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Apical periodontitis and endodontic status in a Trakya population with cancer and autoimmune diseases: A cross-sectional study

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Purpose: The aim of this cross-sectional study was to compare the endodontic and periapical status of patients with cancer or autoimmune diseases (AD) with that of healthy patients matched by age and sex. Additionally, the cancer and AD groups were compared.

Methods: Digital radiographs of 100 patients with cancer, 100 patients with autoimmune diseases, and healthy patients (200) matched for age and gender were evaluated. The total number of teeth, root canal-filling teeth (RCFT), quality, presence and number of apical periodontitis (AP) were examined.

Results: No significant differences were observed in terms of teeth with AP periodontitis between the cancer and control groups, as well as between AD and control groups. The results of the univariate logistic regression analysis revealed a positive association between cancer and the values of RCFTs and inadequate RCFTs (iRCFT) (RCFT $p < 0.001$; iRCFT $p = 0.018$), as well as a positive association between autoimmune disease and RCFTs ($p = 0.001$).

Conclusion: The results showed that AP was similar between the cancer and AD and control groups. Patients with a history of cancer or AD who are clinically considered high-risk should attend regular dental visits.

Keywords: Autoimmune diseases; neoplasms; observational study; periapical periodontitis; risk factors.

Introduction

Apical periodontitis (AP) is the local tissue response to pulp infection caused by dental caries, trauma, and abrasion (1). A 2021 systematic review investigating the prevalence of AP reported that 52% of adults worldwide had at least one tooth with AP (2). The pathological process of AP is related to the relationship between host immunity and the virulence of the infectious pathogens (3), and the role of host immunity is important (4). The relationship between AP and systemic disease has been frequently investigated, and the concept of endodontic medicine has emerged (5). Apical periodontitis occurs in response to endodontic infection, initiating an immune response, and the patient's systemic status may be affected (6). Previous studies have shown that microorganisms and toxins in the periapical tissue can pass from the root canal system into the bloodstream during/after endodontic treatment of tooth (7,8). Conversely, systemic diseases can alter the

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inflammatory response in the localized lesion, increasing the destruction of periapical tissues (6).

The relationship between the oral microbiota and systemic diseases has been frequently investigated in recent years (9). Oral microbiota is associated with many diseases, including cancer, bacterial endocarditis, rheumatoid arthritis, and cardiovascular disease (10-13).

Cancer is a disease characterized by the uncontrolled proliferation of abnormal cells that invade normal tissues and spread throughout the body (14). Oral complications of cancer and cancer treatments cause acute and late symptoms. Acute oral complications include salivary changes, mucositis, and infection. Complications in survivors include neurosensory changes; salivary, gustatory, and functional changes; oral and dental infections; and necrosis of the jaw (15). These complications are important for the quality of life of the cancer survivors. Chemotherapy involves the use of chemotherapeutic drugs that act by destroying and/or controlling the growth of cancer cells. Chemotherapy can predispose to mucosal deterioration, ulceration, and secondary infections (16). Radiation and chemotherapy, together or separately, can significantly damage oral and surrounding tissues (16).

Autoimmune Disorders (AD) are a group of disorders with variable clinical manifestations that exhibit self-reactive immune response (17). The etiology of autoimmune diseases includes genetic and environmental factors (18). Today, 100 autoimmune diseases have been identified (19). Some of these include those specific to certain organs, such as inflammatory bowel disease, autoimmune hepatitis, and Sjögren syndrome, or those that affect more than one organ, such as systemic lupus erythematosus, rheumatoid arthritis, and dermatomyositis (19). The long-term presence of chronic inflammatory disease causes immune system disorders and affects the levels of circulating inflammatory cytokines (20). Therefore, AP, which depends on the balance between microorganisms and host immunity, may be affected (21). In addition, immunosuppressive agents used to treat autoimmune diseases are associated with AP (22).

