Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Clinicopathological Spectrum of Biopsy-Proven Gingival Lesions According to the 2017 Periodontal Disease Classification: A Five-Year Retrospective Analysis

Songul Şahin

songulsahin34@gmail.com

Çankırı Karatekin University

Başak Karasu

Çankırı Karatekin University

Zehra Şahin

Istanbul University Cerrahpaşa

Övgü Aydın Ülgen

Istanbul University Cerrahpaşa

Research Article

Keywords: Gingiva, Biopsy, Squamous Cell Carcinoma, Fibroma, Clinicopathological Correlation

Posted Date: April 21st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9212343/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Aim

The aim of this retrospective study was to evaluate the frequency and distribution of biopsy-proven gingival lesions in our patient population according to the framework of the 2017 periodontal disease classification and to assess the concordance between clinical provisional diagnoses and definitive histopathological diagnoses.

Materials and Methods

The records of 58 patients who underwent gingival biopsy within the specified study period were retrospectively reviewed. Demographic data, lesion location, biopsy type, clinical provisional diagnosis, and definitive histopathological diagnosis were recorded and analyzed. Diagnostic concordance between the clinical and histopathological diagnoses was evaluated.

Results

The most frequent definitive diagnoses were fibroma (n = 12, 20.7%) and non-specific inflammation (n = 12, 20.7%). The overall malignancy rate was 5.2% (3/58), all of which were diagnosed as squamous cell carcinoma (SCC), a rate slightly higher than that reported in the literature. Among the 12 cases with a clinical provisional diagnosis of SCC, only 25% were confirmed histopathologically. Reactive and inflammatory lesions accounted for the majority of false-positive clinical diagnoses.

Conclusion

Reactive lesions constituted the majority of gingival biopsies in this cohort, while the relatively elevated malignancy rate suggests a high level of biopsy selectivity in our clinic. The low diagnostic accuracy observed for the clinical provisional diagnosis of SCC highlights the challenge posed by reactive lesions that clinically mimic malignancy and underscores the indispensable role of histopathological examination as the gold standard for definitive diagnosis.

INTRODUCTION

The gingiva and other oral mucosal tissues are frequent sites for a wide range of pathological lesions. These include plaque-induced conditions as well as numerous non–plaque-induced lesions, some of which may reflect underlying systemic diseases or

disorders. When the etiology is unrelated to dental plaque, such lesions typically do not resolve following plaque removal, highlighting the need to recognize their distinct clinical behavior and diagnostic implications. [1]

A broad spectrum of neoplastic and non-neoplastic lesions may develop on the gingiva. Non-neoplastic lesions are generally inflammatory or represent reactive responses to irritation or minor injury, and most localized gingival enlargements fall into this category. Common examples include pyogenic granuloma, peripheral ossifying fibroma, and inflammatory conditions such as plaque-induced gingivitis and periodontitis.[2, 3] Drug-induced gingival enlargement is another clinically relevant condition observed in patients receiving anticonvulsants, immunosuppressants, or antihypertensive medications[2]

In contrast, neoplastic lesions exhibit autonomous and progressive growth and may follow either a benign or malignant course. Among biopsy-proven gingival lesions, fibroma represents the most frequent benign neoplasm and oral squamous cell carcinoma (SCC) constitutes the majority of malignant tumors.[2, 4]

Non–dental plaque-induced gingival diseases (NDPIGD) were first defined in the 1999 American Academy of Periodontology (AAP) classification [5], although many neoplastic and non-neoplastic entities were not included in that system. The 2018 classification jointly developed by the European Federation of Periodontology (EFP) and the AAP introduced major updates and expanded the spectrum of conditions by incorporating lesions such as leukoplakia and SCC, thereby broadening the categories relevant to periodontal diagnosis and management[6]. Because these conditions vary widely in pathogenesis and are infrequently discussed in periodontal literature, clinicians may be unfamiliar with their clinical presentation. Within this contemporary framework, NDPIGD encompass a diverse range of inflammatory, immune-mediated, reactive, and neoplastic lesions.

