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The Role of Radiotherapy for the Treatment of Advanced Maxillary Sinus Squamous Cell Carcinoma: A Literature Review

Review Article

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Abstract

The maxillary sinuses have pneumatic cavities, enabling direct communication with the nasal cavity. These cavities can be affected by a series of malignant neoplasms. A descriptive narrative literature review of the proposed topic was carried out using scientific articles as a bibliographic basis in databases such as BVSalud, PubMed, Scielo and Google Scholar. The literature showed that the majority of cases of these neoplasms are squamous cell carcinoma, a malignant epithelial neoplasm, which may be non-keratinized. Neoplasms of the maxillary sinuses are asymptomatic in their initial stages, which means that diagnoses are made in advanced stages. Imaging exams are important for diagnosing these neoplasms, with emphasis on computed tomography, which makes it possible to carry out a precise analysis of bone location, extension and destruction. This survey aims to evaluate cases of advanced neoplasia of the maxillary sinuses and we observed that radiotherapy doses greater than 6500 cGy were correlated with better local control in patients treated with exclusive radiotherapy and in relation to lymph nodules in the neck, failures occurred in a low percentage of treated cases (8%) in patients not treated electively. We conclude that exclusive radiotherapy for advanced neoplasia of the maxillary sinuses is a good alternative for those cases in which they are not candidates for surgery or even refuse to be offered it. Thus, since there is a lack of literature on this topic, there is a need for new studies that can help patients with advanced maxillary sinus carcinoma in inoperable cases.

Keywords: Head and Neck Cancer; Squamous Cell Carcinoma; Maxillary Sinus Neoplasms; Radiotherapy

Introduction

The face is mostly made up of the mandibular and maxillary bones, paranasal sinuses, nose and oral cavity. Due to the close anatomical proximity between facial structures, it is common for diseases that affect one component of this set to affect a neighbour more. Both the oral cavity and the nose act together actively in the vital functions of nutrition and breathing respectively and it is not uncommon for pathology that develops in one to affect the other structure [1].

The paranasal sinuses are a set of structures made up of the frontal sinus, sphenoid sinus, ethmoidal cells and maxillary sinuses, which are pneumatic cavities lined by the respiratory epithelium and mucosa, located inside their respective bones, having direct communication with the cavity nasal [1-4]. The maxillary sinuses are the largest and are located bilaterally within the maxila, presenting a pyramidal shape [1,3,4].

Due to this large volume of the maxillary sinuses, it is possible for tumors to develop without presenting any symptoms, which means that when the patient presents any signs or symptoms, the tumors are already at an advanced stage [3,5]. Clinically, the signs are indistinguishable in the early stages [5]. Carcinomas of the maxillary sinuses are considered extremely rare and aggressive lesions; they correspond to 0.2% to 0,8% of all cancers and approximately 3% to 6% of head and neck cancers 3,2,38. Approximately 50% of sinonasal tumors begin in the maxillary sinuses and approximately 15% to 30% begin in the nasal cavity [5,6].

Malignant tumors of the maxillary sinuses have different characteristic when compared to other tumors located in the head and neck region. These malignant neoplasms can lead to significant mortality, as well as debilitating disfigurements [3]. Initially, the symptoms of maxillary neoplasms are nasal obstruction, epistaxis and runny nose 5. In advanced cases, intracranial and orbital, hyperesthesia, facial edema, cranial nerve neuropathy [5].

Maxillary sinus carcinoma is uncommon and represent 0.2% to 0.8% of neoplasms, 3% of head and neck carcinomas and 80% of paranasal sinus tumors [7,8]. The majority of tumors that occur in maxillary antrum are of epithelial and squamous cell carcinomas account for more than 80% of all cases of malignant neoplasms [7]. Treatment options for advanced cancer depend on where the disease started and whether and how widespread it is. As a general rule, the tumor

that has spread will need to be treated with systemic therapy, such as chemotherapy or hormone therapy. Local therapies, such as surgery or radiation therapy, only target a certain region of the body. However, they can also be used to prevent or relieve certain symptoms [9].

