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Research article

Survey of pathology reports with no definitive diagnosis in oral lesions: the necessary skills for the clinicians

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ABSTRACT

Purpose: Biopsy plays a crucial role in definitive diagnosis of lesions and consequently, appropriate treatment of them. Clinicians should correctly do the biopsy in accordance to the existing principles and guidelines to prevent adverse effects on the pathologist's diagnosis. This study aimed to determine the frequency and reasons for not providing definitive histopathological diagnosis of the biopsy samples belong to the laboratory of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Hamadan University of Medical Sciences.

Methods: Archival reports belong to 2006–2016 period of the related laboratory were studied to determine the reports with no definitive histopathological diagnosis.

Results: Out of 1018 archived reports; 90 reports (8.84%) had no definitive diagnosis. The most common reasons found were incompatibility between the clinical/radiographical diagnosis and histopathological findings for 42 cases (46.66%), absence of adequate information about the clinical/radiographical findings for 17 cases (18.88%) and inappropriate quality of samples for 13 cases (14.44%), respectively.

Conclusion: The reasons for not providing definitive histopathological diagnosis of the biopsy samples in present study indicated that preparation, assessment and diagnosis of microscopic slide by pathologists do not separate from the clinician performance.

1. Introduction

Histopathological assessment of tissue sample obtained by biopsy technique is essential to achieve definitive diagnosis of the lesions [1]. Biopsy is often performed prior to initiation of treatment and is the most accurate method to reach a definitive diagnosis. Histopathological features of the lesion, its differentiation from other lesions and its amount of extension can be studied by biopsy. Moreover, biopsy results can predict course of the disease and prognosis of the lesion [2]. Oral mucosal biopsy is a simple minor surgical procedure in dentistry [3]. However, more than a proper surgical technique is required for a précised pathological report [4]. Adherence to the existing protocols and guidelines before, during and after taking a biopsy sample is imperative to achieve the best result and offer an accurate/definitive diagnosis [3, 5]. This study aimed to determine frequency and reasons for lack of definitive histopathological diagnosis on biopsy samples belong to the laboratory of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Hamadan University of Medical Sciences during 2006–2016.

2. Materials and methods

This cross-sectional study evaluated all the pathology reports belonging to archive of the laboratory of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Hamadan University of Medical Sciences from 2006 to 2016. The pathology reports with no definitive histopathological diagnosis were identified and extracted alongside with the pathology assessment request forms and the related slides. The reports, forms and slides were reviewed by two experienced oral pathologists to determine and confirm the reason(s) of not providing definitive diagnosis. In cases of disagreements a third investigator was consulted. Regarding to the previous studies [2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13] which presented the influencing factors on histopathological interpretation, the reasons for verification of the cases with no definitive diagnosis were assigned to one of the following categories:

Group A: Inadequate quantity of sample
Group B: Poor quality of sample

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Group C: Poor quality and inadequate quantity of sample
Group D: Absence of clinical/radiographical diagnosis
Group E: Incompatibility of clinical/radiographical diagnosis and histopathological findings
Group F: Need for special techniques/tests
Group G: Incompatibility of clinical/radiographical diagnosis and histopathological findings + the need for special techniques/tests
Group H: Using an inappropriate fixative

This study was approved by the research ethics committee of Kurdistan University of Medical Sciences (IR.MUK.REC.1396.10.161396.126).

3. Results

A total of 1018 pathology reports retrieved from the applied archive were evaluated; out of which, 90 reports (8.84%) did not have a definitive diagnosis for the submitted biopsy sample. Of these 90 reports, 46 (51.11%) were incisional and 34 (37.77%) were excisional biopsy. In 10 cases (11.11%), type of biopsy was unknown. Table 1 shows the frequency distribution of samples with no definitive diagnosis based on the grouping provided for the reasons. In each group, the samples with no definitive diagnosis were as followed:

3.1. Group A

3.1.1. Peripheral samples (incisional biopsy)

Seven samples: one sample had inadequate (too small) length and width, five samples did not have adequate depth/thickness of connective tissue and one sample did not have adequate width, length and depth. The clinical differential diagnosis were mucocutaneous diseases such as oral lichen planus (OLP), bullous OLP, *Mucous* membrane pemphigoid (MMP) and lichenoid reaction in six samples and oral squamous cell carcinoma (OSCC) in one sample.

