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Soft tissue pathosis associated with asymptomatic impacted lower third molars

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Abstract

Objective: The aim of this study was to identify the prevalence of pathological changes in the pericoronal tissue of asymptomatic impacted lower third molars and to assess the correlation between pathological changes and patient demographic, radiographic and morphological characteristics.

Study Design: Follicles associated with fully impacted lower third molars were submitted for histological examination after surgical extraction from 50 patients. The correlation between pathological changes in the dental follicle and age, gender, depth of impaction, angular position, and coverage and tooth development was analyzed.

Results: Cystic changes were observed in 10% of specimens and inflammatory changes in 62%. Incidence of pathological changes was significantly higher in Class B impacted teeth when compared to Class C impacted teeth. A significant correlation was found between epithelial cell activity and the completion of tooth development.

Conclusion: We recommend monitoring all third molars whether or not they are symptomatic and conducting histopathological analyses on all surgically extracted follicle tissue.

Key words: *Impacted lower third molar, pericoronel tissue, radiograph, pathology.*

Introduction

Tooth formation occurs in the development sac, also known as a dental follicle (DF) or dental sac (DS) that surrounds the dental papilla and enamel organ (1). The DF is responsible for coordinating resorption and deposition in the bone opposite the region of eruption through intraosseous movement (2) and is also responsible for the structure of the periodontal ligament and cement (1,3). Despite this important role in eruption physiology, previous studies have reported that the DF may undergo cystic degeneration and/or neoplastic transformation (1, 4-7). The DF appears radiographically as a pericoronal radiolucency, the width of which is of the utmost importance in identifying DF pathology (3). Previous studies

have suggested that a pericoronal radiolucency 2.5 mm or larger on a panoramic radiograph may indicate an abnormality (4-8).

Extraction of impacted mandibular (lower) third molars (ILTMs) is one of the most frequent procedures performed by oral and maxillofacial surgeons (6, 8-12). Because most dental practitioners discard extracted unerupted third molars rather than send them for histopathological analysis, no accurate information is available regarding the prevalence of pathological formations (9). While there is a consensus that ILTMs should be extracted when pathological changes and serious clinical symptoms are observed, there is no agreement regarding the prophylactic extraction of ILTMs (8-10,13). As a result, some clinicians espouse prophylactic extraction, while others favor observation and periodic monitoring (6,9,10,13).

The aim of this study was to determine the prevalence of pathological changes in the pericoronal tissue of clinically and radiographically asymptomatic lower third molars and to assess the correlation between pathological changes and various patient demographic, radiographic and morphological characteristics.

Materials and Methods

This study was approved by the Ethics Committee of the Atatürk University Faculty of Dentistry, and all participants gave their informed consent. Patients were selected from among those visiting our clinic for removal of asymptomatic ILTMs fully impacted and with follicular spaces smaller than 2.5 mm, over a period of ten months, from January 2009 to November 2009. Only patients who were in good medical health and had not taken any drugs for 30 days before surgery were included. Patients with any signs or history of infection or impacted mandibular third molars with a widened pericoronal region were excluded. From a total of 978 patients, 50 were selected. For the study, only 1 tooth was surgically extracted, even if both third molars required extraction.

Radiographic analysis was conducted using panoramic radiographs (OPTs). All images were exposed for 0.2 s using an Evaluation X 3000-2C x-ray unit (New Life Radiology Srl, Grugliasco, Turin, Italy) operated at 70 kVp and 8 mA with a focus-receptor distance of 30 cm. All images were exposed to 60-80 kV and 1-10 mA from an x-ray unit (Marita, MFG Corp., Kyoto, Japan) for 16.2 s with three rotation centers and a constant magnification of x1.3. The pericoronal space was measured from the mesial, distal and occlusal surfaces, and the largest width was recorded. The follicular space was measured from panoramic radiographs independently by the three authors, and the largest width was recorded, disregarding the manufacturer's reported magnification factor.

The depth of the ILTM impaction was recorded according to Nordenram (14), as follows: Class A (high occlusal level), the most superficial part of the third molar is located on a level with the occlusal plane; Class B (medium occlusal level), the most superficial part of the third molar is located between the occlusal plane and the cement-enamel junction of the second mandibular molar; and Class C (Deep occlusal level), the most superficial part of the third molar is located apically to the cement-enamel junction of the second mandibular molar. (Since this study included only fully impacted third molars, no Class A teeth were included.) Third molar angulation was determined according to Shiller (15), as follows: vertical (V), 0-10°; mesioangular (M) or distoangular (D), 11°-70°; horizontal (H), ≥71°; and a group of cases with inverted or buccolingual angulation were combined as inverted (I). Third molar development was estimated using Kohler et al.'s (16) modification of the method described by Gleiser and Hunt (17). Only teeth between Phase 7 (root 3/4 calcified) and Phase 10 (complete root formation, root canals terminally convergent) were included in the study. Molar coverage was classified as either total mucosa, or partial bone coverage or total bone coverage.

