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ASSOCIATION BETWEEN THE PRESENCE OF ODONTOGENIC INFLAMMATORY CYSTS AND SYSTEMIC IMMUNE RESPONSE BEFORE AND AFTER THEIR SURGICAL THERAPY

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Abstract

Odontogenic inflammatory cysts are pathological lesions that are often present in clinical practice and they represent potential focal points with an impact on other organs and systems in the body.

The aim of the study is to determine the association between the presence of odontogenic inflammatory cysts and the systemic immune response.

63 patients diagnosed with odontogenic inflammatory cysts were included in the study and divided into three groups (Group 1-patients with radicular cysts-23, Group 2-patients with residual cysts-20 and Group 3-patients with periodontal cysts-20). Values of IgA, IgM and IgG in serum were examined before and one month after the surgical therapy in the device Cobas 6000 model c501 (Roche, Germany).

In all three investigated parameters of humoral immunity (IgA, IgG and IgM in serum), in patients IgA and IgG values before and one month after the intervention in the three groups of patients did not indicate a significant difference for a consequent (p=0.4352 vs p=0.4090), (p=0.1489 vs. p=0.2456). The comparison of the three groups of patients regarding the level of IgM in serum indicated a significantly higher value of this parameter in patients before the intervention (p=0.0006) as well as one month after the intervention (p=0.0120) and significant difference in periodontal compared to residual cysts (p=0.0061)

Surgical intervention of odontogenic inflammatory cysts (cistaectomio in toto) affected the values of systemic immunoglobulins, especially the differences in IgM levels. These findings suggest that IgA, IgG, and IgM may play an important role in the occurrence, development, and persistence of cystic lesions

Keywords: Odontogenic inflammatory cysts, immunological analysis, systemic immune response, immunoglobulins IgA IgG and IgM

Introduction

Odontogenic inflammatory cysts are pathological lesions that are often represented in clinical practice and they can end up with complications due to their untimely set up diagnosis or their untimely or inadequate therapy. Odontogenic cysts can be also potential focal points with an impact on other organs and systems in the human body. The actuality of the study of these pathological lesions is emphasized, which is increasing due to the search for answers to numerous controversies and enigmas that follow the complex and insufficiently clarified etiopathogenetic changes that occur during their formation, growth and their persistence in the oral cavity.

It is explained that cysts are usually the result of more complex pathogenetic mechanisms in which the influence of the pathogenetic effect of the causative agent and the reduced immune defense locally in the tissue, but also more widely in the body[1].

Despite numerous disagreements among authors regarding the mechanism of cyst growth, there are like-minded scientists who believe that the epithelium for odontogenic inflammatory cysts originates from the remains of Hertwing's membrane found in the periodontium of the teeth, and is a consequence of its complete disintegration [2].

These collections of epithelium are called epithelial islands of Malaise and they are in a state of rest until some stimulus acts on them. Under the influence of bacteria and their products or under the influence of some other factors (mechanical, chemical and antigens), the metabolic activity of these cells changes and their proliferation begins. [3]

It follows from this that the basic precondition for the appearance of inflammatory cysts is the previous presence of an epithelium at the site of cyst development and an inflammatory stimulus. [4]

Of exceptional importance is the characteristics of odontogenic inflammatory cysts to persist for a long time, even several years without any symptoms, without clinical manifestations as a result of the established balance between the human immune defense reactions and the agents that are present at the cystic lesion [5].

In recent years, immunopathological reactions have been considered to play a dominant role in the pathogenesis of cysts. Piatelli et al. [6] consider that the appearance and development of inflammatory cysts is conditioned by immune reactions. In a narrower sense, immune mechanisms are based on the action of non-specific and specific immunity through the activity of the humoral and cellular immune response. Seen from that aspect, there are numerous theories that arise from many researches whose problems are precisely related to the immunological interactions in the periodontal tissue complex [7].