Periodontal and endodontic diseases are similar in terms of pathogenesis. Both diseases are generally chronic and have similar microbiota. The aim of treatment for both diseases is to control microbial factors, stop local chronic inflammation, and ensure tissue repair (6). Therefore, apical periodontitis may also be affected by the systemic conditions associated with periodontal disease. As observed in autoimmune diseases, impaired immune response may negatively affect pulp and periapical tissue repair (6). It has been reported that patients with periodontitis, a common gum disease, have a 2-5 times higher risk of developing any cancer than healthy individuals (9). Women with periodontitis are two to three times more likely to develop breast cancer than women without periodontitis (23). Previous studies have examined the relationship between periapical disease and autoimmune disease (22) or between periodontal disease and cancer (23). However, no studies have examined and compared the overall relationship between autoimmune diseases and periapical disease, cancer and periapical disease, and cancer and autoimmune disease.

The aim of this study was to evaluate the endodontic and periapical status of patients with cancer or autoimmune disease by comparing them with age- and sex-matched healthy patient groups. In addition, cancer and autoimmune disease groups were compared.

The null hypothesis was that there would be no association between cancer and autoimmune disease and endodontic/periapical status.

Materials and Methods

Ethical approval was obtained from The Ethics Committee of the University of Trakya. (Decision no : 05/30, Date: 18/03/2024). The study was conducted under the principles of the Declaration of Helsinki.

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist and statement were followed.

The medical and dental records of patients at the Trakya University Faculty of Dentistry Hospital who underwent a dental check-up and a panoramic radiography taken between 2020 and 2024 were reviewed.

Medical/dental records and radiographic data were anonymized electronically.

Case selection

Study group 1 (Autoimmune diseases): One hundred patients (male or female) who were at least 18 years old, diagnosed with an autoimmune disease, had no history of systemic diseases other than autoimmune disorders, and had digital panoramic radiography were in the experimental group. Patients diagnosed with autoimmune diseases and who had been using immunomodulatory drugs for at least 3 months were included in the study. The diseases and number of patients included in the current study were as follows: Rheumatoid arthritis, 39 patients; Multiple Sclerosis, 19 patients; Systemic Lupus Erythematosus, 18 patients; Sjögren syndrome, 10 patients; Myasthenia Gravis, 14 patients. A total of 100 healthy age- and sex-matched participants who reported no history of systemic diseases were selected to form the control group.

Study group 2 (Cancer): 100 patients (male or female) who were at least 18 years old, diagnosed with cancer, received at least 6 months of radiotherapy/chemotherapy, had no active cancer/treatment and no additional systemic disease, and had digital panoramic radiography. The diseases and number of patients included in the current study were as follows: Head and neck region cancers, 12 patients; breast cancer, 45 patients; lung cancer, 12 patients; lymphoma, 10 patients; leukemia, 13 patients; and colon cancer, 8 patients. 100 healthy age- and sex-matched participants who reported no history of systemic diseases were selected to form the control group. Only those who had not undergone dental examination before starting radiotherapy and had no dental follow-up after radiotherapy were selected.

Exclusion criteria

Patients with systemic diseases such as diabetes and hypertension were excluded from the study.

Patients receiving drug treatment for different diseases were excluded, and patients with poor or incomplete clinical documentation were excluded from the study.

Data collection

The patients' medical and dental histories were obtained from the records, including the patient's sociodemographic variables (age, gender). All patients were radiographically examined.

The following information was recorded:

- Systemic status of patients (cancer or autoimmune disease)
- Age
- Sex
- The number of teeth present
- Number and presence of Root Canal Filling Teeth (RCFT)
- Number and presence of teeth with AP
- Number and presence of RCFT with AP
- Number and presence of inadequate RCFT (iRCFT)
- Number and presence of iRCFT with AP

Radiographic Assesment

The panoramic radiographs were analyzed by an endodontist and an experienced dentist using a standard examination method to determine the periapical and endodontic status of the patients.The examiners were masked and blinded to whether the radiograph was a test or control group. As in previous similar studies (24,25), the 2 reviewers were calibrated according to the criteria established before their evaluation. All radiographs were analyzed simultaneously to ensure consensus in the interpretation of radiographic findings. In case of disagreement between observers, a 3rd experienced specialist endodontist was consulted.