The main type of radiation therapy used to treat nasal cavity and paranasal sinus cancer is external beam radiation (EBRT). External beam radiation therapy focuses a beam of radiation from a machine outside of the body onto the cancer. These tumors are close to the eyes, brain, glands, nerves, and blood vessels [9]. The face is mostly made up of the mandibular and maxillary bones, paranasal sinuses, nose and oral cavity. Due to the close anatomical proximity between facial structures, it is common for diseases that affect one component of this set to affect a neighbour more. Both the oral cavity and the nose act together actively in the vital functions of nutrition and breathing respectively and it is not uncommon for pathology that develops in one to affect the other [1].

The paranasal sinuses are a set of structures made up of the frontal sinus, sphenoid sinus, ethmoidal cells and maxillary sinuses, which are pneumatic cavities lined by the respiratory epithelium and mucosa, located inside their respective bones, having direct communication with the cavity nasal [1-4]. The maxillary sinuses are the largest and are located bilaterally within the maxila, presenting a pyramidal shape [1,3,4].

The maxillary sinuses grow after birth until approximately age [3]. After this period, there is a slow progression until the age of 7, and then there is a further acceleration of growth, reaching its greatest proportion around 12 to 14 years of age, a period that coincides with the end of the permanent teeth with the closure of the growth of the alveolar process of the maxila [3,4].

Due to this large volume of the maxillary sinuses, it is possible for tumors to develop without presenting any symptoms, which means that when the patient presents any signs or symptoms the tumors are already at an advanced stage [3]. Clinically, the signs are indistinguishable in the early stages [5]. Carcinomas of the maxillary sinuses are considered extremely rare and aggressive lesions; they correspond to 0,2% to 0,8% of all cancers and approximately 3% to 6% of head and neck cancers [2,3]. Squamous cell carcinoma is a malignant epithelial neoplasm thar originates from the epithelium of the mucosa lining the nasal cavities [10]. Approximately 50% of sinonasal tumors begin in the maxillary sinuses and approximately 15% to 30% begin in the nasal cavity [5].

Malignant tumors of the maxillary sinuses have different characteristic when compared to other tumors located in the head and neck region. These malignant neoplasms can lead to significant mortality, as well as debilitating disfigurements [3]. Initially, the symptoms of maxillary neoplasms are nasal obstruction, epistaxis and runny nose. In advanced cases, intracranial and orbital, hyperesthesia, facial edema, cranial nerve neuropathy [5].

After carrying out the clinical examination, an investigation of malignant tumors must be initiated through imaging tests such as X-rays, computed tomography and magnetic resonance imaging. Such exams are important to identify the topography of the lesion, as well as to define its local extension [3,5]. The delay in detecting this pathology occurs mainly due to professionals neglecting the presence of symptoms 3. The maxillary sinuses are extremely important for head and neck surgeon's oncologist due to their intimate relationship with mouth structures and the sinus pathologies can lead to incorrect diagnoses of odontogenic changes that also affect the maxillary sinuses, such as tumors originating from the upper gums in the oral cavity [1,3,4].

This literature review aims to gather information about malignant neoplasms of the maxillary sinuses, which could serve as an informational source for professionals in the health sector and also head and neck surgery.

Literature Review

Malignant neoplasms of the maxillary sinuses are considerably rare lesions. These correspond to approximately 0,2% to 0,8% of all neoplasms and 3% to 6% of head and neck neoplasms, the incidence of which is appoximately1 in every 100.000 people per year [7,8,11]. These neoplasms have a predilection for males, appearing between 50 and 70 years of age [2,4,8,9,12,13]. Most neoplasms of the paranasal sinuses originate in the maxillary sinuses; however, as these are normally only diagnosed in advanced stages, determining the exact place or origin becomes a difficult task [3,4,11,12].