Modern knowledge about the nature of immune reactions is great, but it is still not possible to define their principles in full.

The body can respond to the stimulus from foreign antigens by creating specific antibodies (systemic-humoral immune response) or by activating sensitized T lymphocytes (cellular immune response) [8].

The systemic- humoral immune response is mediated by antibodies, which are the final product of plasma cells, and represent the final form in the differentiation of B-lymphocytes. When soluble antigens enter the lymphatic system (usually through the lymph nodes) they are recognized by antigen presenting cells such as macrophages and dendritic cells. Antigens are presented in complex with HLA Class-II molecules on T lymphocytes that contain CD4 receptors known as 'helper cells'. Activated helper cells secrete cytokines such as interleukin IL-4 which stimulates B lymphocytes to differentiate into plasma cells and memory B cells. Plasma cells initially produce IgM antibodies. Interaction with other receptors presented on B lymphocytes with T lymphocytes and their receptors induces the production of IgG antibodies. The strength of the immune response is regulated by T helper and T suppressor lymphocytes (T lymphocytes that have CD8 receptors). Helper cells increase the immune response, and suppressor cells stop the immune response or regurgitate antibody production. Odontogenic inflammatory cysts are characterized by great diversity, which results in the different morphological characteristics between them.

According to certain scientific data, it is considered that immunopathological reactions play a dominant role in the pathogenesis of cysts. In a narrower sense, immune mechanisms are based on the action of non-specific and specific immunity through the activity of the humoral and cellular immune response.

The importance of immune mechanisms and their activation under the influence of stimuli from foreign antigens is indicated, during which the body can respond by creating specific antibodies (systemic-humoral immune response) or by activating sensitized T lymphocytes (cellular immune response).

According to the latest revision of the World Health Organization (WHO) Classification of odontogenic inflammatory cysts from 2017 [9] odontogenic cysts are divided into two large groups:

- Radicular (apical, residual, periodontal-lateral cysts) and
- Collateral inflammatory cysts.

Inflammatory origin of the most common cysts in the jaws (radicular cysts) is associated with the presence of avital tooth, the residual cysts are usually left in the jaws after the extraction of the affected teeth and the periodontal radicular cysts are usually associated with the lateral root canal of the affected teeth.

The etiopathogenesis of these pathological lesions is still completely unknown. It is considered that it is through immunohistochemical analyzes using immunohistochemical markers that a more uniform approach to establishing the diagnosis is possible and they are indicators in the prognosis of the pathology of odontogenic inflammatory cysts. Regardless of which group they belong to, odontogenic inflammatory cysts are insufficiently investigated from an etiopathogenetic point of view.

Aim

The aim of this study is to determine the association between the presence of the local cystic lesion and the systemic immune response of the body by verifying the changes of the levels of immunoglobulins in the serum of patients before and one month after surgical therapy.

Materials and methods

In order to realize the set goal, research was done at the Dental Clinical Center St. Panteleimon - Oral Surgery Clinic, Institute of Pathological Anatomy and PHI University Institute of Clinical Biochemistry-Skopje

In this study, 63 systemically healthy patients (male and female) aged from18 to 65 years with a clinically established diagnosis of radicular inflammatory cysts were included.

The studied group of 63 patients with a diagnosis of odontogenic inflammatory radicular cysts was divided into three groups:

- Group 1-patients with presence of radicular cysts
- Group 2-patients in whom residual cysts were found
- Group 3-patients in whom periodontal cysts were detected

Clinical and paraclinical examinations were performed individually for all patients.

Inclusion criteria in the studied group is the presence of a radicular inflammatory cyst in the jaws (radicular, residual or periodontal), patients of both sexes (m/f). Patients in good health, without acute diseases (ASA I classification) who are conscientious and understand the significance of the intervention and who may respond to subsequent control studies.

