Journal of Kathmandu Medical College, Vol. 12, No. 2, Issue 44, Apr.-Jun., 2023

Assessment of inconclusive biopsies at a tertiary care dental hospital

Manandhar DK,[1] **Bajracharya D,**[2] **Badhu A,**[1] **Koju S,**[1] **Ojha B,**[3] **Bhandari P**[3]

[1]Dhan Kumari Manandhar, Postgraduate Resident; [2]Dipshikha Bajracharya, Professor and Head; [1]Akanksha Badhu; [1]Sushmit Koju, Postgraduate Resident; [3]Bidhata Ojha; [3]Pradeep Bhandari, Lecturer; Department of Oral and Maxillofacial Pathology, Kantipur Dental College Teaching Hospital and Research Centre, Basundhara, Kathmandu, Nepal.

Abstract

Background: Biopsy has crucial role in definitive diagnosis of lesions followed by appropriate treatment of the same. There are situations to clinicians when the report from the oral pathologists comes as "inconclusive biopsy", instead of a definitive diagnosis.

Objectives: To determine the frequency and reasons for inconclusive biopsy as the final diagnosis, in biopsy samples obtained for histopathological evaluation.

Methods: This retrospective chart review was conducted in a total of 982 biopsy reports from the archive of the Department of Oral Pathology of Kantipur Dental College. Reports from 2016 to 2021 A.D were assessed after institutional ethical approval utilising convenience sampling. Clinical details were assessed from the patient's biopsy requisition form. Inconclusive diagnosis as the final sign-outs were evaluated, to analyse the reasons for such reports according to the standard criteria. For analysis, SPSS v.20 software was used.

Results: Out of 982 biopsy reports, 140 (14.2%) inconclusive biopsy reports were recovered. The reasons for inconclusive biopsy in descending order was 129 (92.1%) poor quality of sample, five (3.6%) insufficient biopsy, three (2.1%) inappropriate fixative, two (1.4%) both insufficient and poor-quality sample and one (0.7%) lack of clinical or radiographic details. Comparison between central and peripheral inconclusive reports was not statistically significant ($p > 0.05$).

Conclusion: This study indicates that careful surgical approach is a must along with proper transportation of the biopsy sample and a detailed clinical and radiographic information to avoid inconclusive biopsy reports.

Key words: Histopathological report; Inconclusive biopsy; Oral pathologist.

Access this article online

Website: www.jkmc.com.np

DOI: https://doi.org/10.3126/jkmc.v12i2.53544

HOW TO CITE

Manandhar DK, Bajracharya D, Badhu A, Koju S, Ojha B, Bhandari P. Assessment of inconclusive biopsies at a tertiary care dental hospital. J Kathmandu Med Coll. 2023;12(2):75-79.

Submitted: Jan 23, 2023
Accepted: May 21, 2023
Published: Jun 30, 2023

Address for correspondence

Dr. Dhan Kumari Manandhar
Postgraduate Resident, Department of Oral Pathology,
Kantipur Dental College Teaching Hospital and Research Centre,
Basundhara, Kathmandu, Nepal.
E-mail: docdhana006@gmail.com

ISSN: 2019-1785 (Print), 2091-1793 (Online)

INTRODUCTION

Biopsy is performed prior to initiation of treatment and is the most accurate method to reach a definitive diagnosis.[1] Oral biopsy is not limited to diagnosis only, but is also very useful to determine nature of lesions: benign or malignant; and for planning effective treatment strategies.[2] There are surprising and disappointing situations when the report from the oral pathologist comes as "not from the representative area" and "inadequate specimen size", instead of a final diagnosis.[3] Inadequate biopsy specimens, tissue artifact incurred at surgery, inappropriate sampling of tissue for suspected pathologic condition type, or insufficient clinical history among other deficiencies hamper the pathologists in their interpretation. Proper tissue preparation for microscopic analysis depends on steps taken by surgeon, assistant, and histotechnician to reduce artifacts' inclusion.[4] Finding out the possible causes for inconclusive biopsy reports may be helpful to get desired biopsy report, ultimately satisfying to the surgeon(s) involved, oral pathologist interpreting the

specimen, and the patient seeking for the best medical service. Thus, present study attempted to determine the frequency and reasons for inconclusive biopsy as the final diagnosis in biopsy samples obtained for histopathological evaluation at a tertiary care dental hospital.

