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Ameloblastoma and It's Prevalence - A Review

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Abstract

Ameloblastoma is a locally invasive odontogenic tumor that predominantly affects the jaw. Approximately 80% of ameloblastoma arise in the mandible, mostly around the third molar, with the remaining 20% occurring in the upper jaw. The aggressive invasive characteristic of ameloblastoma can cause complications including chewing and speaking difficulties, as well as the deterioration of surrounding bone. Serious issues including mortality arise if the tumor is not treated. It makes for 1% of head and neck malignancies and 9-11% of odontogenic tumors [4].

The literature review provides details about this tumor's numerous traits. To obtain a thorough understanding of this illness, the literature review explores the domains of molecular pathogenesis, histology, and epidemiology. The microscopic characteristics of this tumor, such as its distinctive odontogenic epithelium and the existence of many histological subtypes, as well as the genetic mutations, signaling pathways, and molecular markers connected to it. Comprehending these histological features facilitates precise diagnosis and categorization of Ameloblastoma, as well as the identification of putative therapeutic targets and the creation of tailored treatments. The primary issue in the surgical care of ameloblastoma is tumor recurrence, particularly when the tumor is not entirely removed. In certain circumstances, further therapies such as radiation therapy or chemotherapy may be required to prevent recurrence or manage severe cases. In this article, the prevalence of ameloblastoma in India and the United States is compared, taking into account variables including age, gender, geography, diagnosis, and therapy[7].

Introduction

The behavior of epithelial tumors is categorized, and odontogenic and non-odontogenic cancers are separated based on where they are found in the oral cavity. Odontogenic malignancies include ameloblastoma in their classification. Due to the dental lamina's relics, it developed. The Greek word "blastos," which means "germ," and the English word "amelo," which signifies

enamel, are the roots of the phrase "ameloblastoma." The odontogenic epithelium is a slowly developing and invasive tumor, which makes it the most common odontogenic tumor of the jaw [6].

Ameloblastoma development has been associated with remains of odontogenic epithelial tissue, the enamel organ, and the lining of an odontogenic cyst. According to Milman et al. (2016), it is the most prevalent tumor in the jaws and makes up around 1% of head and neck tumors. The mandible is the area most frequently impacted. It is included in the group of tumors developing from odontogenic epithelium with mature fibrous stroma but without odontogenic ectomesenchyme. In the World Health Organization (WHO) Classification of Odontogenic Tumors from 2005[5] Epithelial remnants, enamel organs, and the lining of the odontogenic cyst were implicated in the development of odontogenic tumors, which are also general factors in the development of ameloblastoma. This idea can be supported by the similar experiences of the cytokeratin and vimentin profiles between developing tooth germs and ameloblastomas.

Clinical feature

Ameloblastoma tumors were mostly found in the mandible, sparing the maxilla of any lesions. The anterior region was the most often impacted area, followed by the posterior mandible. The left posterior body-ramus-angular region was more frequently affected than the right side in each of the four quadrants. The clinical presentation of ameloblastoma can range from an unappealing orofacial enlargement to a benign intraoral swelling that most patients are unaware of. The display of symptoms like pain, fistula, ulcer, tooth mobility, paranesthesia, purulent discharge, Trismus in the affected region, and ill-fitting dentures is a common issue faced by people who are using dentures. Males are more impacted than females, with the majority of the younger generation experiencing it during their decade [1].

Classification

According to WHO categorization, histological characteristics are the prognostic factor that has the most impact. These traits are further categorized into three different forms of ameloblastoma: desmoplastic, solid, and peripheral[2]. A multicystic foci will appear due to the invasion of the bone in the solid or multicystic tumor, and the tumor is monopolized by the stomal aspects in a desmoplastic lesion that resembles similar to the fibro-osseous lesions during the imaging procedure. Malignancy is extraosseous and demonstrates a connection with the stratified oral mucosal epithelium in peripheral ameloblastoma. In the mandible, where it most typically affects the molar ramus area, a group of intraosseous ameloblastomas is known as central ameloblastoma.