Exclusion criteria for the members of the study group were patients with a diagnosis of odontogenic inflammatory cysts who were not on anti-inflammatory and antibiotic therapy 4-6 weeks before the surgical intervention, patients with cardiovascular diseases, liver disorders, malignancies, patients on bisphosphonate therapy, chemotherapy, pregnant women and lactating women.

The obtained values of the studied group were compared before and one month after therapy from an immunological point of view. Participants from both groups signed an Informed Consent before the start of the trial.

The research was approved by the Ethics Commission of the Faculty of Dentistry with number 02-3152/3 on 23.12.2021.

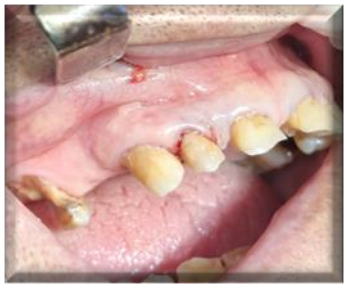
Detailed anamnesis from the patients, clinical examination and paraclinical examinations were used as work methods during the research. Based on these procedures, a diagnosis was made, surgical therapy was applied, and statistical processing was performed on the data obtained from the examination.

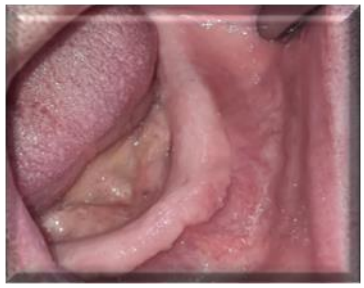
Medical history data obtained personally from patients included general, main complaints and personal history of current and past illnesses including allergies and also family history.

The clinical examination included extraoral status, intraoral status and dental status. (Figures 1, 2, 3).

With extraoral status we saw the extraoral changes, while intraoral status included the changes intraorally. With dental status, a review was made regarding the restoration of the dentition.

The detailed examination was performed by inspection and palpation, percussion (horizontal and vertical), and the vitality of the affected teeth was determined. We also perceive the presence or absence of the Dipitren`s sign which is the pathognomy sign of the presence of inflammatory odontogenic cyst.





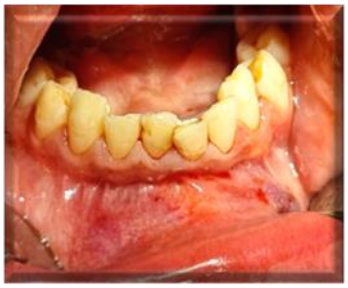


Figure 1. Clinical examination of radicular cys;t **Figure 2.** Clinical examination of residual cyst; **Figure 3** Clinical examination and periodontal cyst.

The following examinations were included in the paraclinical investigations of the studied group: radiological, histopathological and immunological. Based on the clinical symptoms and the radiographic finding, a preliminary diagnosis was made, the clinical diagnosis is made during the operative treatment, while the definitive diagnosis is always based on a histopathological finding which is necessary. Surgical intervention was performed at the Oral Surgery Clinic. The surgical procedure began with disinfection of the operative field with a 1% solution of Betadine (providon-iodine), and then the application of anesthesia with mepivacaine (Scandonest3%) to anesthetize the operative field.

The operative procedure began with an incision and formation of a mucoperiosteal flap in order to obtain a visual control of the operative field. The mucoperiosteal flap was raised in full thickness with a raspatorium, osteotomized in order to expose the cystic sacus. Enucleation of the cysts was done in toto-Cistaectomio (Partch II) (Figure 4). If the tooth was preserved in the oral cavity, it was apicotomized through resection of the root of the tooth during surgical-endodontic therapy procedures with the application of orthograde filling or with the use of retrograde filling in order to ensure retrograde (apical) hermetic canal obturation. When the affected tooth or teeth had a bad prognosis, they were extracted. The postoperative control consisted of a first control examination which was the next day, and then 7 days after the surgical intervention. The material taken from the pathological lesion (Figure 5) was applied in a sterile syringe filled with physiological solution at the Oral Surgery Clinic and it was transported and analyzed at the Institute of Pathological Anatomy (Figure 6) for establishing the definitive diagnose.