All teeth were recorded (except for impacted teeth).

The radiographs were viewed by the same technician using the same device (Vatech PaX-i3D; South Korea) without changing the contrast and brightness.

Teeth were defined as RCFTs in the presence of radiopaque material in the root canals.

The quality of the RCFT was assessed according to the length and taper of the root filling (26). If all canals are filled without voids, if the root canal fillings are 0-2 mm shorter than the radiographic apex, and if there is a consistent taper from the orifice to the apex, RCFT is considered adequate. If any of the required criteria are missing, the root canal treatment is considered inadequate.

The periapical status was evaluated using the periapical index (PAI) according to previously defined criteria (27). Each tooth was assigned a PAI point based on visual references from the five categories on the scale. If the width of the periodontal ligament space was within normal limits and there was no break in the continuity of the lamina dura, PAI scores were defined as 1 and 2, whereas widening of the periodontal ligament and a break in the lamina dura and/or periapical tissues were defined as PAI 3 to 5. In multirooted teeth, the root with the highest score was used as reference.

Teeth with a PAI score > 2 were considered to have AP.

Statistical Analysis

The statistical analysis of the data was performed using IBM SPSS Statistics software. Pearson's chi-square test was used to compare categorical variables, and Mann–Whitney U statistical analyses were used to compare continuous variables between two groups because they were not normally distributed (Kolmogorov-Smirnov $p < 0.05$). The relationship between diseases and dental characteristics was evaluated using logistic regression analysis. $P < 0.05$ was considered statistically significant.

Results

The study included all patients with cancer and autoimmune diseases who met the inclusion and exclusion criteria.

There were 100 patients with autoimmune diseases included in our study, 33 men and 67 women, ranging in age from 17 to 78 years (mean ± SD: 49.45 ± 15.18 years), and 100 patients with cancer, 19 men and 81 wom-

en, ranging in age from 22 to 89 years (mean ± SD: 57.31 ± 12.07 years).

A total of 200 systemically healthy patients (52 males and 148 females) aged between 17 and 89 years were included.

The mean total number of teeth was 20.76 ± 7.57 in cancer patients, 19.89 ± 8.33 in the cancer control group, 22.63 ± 6.67 in autoimmune patients, and 22.97 ± 8.07 in the autoimmune control group.

The number and presence of RCFTs were significantly higher in the autoimmune disease group than in the control group (p = 0.001) (Table 1).

No significant differences were observed between the autoimmune disease and control groups in terms of teeth with AP periodontitis or other variables (p > 0.05) (Table 1) .

The results of the univariate logistic regression analysis showed a positive association between autoimmune disease and RCFTs (p = 0.001) (Table 2).

Each additional tooth with RCFT, patients had an increased risk of being in the autoimmune disease group (for number of RCFT OR, 4.125; 95% CI, 2.122 to 8.018; p = 0.001) (Table 2).

The number and presence of RCFTs and iRCFTs were significantly higher in the cancer group than in the control group (RCFTnumber&presence; p = 0.001, p = 0.001; iRCFTnumber; p = 0.03; iRCFTpresence; p = 0.018) (Table 3).

No significant differences were observed between the cancer group and control group in terms of teeth with AP periodontitis or other variables (p > 0.05) (Table 3) .