According to recent theories, varying aggressive tendencies and the risk of metastatic disease are explained by genetic and molecular aberrations. The two primary histological development patterns in ameloblastomas are plexiform and follicular, with the latter further broken down into acanthomata, granular, spindle, and basal forms. The most often occurring kind of ameloblastoma is solid or multicystic.

Ameloblastomas, on histological examination, look benign and in persistent cases, have the potential to develop into cancer. According to Ragunathan et al. (2002), malignant ameloblastoma is further divided into primary intraosseous ameloblastic carcinoma, secondary intraosseous ameloblastic carcinoma, and secondary peripheral ameloblastic carcinoma.

Epidemiology

Numerous theories were proposed for tumor formation. In the earlier theory regarding the formation of ameloblastoma, the pre-ameloblasts' failure to develop into ameloblasts during the bell stage of tooth development was attributed to the absence of the intermediate alkaline phosphate, an essential substance needed to break down the nutritional components that would be transferred to ameloblasts during the bell stage [5]. A decrease in the production of enamel and ameloblast activity further strengthens this concept. The multicystic ameloblastoma was caused by the coalescence of micro-cysts, which arise when the stellate reticulum deteriorates in epithelial tumor nests with larger cystic regions. Inflammation, inadequate nutrition, general extraction-related irritation, and dental caries have all been linked to genetic factors that affect tooth development, morphogenesis, cytodifferentiation, and tooth patterning, some of which are significantly altered in ameloblastic tissues. These factors are all involved in the molecular-level development of ameloblastoma.

Molecular Pathways and Cellular Mechanisms in Ameloblastoma

The main reason for the uncontrolled cellular growth in ameloblastoma is caused by the Disruption of the major molecular pathway known as the mitogen-activated protein kinase (MAPK) signaling system, according to research based on ameloblastoma tissues, cell lines, and transgenic mice. The majority of ameloblastomas are connected to the BRAF protein kinase, a serine/threonine protein kinase that promotes the MAPK/ERK signaling pathway and is closely related to melanoma. BRAF protein constitutive activation downstream of MEK/ERK ultimately causes cancer. The most notable molecular event is the mutated BRAF gene, which causes glutamic acid (E) to replace the amino acid valine (V) at position 600 (mutated BRAF V600E). Even in the absence of external growth cues, the mutant BRAF V600E protein persistently signals downstream in the MAPK pathway, causing cancer cells to proliferate uncontrollably. The development of ameloblastomas and the ongoing activation of BRAFV600E are factors in the disease's progression[3]. Younger patients were found to have this BRAF mutation more frequently, mainly in the mandibular area. The maxillary BRAF wild-type ameloblastomas, however, were more common and recurred less frequently [2]. Ameloblastoma tumors exhibit aggressive invasion into the bone, with osteoclasts playing a critical role in bone resorption. The presence of Receptor Activator of Nuclear Factor Kappa B (RANK), Receptor Activator of Nuclear Factor Kappa B Ligand (RANKL), and Osteoprotegerin (OPG) are essential for osteoclast formation and bone remodeling. Bone remodeling is influenced by the interaction of the kappa B receptor activator (RANK) on osteoclast precursors and its osteoblast membrane-bound ligand (RANKL). The osteoprotegerin (OPG), also known as soluble receptors, is found on osteoblasts and it forms a connection with RANKL to modify the interactions between RANK and RANKL[2]. Because RANK-RANKL signaling dysregulation and changed OPG levels have been associated with lesional bone loss in ameloblastoma, RANKL and OPG are expressed differentially in distinct forms of ameloblastoma.

The histological characteristics of the enamel organ are quite like those of the benign, locally aggressive odontogenic tumor known as ameloblastoma. The average age of ameloblastoma patients was 39.1 years in industrialized countries against 27.7 years in developed countries.