Although there are several neoplasms thar can affect this region, squamous cell carcinoma represents approximately 80% - 90%, being considered the most common malignant neoplasm of the paranasal sinuses [3,4,13]. The remaining percentage is represented by adenocarcinomas, melanoma, soft and hard tissue sarcomas, and lymphomas [3,4]. Squamous cell carcinoma is a malignant epithelial neoplasm that originates from the epithelium of the mucosa lining the nasal cavities or paranasal sinuses; these can be quarantines or non-keratinized [3,14]. It is a tumor that can manifest itself in several different forms of malignancy, with the most important characteristics such as: anaplasia (when cell formation deviates from normality), rapid growth, tissue destruction and metastases capacity. There are some lesions considered precursors to squamous cell carcinomas; approximately 10% of HPV infections, in nasosinusal carcinomas [3].

Malignant nasosinusal neoplasms are divided according to their origin and can be epithelial (squamous cell carcinoma; adenoid cystic carcinoma and adenocarcinoma) and non-epithelial (chondrosarcoma; olfactory neuroblastoma and mucosal melanoma). As for the occurrence of metastasis, the distance is considerably low when talking about squamous cell carcinoma of the maxillary sinuses; bones and lungs are most affected by distant metastasis. The probability of metastasis occurring in regional lymph nodes is greater when it comes to squamous cell carcinomas (10%) compared to adenoid cystic carcinoma 3. Carrying out a differential diagnosis should take into account the possibility of undifferentiated sinus carcinoma, carcinoma mucoepidermoid carcinomas and adenocystic carcinomas [4]. The most common type of adenocarcinoma is those with a tubular, papillary and cystic structure. These occur mainly in smokers and workers who come into contact with wood dust such as beech, ebony and oak. Some studies indicate that constant contact with formaldehyde, nickel, chromium and isopropyl alcohol are also related to the development of this neoplasm [12].

Melanoma occupies second place in the ranking of malignant neoplasms, but its incidence does exceed 30%. This is considered a rare malignant neoplasm in the sinuses. Their nasal lesions are usually polypoid, solid, pigment or not. Sinus sarrcomas have a much lower incidence than carcinomas; represent less than 15% of malignant neoplasm in this region. In ascending order, the most common sarcomas are fibrossarcoma, chondrosarcoma, reticular cell sarcoma, osterosarcoma of osteogenic sarcoma and embryonal rhabdomyosarcoma. Lymphomas, in turn, represent less than 10% of malignant neoplasms of the facial sinuses. These processes have a greater incidence in the nasopharynx region, due to the greater amount of lymphoreticular tissue present in this region; This is among the three most common malignancies in the nasopharynx of children [12].

Due to the location of these neoplasms and the absence of early symptoms, the diagnosis is made late [3,4,7,8,13]. Initially, when the lesions are limited to the maxillary sinuses, it is possible to observe nonspecific symptoms, such as mucopurulent rhinorrhea, unilateral nasal obstruction and epistaxis. These signs and symptoms commonly lead to erroneous diagnoses such a nasal polyp, chronic sinusites, tear duct obstruction and cranial arthritis [3,4,7,11,13]. Facts such as the unilatterality and perpetuation of these symptoms can help in the suspicion and diagnosis of malignant neoplasms in the paranasal

sinuses [3,14]. Before causing bone destruction, the first lesions may only appear as soft tissue masses located inside the breasts. These can expand in size, affecting the entire breast, presenting radiographic evidence of boné destruction, even before symptoms occur. It is possible to find in approximately 40% to 60% of cases the occurrence of bulging of the oral cavity, facial asymmetry and expansion of the neoplasm into the nasal cavity [4].

When the neoplasm exceeds the limits of the sinus cavities, it may end up causing some symptoms such as trigeminal nerve paresthesia and headaches, ophthalmic symptoms such as recurrent conjuntivitis, exophthalmos and diplopia or even dental symptoms such as mobility of the upper teeth and painful symptoms [3]. Lesions can extend medially to the nasal cavity, anterolateally to the soft tissues and buccal mucosa, down to the floor of the maxillary sinus, palate and alveolus, subsequently affecting the pterygoid muscles and pterygopalatine fossa [3,5]. They can reach the orbital fissure and the carvernous sinus by climbing through the pterigoid fossa [3,4,5].