Given that many gingival and oral soft-tissue lesions cannot be reliably diagnosed on the basis of clinical and radiographic findings alone, histopathological examination via biopsy remains essential for achieving diagnostic accuracy and informing appropriate treatment strategies [1, 2, 4, 7]

Periodontists and oral pathologists therefore play complementary roles in the differential diagnosis, management, and referral process for gingival lesions. Despite their clinical relevance, epidemiological data on gingival lesions remain limited, with only a small number of studies from different regions reporting their distribution and characteristics. Consequently, updated information is needed to better understand the spectrum of biopsy-proven lesions affecting the gingiva.

Therefore, the aim of the present study was to evaluate the frequency and distribution of biopsy-proven gingival lesions in our patient population in accordance with the framework of the 2017 periodontal disease classification.

MATERIALS AND METHODS

Study Design

This retrospective study was conducted by reviewing the pathology archives of two centers with different institutional capacities: Cerrahpaşa University Faculty of Medicine and Çankırı Karatekin University Faculty of Dentistry. Records dated between 2019 and 2025 were examined. A total of 1,695 oral biopsy specimens were screened, from which cases identified as “gingiva” and possessing a definitive histopathological diagnosis were selected. Ultimately, 58 biopsy-proven gingival lesions met the inclusion criteria and were included in the analysis.

For each case, demographic and clinical variables were collected from the institutional pathology database, including the patient’s age at the time of biopsy, sex, clinical preliminary diagnosis, the type of biopsy performed, the definitive histopathological diagnosis, and the biological behavior of the lesion classified as benign, malignant, or premalignant. The anatomical site of the lesion was also documented in detail, specifying the exact gingival region involved (e.g., maxillary posterior gingiva or mandibular anterior free gingiva). All data were systematically recorded using a standardized extraction form for subsequent analysis.

Three main analytical components were evaluated: demographic profiling, diagnostic concordance between clinical provisional diagnoses and definitive histopathological findings, and the overall pathological spectrum of gingival biopsy specimens. As part of the pathological spectrum assessment, the most frequently encountered gingival lesions were identified, the proportion of malignant cases within the total biopsy pool was calculated, and the distribution of premalignant lesions was examined. Collectively, these analyses were used to establish the characteristic pathological profile of gingival biopsy material processed in our institution.

Inclusion criteria consisted of biopsy cases from individuals of any age and sex in which the lesion originated from the gingiva and a complete, definitive histopathological diagnosis was available.

Exclusion criteria comprised biopsy records originating from non-gingival sites (buccal mucosa, lip, tongue, or palate), salivary gland pathologies, and intraosseous lesions secondarily extending to the gingiva. Additionally, non-specific inflammatory conditions such as plaque-induced gingivitis or periodontitis, as well as entities classified in the 2017

periodontal disease framework under endocrine, nutritional and metabolic disorders, traumatic lesions, and gingival pigmentation were excluded, as these conditions typically do not require biopsy for diagnosis and are therefore not submitted for histopathological evaluation. Duplicate biopsy specimens obtained from the same patient representing the same lesion were also excluded to avoid repeated sampling of a single pathological entity.

Diagnostic concordance was assessed by evaluating the correlation between the clinicians' preliminary diagnoses made in the presence of suspected malignancy (particularly suspected SCC) and the definitive histopathological diagnoses issued by the pathology laboratory. The histopathological diagnosis served as the gold standard for all cases. Final diagnoses were further categorized according to the updated classification of gingival lesions proposed by the 2017 World Workshop on Periodontal and Peri-Implant Diseases and Conditions.

Table 1
Classification of Biopsy-Proven Gingival Lesions According to the 2017 Periodontal Disease Framework[6]

Category	Subcategory	Disease / Condition
Specific Infections	**Viral origin**	Verruca vulgaris
	Fungal origin	Candidosis
Inflammatory and Immune Conditions	**Hypersensitivity Reactions**	Contact allergy
		Plasma cell gingivitis
		Erythema multiforme
	Autoimmune Diseases of the Skin and Mucous Membranes	Pemphigus vulgaris
		Pemphigoid
		Lichen planus
		Lupus erythematosus
	Granulomatous Inflammatory Lesions (Orofacial Granulomatosis)	Crohn’s disease
		Sarcoidosis
Reactive Processes	**Epulides**	Fibrous epulis
		Calcifying fibrous granuloma
		Vascular epulis (pyogenic granuloma)
		Peripheral giant cell granuloma
Neoplasms	**Premalignancy**	Leukoplakia
		Erythroplakia
	Malignant Neoplasms	Squamous cell carcinoma
		Leukemic cell infiltration
		Lymphoma
		— Hodgkin lymphoma

Category	Subcategory	Disease / Condition
		— Non-Hodgkin lymphoma

Statistical analysis

Statistical analysis was executed using the Microsoft Excel computer software.