Studies and Trails

Based on studies carried out using easily accessible oral biopsy samples. Each patient's age, gender, and anatomical location were recorded using the clinical information included in the biopsy reports. The most recent theories given by the WHO were used to evaluate a selection of histopathology slides stained with hematoxylin and eosin. Histological evidence of the solid/multicystic ameloblastoma subtypes was required for inclusion. In the 58 ameloblastomas seen during the 13-year observation period, 27 instances (46.5%) and 31 cases (53.4%) were unicystic and solid, respectively[4]. Following histological examination of these 31 multicystic ameloblastomas, four subtypes were identified: follicular, which accounted for 54.8% of cases, acanthomatous, which accounted for 29% of cases, plexiform and granular cell, which accounted for 6.5% of cases, and desmoplastic. The male-to-female ratio for all ameloblastomas was 2.1:1, with males accounting for 21 (67.8%) and women for 10 (32.2%) of these occurrences[4]. Patients ranged in age from 21 to 73, with a median age of 39.5 years. Eight cases (25.8%) and eleven (35.5%) of these cases, respectively, received their diagnoses in their third and fourth decades of life [5].

Racial and regional factors affect the distribution of odontogenic tumors. The distribution of multicystic and unicystic ameloblastomas was about 53.4% and 46.5%, respectively, and no peripheral variants existed[5]. The two most common variations were the follicular subtype and acanthomata's ameloblastoma. According to several academic sources, Plexiform is the second most frequent subtype, after follicular, and the variability may be brought on by the study population's wide ethnic makeup. The least common subtype, basal cell ameloblastoma, was absent in any lesions. Histological subtypes and clinical symptoms are not correlated in this study. The mandibular molar ramus region is the most often impacted area[5]. In every form of ameloblastoma, the posterior mandible is the area that is most frequently affected. Desmoplastic ameloblastoma, which tends to develop in the maxillary anterior region, was present in the mandibular posterior region and was of the acanthomatous subtype. The swelling was the major diagnosed clinical symptom subsequently followed by a pain-and-swelling combination. Most of the lesions are unilateral generally there would be no correlation between the histological categories and clinical symptoms[6].

Molecular Pathogenesis

To explain the pathogenesis of ameloblastoma various signaling pathways were identified. A homolog of the drosophila segment polarity gene that enscripts a secreted protein is Sonic Hedgehog (SHH) which in turn activates the membrane receptor complex formed by patched 1 (PCTH 1) [6]. SHH signaling is mediated from the cytoplasm to the nucleus as a result of the release of the PCTH-SHH binding SMO, activation of the glioma-associated (GLi 1) family transcription factor gene, and SHH signaling. In cases of ameloblastoma. SHH, SMO, and GLi 1 all had high expression levels. Compared to healthy stromal cells, cancerous cells have a higher PCTH 1 signal. SHH signaling molecules are important in the stages of ameloblastoma, such as during cell proliferation and the connection between the epithelium and mesenchyme[3]. The activity of enamel epithelial cells and the emergence of tumors were discovered to be greatly affected by WNT 5a signaling in ameloblastoma. The primary function is the resilience of catenin and its transport into the nucleus, whereupon it performs its influence on gene transcription. Suppression of WNT 5a inhibits enamel epithelial cell

motility while overexpression increases it. In keratinizing cells, acanthomatous ameloblastomas displayed an elevated BMP-7 reactivity. Low levels of BMPs, BMPRs, and CBFA1 reactivity were seen in ameloblastic carcinomas.

