THE IMPORTANCE OF IMPLEMENTING IMMUNOHISTOCHEMICAL METHODS IN THE DIFFERENTIAL DIAGNOSIS OF ODONTOGENIC KERATOCYST AND AMELOBLASTOMA

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ABSTRACT

The clinical similarity between odontogenic keratocyst and ameloblastoma requires the use of additional diagnostic methods to determine accurate diagnosis. Immunohistochemistry is used in the pathohistological diagnostics of odontogenic keratocysts and ameloblastomas, as well as in decision-making regarding the appropriate therapy and extent of surgical radicality, because their characteristics, such as recurrence and invasiveness, are imperative in therapy planning.

Keywords: odontogenic keratocyst, ameloblastoma, immunohistochemistry, recurrence.

Introduction

Odontogenic keratocyst and ameloblastoma are classified as benign lesions with a high recurrence rate and invasive growth [1, 2]. Accurate differential diagnosis of odontogenic keratocyst and ameloblastoma is of great importance due to their frequent recurrences and different treatment approaches. Immunohistochemical methods are used in pathohistology to determine an accurate diagnosis, indicate the risk of recurrence and potential malignant alterations and are therefore used in the differential diagnosis of cysts and tumors.

Characteristics of odontogenic keratocyst and ameloblastoma

Odontogenic keratocyst is classified as a cyst of odontogenic origin [3, 4]. Odontogenic keratocyst is usually located in the posterior part of the mandible [2, 3, 4]. In the upper jaw the odontogenic keratocyst can invade the maxillary sinus and nasal cavity and even the orbit, infratemporal fossa and base of the skull [5]. Recurrence of odontogenic keratocyst can cause the presence of satellite cysts and the inability to completely remove the odontogenic keratocyst due to its structure and expansive growth. Accurate diagnosis and appropriate treatment of odontogenic keratocysts are of great importance due to their frequent recurrences that grow rapidly and potentially transform into malignancy [1, 6, 7] (Figure 1).

Ameloblastoma is a neoplasm of odontogenic epithelial origin characterized by invasive growth that destroys the jawbone and a high possibility of postoperative recurrence [2]. The usual localization of ameloblastoma is ramus of the mandible. Malignant ameloblastoma is associated with metastases and has histological features of ameloblastoma in contrast to ameloblastic carcinoma which has features of a true malignant neoplasm [9] (Figure 2).

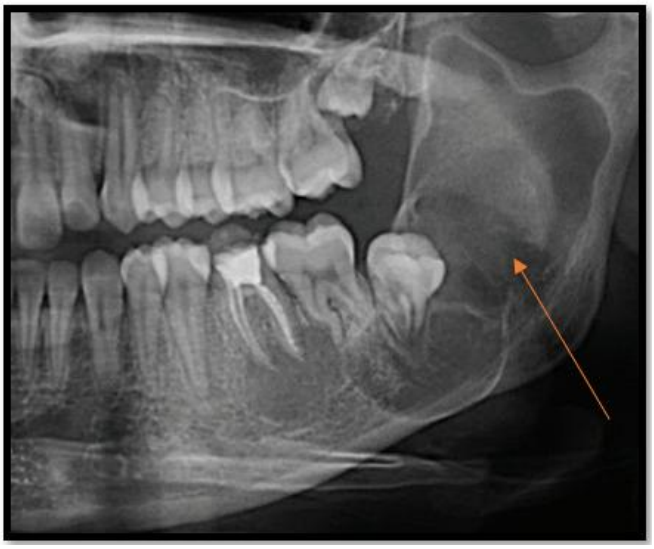

Figure 1: Radiographic image shows radiolucency in the posterior part of the mandible that indicates an odontogenic keratocyst. Source: Şen B, Dündar N, Aslan E, Işık G, Özyiğit Büyüktalancı D, 2024 [8]