RESULTS

A total of 58 cases met the inclusion criteria, representing 3.4% (58/1695) of all oral biopsy specimens reviewed. The mean age of the patients was 49.1 years, ranging from 10 to 83 years. The sex distribution was female-predominant, with 36 women and 22 men.

The distribution of all cases according to their definitive histopathological diagnoses is summarized in Table 2. Analysis of the biopsy-proven gingival lesions demonstrated a clear predominance of benign pathology. Reactive lesions accounted for the majority of cases (65.5%), indicating that most biopsied gingival specimens represented non-neoplastic proliferations associated with local irritation or inflammatory stimuli rather than malignant or autoimmune processes. Among all diagnoses, non-specific inflammation (NOS) was the most frequent entity, constituting 31% of cases, followed by fibroma (20.7%). This pattern suggests that a substantial proportion of gingival biopsy submissions arise secondary to traumatic insults such as biting habits or prosthetic irritation or odontogenic inflammatory conditions. Overall, the distribution highlights that benign, irritation-related lesions represent the primary indication for gingival biopsy within the study population.

A well-circumscribed reactive connective tissue lesion characterized by a dense collagenous stroma located beneath a hyperplastic stratified squamous epithelium

Infiltration of squamous cell carcinoma within the connective tissue, with keratin pearl formation (arrow)

The stratified squamous epithelium shows spongiosis and basal cell vacuolization, with the presence of dyskeratotic cells (arrow). A band-like lymphocytic infiltrate is observed in the underlying connective tissue.

Table 2
Distribution of the Gingival Biopsy Series (N = 58) According to Definitive Histopathological Diagnoses

Definitive Histopathological Diagnosis	Number of Cases (n) (F/M)	%	Mean age (years)
Reactive Processes	**38**	**%65,5**	**42,6***
Fibroma	12	%20,7	48,8
NOS (Non-specific Inflammation)	18	**%31,0**	38,5
Pyogenic granuloma	4	%6,9	51,6
Granulation Tissue	3	%5,2	41,3
Peripheral Giant Cell Granuloma	1	%1,7	10,0
Inflammatory and Immune Conditions	4	**%6,9**	**61,9***
Lichen planus	3	%5,2	73,7
Pemphigus/Pemphigoid	1	%1,7	28,0
Specific Infections	6	%10,3	
Verruca vulgaris	4	%6,9	46,5
Fungal Infection	2	%3,4	61,0
Malignant Neoplasms	**3**	**%5,2**	**74,0**
Squamous cell carcinoma	3	%5,2	74,0
Premalignancy	1	%1,7	52,0
Leukoplakia	1	%1,7	52,0
Other Neoplasms / Rare Diagnoses	7	**%12**	**56,1***
Squamous Papillomatous Lesion	3	%5,2	72,5
Vascular Malformation	2	%3,4	57,0
Intramucosal Melanocytic Nevus	1	%1,7	21,0
Low-Grade Dysplasia (Papillary)	1	%1,7	83,0
Total	**58**	**%100**	**49,8***

Inflammatory and immune lesions were observed exclusively in women, consistent with the well-documented female predominance of oral lichen planus. Reactive lesions occurred in both sexes; however, pyogenic granuloma was more frequently diagnosed in women

likely reflecting hormonal influence whereas irritation fibroma was more common in men. Malignant lesions demonstrated a marked male predominance, with three of the four SCC cases occurring in men. Age patterns varied considerably across diagnostic categories. Women with reactive lesions were generally younger (mean age: 32 years) compared with men (mean age: 41 years), reflecting the tendency of hormonally influenced lesions to occur in younger females. Inflammatory and immune lesions showed a higher mean age (54 years), and all cases occurred in women. In contrast, malignant lesions exhibited a sharp age-related disparity: the single female case occurred at 45 years, whereas male patients presented at a much older age (mean: 70 years), indicating a substantially increased cancer risk in older men.

Only 5.2% of all cases (3 patients) were diagnosed as malignant. All malignant lesions corresponded to SCC, the most common oral cancer. Although the overall proportion of malignancy was low, the advanced mean age of these patients (74 years) underscores the need for increased clinical vigilance when evaluating gingival lesions in older individuals.

