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Histopathologic Changes in Dental Follicle Associated with Radiographically Normal Impacted Lower Third Molars

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ABSTRACT

Impacted third molar extractions are one of the most common oral surgical procedures. In cases where a pathological condition is observed, it is relatively easy to decide on surgery. However, cystic changes can be observed in follicular tissues even in cases where pathological changes are not observed on radiography. The present study aimed to evaluate the histopathologic changes in dental follicles associated with radiographically normal impacted lower third molar. One hundred and one dental follicles were obtained after third molar surgeries. The patients with follicular width of less than 2.5 mm in the panoramic radiographs were included in the study. The relationships between pathological changes in follicular tissues and angular position of impacted teeth, age and gender were statistically examined. Cystic changes were observed in 65 (64.3%) of 101 follicles examined. The relationship between cystic changes and the angular position of impacted lower third molars was statistically significant ($p < 0.05$). Cystic changes were observed in 13 (43.3%) of 30 mesioangular teeth, 24 (80%) of 30 vertical teeth, 19 (65.5%) of 29 horizontal teeth, and 9 (75%) of 12 distoangular teeth. About 60% of cystic changes and 64.06% of inflammation occurred in patients between the ages of 20 and 30. Cystic changes can be observed in the follicular tissues of impacted lower third molars that are radiographically normal. There is a probability of histopathological changes, especially in patients over the age of 20 years and in the impacted lower third molars in the vertical position.

Keywords: *Dental follicle; dentigerous cyst; impacted teeth; oral surgery; pathology*

INTRODUCTION

The surgical removal of impacted lower third molars (ILTM) is one of the most frequently performed oral surgery procedures (Marciani, 2007; Altan & Soylu, 2018). Infection, cystic pathologies, odontogenic tumours, and root resorption in adjacent teeth are observed among the extraction indications of ILTM (Altan & Akbulut, 2019). Furthermore, there is still no consensus on the prophylactic extraction of asymptomatic ILTM. Prophylactic extraction indications include minimising the risk of pathological variables such as cysts and tumours, increased surgical difficulty with advanced age, and mandibular fracture risk (Adeyemo, 2006).

A dental follicle is a tissue of mesenchymal origin surrounding the developing tooth germ. During the root development of a tooth, periodontal ligament, cementum, and alveolar bone are formed by dental follicle progenitor cells (Yokoi *et al*., 2007). On the radiograph, it is a homogeneous radiolucency band observed around the crown of a developing tooth, and this radiolucent area is defined as the follicular space (Saravana & Subhashraj, 2008). The dental follicle may be the source of odontogenic cysts and tumours due to its odontogenic components showing proliferative potential. As a result of pathological degenerations observed in the dental follicle of an impacted tooth, there is the potential to develop odontogenic cysts or tumours such as dentigerous cyst, odontogenic keratocyst or ameloblastoma from the dental follicle (Rakprasitkul, 2001).

Radiographically, when pericoronal radiolucency width is less than 2.5 mm, follicular tissue is suggestive as normal or not associated with any pathologies (Rakprasitkul, 2001). Nevertheless, whether this evaluation provides complete reliability is controversial. The incidence of pathological changes associated with follicles of impacted teeth was observed at higher levels than those observed or reported radiographically (Adelsperger *et al*., 2000; Rakprasitkul, 2001; Baykul *et al*., 2005).

The present study aimed to evaluate the incidence of histopathologic changes in dental follicles associated with radiographically normal ILTM and determine the relationship between cystic changes in follicle tissues and age, gender, and the angular position of the impacted tooth.

MATERIAL AND METHODS

Patients

The study included 101 healthy patients whose ILTM were extracted for various reasons at Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Tokat Gaziosmanpaşa University. All participants included in the study signed an informed consent form. The study was conducted following the Declaration of Helsinki, and the protocol was approved by Tokat Gaziosmanpaşa University Clinical Research Ethics Committee for the study (Project number: 19-KAEK-081) (ClinicalTrials.gov Identifier: NCT04708119). The patients' panoramic radiographs were examined, and the impacted teeth were divided into four groups: vertical, horizontal, mesioangular, and distoangular, according to their angular positions. Patients with a follicular width of less than 2.5 mm associated with an impacted lower third molar radiographically were included in the study. The follicular tissues were also excised after tooth extraction. Soft tissue samples taken during surgical removal of ILTM were evaluated in the pathology department.