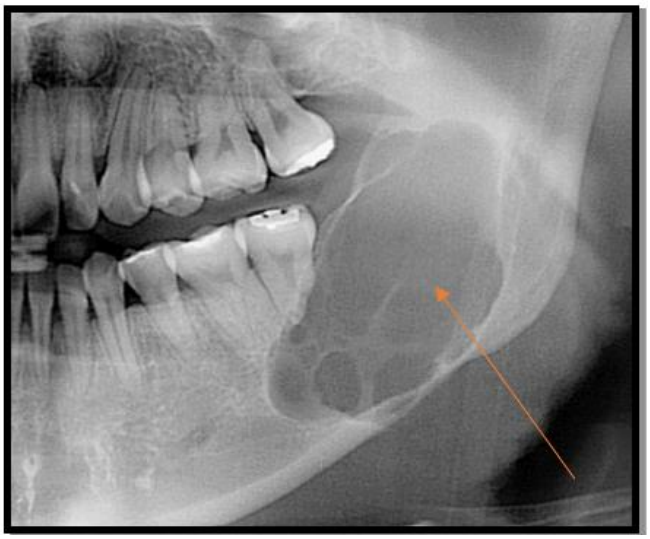

Figure 2: Radiographic image shows radiolucency in the posterior part of the mandible that indicates an ameloblastoma. Source: Kim JE, Cho JB, Yi WJ, Heo MS, Lee SS, Huh KH, 2025 [10]

Immunohistochemistry

Immunohistochemistry is an important pathohistological diagnostic method that can detect markers in a tissue sample. Multiplex immunohistochemistry/immunofluorescence is an improved method that can be used to detect multiple markers in a single tissue sample [11]. Immunohistochemical methods are used in clinical diagnostics - especially in oncological pathology, prognosis and therapy of diseases, they are based on the reaction between specific antibodies and antigens in a tissue sample in order to identify specific markers that can be used for differential diagnosis, classification of diseases and assessment of the course of the disease. Immunohistochemical methods can be used to differentiate benign from malignant tumors, classify pathological lesions, identify the origin of metastases and in the differential diagnosis of cysts and cystic neoplasms of the jaw [12, 13]. The implementation of immunohistochemistry represents a major advance in diagnostics [12].

The aim of this review is to present the importance and possibilities of pathohistological diagnostics using immunohistochemical methods in the diagnosis and differential diagnosis of odontogenic keratocysts and ameloblastomas.

Materials and Metods

The process of searching for relevant scientific literature consisted of reviewing and analyzing electronic scientific databases: Pubmed, Science Direct, Google Scholar and Cochrane Library. A total of 57 articles were reviewed, while 23 articles were included in the review. Data from textbook literature was also used in this review.

Discussion and Conclusion

Research has shown that the biological behavior of cysts and tumors is dictated by their proliferative activity, therefore the expression of cell proliferation markers in immunohistochemistry can be very useful in clinical application [14]. Overexpression of markers indicating the risk of recurrence of odontogenic keratocysts may help during treatment planning and influence the decision on more radical approaches in terms of extraction of teeth affected by the pathological lesion and more extensive osteotomy to prevent recurrence [15]. Many factors influence the occurrence of recurrences of odontogenic keratocysts, which is why precise diagnostics is necessary with the implementation of additional examinations such as immunohistochemical methods in order to reduce the frequent recurrences with appropriate therapy, that is, by conservative treatment of pathological lesions with a good prognosis and a more radical approach in the case of an estimated risk of recurrence which may include jaw resection [16]. Different expressions of immunohistochemical markers provide insight into information about the characteristics and biological behavior of odontogenic lesions and enable precise differential diagnostics and individualized treatments improving their success [17].

According to the available results, a higher expression of the COX-2 marker was found in odontogenic keratocysts than in ameloblastomas [18].

Calretinin is a specific tumor marker for ameloblastoma. Studies have shown that the immunohistochemical expression of calretinin is higher in ameloblastoma than in odontogenic keratocysts, which indicates a difference in the invasiveness of these lesions [14, 19]. Calretinin can be used in immunohistochemistry for the differential diagnosis of odontogenic keratocyst and ameloblastoma as well as for the evaluation of their biological behavior [19]. Based on the findings, it can be concluded that the evaluation of this immunohistochemical marker may provide significant information about the biological behavior of odontogenic keratocyst and ameloblastoma, which significantly contributes in differential diagnostics and consequently impacts treatment approach.