3.1.2. Central samples (incisional biopsy)

Two samples: they had very small size. Differential diagnosis were periapical granuloma and periapical cyst for one case as well as residual cyst and odontogenic keratocyst (OKC) for other case.

3.2. Group B

3.2.1. Peripheral samples (incisional biopsy)

Eight samples: two samples did not have the superficial epithelium and six samples had ulceration and severe inflammation microscopically. Some of the differential diagnosis offered were OLP, pemphigus vulgaris, MMP and OSCC.

3.2.2. Central samples (incisional biopsy)

Four samples: they did not have epithelial lining of the cyst microscopically (meanwhile there was no evidence supporting the degradation of lining by inflammation). Differential diagnosis included OKC, dentigerous cyst and periapical cyst.

3.2.3. Peripheral samples (excisional biopsy)

One sample: it had microscopic feature of an ulcerative tissue. Differential diagnosis was OLP and pemphigus vulgaris.

3.3. Group C

3.3.1. Peripheral samples (incisional biopsy)

One sample: it had too small size and did not have superficial epithelium. OLP was the clinical diagnosis offered.

3.4. Group D

3.4.1. Peripheral samples (incisional biopsy)

One sample: it had histopathological feature of mucosal tissue with epithelial lining and insignificant inflammation of connective tissue.

3.4.2. Central samples (incisional biopsy)

Three samples: they had histopathological features compatible with an inflammatory odontogenic cyst.

3.4.3. Peripheral samples (excisional biopsy)

One sample: it had microscopic feature of an inflammatory hyperplasic lesion.

3.4.4. Central samples (excisional biopsy)

Nine samples: Five samples had histopathological feature of an infected odontogenic cyst. Two samples had a microscopic feature of bone tissue, and two samples had a microscopic feature of inflammatory connective tissue.

3.4.5. Peripheral and central samples (unknown biopsy type)

Three samples: Two samples were peripheral and one sample was central. Histopathological features of peripheral and central samples were inflammatory oral mucosal tissue and inflammatory connective tissue, respectively.

3.5. Group E

Microscopic feature of all lesions in this group did not have the required histopathological criteria to confirm the suggested clinical/

Table 1. Frequency distribution of samples with no definitive diagnosis based on the grouping provided for reasons.

Type of Biopsy	N (%)	A group	B group	C group	D group	E group	F group	G group	H group
Peripheral IB	31	7	8	1	1	10	4	0	0
Central IB	15	2	4	0	3	5	1	0	0
Total of IB	46 (51.11)	9	12	1	4	15	5	0	0
Peripheral EB	11	0	1	0	1	8	1	0	0
Central EB	23	0	0	0	9	13	0	1	0
Total of EB	34 (37.77)	0	1	0	10	21	1	1	0
Peripheral UBT	5	0	0	0	2	3	0	0	0
Central UBT	5	0	0	0	1	3	0	0	1
Total of UBT	10 (11.11)	0	0	0	3	6	0	0	1
Total of Biopsies (%)	90 (100)	9 (10)	13 (14.44)	1 (1.11)	17 (18.88)	42 (46.66)	6 (6.66)	1 (1.11)	1 (1.11)

N- Number.
IB- Incisional Biopsy.
EB- Excisional Biopsy.
UBT- Unknown Biopsy Type.

radiographic diagnosis. In other words, the microscopic feature of these lesions was non-specific for the suggested diagnosis despite the fact that all samples had adequate quality and quantity.

3.5.1. Peripheral samples (incisional biopsy)

Ten samples: Eight samples had the microscopic feature of non-specific inflammatory oral mucosal tissue. The clinical diagnosis included OLP, MMP, and lichenoid reaction.

One sample had histopathological feature of epithelial dysplasia along with inflamed connective tissue. The clinical diagnosis included OSCC and salivary gland tumor. One sample had clinical diagnosis of a reactive lesion with a non-specific microscopic feature.