Extractions were performed under local anesthesia without any kind of sedation (oral, nasal or venous) and were standardized to as great an extent as possible. Articaine HCl 2.5% plus 1:100,000 epinephrine (Ultracaine D-S Forte Ampul; Aventis, Istanbul, Turkey) was used for the inferior alveolar and buccal nerve blocks. A standard incision was used, from the anterior border of the ramus to the distobuccal corner of the second molar, following the buccal gingival sulcus along the second molar. A vertical incision was made from the mesiobuccal corner of the second molar to the mucogingival line. After periosteal elevation, bone on the buccal and distal sites was removed with a round bur using abundant saline irrigation. In all cases, the third molar was carefully extracted. Following the extraction, the pericoronal tissue was carefully curetted, and the soft tissue was sent for histopathological analysis. Closure was done with 3-4/0 silk sutures. Tissue samples were immersed in 10% neutral-buffered formaldehyde for 48-52 hours and dehydrated using a graded ethanol series. Samples were embedded in paraffin wax, serially sectioned into 5-µm slices using a Leica RM2125RT microtome (Leica, Germany) and mounted on glass slides. The prepared sections were stained with hematoxylin and eosin (H&E) and examined under a Nikon Eclipse E600 light microscope (Nikon, Japan) equipped with a digital color camera attachment (Nikon DS-Fi1, Japan). Slides were viewed independently by three histologists. Diagnoses were recorded when all three histologists were in agreement. In cases of disagreement, a consensus diagnosis was recorded after a joint review. Specimens were classified as cystic if they showed a

dense fibrous connective tissue wall lined with several layers of stratified squamous epithelium (6). Epithelial cell activity was recorded as follows: inactive (less than 20 layers of epithelial cells and no epithelial projections into the connective tissue), hyperplasic (more than 20 layers and/or epithelial projections) or absent (no epithelial cells observed) (1). Connective tissue was classified as dense or loose. Inflammation was classified as acute, chronic or absent. Calcification was recorded as either present or absent.

Histopathological data was analyzed according to the radiographic criteria described above and by gender and age, with patients aged 25 years or younger in one group and patients older than 25 years of age in another group. A chi-square test was conducted with gender, age and radiographic findings as independent variables and histopathological parameters as dependent variables (Statistical Analysis System, Windows Ver. 9.0, Cary, NC, USA). If the number of observations was insufficient, Fisher's exact test was applied. The level of significance was set at $p < 0.05$.

Results

Of the 50 patients included in the study, 56% were female (n = 28), and 44% were male (n = 22). Mean age was 20.97 ± 1.96 (age range 16-25) in the 25 years or younger age group (n = 31) and 33.00±8.76 (age range: 26-59) in the 25 and older age group (n = 19). Mean age for women and for men was 24.71 ± 6.32 (16-45) and 26.59 ± 9.95 (16-59), respectively.

Correlations between ILTM pathology and demographic factors are given in (Table 1), and correlations between ILTM pathology and radiographic and morphological factors are given in (Table 2).

Cystic changes were found in 10% (n = 5) of specimens. Eighty percent of the cystic changes (n = 4) were in the younger age group; the differences between younger and older patients was not statistically significant. Cystic changes were also seen in 4 female patients and 1 male patient, but again, this difference was not statistically significant. No correlation was found between cystic change and depth of impaction. Two out of 17 mesioangular teeth (11.8%), 1 out of 8 distoangular

Table 1. Histopathological findings according to patient age and gender.

		Age		Sex	
Histopathological Features	**Subclass**	**≤25 years (n = 31)**	**>25 years (n= 19)**	**F (n=28)**	**M (n = 22)**
Cell Activity	Absent	5	3	4	4
	Hyperactive	15	14	19	10
	Inactive	11	2	5	8
	(X^2; p)	4.1; 0.13		2.8; 0.25	
Inflammation	Absent	13	6	11	8
	Acute	3	1	4	0
	Chronic	15	12	13	14
	(X^2; p)	1.1; 0.58		3.9; 0.15	
Connective tissue	Dense	6	3	6	3
	Loose	25	16	22	19
	(X^2; p)	0.1; 0.75		0.5; 0.48	
	Absent	31	18	27	22
	Present	0	1	1	0
	(X^2; p)	1.7; 0.20		0.8; 0.37	
Cyst	Absent	27	18	24	21
	Present	4	1	4	1
	(X^2; p)	0.8; 0.38		1.3; 0.25	

F; Female, M; Male.