METHODOLOGY

This was a retrospective chart review with an observational analytical cross-sectional design conducted in the department of Oral Pathology at Kantipur Dental College. Ethical clearance was taken from the institutional review board (Ref. 8/022) before commencing the study. The authors evaluated all the pathology reports belonging to archive of the laboratory of the Department of Oral Pathology of a Dental College from 2016 to 2021 A.D. Convenience sampling technique was utilised.

The sample size was calculated using data from a previous study[1] in which the prevalence of inconclusive biopsy report was 8.8%, using the formula:

$$n = \frac{z^2pq}{e^2}$$

where, z = 1.96 (standard normal deviate at 95% confidence level), p = 8.8% (prevalence), q = 1-p (1-0.088 = 0.912), e = 0.05 (5% margin of error taken), n = sample size required per group = 123.32 ≈ 124. After adding 10% of the sample size for permissible error, n = 124+10% of 124 = 135.66 ≈ 140. A total 140 samples of biopsy reports with inconclusive biopsy as the final report were included in the study and biopsy reports with definitive diagnosis provided were excluded from the study. The pathology reports with inconclusive biopsy were identified and extracted alongside with the pathology assessment request forms. The hospital where the study was conducted was labelled as central institute and the other referral centres were labelled as peripheral institutes. The reports were categorised accordingly. The reports and forms were then reviewed to determine and confirm the reason(s) for not providing definitive diagnosis. The reasons for verification of the cases with inconclusive biopsy were assigned to one of the following categories:

Group A: Inadequate quantity of sample. This included specimens with inadequate length and width, inadequate thickness and depth of connective tissue.

Group B: Poor quality of sample. This included specimens lacking overlying epithelium, presence of ulceration and severe inflammation.

Group C: Poor quality and inadequate quantity of sample. This included specimens with both of above features.

Group D: Absence of clinical/radiographical diagnosis. This included specimen with no clinical and/or radiographic diagnosis provided.

Group E: Using an inappropriate fixative. This included specimen sent in inappropriate fixative (e.g., saline) resulting in lysis/degradation.

Data were collected and statistical analysis was done using IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA) and Pearson Chi-square test was applied.

RESULTS

Out of 982 biopsy reports assessed, 140 (14.2%) inconclusive biopsy reports were recovered from the Department of Oral and Maxillofacial Pathology, Kantipur Dental College and Hospital. Among the inconclusive biopsy reports, 79 (56.4%) were from the central institute where this study was performed and 61 (43.6%) were from the peripheral centres referred to the central institute. Most common reason for no definitive diagnosis was Group B: poor quality of sample (Table 1). No statistically significant difference between inconclusive biopsy at central and peripheral institutes was observed (Table 2).

Reasons	Frequency (Percent)
Group A: Insufficient	5 (3.6)
Group B: Poor quality	129 (92.1)
Group C: Insufficient and poor quality	2 (1.4)
Group D: Lack of clinical or radiographic diagnosis	1 (0.7)
Group E: Inappropriate fixative	3 (2.1)
Total	**140 (100)**

Table 2: Comparison of inconclusive biopsies between central and peripheral institutes

Institute	Reasons					Total	Pearson Chi-square
	Insufficient	Poor Quality	Insufficient and Poor Quality	Lack of clinical or radiographic diagnosis	Inappropriate fixative		
Central	2	77	-	-	-	79	0.064 (non-significant)
Peripheral	3	52	2	1	3	61	
Total	**5**	**129**	**2**	**1**	**3**	**140**	

DISCUSSION

A biopsy is considered to be the gold standard of diagnostic procedures as it helps in confirming or denying a diagnosis.[3] Arriving at the proper diagnosis depends on various factors and proper planning for biopsy making is equally essential. This begins from the history taking and the clinical examination followed by proper surgical skills, tissue handling, transportation, processing and ultimately the knowledge of a pathologist.[5]

According to Ghoreishi et al. 8.84% of biopsy reports had no definitive diagnosis.[1] In present study, 140 (14.2%) samples out of 982 biopsy specimens were reported as inconclusive biopsy. Among them, 79 (56.4%) were specimens from the central institute while 61 (43.6%) were from peripheral centres.