The results of the univariate logistic regression analysis re-

Table 1. The mean, standard deviation, and p values of the amount of removed dentin thickness in experimental groups (%)

	Control Group	AD	p
RCFT (Mean±SD (Min.-Max.)	1.39 ± 1.93 (0-13)	2.6 ± 2.19 (0-8)	0.001
RCFT (n, %)			
None	44 (44%)	16 (16%)	0.001
Any	56 (56%)	84 (84%)	
Teeth with AP (Mean ± SD (Min.-Max.)	0.71 ± 0.96 (0-4)	0.74 ± 0.91 (0-4)	0.619
Teeth with AP (n, %)			
None	55 (55%)	50 (50%)	0.479
Any	45 (45%)	50 (50%)	
RCFT+AP (Mean ± SD (Min.-Max.)	0.33 ± 0.65 (0-4)	0.39 ± 0.69 (0-3)	0.621
RCFT+AP (n, %)			
None	74 (74%)	72 (72%)	0.750
Any	26 (26%)	28 (28%)	
iRCFT (Mean ± SD (Min.-Max.)	0.55 ± 0.9 (0-4)	0.7 ± 1.11 (0-4)	0.464
iRCFT (n, %)			
None	66 (66%)	62 (62%)	0.556
Any	34 (34%)	38 (38%)	
iRCFT+AP (Mean ± SD (Min.-Max.)	0.4 ± 0.72 (0-4)	0.42 ± 0.65 (0-3)	0.587
iRCFT+AP (n, %)			
None	70 (70%)	66 (66%)	0.544
Any	30 (30%)	34 (34%)	

Pearson Chi-Square, Mann Whitney U. (AD: Autoimmune Disease; RCFT: Root Canal Filling Teeth; AP: Apical Periodontitis; iRFCT: inadequate Root Canal Filling Teeth).

Table 2. Association of endodontic and periapical conditions with independent variables: a univariate logistic regression analysis

Groups	Variable	p	ODDS RATIO (95% C.I.)
Cancer	RCFT	0.001	6.143 (3.089 - 12.217)
Autoimmune Disease	RCFT	0.001	4.125 (2.122 - 8.018)
Cancer	iRCFT	0.018	2.04 (1.127 - 3.69)

(RCFT: Root Canal Filling Teeth; iRFCT: inadequate Root Canal Filling Teeth)

Table 3. Comparison of endodontic and periapical conditions between the cancer and control groups

	Control Group	Cancer	p
RCFT (Mean ± SD (Min.-Max.)	1.33 ± 2.05 (0-11)	2.6 ± 2.4 (0-11)	0.001
RCFT (n, %)			
None	50 (50%)	14 (14%)	0.001
Any	50 (50%)	86 (86%)	
Teeth with AP (Mean ± SD (Min.-Max.)	0.83 ± 1.07 (0-4)	0.9 ± 1.07 (0-4)	0.522
Teeth with AP (n, %)			
None	51 (51%)	45 (45%)	0.396
Any	49 (49%)	55 (55%)	
RCFT+AP (Mean ± SD (Min.-Max.)	0.33 ± 0.64 (0-3)	0.54 ± 0.83 (0-4)	0.056
RCFT+AP (n, %)			
None	75 (75%)	63 (63%)	0.067
Any	25 (25%)	37 (37%)	
iRCFT (Mean ± SD (Min.-Max.)	0.47 ± 0.95 (0-5)	0.7 ± 1.07 (0-5)	0.03
iRCFT (n, %)			
None	73 (73%)	57 (57%)	0.018
Any	27 (27%)	43 (43%)	
iRCFT+AP (Mean ± SD (Min.-Max.)	0.47 ± 0.8 (0-3)	0.49 ± 0.73 (0-3)	0.565
iRCFT+AP (n, %)			
None	68 (68%)	63 (63%)	0.457
Any	32 (32%)	37 (37%)	

Pearson Chi-Square, Mann Whitney U.(RCFT): Root Canal Filling Teeth; AP: Apical Periodontitis; iRFCT: inadequate Root Canal Filling Teeth).

vealed a positive association between cancer and the values of RCFTs and iRCFTs (Table 2).