Histopathological Evaluation

The excision materials obtained for the study were subjected to routine tissue follow-up procedures at Department of Pathology, Faculty of Medicine, Tokat Gaziosmanpaşa University. The samples were fixed in 10% formalin solution for 24 hours for light microscope examination and were blocked using the routine paraffin blocking method. The samples were prepared by obtaining sections with microtome from the blocks. These preparations were stained with haematoxylin and eosin, and evaluated under a light microscope. In the histopathological examination, squamous epithelium, keratinisation, odontogenic epithelial residue, and fibrosis were either present or absent, and inflammation was scored as 0 (absent), 1 (mild), 2 (moderate), or 3 (severe). During the microscopic evaluation of follicular tissues, soft tissue samples with stratified squamous epithelium were identified as cystic (Rakprasitkul, 2001).

The relationship between histopathological changes observed in the radiographically normal dental follicles and gender and the teeth' angular positions was statistically evaluated.

Statistical Analysis

Before the data were collected, G*Power version 3.1.9.2 was performed for power analysis to estimate the sample size. The sample size of 89 was calculated to provide 95% power with an alpha of 5%. The final sample size consisted of 101 patients, considering the possibility of losses throughout the study.

Data are presented as percentage and frequency or mean +/- standard deviation. The chi-square test was used to compare the categorical data between groups. A p-value < 0.05 was considered as significant. The obtained data were analysed with SPSS 19 (IBM Corp., Armonk, NY, USA).

RESULTS

One hundred one patients (74 females, 27 males) were included in the study. The ages of the participants varied between 18 and 53 (mean: 22.24 ± 5.37). The study results showed that 60% of the cystic changes in the follicles and 64.06% of the inflammation were observed in patients between the ages of 20 and 30 (Figs. 1 and 2). Cystic changes were observed in 65 (64.3%) of 101 follicles examined. A statistically significant relationship was observed between the angular position of ILTM and cystic degenerations ($p < 0.05$). Cystic changes were observed in 13 (43.3%) of 30 mesioangular teeth, 24 (80%) of 30 vertical teeth, 19 (65.5%) of 29 horizontal teeth, and 9 (75%) of 12 distoangular teeth. Inflammatory changes were found in 63.3% ($n = 64$) of the samples. Severe inflammation was mainly observed in the vertical group, and there was a statistically significant difference with the other groups ($p < 0.05$). Keratinisation was observed only in the vertical group ($p < 0.05$). There was no significant difference between the angular position of ILTM regarding odontogenic epithelial residue and fibrosis ($p > 0.05$) (Table 1). No statistically significant difference by gender was observed in all histological parameters ($p > 0.05$).

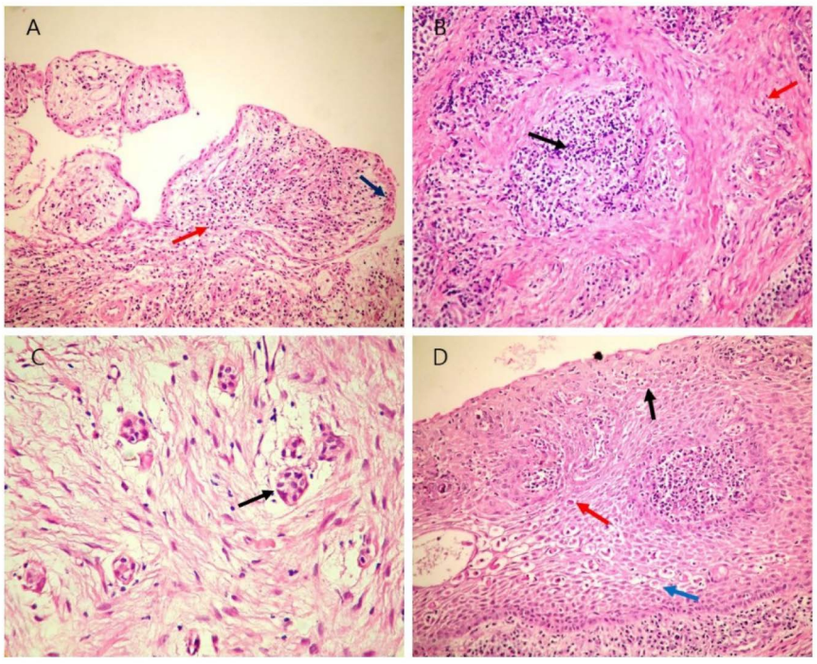

Fig. 1 (A) Atrophic epithelium (blue arrow) lining the cyst and lymphocytes (red arrow) in the loose stroma (HE × 400). (B) Intense chronic inflammation (black arrow) infiltrating the collagenised cyst wall (red arrow) (HE × 200). (C) Odontogenic epithelial remnants (black arrow) in the cyst wall (HE × 400). (D) Histological appearance of epithelial inflammation (black arrow), spongiosis (blue arrow), single cell keratinisation (red arrow) (HE × 400).