3.5.2. Central samples (incisional biopsy)

Five samples: two samples had differential diagnosis of OKC and ameloblastoma but its histopathologic feature was consistent with an infected odontogenic cyst. Three samples had differential diagnosis of eosinophilic granuloma, osteomyelitis and osteosarcoma/osteomyelitis. The microscopic feature of all three samples was non-specific and indicated an inflammatory connective tissue along with one piece/pieces of normal bone tissue.

3.5.3. Peripheral samples (excisional biopsy)

Eight samples: Clinical differential diagnosis offered for the samples in this group ranged from benign soft tissue lesions to salivary gland lesions. Their histopathological feature was non-specific and included inflammatory connective tissue along with limited areas of ulceration at the surface of samples.

3.5.4. Central samples (excisional biopsy)

Thirteen samples: Three samples with the radiographic diagnosis of central giant cell granuloma had only a histopathologic feature of inflammatory connective tissue. Ten cases with differential diagnosis of one of the odontogenic cysts/tumors showed histopathologic feature of a cyst. However, due to complete degeneration of epithelial lining of the cyst by inflammation, it was impossible to determine its type.

3.5.5. Peripheral and central samples (unknown biopsy type)

Six samples: Three samples were peripheral and three samples were central with non-specific histopathological feature, which were not compatible to clinical/radiographic differential diagnosis. The suggested diagnosis included lichenoid reaction, reactive lesion and mucocele. The suggested radiographic diagnosis was OKC and periapical cyst.

3.6. Group F

3.6.1. Peripheral samples (incisional biopsy)

Four samples: Two samples had clinical diagnosis of OLP and lupus erythematosus (with recommendation for performing direct immunofluorescence). One sample had a microscopic feature similar to that of benign spindle cell tumors; one sample had an appearance of malignant spindle cell tumors microscopically (with recommendation for performing immunohistochemistry tests).

3.6.2. Central samples (incisional biopsy)

One sample: it had the diagnosis of a malignant bone tumor but its histopathological feature was similar to that of malignant small round cell tumors (with recommendation for performing immunohistochemistry tests).

3.6.3. Peripheral samples (excisional biopsy)

One sample: it had clinical diagnosis of OSCC but its histopathological feature was similar to a high-grade mucoepidermoid carcinoma (with recommendation for performing immunohistochemistry tests/staining with mucin).

3.7. Group G

3.7.1. Central samples (excisional biopsy)

One sample: it had radiographic diagnosis of OKC and histopathological feature of a soft tissue tumor probably with neural origin (with recommendation for performing immunohistochemistry tests).

3.8. Group H

3.8.1. Central samples (unknown biopsy type)

One sample: the sample with radiographical diagnosis of OKC microscopically showed tissue degradation/lysis since it had been sent to the lab in an inappropriate fixative (saline).

4. Discussion

In present study of 1018 samples; 90 (8.8%) did not have a definitive diagnosis in their histopathology report. In other words, the laboratory pathologist(s) had problem in accurate histopathological interpretation of these samples.

Nine samples (10%) had inadequate quantity for a definitive histopathological diagnosis (group A). A biopsy sample is adequate when the clinician takes sufficient dimensions including the depth of tissue for microscopic assessment [14]. Peripheral incisional biopsy samples in group A were small and superficial. Thus, assessment and definitive confirmation of presence/absence of diagnostic features of mucosal disorders (included in the list of clinical differential diagnosis) was impossible. In samples with clinical diagnosis of OSCC, it was impossible to determine the occurrence of invasion of malignant cells into the underlying connective tissue due to their inadequate depths. Definitive diagnosis of central incisional biopsy samples in group A required adequate amount of tissue, preferably the entire lesion. Adequate amount of tissue enables definitive determination of presence/absence of cystic epithelial lining (for differentiation between periapical granuloma and odontogenic cyst) and its histopathological characteristics (for determining the type of odontogenic cyst). Chen et al. [9] reported four cases (13.3%) of tissue inadequacy, which resulted in incompatibility between the pathologist's diagnosis in primary and secondary biopsies [9].

Samples in group B did not have adequate quality for a definitive histopathological diagnosis. Biopsy should include a part of tissue that indicates the lesion [6]. Biopsy from necrotic, ulcerative or erosive areas has limited diagnostic value [7, 8, 15] and often shows non-specific inflammatory changes [8].