Table 2. Histopathological findings according to radiographic features of the third molar.

		Radiographic Features										
		Depth[1]		Angulation[2]				Coverage[3]			Tooth Development[4]	
Histopathological Features	Subclass	B	C	MA	DA	H	V	BC	MC	MBC	C	IC
Cell Activity	Absent	7	1	2	4	2	0	3	1	4	3	5
	Hyperactive	26	3	11	2	10	6	9	7	13	22	7
	Inactive	10	3	4	2	6	1	17	0	6	5	8
	(X^2; p)	1.2; 0.54		10.7; 0.09				4.6; 0.33			7.2; 0.03	
Inflammation	Absent	13	6	5	5	8	1	12	1	6	9	1
	Acute	4	0	2	0	1	1	2	0	2	3	1
	Chronic	26	1	10	3	9	5	5	7	15	18	9
	(X^2; p)	7.9; 0.02		5.2; 0.52				11.1; 0.03			2.1; 0.34	
Connective tissue	Dense	8	1	3	2	1	3	5	1	3	5	4
	Loose	35	6	14	16	17	4	14	7	20	25	16
	(X^2; p)	0.1; 0.78		5.9; 0.17				1.4; 0.49			0.1; 0.76	
Calcification	Absent	42	7	16	8	18	7	19	7	23	29	20
	Present	1	0	1	0	0	0	0	1	0	1	0
	(X^2; p)	0.2; 0.68		2.0; 0.58				5.3; 0.07			0.7; 0.40	
Cyst	Absent	39	6	15	7	17	6	15	8	22	27	18
	Present	4	1	2	1	1	1	4	0	1	3	2
	(X^2; p)	0.3; 0.57		0.7; 0.88				4.3; 0.12			0.00; 1.00	

DF; Dental Follicle.
1B; Class B, C; Class C.
2MA; Mesioangular, DA; Distoangular, H; Horizontal, V; Vertical.
3BC; Bone Coverage, MC; Mucosa Coverage, MBC; Mucosa and Bone Coverage.
4C; Complete, IC; Incomplete.

teeth (12.5%), 1 out of 18 horizontal teeth (5.6%) and 1 out of 7 vertical teeth (14.3%) exhibited cystic changes; however, the differences between teeth of different angulation were not statistically significant. Moreover, no statistically significant differences were seen between cystic change and tooth coverage or development (Fig. 1).

Inflammatory changes were found in 62% (n = 31) of the specimens; 58.06% of the inflammatory changes (n = 18) were in the younger age group. The difference between age groups was not statistically significant. Inflammatory changes were seen in 17 female patients (54.84%) and in 14 male patients (45.16%), but again, the differences between the women and men were not statistically significant. A statistically significant correlation was found between inflammation and depth of impaction (p = 0.02), with the incidence of inflammation higher among Class C ILTMs in comparison to Class B ILTMs. There was also a statistically significant correlation between inflammation and coverage (p = 0.03), with 7 out of 8 ILTMs (87.5%) covered by mucosa, 17 out of 23 ILTMs (73.9%) partially covered by bone and 7 out of 19 ILTMS (36.8%) completely covered by bone exhibiting inflammatory changes. The majority of teeth with inflammation (38.7%) had mesioangular angulation, followed by those with horizontal angulation (32.3%), vertical angulation (19.4%) and distoangular angulation (68%); however, the differences between inflammation rates by angulation were not statistically significant. Moreover, no correlation was found between inflammation and tooth development (Fig. 2).

No correlation was found between epithelial cell activity and age, gender, depth of impaction, angulation or coverage; however, a statistically significant correlation