A small number of lesions with premalignant potential were identified, including leukoplakia and low-grade dysplasia. Notably, the patient diagnosed with low-grade dysplasia was 83 years old, which is clinically relevant given the risk of malignant transformation and the need for close follow-up in elderly individuals.

Within the category of specific infections, viral lesions predominated. Verruca (6.9%) and papilloma (5.2%), both of which may be associated with HPV infection, were the most frequently observed lesions in this group.

As shown in Table 3, diagnostic accuracy for clinically suspected SCC was low, with only 25% of clinically suspected cases being confirmed by definitive histopathological examination. The majority of false-positive SCC suspicions resulted from non-specific inflammatory conditions and reactive lesions, both of which commonly mimicked malignant features on clinical presentation.

Table 3
Diagnostic Concordance Between Clinical Suspicion of Squamous Cell Carcinoma and Definitive Histopathological Diagnoses

Preliminary diagnosis	Definitive Histopathological Diagnosis	Number of cases (n)	(%)	Clinicopathological Agreement
SCC suspicion	SCC	3	25%	True Positive (Concordant)
SCC suspicion	NOS	4	33%	False positive
SCC suspicion	Granulation tissue	2	17%	False positive
SCC suspicion	Squamous Papillomatous Lesion	1	8%	False positive
SCC suspicion	Vascular Malformation	1	8%	False positive
SCC suspicion	Low-Grade Dysplasia	1	8%	False positive
Total		12	100%	25% agreement

DISCUSSION

This retrospective analysis of 58 cases delineates the spectrum of NDPIGD-related gingival biopsy specimens encountered in our clinic.

The overall female predominance and the wide age range observed in our cohort reflect demographic patterns commonly reported in oral pathology services, where females more frequently seek dental care and where age strongly influences lesion type.

In the present study, fibroma and non-specific inflammation emerged as the most frequently diagnosed gingival lesions. This distribution aligns with the prevailing evidence that the majority of biopsy-proven gingival lesions are benign or reactive in nature. Interestingly, our findings diverge from several previously published series in which pyogenic granuloma is reported as the most common reactive lesion of the gingiva. In contrast, fibroma demonstrated a higher prevalence in our cohort (20.7%). This discrepancy may reflect regional or demographic differences, as well as potential variation in biopsy referral patterns or selection criteria within our clinical setting. Moreover, the predominance of fibroma may suggest an increased local occurrence of lesions with distinctive histopathological characteristics, such as the “gingival fibroma” pattern described by Bawazir and Islam, underscoring the importance of context-specific diagnostic profiling in understanding lesion patterns across populations.

Inflammatory and immune lesions were observed exclusively in women, consistent with the well-documented female predominance of oral lichen planus.

Reported rates of malignancy in large gingival biopsy series typically range between 1% and 5%.[8] The 5.2% prevalence of SCC observed in our cohort is slightly above this expected range; however, this finding should be interpreted in light of our relatively low annual biopsy volume compared to major referral centers. The combination of a smaller case load and a proportionally higher malignancy rate likely reflects the “high-selectivity principle” that characterizes biopsy referral patterns in our clinic. In this context, clinicians tend to submit biopsies primarily for lesions that are clinically suspicious, diagnostically challenging, or carry a higher perceived risk, while routine benign lesions are more often managed without surgical sampling. This selective approach may therefore yield a case mix that is enriched with malignancies relative to high-volume settings.

Consistent with epidemiological trends malignant lesions in our study occurred predominantly in older men, reinforcing the well-established association between age, male sex, and oral cancer risk.[8, 9]

The finding that only one quarter of clinically suspected SCC cases were confirmed as malignant highlights the diagnostic challenge posed by reactive lesions that mimic carcinoma. Non-specific inflammation and granulation tissue were the most common sources of false-positive clinical impressions, often presenting with ulceration or irregularity that raised unwarranted suspicion. This observation reinforces the critical role of biopsy in distinguishing true malignancies from benign mimickers, as previously emphasized by Fitzpatrick et al., who noted that even malignant variants may overlap clinically with reactive masses. Factors such as advanced patient age, persistent lesion behavior, and the presence of atypical surface changes should therefore prompt clinicians to maintain a low threshold for biopsy when SCC is a diagnostic consideration.