Even today, the pathogenesis of sinus neoplasm is not fully understood. It is believed that this is related to genetic mutations, with the association of environmental carcinogens such as physical agents and viroses, due to a variety of factors. Exposure to formaldehyde, dichloroethyl sulfide and diisopropyl sulfate are cited as some physiological factors thar may be related to neoplasms [13]. It is known thar even after 40 years or more, since contact with carcinogens, their effects are still present, even if exposure has ceased 3. Among the various viral agents suspected of being related to the development of malignant neoplasms of the maxillary sinuses, human papillomavirus (HPV) stands out, especially types 16 and 18 and, to a lesser extent, types 6 and 11 [13]. Studies are being carried out on the mutation of the gene that encodes the p 53 protein, due to its influence on the development of head and neck carcinomas, since this problem participates in the mechanisms that carry out the repair of genetic material [3].

Substances used as contrast in imaging exams such as thorium dioxide, which was widely used in the 30s and 40s, is considered a carcinogen [4]. Prolonged and abusive use of alcohol and Tabacco appears to be related to the emergence of theses cancers, however, there is no direct relationship with the development of neopl asms of the maxillary sinuses [13,15].

In panoramic radiographs of patients who have malignant neoplasms in the maxillary sinuses, the sinusses may presented shadowing, with visible destruction of the bone walls. Faced with such a clinical situation, it is necessary to complement the imaging study through computed tomography and magnetic resonance imaging. These exams play an important role in determining the therapeutic possibilities for injuries on an individual basis, especially when they reveal their extensions and tissue destruction [4].

Radiographs and imaging studies show aggressive characteristics of neoplasm, such as slow or accelerated growth of the lesion. Radiographic examination shows whether the maxillary sinus is infected or not. The normal breast has clear and precise walls. The inflamed sinus has na opaque glass appearance. Panoramica radiography offers a view of the sinus antrum and its relationship with the upper teeth [3]. When it comes to diagnosis through images, computed tomography is the first choice, as it allows the assessment of the extent of the lesion in question and the possible involvement of neighboring bone structures. Magnetic resonance imaging is also widely used, especially to perform the precise differentiation of surrounding inflammatory tissue from neoplastic tissue [8,11].

Magnetic resonance imaging is a non-invasive method and evaluates the behavior of some elements and this method does not deal with ionizing radiation, being widely used in the field of oral and maxillofacial surgery [3]. Maxillary sinus tumors can be divided into epithelial and non-epithelial. Epithelial cells can be observed under microscopic view. Thus, the invasion of these cells into the connective tissue can be seen. The histological lineages that make up neoplasms are diverse and have distinct clinical behaviours. Determining the histopathological type is very importance for prognosis, because this, better results can be obtained for patients who have the neoplasm. The histopathological diagnosis of the type of tumor must be made before determining the treatment to be performed [3]. In nasal and paranasal tumors, it is recommended to perform na incisional biopsy, where part of the lesion is removed for an excisional biopsy, when the entire lesion is removed. In cases of advanced stage tumors, which have reached deeper areas, endoscopic or surgical biopsy may be chosen [16].

Treatment for malignant neoplasms of the maxillary sinuses consists of surgical procedures, chemotherapy and radiotherapy; however, due to the asymptomatic appearance of these lesions, the prognosis is not good due to detection at advanced stages [12]. Surgical treatment is essential for tumors of the paranasal sinuses and nasal cavity. It is almost always combined with other treatments such as radiotherapy and chemotherapy for a better treatment result [17]. When it involves the maxillectomy is performed, where part of the jawbone is removed. It is necessary to know the location of the tumor and whether it involves adjacent tissues such as bone, muscle, skin, orbit to perform a maxillectomy. The incision is made by the surgeon, on the side of the nose and from the eyebrow to the upper eyelid or the incision can be made under the upper lip, the bone of the hard palate, the upper teeth on one side of the mouth, part or all of it can be removed of the orbit, part of the facial bone and upper bone part of the nose [18].