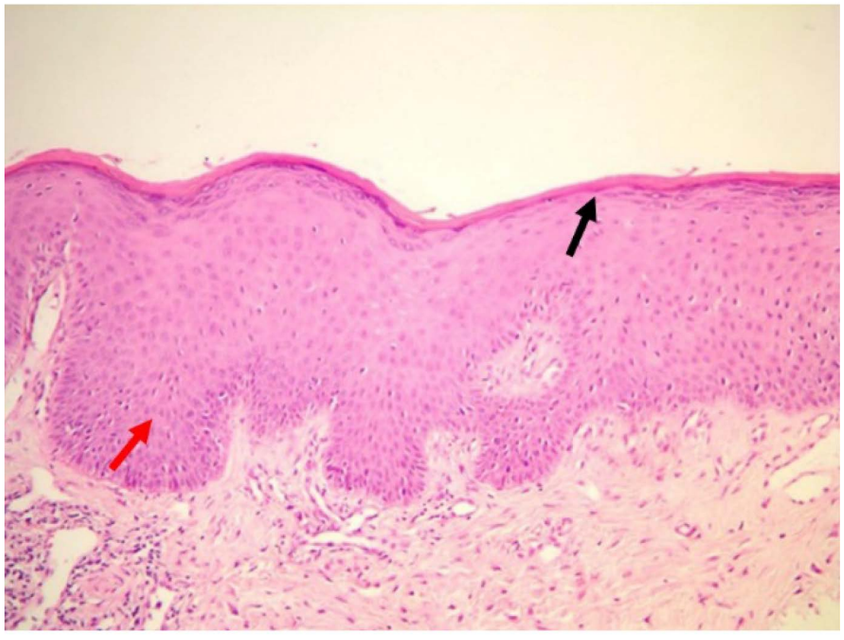

Fig. 2 Histopathological appearance of hyperplastic squamous epithelium (red arrow) and keratinisation (black arrow) (HE × 400).

Table 1 Histopathological findings according to angulation of the impacted lower third molar (n = 101)

Histopathological features		Angulation of the impacted lower third molar				χ^2	p
		Mesioangular (%)	Vertical (%)	Horizontal (%)	Distoangular (%)		
Stratified squamous epithelium	Absent	17 (56.7)$^{(a)}$	6 (20.0)$^{(b)}$	10 (34.5)$^{(ab)}$	3 (25.0)$^{(ab)}$	9.590	0.022*
	Present	13 (43.3)$^{(a)}$	24 (80.0)$^{(b)}$	19 (65.5)$^{(ab)}$	9 (75.0)$^{(ab)}$		
Inflammation	Absent	18 (60.0)$^{(a)}$	7 (23.3)$^{(b)}$	9 (31.0)$^{(b)}$	3 (25.0)$^{(b)}$	29.224	0.001*
	Low	6 (20.0)$^{(ab)}$	2 (6.7)$^{(b)}$	10 (34.5)$^{(a)}$	2 (16.7)$^{(ab)}$		
	Moderate	4 (13.3)$^{(a)}$	2 (6.7)$^{(a)}$	3 (10.3)$^{(a)}$	1 (8.3)$^{(a)}$		
	Severe	2 (6.7)$^{(a)}$	19 (63.3)$^{(b)}$	7 (24.1)$^{(ac)}$	6 (50.0)$^{(bc)}$		
Keratinisation	Absent	30 (100.0)$^{(a)}$	22 (73.3)$^{(b)}$	29 (100.0)$^{(a)}$	12 (100.0)$^{(a)}$	20.562	<0.001*
	Present	0 (0.0)$^{(a)}$	8 (26.7)$^{(b)}$	0 (0.0)$^{(a)}$	0 (0.0)$^{(a)}$		
Odontogenic epithelial residues	Absent	18 (60.0)$^{(a)}$	17 (56.7)$^{(a)}$	21 (72.4)$^{(a)}$	10 (83.3)$^{(a)}$	3.731	0.292
	Present	12 (40.0)$^{(a)}$	13 (43.3)$^{(a)}$	8 (27.6)$^{(a)}$	2 (16.7)$^{(a)}$		
Fibrosis	Absent	6 (20.0)$^{(a)}$	2 (6.7$^{(a)}$	3 (10.3)$^{(a)}$	0 (0.0)$^{(a)}$	4.592	0.204
	Present	24 (80.0)$^{(a)}$	28 (93.3)$^{(a)}$	26 (89.7)$^{(a)}$	12 (100.0)$^{(a)}$		

Notes: Data are given in n (percentages of rows). * Significant at the $p < 0.05$ level.
There is no statistical significance between the columns belonging to the same superscript letters.