When the tissue sample is obtained with excessive force, the epithelial part can be significantly damaged [2]. The vesiculobullous lesions are easily ruptured into the oral cavity [7] and even the slightest carelessness and improper handling can result in loss of their epithelial structure. This might be the reason for samples with no epithelial lining in groups B and C.

Lack of information and/or improper list of clinical/radiographical differential diagnosis by the clinicians can significantly limit the correctness of interpretation for the samples [4, 10]. The suggested clinical/radiographical diagnosis is important for the pathologist because it provides him/her with an idea about what is witnessed and assumed by the clinician [5]. In group D, the histopathological feature of the samples was non-specific and could be attributed to several lesions. For example, tissue hyperplasia with an inflammatory/traumatic origin might confined to several lesions. The diagnosis of this group of lesions is always clinical-pathological ones [16]. OLP, lichenoid reactions and systemic lupus erythematosus can all have similar histopathological features. Thus, it is imperative to provide complete history, clinical description and specific diagnostic techniques/tests (serology and/or immunofluorescence) [11]. Novis [17] also reported that not providing clinical diagnosis was among the most common errors in sending a sample for histopathological analysis.

Despite the presence of clinical/radiographical differential diagnosis, disagreement between them and histopathological findings (group E) was noted in 42 cases (46.66%). Although size of the samples seemed adequate in this group it should be noted that larger biopsy taken from a suitable site might have higher amount of tissue indicative of lesion and enhance reaching a diagnosis [9]. Moreover, if clinician is unsure about the most appropriate site to do a biopsy, he/she should refer the patient to a specialist in the related field. Incorrect biopsy can falsely assure the patient and the clinician [18] as well as the pathologist as signatory of the pathology report while not aware of this mistake. Chen et al. [9] reported incorrect biopsy in 18 cases (60%).

Inflammation masks the diagnostic features of tissue [19]. It can cause changes in epithelial lining of odontogenic cysts [9]. For samples having these changes, differentiation between an infected developmental odontogenic cyst and an inflammatory odontogenic cyst, based on incisional or unknown biopsy type, is impossible. Sometimes inflammation may cause complete degradation of epithelial lining of the cyst; as a result, the type of cyst is not determinable even in excisional biopsy (group E). Chen et al. [9] reported 3.4% error in diagnosis of lesions such as OKC due to masking inflammation. This might be a reason for why a definitive diagnosis of inflammatory odontogenic cyst (such as periapical cyst) was not offered for the samples in group E and the odontogenic cysts with inflammation in other groups. In these lesions, we had to make sure that either the sampling is correct or the entire lesion requires evaluation to reach a definitive diagnosis.

In some lesions, a definitive diagnosis cannot be made based on microscopic observation of hematoxylin-eosin stained slides due to variable and overlapping patterns [12]. Soft tissue tumors can be categorized in this group which definitive diagnosis of them may require specific techniques/tests. Immunohistochemical studies play an important role in this regard, occasionally [20]. In groups F and D, 6 cases (6.66%) required further tests such as immunohistochemical and/or immunofluorescence studies. In this study, immunohistochemical tests had been requested for 4 cases (4.44%) out of 90 samples. Ajura et al. [12] reported immunohistochemical analysis requests for 197 (2.1%) out of 9523 samples. To prevent tissue autolysis and degradation the tissue sample should be immediately placed in a fixative after biopsy [2, 13, 21]. 10% buffered formalin is the best fixative for this purpose [6, 10]. In some cases, unsuitable solutions such as tap water, distilled water or saline solution are used [7, 21]. Saline does not cause tissue fixation [4] (group H) and should not be used even for a short time [22].

5. Conclusions

Findings indicated that the preparation of microscopic slide, its assessment and diagnosis by pathologists do not separate from the clinician performance. Not adhering to the recommended biopsy principles and guidelines may result in no definitive histopathological diagnosis of the lesion. This can necessitate a second biopsy and delay diagnosis and treatment especially for premalignant and malignant lesions. Meanwhile, it can have an adverse psychological impact on patients and ruin their trust on clinicians and the health care system. Finally, theoretical and practical training of clinicians with the aim of reducing adverse factors affecting definitive histopathological diagnosis seems necessary.

Declarations

Author contribution statement

S. Ghoreishi and F. Baghaei: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

M. Zargaran: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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