Wang et al. [19] reviewed 98 patients with maxillary sinus squamous cell carcinoma (MSSCC) and they stated that the surgery-based treatment is still the first-line therapeutic strategy for MSSCC and neoadjuvant chemoradiotherapy followed by is highly recommended for MSSCC patients, especially those with advanced tumors or requesting high quality of life.

Bhasker et al. [20] the author stated that regarding the treatment of carcinoma of the maxillary sinus show feasibility and efficacy of multimodal therapy. Radical radiotherapy appears to be a feasible alternative in cases of inoperable tumors being the locoregional relapse remains a significant pattern of failure.

Ozsaran et al. [21] evaluate the outcome of patients with maxillary sinus carcinoma after radiotherapy regarding local control, prognostic factors and morbidity of treatment. They concluded that high rates of local control can be achieved with surgery and radiotherapy. Su et al. [22] concluded that there is no satisfactory treatment for advanced maxillary sinus squamous cell carcinoma, and the treatment strategy is controversial. The authors stated that the efficacy of multimodality therapy is better than that of single therapy strategy for advanced maxillary sinus squamous cell carcinoma. So, the best treatment pattern for advanced maxillary sinus squamous cell carcinoma needs further research.

Giri et al. [23] evaluated 41 cases of advanced maxillary sinus carcinoma were treated at the University of Kansas Medical Center and they observed that a dose greater than 6500 cGy correlated with better local control in patient treated with radiotherapy alone. They concluded that radiation therapy is an equally good alternative for those who are not surgical candidates or refuse surgery. Stern et al. [24] the authors observed that those patients who underwent radiotherapy alone or chemotherapy presented with either metastatic or locally advanced disease and were treated with palliative intent, therefore, comparison between this group and standard therapy groups Was impossible in this retrospective review. Although it is tempting to speculate thar combination therapy improved locoregional control and survival in patients with more advanced disease, none of the data presented in this review reach statistical significance. The authors concluded that locoregional tumor progression remains a significant pattern of failure.

Santos et al. [6] related that the squamous cell carcinoma arising at maxillary sinus is a rare neoplas, characterized by aggressive growth pattern and glooming prognosis. There are no studies describing specifically its epidemiology in the South America. Maxillary sinus squamous cell carcinoma is an aggressive tumor normally diagnosed at the advanced stage and most patients presented unfavourable prognosis and reduced survival rate.

Discussion

Advanced cancer usually cannot be cured, but it can and should be treated. At any stage of the disease, the objective of treatment must be clear. The patient needs to know whether the objective is to cure the disease, slow its growth and increase survival or to cure the disease are the same as those used to slow its development or alleviate symptoms, relieve symptoms. This can sometimes be confusing because some treatments used to cure the disease are the same treatments used to slow its development or alleviate symptoms.

It was shown in the studies by Mendonça et al. [25] and Santos [2] that there is a higher prevalence of squamous cell carcinoma in the maxillary sinuses when compared to all other malignant neoplasms that affect this region. It was also demonstrated the predilection of this for males, Caucasian, between the 5th and 7th decade of life.

The study by Maciel et al. [26] showed that although computed tomography is an extremely useful tool for making diagnoses, simple diagnosis is not enough. It is necessary for the head and neck surgeon to have sensitivity and knowledge so that he can understand it and then enjoy its full potential. Souza et al. [10] emphasize the important role played by computed tomography and magnetic resonance imaging, which enable na accurate analysis of tumor extension and dissemination, favouring therapeutic planning, enabling better prognosis, Rege [27] also demonstrated the importance role of CT scans, emphasizing their potential to assist in the early diagnosis of asymptomatic patients.