DISCUSSION

Third molars are the last teeth to complete eruption in the jaws, and mandibular third molars are the teeth with the highest probability of impacting among all teeth (Damlar *et al.*, 2014). Surgical removal of these teeth for various indications is one of the most common oral surgical procedures. It is usually easy to extract third molars associated with a pathological condition. Complications such as infection, swelling, pain and nerve damage that can be observed due to surgical procedure in asymptomatic cases would reduce the patient's quality of life causing both the patient and the clinician to avoid prophylactic tooth extractions. However, the complications and difficulties of impacted third molar surgery increase as pathologies associated with impacted teeth, systemic diseases, and postoperative morbidity increase with age (Adeyemo, 2006). These reasons support prophylactic tooth extraction.

In addition, the authors, who thought that prophylactic impacted third molar extractions were necessary, suggested that a high rate of cystic degeneration was observed in follicles with pericoronal radiolucency less than 2.5 mm (Eliasson *et al.*, 1989). Although different clinical and radiographic markers are used in the diagnosis of cystic pathologies, histopathological examination in oral pathology is the gold standard and necessary to confirm the clinical diagnosis (Patel *et al.*, 2011). Obtaining comprehensive information about the character of cystic pathologies is essential for the clinician to determine the right treatment options and to guide the patient when necessary. The present study determined that pathological changes may occur in impacted teeth even if they are considered radiographically normal.

Most dentists frequently discarded follicular tissues after impacted tooth extraction and did not send soft tissues for histopathological examination. Therefore, there is minimal data on pathological changes in the follicles associated with impacted third molars. The cystic changes in impacted third molars were reported to be 23% (Yildirim *et al.*, 2008), 34% (Adelsperger *et al.*, 2000), 35% (Rakprasitkul, 2001), 37% (Glosser & Campbell, 1999), 46% (Saravana &

Subhashraj, 2008), and 50% (Baykul *et al.*, 2005). In the present study, cystic changes were observed in 64.3% of the dental follicles obtained from radiographically normal impacted lower third molars.

A previous study by Tegginamani and Prasad (2013), showed different results when compared with the present study. Both studies had similar age averages and similar study groups; however, there were differences in the distributions between the groups and the high incidence of cystic degeneration observed in the dental follicles of vertically impacted teeth.

When the impacted mandibular third molar position was compared with the incidence of pathological changes in the follicular tissue, it was observed that the pathological variables in the follicular tissues were the most sensitive to different angular positions of the impacted lower third molars. Many authors reported the relationship between the angular positioning of the ILTM and pathology. However, the results of the studies are contradictory. In our study, the vertically impacted teeth showed a higher tendency to pathological changes. Knutsson *et al.* (1996) and Eliasson *et al.* (1989) found higher rates in horizontally positioned teeth. While Yıldırım *et al.* (2008) reported higher rates of pathological changes between the teeth in vertical and mesioangular positions, Baykul *et al.* (2005) reported higher rates between the vertically positioned teeth. The differences in results may also be related to the inclusion criteria among the studies.

Chronic inflammation might lead to chronic irritation and stimulate epithelial cells' proliferation (de Paula *et al.*, 2000). Edamatsu *et al.* (2005) argued a potential direct relationship between the severity of inflammation and proliferation, and they theorised that inflammatory changes could rearrange the cell cycle of dental follicle epithelial components. Following this recommendation, Edamatsu *et al.* (2005) and Cabbar *et al.* (2008) reported high Ki67 and MCM2 cell proliferation markers in inflamed dental follicles. In the present study, severe inflammation was more prevalent in vertically positioned teeth.

Many studies reported a correlation between cystic changes in dental follicles and age. It has been reported that follicular pathological changes are observed at a higher rate in older age groups than the second decade (Glosser & Campbell, 1999; Adelsperger *et al.*, 2000; Rakprasitkul, 2001). In our study in which cystic changes occurred between the ages of 18 and 53, the patients' mean age was 22. Our study determined that 60% of cystic changes and 64.06% of inflammation occurred in patients between the ages of 20 and 30 years old. This result is consistent with previous reports. The present study found cystic changes primarily in women, and different female/male ratios were reported in previous studies (Daley & Wysocki, 1995; Baykul *et al.*, 2005). The reason for the gender difference still remains unclear (Adelsperger *et al.*, 2000; Rakprasitkul, 2001; Yildirim *et al.*, 2008).

CONCLUSION

Radiographically, when pericoronal radiolucency width is less than 2.5 mm, follicular tissue is suggestive as normal. However, our results indicate that radiographic analysis may not be reliable for evaluating follicular tissues. Cystic changes may be observed in the histopathological examination of radiographically normal ILTM. It may be suspected of the probability of cystic changes, especially in patients over the age of 20 years old and in the impacted lower third molars in the vertical position. Therefore, it is recommended to monitor all third molars regardless of whether they are symptomatic. Furthermore, it is recommended to perform histopathological analysis on all surgically removed follicular tissues.

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