This dataset reflects the typical diagnostic profile encountered in an oral pathology service. The majority of gingival biopsies corresponded to benign, reactive lesions associated with trauma or local inflammation. Patient age emerged as a key determinant, with an increasing likelihood of autoimmune or malignant pathology in older individuals particularly those over 60 years of age. More serious diagnoses, such as lichen planus and SCC, were predominantly clustered within this older age group.

CONCLUSION

This retrospective analysis confirms the predominance of reactive lesions particularly fibroma within our gingival biopsy series, while the 5.2% malignancy rate reflects the high diagnostic selectivity of our clinical referral pattern. Nonetheless, the low accuracy of clinical suspicion for SCC underscores the indispensable role of histopathological

examination as the gold standard for establishing a definitive diagnosis and enabling timely interventions that reduce patient morbidity and mortality. In daily practice, clinicians should remain highly vigilant when encountering atypical or persistent reactive lesions that may clinically resemble malignancy. At the same time, the notable proportion of false-positive SCC suspicions highlights the potential risk of overdiagnosis, emphasizing the need for balanced clinical judgment that avoids unnecessary alarm while ensuring that genuinely suspicious lesions are not overlooked. Together, these findings reinforce the importance of maintaining an appropriate threshold for biopsy and integrating clinical assessment with histopathological confirmation to optimize diagnostic accuracy.

Abbreviations

The following abbreviations are used in this manuscript:

SCC: Squamous Cell Carcinoma

NDPIGD: Non–dental plaque-induced gingival diseases

AAP: American Academy of Periodontology

EFP: European Federation of Periodontology

H&E: Hematoxylin and Eosin

NOS: Non-specific Inflammation

F/M: Female / Male

HPV: Human Papillomavirus

Declarations

Institutional Review Board Statement: This observational cross-sectional study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Cankiri Karatekin University, Health Sciences, Turkey (Approval No: 12.03.2026/29).

Clinical trial number: Not applicable.

Informed Consent Statement: General written informed consent for the use of clinical data and biological materials for research, education, and publication purposes was obtained from all patients prior to their routine clinical and surgical procedures. Due to the retrospective nature of the study, the requirement for additional study-specific informed consent was waived.

Consent for publication: Not applicable.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request. Individual CBCT and clinical measurement datasets are not publicly available due to privacy and ethical restrictions.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Funding: This research received no external funding

Author Contributions: Conceptualization, S.Ş. and B.K.; methodology, S.Ş.,Ö.A.Ü. and Z.Ş.; software, S.Ş.; validation, B.K.,Ö.A.Ü., Z.Ş. and S.Ş.; formal analysis, B.K. and Z.Ş.; investigation, Z.Ş.; resources, B.K.; data curation, Z.Ş. and S.Ş.; writing—original draft preparation, B.K. and Z.Ş.; writing—review and editing, B.K.,Ö.A.Ü. and S.Ş.; visualization, S.Ş.; supervision, Z.Ş.; project administration, B.K.; funding acquisition, S.Ş. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: No external funding or additional support was received for this study.

References

1. Gupta V, Kaur H, Mishra D et al. (2022) Distribution of biopsied gingival lesions according to the proceedings from the 2017 World Workshop classification: A three-year retrospective study. Dent Med Probl 59:105–110. https://doi.org/10.17219/dmp/141555
2. Li X, Zhang J, Zhang H, Li T. Biopsied non-dental plaque-induced gingival diseases in a Chinese population: a single-institute retrospective study. BMC Oral Health. 2021;21:265. https://doi.org/10.1186/s12903-021-01614-z.
3. Manjunatha B, Sutariya R, Nagamahita V, et al. Analysis of gingival biopsies in the Gujarati population: A retrospective study. J Cancer Res Ther. 2014;10:1088. https://doi.org/10.4103/0973-1482.137929.
4. Carbone M, Broccoletti R, Gambino A, et al. Clinical and histological features of gingival lesions: A 17-year retrospective analysis in a northern Italian population. Med Oral Patol Oral Cir Bucal. 2012;e555–61. https://doi.org/10.4317/medoral.17809.
5. Armitage GC. Development of a Classification System for Periodontal Diseases and Conditions. Ann Periodontol. 1999;4:1–6. https://doi.org/10.1902/annals.1999.4.1.1.
6. Chapple ILC, Mealey BL, Van Dyke TE, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol. 2018;89. https://doi.org/10.1002/JPER.17-0719.