Midkine is a heparin-binding growth factor that is expressed during tooth formation. This protein has been overexpressed in ameloblastomas, particularly ameloblastic carcinoma since ameloblastomas arise from the odontogenic apparatus. This protein in ameloblastoma, particularly solid/multicystic lesions, signals three symptoms, including protein growth, tumor progression, and tumor activity.cancers' initial development and growth There is a significant role for growth factors and their receptors. FGF1 and FGF2 were detected in the basement membrane and stellate reticulum, respectively, with the former being strongly expressed in ameloblastoma- and stellate reticulum-like cells. Angiogenesis is a process that is necessary for the tumor to become metastatic [6]. Vascular endothelial growth factor (VEGF) is a crucial element needed for this procedure, and its response was poor in cases of acanthomatous ameloblastomas, which also had the lowest expression of VEGFA in keratinizing cells in granular cell ameloblastomas and granular cells in granular cell ameloblastomas. Platelet-derived growth factor (PDGF) and its receptor (PDGF-R) levels were higher in malignant ameloblastomas[6].

Management of the Ameloblastoma

With the use of the outcomes from the clinical findings and histopathology and various imaging procedures, a successful management for the disease can be found. Plain film radiography, cone-beam computed tomography, conventional CT, magnetic resonance imaging (MRI), and functional imaging that combines positron emission tomography (PET) with conventional CT are the various imaging techniques used for ameloblastoma. The application of the MRI will provide information on the soft tissue within and close to the afflicted areas as well as the bone components. They are helpful for identifying the extensions of maxillary ameloblastomas throughout the maxillary sinuses, orbits, and skulls. It is helpful to utilize a PET/CT scan to determine how much soft tissue is impacted by malignant ameloblastoma.

Surgical methods can be utilized for the treatment of the ameloblastoma. Enucleation and cauterization, curettage, cryotherapy, or marsupializations are some examples of conservative surgical treatments [1]. In conservative surgery, facial disfiguration is avoided, natural tissues are protected, and the patient's quality of life is improved. However, conservative surgery is more likely to fail, particularly when aggressive ameloblastoma is present. For biologically aggressive subtypes of primary and recurrent ameloblastomas, radical surgical therapy is typically the treatment of choice. Wide bone margin tumor removal is followed by immediate or delayed bone repair of the surgical defect using tissue transplants and prosthetic rehabilitation. Nonsurgical treatments for ameloblastoma include helical tomotherapy, image-guided radiation therapy, intensity-modulated radiation therapy, and proton beam therapy[1]. Other medication regimens can be used in addition to radiation therapy and surgical resection. These include the regimens of doxorubicin, cisplatin, gemcitabine, and carboplatin, as well as the combinations of vinblastine, cisplatin, and bleomycin, adriamycin, cisplatin, and cyclophosphamide. As a result of recent developments in the molecular signaling networks linked to the pathophysiology of ameloblastoma, targeted therapeutics have been created[5]. Numerous MAPK-specific drugs precisely inhibit the actions of mutant BRAF and MEK

to prevent the dysregulated proliferation and differentiation of ameloblastic cells. These include vemurafenib and dabrafenib, which block the mutated BRAF gene, and trame-tinib, an inhibitor of the mutated MEK gene. complicated polycomb protein Bmi 1, also known as the polycomb group RING finger protein, is essential for DNA damage repair and is necessary for a number of signaling pathways, including Wnt, notch, hedgehog (Hh), and Akt. This complex's abnormal activity may result in several different mutations. The expression of CD 133 and Bmi-1 was positive in melanoma, odontogenic epithelial cells, and metastasizing ameloblastomas[6]. Sensitivity to CD 133 and Bmi-1 in ameloblastic carcinomas was also detected. Ameloblastomas and tooth germs did not express CD 133 as robustly as malignant ameloblastic tumors did.

Conclusion

Patients with ameloblastoma in impoverished nations may arrive with massively enlarged lesions before seeking care because of ignorance and inadequate healthcare facilities. Proper diagnosis and health awareness can act as factors for an effective prognosis. Several cellular processes play a role in the development of ameloblastoma. A range of substances and gene mutations influence odontogenic epithelium growth and development, and these features appear to be mediated by a number of molecular pathways. Being familiar with the pathogenic process of ameloblastoma and its development allows researchers to establish new therapeutic methods, such as molecular-targeted treatment for odontogenic tumors.

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