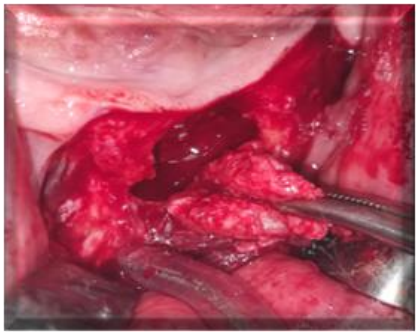


Figure 4. Enucleation of cyst in toto-Partch II

Figure 5. Odontogenic inflammatory cyst

Figure 6. Material taken for histopathological analysis

The immune status was examined in all patients and it was registered as a quantitative and qualitative measure of systemic-humoral immunity in the blood. Venous blood samples (9 ml) were taken at the Clinic for Clinical Biochemistry by the Vacutainer venipuncture method (Figure 7), before surgical therapy and one month after and the presence of the humoral immune response was monitored by determining the values of immunoglobulins in serum.

Figure 7. Taking venous blood for immunological examination

Immunoglobulins in serum were determined in the device Cobas 6000 model c501 (Roche, Germany) (Figure 8), which is a biochemical analyzer of spectrophotometric, immunoturbidimetric and ion selective method of determining the concentrations of biochemical analytes, in our case it is blood [11, 12,13].

Figure 8. Apparatus Cobas 6000 model c501 (Roche, Germany)

Standard values for IgA according to CRM 470 Protein Standardization=0.7 4 g/L 4.38 25.0 µmol/L 70 400 mg/dL

Standard values for IgG according to CRM 470 Protein Standardization-7-16 g/L 46.7-107 µmol/L 700-1600 mg/dL

Standard values for IgM according to CRM 470 Protein Standardization-0,4-2.3 g/L 0.4-2.4 µmol/L 40-230 mg/dL

Serum immunoglobulin values were evaluated before surgical treatment of the cyst and one month after it when complete clinical healing of the wound occurred in the absence of postoperative complications or early recurrences.

Results

The research was a prospective monocentric randomized clinical study that was performed in the period 2021/2023 at the Dental Clinical Center "St. Pantelejmon "-Clinic for Oral Surgery - Skopje in collaboration with the Institute of Pathological Anatomy at the Faculty of Medicine in Skopje and PHI University Institute for Clinical Biochemistry - Skopje.

According to the set criteria for participation in the study, 63 patients with a diagnosis of odontogenic inflammatory cyst were selected. In addition, based on the type of inflammatory cyst, patients were divided into three groups: a) Group 1 – radicular cysts; b) Group 2 - residual cysts; and c) Group 3 - periodontal cysts. All patients in the research were monitored pre and post-operatively in relation to selected clinical and paraclinical immunological investigations. In this part of the analysis, a comparison was made between the three groups of odontogenic inflammatory cysts (radicular, residual, periodontal) in relation to each of the analyzed B lymphocytes IgA, IgG and IgM in serum. The intergroup comparison was made for two times, before and one month after the surgical intervention.

Ig A - intergroup comparison at two times Among the three types of inflammatory odontogenic cysts (radicular, residual, and periodontal) a comparison was made regarding B lymphocyte IgA in serum at two times, before and one month after the surgical intervention (Table 1).