In odontogenic keratocysts, the expression of Bcl-2, CK17, CK19 and CK10 immunohistochemical markers was recorded [13, 20]. Bcl-2, CK17 markers were also recorded in ameloblastoma, but in different places compared to odontogenic keratocysts [13]. Current research suggests that increased expression of the CD10 marker indicates tumor progression, therefore this marker can be an indicator of the invasiveness of ameloblastoma and odontogenic keratocyst [21].

Research data suggest that the expression of the immunohistochemical marker Bcl-x is increased in ameloblastoma compared to odontogenic keratocyst, which may be an indicator of the invasiveness of ameloblastoma, indicating the importance of this marker in diagnostics [22]. Disease progression may be monitored by evaluation of CK10 and Bcl-x immunohistochemical markers which indicate invasiveness of odontogenic keratocyst and ameloblastoma.

Identification of overexpression of CD34 and Ki-67 markers by immunohistochemical methods can indicate the risk for the development of recurrence of odontogenic keratocysts and help in its prevention. The Ki-67 marker enables the assessment of proliferative activity and the possibility of recurrence of odontogenic keratocysts [23]. Ki-67 can also be used to assess the risk of recurrence of ameloblastoma [15, 24]. Ki-67 and p53 markers are very significant in assessing the extent of surgical procedure in odontogenic keratocysts [17]. According to the literature review it can be concluded that Ki-67 and p53 markers used in immunohistochemical methods can be significant in assessing the risk of recurrence and malignant alteration of ameloblastoma [25]. Ki-67 and p53 markers can be used to differentiate benign from malignant pathological lesions [26]. Increased values of the immunohistochemical markers Ki-67, p53, Bcl-2 and PCNA, which play a significant role in the pathogenesis of odontogenic lesions, in odontogenic keratocysts indicate a risk of recurrence [17]. Increased immunohistochemical expression of the Ki-67 marker indicates the need for more radical surgical procedures in odontogenic keratocysts, while in the presence of Bcl-2 markers in recurrences of odontogenic keratocysts inhibition of the Bcl-2 protein can be attempted which requires additional clinical trials and research [17]. The implementation of Ki-67 and p53 immunohistochemical markers can provide information significant for decision-making regarding the extent of surgical procedure as their increased expression indicate the risk of recurrence of odontogenic keratocyst and ameloblastoma.

Through the use of PTCH1 immunohistochemical marker it is possible to detect mutations of PTCH1 gene of the SHH pathway that affect the behavior of odontogenic keratocysts and ameloblastoma, therefore, by inactivating these mutations a therapeutic effect could be achieved [17]. The PTCH1 gene mutation is an important factor in the development of Gorlin-Goltz syndrome [20].

According to the research results, the expression of the SOX2 marker by immunohistochemical methods is higher in odontogenic keratocyst compared to ameloblastoma [27]. The marker SOX2 has the ability to detect the presence of stem cells, therefore its elevated values may indicate the possibility of self-renewal and proliferation of odontogenic keratocysts [27].

The results of immunohistochemical expression of EGFR and survivin markers in odontogenic keratocysts and ameloblastomas can provide significant information about invasiveness, malignancy and the possibility of recurrence [28]. EGFR marker values are often elevated in malignant lesions which are invasive [28]. According to the research results, EGFR expression is increased in odontogenic keratocysts compared to ameloblastomas [28]. Survivin participates in apoptosis and cell division, therefore, its values are of great importance [28]. According to research elavated values of survivin are found in malignant lesions, it is also found that higher values of survivin are in ameloblastoma compared to odontogenic keratocysts [28].

By implementing immunohistochemical methods in the diagnosis and differential diagnosis of odontogenic keratocysts and ameloblastomas it is possible to identify specific markers (antigens) in a tissue sample by reaction with specific antibodies, thereby obtaining detailed information about the risk of recurrence, biological behavior - invasiveness and the possibility of malignant alteration of pathological lesions.

Immunohistochemical methods confirm the diagnosis, especially when standard pathohistological methods are not precise enough, and based on the information obtained it is possible to predict the development and progression of the disease which enables appropriate therapy planning and improved treatment outcomes in oral and maxillofacial surgery.

Additional research is necessary on specific immunohistochemical markers that can be used for precise diagnostics of odontogenic keratocysts and ameloblastomas.

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