In advanced sinus cancer, radiation therapy is often used as a palliative treatment with the goal of reducing the size of tumors, relieving pain and other symptoms. Sometimes different types of radiation therapy are used simultaneously, especially in combination with radiopharmaceuticals that may be more effective for diseases that have spread to the bones and lungs.

Even if the advanced cancer no longer responds to treatment, there are still action that can be taken to improve the patient´s quality of life for as long as possible. This care, which aims to relieve suffering and improve quality of life, is called supportive treatment.

The majority of maxillary antrum neoplasm are squamous cell carcinomas and in view the location and lack of early symptoms, patients usually have advanced tumors at the time of diagnosis and when small, they are mistakenly diagnosed as chronic sinusitis, nasal polyps, tear duct obstruction or even cranial arteritis [28]. Lymph node blocks in the neck as an initial presentation are infrequent [29]. The low incidence may be associated with weak lymphatic drainage of the maxillary sinus or with clinical inaccessibility to diagnose affected lymph nodes [30]. The topographic distribution of lymph node metástases in neck is usually depend on the tumor site, contiguity and richness of lymphatic capillaries [31]. Patients with extension to the nasopharynx and oral cavity have an incidence of cervical metastases is higher than in other regions [32].

In that literature review of advanced maxillary sinus cancer inoperable, radiotherapy is often used as a palliative treatment with the aim of reducing the size of tumors, used simultaneously, mainly with the combination of radiopharmaceuticals that can be more effective for metastases that have spread to the bones and lungs.

Approximately the majority of maxillary antrum neoplasm are squamous cell carcinomas [33] and in view the location and lack of early symptoms, patients usually have advanced tumors at the time of diagnosis [28] and when the tumors are small, they are mistakenly diagnosed as chronic sinusites, nasal polyps, tear duct obstruction or even cranial arteritis [28] in also 40% to 60% of cases there is alteration of facial nerve.

The presence of lymph nodes in the neck as an initial presentation are infrequent, ranging from 3% to 20% [29]. The low incidence may be associated with weak lymphatic drainage of the maxillary sinus or with clinical inaccessibility to diagnose affected lymph nodes [30]. The topographic distribution of lymph node metastasis in neck is usually depend on the tumor site, contiguity and richness of lymphatic capillaries [31]. Patients with extension to the nasopharynx and oral cavity have an incidence of cervical metastases is higher than in other regions [32].

The incidence of distant metastases is generally low in squamous cell carcinoma of the maxillary sinus [34], being more frequent in the histopathological poorly differentiated subtype. In this case lungs and bones are most affected sites [35]. The poor prognosis of maxillary sinus carcinoma may be due to the late detection of extensive tumor and the impossibility of complete surgical resection. The five-year survival rate ranges from 20% to 40% [28,36].

Finally, the advanced maxillary sinus carcinomas can mean different things to different references according to the American Cancer Society (ACS) so the advanced cancer corresponds to cancer that cannot disappear completely and in which the patient cannot move away from treatment. This kind of neoplasms usually can't be cured, but it can and should be treated. At any stage of the disease, the goal of treatment should be clear. The patient needs do know whether the goal is to cure the disease, slow its growth and increase survival or relieve symptoms. This can sometimes be confusing, because some treatments used to cure the disease are the same ones used to slow its development or relieve symptoms [37,38].

Conclusion

It is extremely important for head and neck surgeon oncologist to be attentive to the simplest signs and symptoms presented by patients and to transmit confidence to them so that they feel comfortable to report what they are feeling, no matter how simple the symptom may be since, as demonstrated in the present review, simple and apparently harmless signs can be indications of the development of malignant neoplasms of the maxillary sinuses. The search for new knowledge on the part of the head and neck surgeon's oncologist are necessary so that they can make more accurate diagnosis. Further studies on this topic are recommended, since there has been a considerable lack of literature on this subject and that new studies can help those affected in diagnosing advanced carcinoma of the maxillary sinus in inoperable cases.

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