7. Dhanuthai K, Boonkhanasan S, Kasarat P, et al. Prevalence and Clinico-pathologic Profile of Biopsied Gingival Lesions from 2 Thai Dental Schools. J Clin Exp Dent. 2024;e1046–52. https://doi.org/10.4317/jced.61932.
8. Mello FW, Miguel AFP, Dutra KL, et al. Prevalence of oral potentially malignant disorders: A systematic review and meta-analysis. J Oral Pathol Med. 2018;47:633–40. https://doi.org/10.1111/jop.12726.
9. Dilsiz A, Sevinç Gül SN. Investigation of Biopsied Non-Plaque-Induced Gingival Lesions in a Turkish Population: A 5-Year Retrospective Study. Eurasian J Med. 2023;55:100–3. https://doi.org/10.5152/eurasianjmed.2023.0088.

Figures

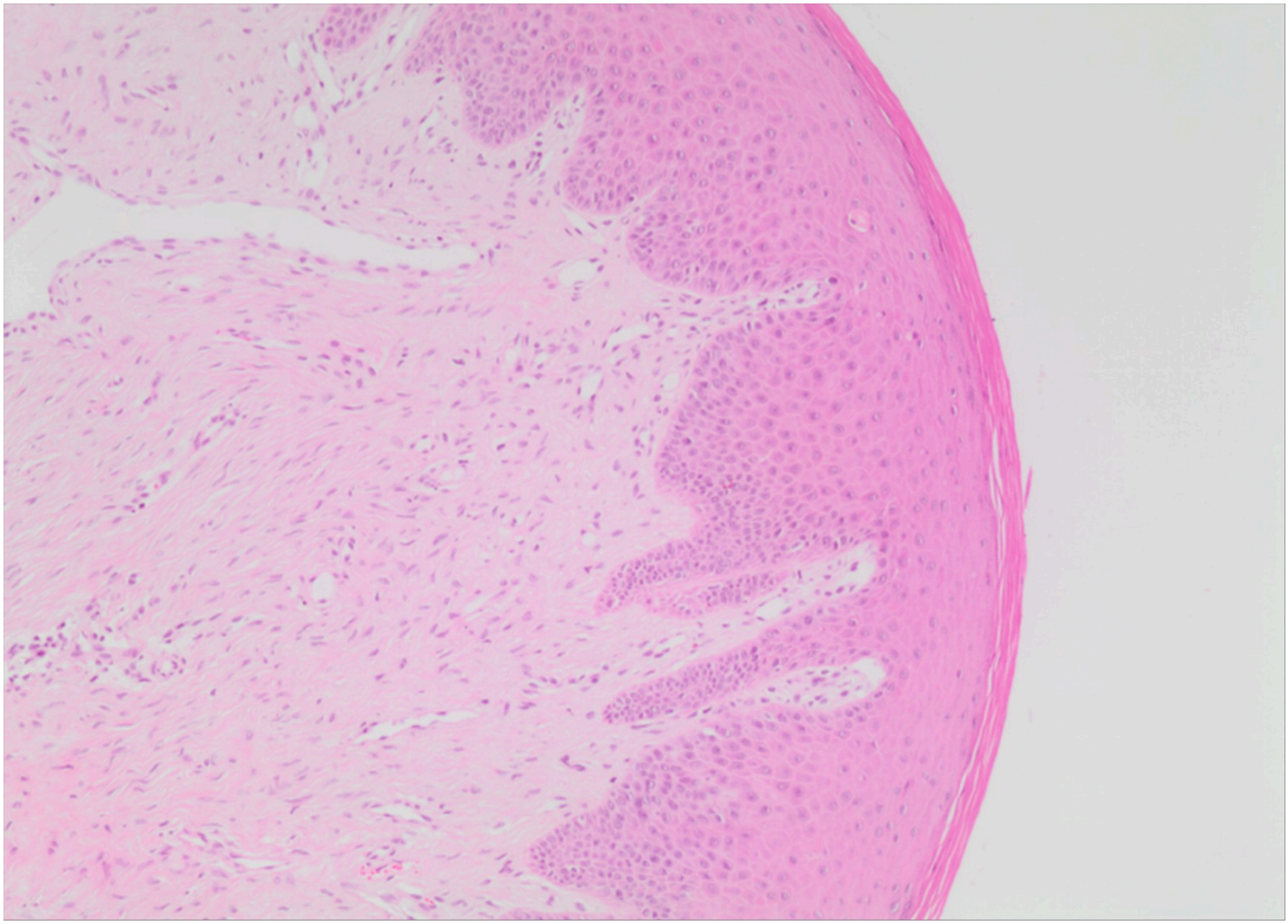


Figure 1

Fibroma (H&E, ×200)