Each additional tooth with the values of RCFT and iRCFT was associated with an increased risk of being in the cancer group (for values of RCFT OR, 6.143; 95% CI, 3.089 to 12.217; p = 0.001; For values of iRCFT OR, 2.040; 95% CI, 1.127 to 3.69; p = 0,018 (Table 2).

There were no differences in endodontic and periapical conditions between the autoimmune disease and cancer group without age and gender matching (p > 0.05).

Discussion

This study investigated the apical periodontitis/endodontic status in patients with autoimmune diseases or cancer and healthy controls. Participants in the control group were matched by sex and age to reduce potential risk factors. Also, autoimmune diseases and cancer were compared in terms of endodontic status and apical periodontitis.

According to the current study, the number and presence of RCFT were significantly higher in the autoimmune disease group than in the control group, whereas the number and presence of RCFT and iRCFT were significantly higher in the cancer group than in the control group. No association was found between AP and cancer or autoimmune disease.

The pathogenesis, progression, and resolution of AP depend on the host immune response and the balance of proinflammatory and proresolution mediators (28). AP may develop due to primary infection in teeth with necrotic pulp or infection in teeth with inadequately treated root canal fillings. The risk of systemic infection spread after root canal treatment increases in patients with immune system suppress (29).

Cancer or cancer treatment may affect the immune response by suppressing the immune system (30). Radiotherapy can cause structural changes in dentin by generating free radicals and can also cause microbial changes (31). It can also change the pH by xerostomia, causing the growth of cariogenic bacteria (31). A study on oral changes in patients with cancer reported that the salivary microbiological profile and salivary pH differed between the cancer and healthy groups (32). The prevalence of dental caries increases with xerostomia and changes in the oral flora of patients undergoing radiation to the head and neck region (33). Because of the aggressive progression of tooth decay, bacteria can reach the pulp, leading to AP (34). According to the results of this study, the AP rate in patients with cancer was similar to that in the control group. Hommez et al. (35) reported that the incidence of AP after head and neck radiotherapy was similar between the groups. However, in a previous study examining the relationship between the dose received after head

and neck radiotherapy and AP, the incidence of AP increased significantly as the dose increased (34). In this study, the similarity in AP rates between the cancer and control groups can be explained by the limited number of patients who received head and neck radiotherapy and the unknown amount of dose received.

The risk of oral side effects is higher among patients receiving chemotherapy (36). The ideal situation is to complete the necessary dental treatment before starting chemotherapy (37). However, this is not always possible because of time constraints, patient's medical condition, and the urgency to start chemotherapy (37). Because the current study evaluated only patients who were at least 6 months post-cancer treatment, dental treatments before or during the illness were unknown. Treatment preferences at dental visits before the patients' cancer history may have influenced the current results.

According to the results, the RCFT and iRCFT rates increased in patients with cancer. As patients undergoing cancer treatment suffer from depressive symptoms, their self-care, including oral hygiene habits, is negatively affected, which can result in caries, periodontal disease, and tooth loss (38). The physical and mental fatigue they experienced during the disease process and their inadequate attention to dental care may explain this result (39).

In this study, 55% of 100 patients with cancer (55 patients) had at least one tooth with AP. These results are consistent with those reported in epidemiological studies (40). According to the results of the study, AP rates were similar between the cancer and control groups. Ding et al. (41) found that breast cancer had no effect on AP. Conversely, another study showed that the number of apical lesions was higher among patients with cancer (42). The reason for the different results may be that the study included patients undergoing active cancer treatment and that the diagnosis of AP was evaluated by clinical examination of the patients in addition to radiographic examination.

Although RCFT and iRCFT values were significantly higher in the cancer group than in the control group, the reason for the similarity of AP may be that dentists make more radical decisions in patients with a history of cancer. Dentists may be inclined to extract teeth with lesions after root canal treatment (43). This condition may occur frequently in patients with cancer in whom the inflammatory response may change.