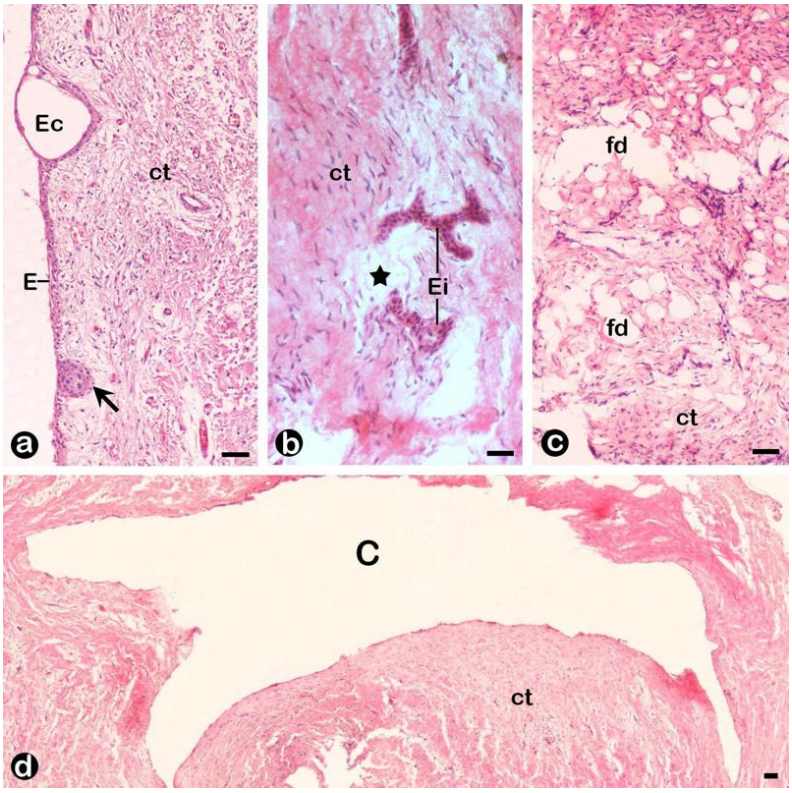

Fig. 1. Light microscopy photographs of a dental follicle.
E: epithelium, Ec: an intraepithelial cyst, arrow: epithelial cell proliferation with a globular appearance, Ei: epithelial cell islands within the connective tissue, asterisk: stromal edema, fd: fatty degeneration, C: a large cyst, ct: connective tissue. Stain: H&E. Bars = 70 µm.

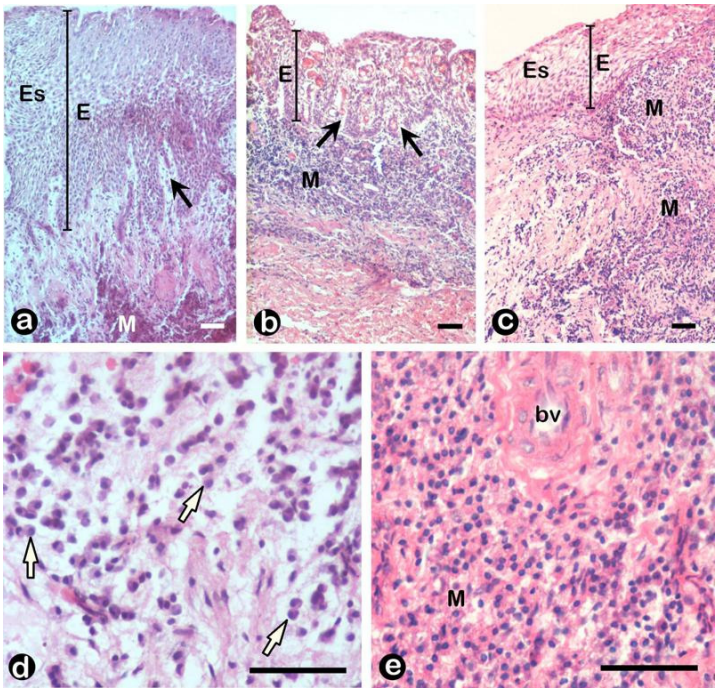

Fig. 2. Light microscopy photographs of a dental follicle.
E: epithelium, Es: epithelial swelling, M: mononuclear infiltrations within the connective tissue, by: blood vessel, black arrow: finger-like projections of subepithelial connective tissue, white arrow: plasma cells. Stain: H&E. Bars = 70 µm.

was found between cellular activity and tooth development (p = 0.03), (Fig. 1).
No correlation was observed between connective tissue density and any of the parameters examined (Fig. 2).
No correlation was observed between calcification and any of the parameters examined. Calcification was seen in only 1 patient (female, under age 25).
No correlation was observed between tooth coverage and any of the parameters examined.