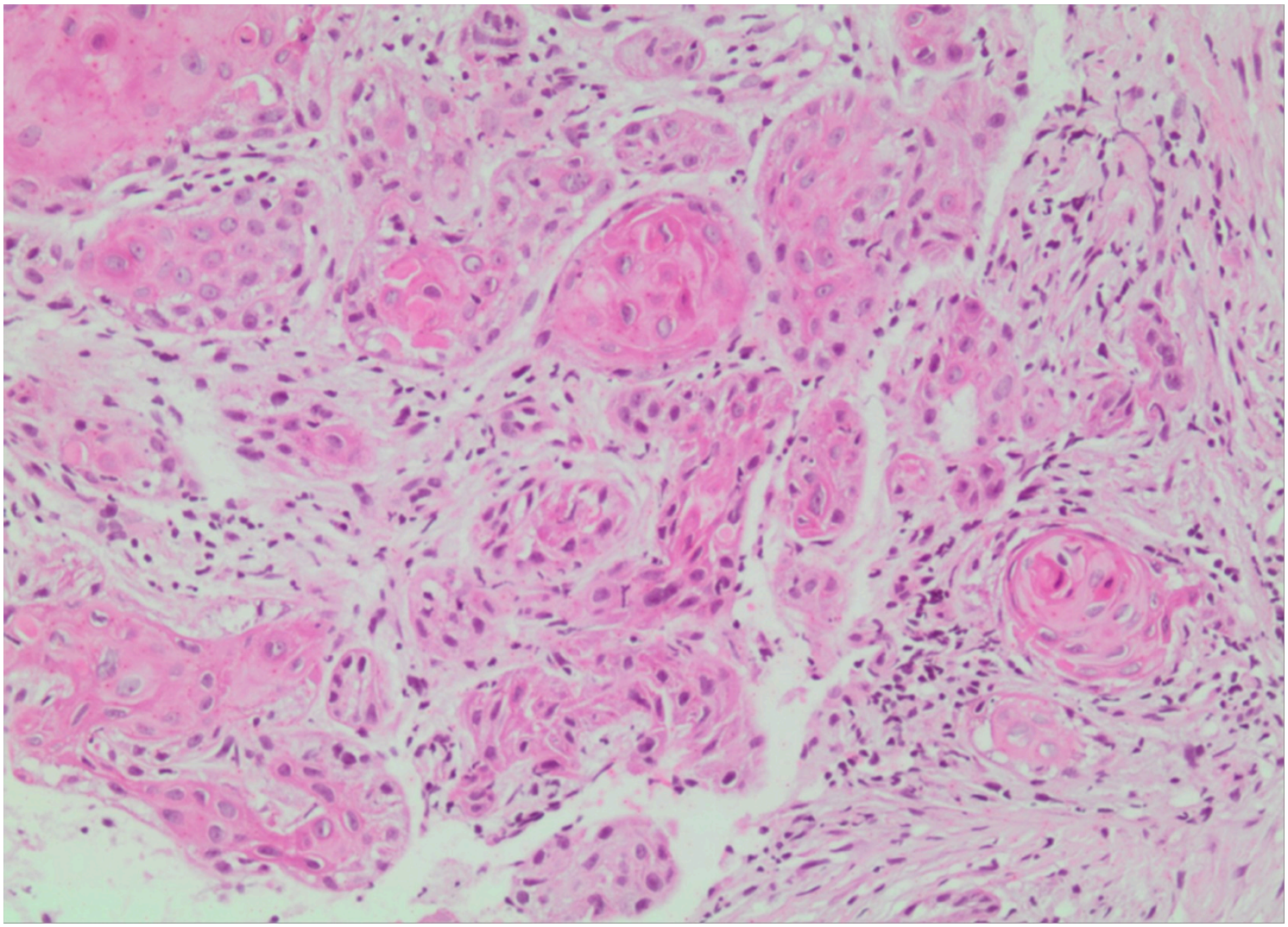


Figure 2

Squamous cell carcinoma (H&E, ×400)