Table 1. Intergroup comparison of odontogenic cysts according to B lymphocytes IgA in serum at two times

Types of Odontogenic cysts	IgA in serum						[1]p
	N	Mean±SD	Min/ Max	Percentiles			
				25th	50th (Median)	75th	
IgA (g/L) – before surgical therapy							
Radicular	23	2,18±0,88	0,8/4,2	1,7	2,1	2,6	X^2=1,664; df=2; p=0,4352
Residual	20	2,29±1,17	0,7/5,4	1,6	2	3,1	
Periodontal	20	1,93±1,00	0,6/3,8	1,1	1,7	2,6	
IgA (g/L) – after surgical therapy							
Radicular	23	2,01±0,86	0,6/4,1	1,6	2,0	2,4	X^2=1,788; df=2; p=0,4090
Residual	20	1,10±0,59	0,3/5,0	0,9	0,9	1,3	
Periodontal	20	1,73±0,90	0,5/3,2	0,9	1,5	2,6	
[1]Kruskal-Wallis H test			*significant for p<0,05				

Intergroup comparison of the three types of odontogenic cysts in terms of B lymphocyte IgA in serum (Table 1) indicated that

IgA (g/L) – before surgery: IgA in serum before intervention had a mean value of 2.18±0.88 g/L in radicular cysts, 2.29±1.17 g/L in residual cysts, and 1, 93±1.00 g/L in periodontal lateral cysts. In 50% of subjects before surgery, IgA was <2.1 g/L in radicular cysts, <2 g/L in residual cysts, and <1.7 g/L in periodontal lateral cysts. For p<0.05, there was no significant difference between the three types of odontogenic cysts regarding the level of IgA in serum before surgery (Kruskal Wallis test: X2(df=2, N=63) =1.664; p=0.4352) (Table 1).

IgA (g/L) – after surgery: IgA in serum after intervention had a mean value of 2.01±0.86 g/L in radicular cysts, 1.10±0.59 g/L in residual cysts and 1.73 ±0.90 g/L in periodontal lateral cysts. In 50% of subjects before surgery, IgA was <2 g/L in radicular cysts, <0.9 g/L in residual cysts, and <1.5 g/L in periodontal lateral cysts. For p>0.05, we did not determine a significant difference between the three types of odontogenic cysts regarding the level of IgA in serum after surgery (Kruskal Wallis test: X2(df=2, N=63) =1.788; p=0, 4090) (Table 1).

Additionally, for p>0.05, intergroup analysis indicated that before surgery, serum IgA level was non-significantly lowest in periodontal lateral cysts, followed by radicular cysts, that is, it was non-significantly highest in residual cysts. After surgery, for p<0.05, serum IgA level was non-significantly lowest in residual cysts, followed by periodontal lateral cysts, i.e. it was non-significantly highest in radicular cysts (Table 1)

IgG - intergroup comparison at two time points

The three types of odontogenic cysts (radicular, residual, and periodontal) were compared in terms of B lymphocyte IgG in serum, at two times, before and one month after the surgical intervention (Table 2).

Table 2. Intergroup comparison of odontogenic cysts according to B lymphocytes IgG in serum

Types of odontogenic cysts	IgG in serum						[1]p
	N	Mean±SD	Min/ Max	Percentiles			
				25th	50th (Median)	75th	
IgG (g/L) – before surgical therapy							
Radicular	23	11,86±2,49	7,6/17	9,9	11,4	13,8	X^2=3,808; df=2; p=0,1489
Residual	20	13,21±2,40	10,2/19,2	11,7	12,8	13,7	
Periodontal	20	12,57±2,07	10,2/17	11,1	11,8	13,2	
IgG (g/L) – after surgical therapy							
Radicular	23	11,50±2,38	7,3/16	9,8	11,2	13,6	X^2=2,808; df=2; p=0,2456
Residual	20	12,67±2,25	9,9/18,4	11,0	12,3	13,3	
Periodontal	20	12,05±1,93	9,1/15,9	10,9	11,1	12,8	

[1]Kruskal-Wallis H test *significant for p<0,05

Intergroup comparison of the three types of odontogenic cysts in terms of B lymphocyte IgG in serum (Table 2) indicated that:

IgG (g/L) – before surgery: preoperative serum IgG had a mean value of 11.86±2.49 g/L in radicular cysts, 13.21±2.40 g/L in residual cysts, and 12, 57±2.07 g/L in periodontal lateral cysts. In 50% of subjects before surgery, IgG was <11.4 g/L in radicular cysts, <12.8 g/L in residual cysts, and <11.8 g/L in periodontal lateral cysts. For p<0.05, there was no significant difference between the three types of odontogenic cysts regarding the level of IgG in serum before surgery (Kruskal Wallis test: X2(df=2, N=63) =3.808; p=0.1489) (Table 2)

IgG (g/L) – after surgery: serum IgG after the intervention had a mean value of 11.50±2.38 g/L in radicular cysts, 12.67±2.25 g/L in residual cysts, and 12, 05±1.93g/L in periodontal lateral cysts. In 50% of subjects before surgery, IgG was <11.2 g/L in radicular cysts, <12.3 g/L in residual cysts, and <11.1 g/L in periodontal lateral cysts. For p<0.05, there was no significant difference between the three types of inflammatory odontogenic cysts in terms of serum IgG levels after surgery (Kruskal Wallis test: X2(df=2, N=63) =2.808; p=0, 2456) (Table 2)

Intergroup analysis, additionally for p>0.05, also indicated that before surgery, the level of IgG in serum was non-significantly lowest in radicular cysts, followed by periodontal lateral cysts, it was non-

significantly highest in residual cysts. After surgery, for p<0.05, the level of IgG in serum was non-significantly lowest in radicular cysts, followed by periodontal lateral cysts, that is, it was non-significantly highest in residual cysts (Table 2)

IgM - an intergroup comparison at two time points

Within the framework of the research, in the three types of odontogenic cysts (radicular, residual, and periodontal), a comparison was made regarding B lymphocyte IgM in serum, at two times, before and 1 month after the surgical intervention (Table 3).

Table 3. Intergroup comparison of odontogenic cysts according to B lymphocytes IgM in serum

Types of odontogenic cysts	IgM in serum						[1]p
	N	Mean±SD	Min/ Max	Percentiles			
				25th	50th (Median)	75th	
IgM (g/L) – before surgical therapy							
Radicular	23	1,11±0,55	0,4/2,7	0,8	0,9	1,3	X^2=14,754; df=2; p=0,0006*
Residual	20	0,93±0,73	0,1/2,6	0,4	0,8	0,9	
Periodontal	20	1,56±0,49	0,8/2,5	1,1	1,6	1,9	
IgM (g/L) – after surgical therapy							
Radicular	23	1,09±0,58	0,3/2,5	0,7	0,8	1,3	X^2=8,850; df=2; p=0,0120*
Residual	20	0,89±0,69	0,1/2,5	0,4	0,7	0,9	
Periodontal	20	1,35±0,52	0,7/2,1	0,9	1,3	1,9	

[1]Kruskal-Wallis H test *significant for p<0,05

Intergroup comparison of the three types of odontogenic cysts in terms of B lymphocyte IgM in serum indicated that (Table 3):

IgM (g/L) – before surgery: IgM in serum before surgery had a mean value of 1.11±0.55 g/L in radicular cysts, 0.93±0.73 g/L in residual cysts, and 1, 56±0.49 g/L in periodontal lateral cysts. In 50% of subjects before surgery, IgM was <0.9 g/L in radicular cysts, <0.8 g/L in residual cysts, and <1.6 g/L in periodontal lateral cysts. For p<0.05, a significant difference was determined between the three types of odontogenic cysts regarding the level of IgM in serum before surgery (Kruskal Wallis test: X2(df=2, N=63) =14.754; p=0, 0006) (Table 3)

In addition, an analysis was made to see what is due to the established significance between the groups of odontogenic cysts in relation to the level of IgM in serum before the intervention. It was observed that:

• for p<0.05, before the intervention, a significantly higher level of IgM in serum was determined in periodontal lateral cysts compared to radicular cysts (Mann-Whitney U Test: Z=-2.885; p=0.0039);

