self-presented to the hospital emergency departments. However, it is more likely that these malignant and potentially malignant oral lesions were first detected by clinicians in the primary care setting, who subsequently facilitated the patient's onward referral for further assessment and biopsy.

In conclusion, this diagnostic pathology service received a high volume of oral biopsies and presented a broad range of histological diagnoses, the majority of which were benign. The frequencies of the most common diagnoses were similar to the frequencies seen in studies from similar populations. This study showed that oral biopsies are not submitted from the primary care setting, but rather from hospital-based units or referral-based specialist practitioners. Further research is needed to determine how malignant and potentially malignant oral lesions are first detected in the primary care setting in Ireland.

Declaration of Conflicts of Interest:
The authors confirm that there are no known conflicts of interest associated with this publication.

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