Discussion

Prophylactic extraction of all ILTMs is reported to occur at rates of between 18% and 54% (10,18), although not all ILTMs cause clinical problems and the percentage of ILTMs that may remain asymptomatic for years is unknown (13). Prophylactic extraction is favored by many surgeons for reasons that include the possibility of pathological change (8,10), the rise in surgical and postsurgical complications with age (1,7,9), the higher costs of extraction if performed after pathology has developed and the quick rate of progression of untreated pathological conditions (9).
Most previous studies relied on radiographic analysis of the dental follicle to identify the presence of pathology (19-21). Radiographic studies have reported cyst development in impacted third molars to occur at rates of between 1% and 1.6% and epidemiological studies at rates of between 0.0002% and 2.31% (18, 21-23). However, radiographic and clinical analysis of DFs may not always agree with histopathological findings (4,5, 7-9), and the absence of symptoms does not necessarily imply the absence of pathology (9). A follicular width greater than 2 mm on periapical radiographs (24) and 2.5 mm on panoramic radiographs has been suggested as an indication of DF pathology in asymptomatic impacted third molars (25). Miller and Bean (26) suggested that disease may be present in minute follicular spaces whereas areas of enlarged radiolucency may be histologically normal, making biopsy imperative. In our study, histopathological analysis showed cystic changes in 10% of ILTMs that were radiographically normal, and previous studies have reported much higher discrepancies (between 23% and 70.5%) (4-9, 11) (Table 3).
Our study found all pathological changes of ILTMs to be more frequent among women. Differences in male/female ratios have also been reported in earlier studies, although the reason for this difference remains unknown (6-9).
In line with studies suggesting that pathological change occurs more frequently after age 20 and is particularly high among individuals aged 20-30 (4,8,11,12), our study found 80% of cystic changes and 58.06% of inflammation occurred in patients aged 20-24. This result is consistent with the previous reports. Therefore, age may be used as an indication for surgical removal of ILTM, as the risk of surgical morbidity also increases as age increases (8). On the other hand, our finding of a higher incidence of pathological changes among patients under age 25 conflicts with our finding that the likelihood of cystic change is independent of tooth development. This inconsistency may be ascribed to the higher number of individuals aged 20-30 among the participants in our study and previous studies.
In our study, vertical and mesioangularly inclined molars showed a greater tendency toward pathological change. The association between the angular positioning of ILTMs and pathology has been reported by many authors; however, the findings among studies are contradictory. Whereas Baykul et al. (8) reported higher rates of pathological changes among vertically positioned teeth and Yildirim et al. (9) reported higher rates among both vertically and mesioangularly positioned teeth, Knutsson et al. (12) and Eliasson et al. (27) reported higher rates among horizontally positioned teeth. This suggests that factors other than those examined may play a role in the emergence of ILTM pathology. Differences in findings may also be related to differences in inclusion criteria among studies. Whereas Baykul and Knutsson et al.'s studies (8,12) evaluated only third molars covered either partially or totally by mucosa, our study and Yildirim et al.'s study (9) analyzed only fully impacted third molars.
In agreement with Werkmeister et al. (28), who reported a relationship between impaction level and severe complications in impacted lower third molars, our study found a strong correlation between depth of im-

Table 3. Histopathological changes in follicular tissue of the third molars with radiographically normal.

Cases	Age range (mean)	% in pathological conditions	
		Cyst	Inflammation
Saravana and Subhashraj (4)	18-44 (28)	46	-
Cabbar et al. (5)	16-69 (28.2)	-	33
Rakprasitkul (6)	13–63 (26)	51	4.8
Adelsperger et al. (7)	15–34 (18.9)	34	-
Baykul et al.(8)	14–45 (21.1)	50	-
Yıldırım et al. (9)	15–68 (24.7)	23	-

paction and the prevalence of pathological changes in DF follicular tissue. In terms of coverage, whereas our study found pathological changes in 11.3% of third molars completely covered by mucosa and 51.3% of those completely covered by bone tissue, Knutsson et al. (12) reported that 19.34% of pathological third molars were completely covered by mucosa, compared to only 2.55% that were covered by bone tissue.

In our study, a direct correlation emerged between ILTM development and cell activity. The increase in cell activity with development may be related to the increases in inflammation also found in this study. De Paula et al. (29) suggested that chronic inflammation may cause chronic irritation and stimulate the proliferation of epithelial cells. Edamatsu et al. (30) suggested a possible direct correlation between severity of inflammation and proliferation, and they theorized that inflammatory changes could reorder the cell turnover of DF epithelial components. In line with this suggestion, Edamatsu et al. (30) and Cabbar et al. (5) reported high levels of Ki-67 and MCM-2 cell proliferation markers in dental follicles with inflammation.

Conclusion

Within the limits of the study population and method, our findings show that radiographic analysis may not be a reliable technique for the evaluation of DF. Although clinically and radiographically asymptomatic, impacted third molars—especially those in Class B that are entirely covered by mucosa and that have completed development—have the potential to undergo pathological change. For this reason, we recommend monitoring all third molars regardless of whether or not they are symptomatic. Furthermore, we recommend that histopathological analysis be conducted on all surgically extracted follicle tissue.

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