• for p<0.05, before the intervention, a significantly higher level of IgM in serum was determined in periodontal lateral cysts compared to residual cysts (Mann-Whitney U Test: Z=-3.368; p=0.0007);

• for p>0.05, before the intervention, there was no significant difference between radicular and residual cysts regarding the level of IgM in serum (Mann-Whitney U Test: Z=1.717; p=0.0861);

IgM (g/L) – after surgery: IgM in serum after surgery had a mean value of 1.09±0.58 g/L in radicular cysts, 0.89±0.69 g/L in residual cysts, and 1, 35±0.52g/L in periodontal lateral cysts. In 50% of

subjects after surgery, IgM was <0.8 g/L in radicular cysts, <0.7 g/L in residual cysts, and <1.3 g/L in periodontal lateral cysts.

For p<0.05, a significant difference was determined between the three types of odontogenic cysts regarding the level of IgM in serum after surgery (Kruskal Wallis test: X2(df=2, N=63) =8.850; p=o,0120 (Table 3)

Additional analysis to understand the reason for the established significance between the three types of odontogenic cysts in relation to serum IgM levels after the intervention indicated that:

• for p>0.05, after the intervention, there was no significant difference between radicular and periodontal lateral cysts regarding the level of IgM in serum (Mann-Whitney U Test: Z=-1.814; p=0.0697) - the level of IgM after intervention it was insignificantly higher in periodontal lateral cysts.

• for p<0.05, after the intervention, a significantly higher level of IgM in serum was determined in periodontal lateral cysts compared to residual cysts (Mann-Whitney U Test: Z=-2.745; p=0.0061);

• for p>0.05, after the intervention, there was no significant difference between radicular and residual cysts regarding the level of IgM in serum (Mann-Whitney U Test: Z=1.631; p=0.1028); =0, 0120) (Table 3)

Discussion

Pathological lesions with unknown etiopathogenesis, which include odontogenic inflammatory cysts, are a special challenge for study. Several professional and scientific publications have been published in the literature that confirm the association of these diseases with the histopathological findings, and more recently the immunohistochemical and immunological analyzes carried out on the cystic lesions, which emphasize the disturbed immune response, connecting these lesions with changes in humoral and cellular immunity.

S. Anil et al. [14] in their study of 45 patients with periapical lesions, 24 of which with periapical granulomas and 21 patients with radicular cysts using the Polyethylene glycol precipitating method of detection, determined an increase in the values of circulating immune complexes (CIC) present in the serum of patients compared to the control group of patients. Their results indicate that the higher the CIC values, the more likely they are to cause systemic changes in immunity in certain individuals with periapical cysts. In them, it is necessary to eliminate the source of antigen in order to prevent the occurrence of systemic complications.

Juliana R.B et at. [15] in their paper discussed the different subpopulations of T lymphocytes, CD4 and CD8+ T lymphocytes, macrophages, plasma cells, eosinophils, different types of cytokines (interleukin [IL]-1, IL-3, IL-6, IL-8 , IL-10, IL-12, IL-17, interferon (IFN)-g, tumor necrosis factor [TNF]-a, transforming growth factor [TGF]-ß, and granulocyte-macrophage colony-stimulating factor) present in the radicular cysts and periapical granulomas and by proving their presence in the inflammatory infiltrate they emphasized the role of the cellular immune response in the modulation of the inflammatory process and bone resorption.

From a pathogenetic point of view, in odontogenic inflammatory cysts there is inflammation, but in the broader sense of the word, as well as because the inflammatory process represents a complex neuro-reflex and neuro-humoral general and local reaction of the body in response to external and internal agents, patients with the presence of odontogenic inflammatory cysts, we should not perceive them only as patients with diseased teeth with cysts present, but as patients whose organism is affected in its entirety.