Apical periodontitis and autoimmune diseases have similar pathological features. Chronic inflammation is common in autoimmune diseases and apical periodontitis and is characterized by the destruction of connective tissue and bone (44).

According to the results, the number and presence of RCFTs were significantly higher in the autoimmune disease group than in the control group. However, no association was found between autoimmune diseases and the AP rate.

Similar to our results, another study reported that patients with Rheumatoid Arthritis (RA) tend to develop AP (45). Previously, Jalali et al. (44) reported no statistically significant difference between RA and control patients in their retrospective study comparing RA patients and controls in terms of the prevalence of periapical rarefying osteitis. In contrast, another cross-sectional study suggested that individuals with RD have at least twice the risk of AP compared with controls (24). In another study, the incidence of AP was significantly higher in patients with autoimmune diseases than in controls (46). Variations in study type and sample size may explain the differences between the studies. Furthermore, these differences between the included studies may be attributed to methodological differences, especially in the diagnosis of AP. In this study, AP was defined only by radiographic examination. Because radiographic changes in cancellous bone are not detected until bone loss reaches the cortical plate, radiographic examination alone may not be sufficient for evaluation, and the results may have been affected by this situation. It is suggested that immunosuppressive agents weaken resistance by decreasing the number of leukocytes and increase the risk of opportunistic oral infections and AP (47). The different findings may be related to the dose and duration of the immunosuppressive agents used and the virulence of the bacteria (48).

Inflammatory and immunological responses are affected by genetic factors and can be explained by the fact that individuals may respond differently to environmental stimuli (46). Genetic polymorphisms may play a role in the etiology of complex diseases (49) .

Cotti et al. (50) showed that existing apical periodontitis healed more rapidly in patients receiving biologics compared with those in the control group, suggesting that treatment that modulates the immune response may affect the healing of apical periodontitis after endodontic treatment. Immunomodulatory therapy and altered immune response in patients with autoimmune disorders may affect the prevalence and prognosis of apical periodontitis after endodontic treatment (51).

Limitations

The current study is a retrospective study that examined patient records. It is difficult to distinguish whether the results are due to the disease, treatment processes, the medication used, or all of them. In addition, since differ-

ent diseases are examined, the diseases studied may show heterogeneity under common immune pathogenesis, and this can affect the endodontic and apical status to different degrees.

The presence of undiagnosed systemic diseases that can affect dental health may have affected the results. Prospective controlled clinical studies are needed because confounding factors cannot be controlled.

Because this was a retrospective study, the time since completion of endodontic treatment could not be assessed. In this cross-sectional study, Whether the lesions were active or healing, and the quality of the coronal restoration was not examined. The quality of the coronal restoration may have affected the outcome of the root canal treatment and therefore the present results.

The presence of periapical lesions and quality of the root canal treatment were evaluated using panoramic radiography. Untreated canals may be missed on panoramic radiographs, or the quality of the canal filling may not be evaluated well due to distortions. During the early stages of AP, changes may not be visible on radiography. Panoramic radiography may cause an underestimation of the lesion because radiographic changes in the cancellous bone are not detected until bone loss reaches the cortical plate (52). Therefore, some teeth with AP in the current study may not have been diagnosed. Additionally, anatomical noise masking of the region of interest to varying degrees on panoramic radiographs may negatively affect the assessment of AP and the quality of the root canal filling. Full mouth periapical radiography and cone beam computed tomography are recommended for root canal and apical status evaluation in subsequent studies.

Conclusion

The results showed that AP was similar between the cancer and autoimmune disease and control groups. Since the current study used a cross-sectional design, the generalizability of the findings is limited. The results of this study require larger prospective studies. Clinically, we recommend that patients with a history of cancer and cancer treatment or autoimmune disease should be considered high-risk patients and should be included in a strict dentist recall system.

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