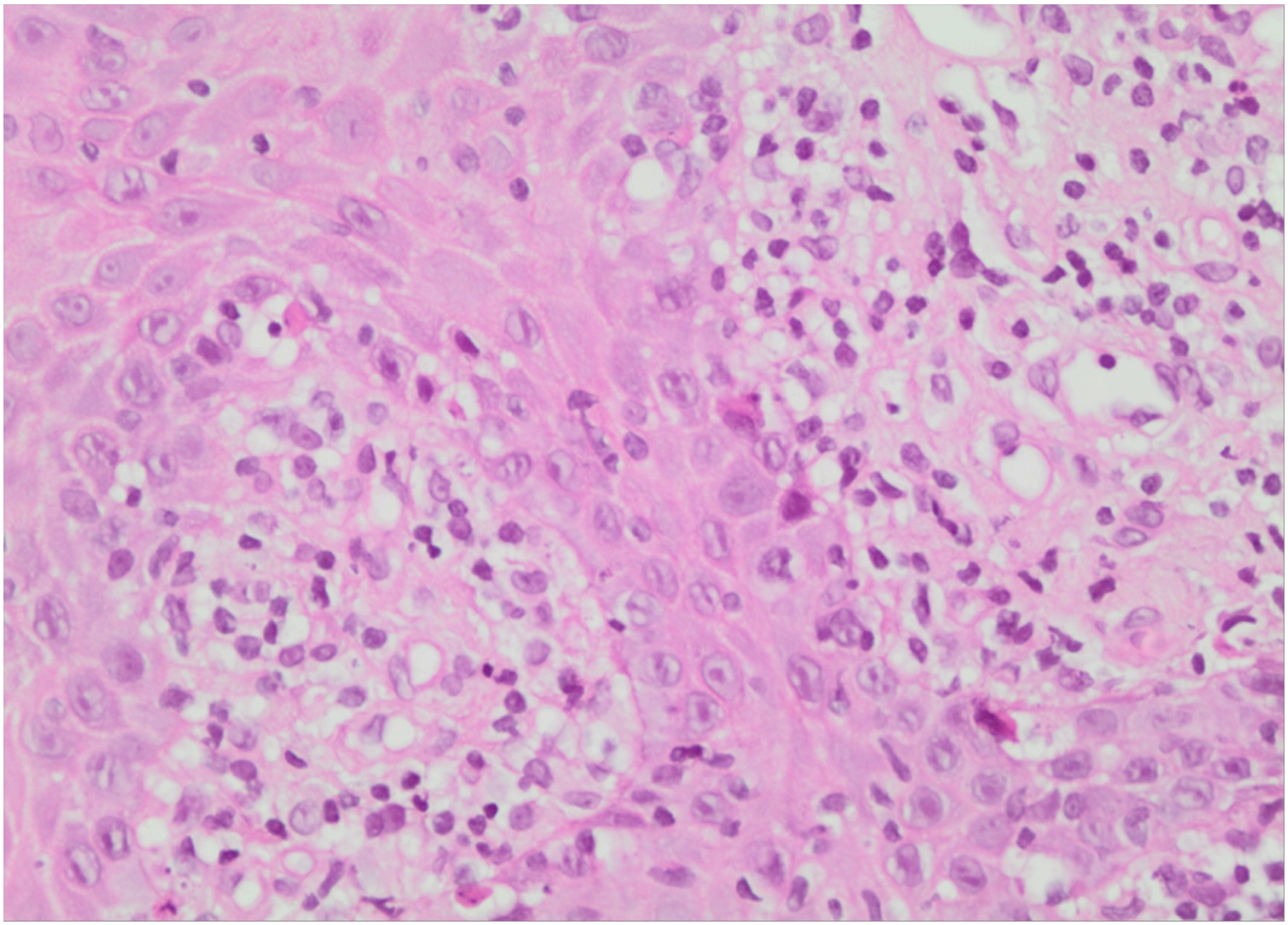


Figure 3

Lichen planus (H&E, ×400)