There is new evidence in the literature that the authors Sadia Ambreen Niazi and Abdulaziz Bakhsh [16] confirm in their study, which refers to how the presence of periapical lesions can modify the systemic levels of inflammatory markers (for example, C-reactive protein high-sensitivity (hs-CRP), interleukin-1β (IL-1β), IL-6, IL-12, IL-10, tumor necrosis factor (TNF-α), matrix metalloproteinases (MMP-8 and MMP-9) , soluble vascular cell adhesion molecule 1 (sVCAM-1), endothelial leukocyte adhesion molecule (E-selectin) and intercellular adhesion molecule (ICAM)), asymmetric dimethylarginine (ADMA) levels,

complement-C3) and immunoglobulins IgA , IgM, IgG in patients. This is significant to highlight the potential negative impact of asymptomatic periapical lesions on the systemic immune response of the body.

Similar results were reached much later by Browne et al. [17] who in their study examined the influence of odontogenic cysts on the humoral immune response and presented the highest values of immunoglobulins in the serum in patients with the presence of radicular cysts (IgA- 488.9 mg/100ml, IgG – 2535.4 mg/100 ml, IgM – 135.6 mg/100 ml), unlike follicular (IgA -2308.4 mg/100 ml, IgG – 1618.2 mg/100 ml, IgM – 155.6 mg/100 ml) and especially odontogenic keratocysts (IgA – 135.6 mg/100 ml, IgG – 491.9 mg/100 ml, IgM – 54.1 mg/100 ml).

The systemic (humoral) immune response in our research was analyzed by determining the values of IgA, IgG and IgM in serum at two times, before and one month after the surgical intervention.

The analysis individually included each of the three groups of patients with different types of cysts such as radicular, residual and periodontal-lateral, and a significant difference was obtained in the values of immunoglobulins in all three groups in both measurements. In the group of radicular cysts (n=23) IgA was significantly elevated by (p=0.0001) before and after surgery, also IgG had a significant difference by (p=0.00004) and IgM a significant difference by (p= 0.0093). In the second group of residual cysts n=20, there was a significantly higher level of IgA in serum before the intervention compared to 1 month after it for (p=0.0005), that is for IgG (p=0.00004) and for IgM for (p=0.0004). In the third group of periodontal lateral cysts, the analysis showed a significantly higher level of IgA in serum before the intervention compared to 1 month after it for (p=0.00008), for IgG for (p=0.0002) and for IgM for (p= 0.00009).

Dimitrovski et al. (18) also obtained statistically significant differences for the values of all immunoglobulins IgA, IgG and IgM only in the group of residual and periodontal cysts before and one month after surgical therapy. In the group of residual cysts obtained a significant difference for IgA, IgG and IgM for (p=0.0371; p=0.0000; and p=0.0276), while in the group of periodontal cysts they obtained a significant difference for the values of IgA, IgG and IgM for (p=0.1966; p=0.0647 and p=0.1237) which is similar to our analysis which indicated a statistically significant difference for immunoglobulin values in all three groups of odontogenic radicular cysts. The difference registered between the average values of immunoglobulins in the studied groups in the study of Dimitrovski et al. are statistically insignificant. A significant difference was only registered for IgA one month after the surgical intervention between all studied groups for p=0.00001. In our research, a mutual comparison was made between the three groups in relation to all types of immunoglobulins IgA, IgG and IgM in the serum, and for IgA and IgG there was no significant difference between the groups, and for IgM, a significantly higher level of IgM in serum was determined in the periodontal laterals. cysts compared to residual and radicular cysts for p=0.0006 before intervention and significantly higher serum IgM level in periodontal lateral cysts compared to residual and radicular cysts for p=0.0120 after intervention and does not match their obtained results.

Conclusion

The results obtained with immunological investigations and the differences in the average values of immunoglobulins before and after surgical therapy of odontogenic inflammatory cysts proved their association and influence on the systemic (humoral) immune response. This confirmed the importance of their early detection and the effectiveness of the therapeutic intervention on the body's immune defense capacity.

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