Out of 140 inconclusive reports, 129 (92.1%) cases of inconclusive report were mainly due to poor quality of specimen. Logan et al. in their study have concluded that biopsy should include a part of tissue indicating the lesion to be from the representative area.[6] Poh et al. in their study have proposed that biopsy from necrotic, ulcerative or erosive areas were supposed to be of limited diagnostic value and often showed non-specific inflammatory changes.[7] In current study, absence of overlying epithelium was the major reason for poor quality of sample in 101 samples. Also, 24 specimens were not from the representative area and 4 of them had no correlation with the differential diagnosis provided. Operating surgeon should be aware of the various biopsy techniques that are available for the oral tissues, as well as the challenges specific to these tissues with the aim to provide a suitably representative sample for the clinician to interpret. An unsuitable, unrepresentative sample is of no use to the clinician and does not help the patient who would be ill served by an unnecessary repeat procedure.[8] An appropriate biopsy must contain tissue that is representative of the lesion which is dependent on three main factors, namely, selection of the biopsy site, the type of biopsy and finally the adequate submission of the specimen to the laboratory.[9]

A total of five (3.6%) cases were of insufficient biopsy. An ideal biopsy sample should have adequate dimensions including the depth of tissue for microscopic assessment.[10] According Guarner et al., it would be impossible to determine the occurrence of invasion of malignant cells into the underlying connective tissue due to their inadequate depths.[11] Hence, a sufficient tissue sample enables definitive determination of presence or absence of cystic epithelial lining and its histopathological characteristics. A biopsy does not necessarily have to be large but very small or superficial biopsies can be inadequate and not diagnostically useful. The biopsy specimen should include as much tissue as is feasible. This applies to incisional biopsies in which only a portion of the lesion is removed.[12] Small biopsies can also be lost or become distorted during processing. Thus, it is important that there is an adequate amount of tissue for assessment.[6]

Likewise inappropriate fixative was noted in three (2.1%) cases as reason for inconclusive biopsy reports in this study. Process of autolysis and bacterial attack start as soon as tissue is removed from the body. So, the first aim of fixation is to arrest these changes.[13,14] Saline was used as transport medium as an alternative. Jain et al. 2011,[4] have mentioned that saline does not cause tissue fixation[12] and should not be used even for a short time.[15] The amount of fixative should be 15–20 times the bulk of tissue to be fixed and must surround the specimen on all sides.[12] Inadequate fixative resulting in improperly fixed tissue might be the reason for inconclusive biopsy report in this study. Delay in fixation and inadequate fixation alters the staining quality of the cells resulting in cellular shrinkage and clumping of cytoplasm. The nuclear chromatin becomes indistinct and nucleoli are sometimes not visible. This knowledge is useful in handling of oral biopsies especially of dysplasia and carcinomas.[16] Both insufficient biopsy and poor quality of sample was the reason for inconclusive reports in two (1.7%) out of 140 cases. Here, the tissue specimen lacked adequate depth and the overlying epithelium were absent in them.

Lack of clinical and radiographic diagnosis led to inconclusive report in one (0.7%) case of 140 samples. Clinical details of the case were not provided along with the tissue specimen. Bernstein et al. have suggested that tissue has to be sent with a proper requisition form,[11] identification details and all relevant clinical details like site, size, shape, colour, dimensions etc.[12] Kahn et al. in their study suggested that clinical and radiographic diagnosis is important for the pathologist because it provides with an idea about what is witnessed and assumed by the clinician.[17]Also, the diagnosis of exophytic lesions is always clinical-pathological ones.[18]

Insufficient and Poor Quality specimen two (1.4%), lack of clinical or radiographic diagnosis one (0.7%) and inappropriate fixative three (2.1%) were encountered in the biopsy specimen received from the peripheral referral centres. Hence, it shows the necessity for proper handling and following the required guidelines for transportation of the biopsy specimen from other centres for definitive histopathological diagnosis.

CONCLUSION

This study indicates careful surgical approach is a must along with proper transportation of the biopsy sample and provision of clinical and radiographic diagnosis to avoid inconclusive biopsy reports. If we take some extra little care for tissue specimen, it can definitely be a great help for the patient, the pathologists and the surgeon in providing a good diagnosis and a good treatment.

ACKOWLEDGEMENT

The authors would like to thank Assistant Professor Dr. Sunita Khanal, Department of Community and Public Health Dentistry for statistical analysis, Dr. Nisha Maharjan, Department of Oral Pathology, Kantipur Dental College, Teaching Hospital and Research centre for the support.

Conflict of interest: None.
Source(s) of support: None.

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