

WELL DIFFERENTIATED SQUAMOUS CELL CARCINOMA OF RIGHT MAXILLARY ANTRUM: A CASE REPORT

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ABSTRACT

Malignant tumors of the nasal cavity and paranasal sinuses are rare, with poorly differentiated squamous cell carcinoma of the maxillary sinus being the most common. Carcinomas of the maxillary sinus are uncommon and comprise 3% of all head and neck cancers, and 80% of all paranasal sinus cancers. Squamous cell carcinoma is the most common malignant tumor at this site, representing 60%–90% of the total cases. We report case of well differentiated squamous cell carcinoma affecting the right maxillary antrum in a 482 year old male along with the importance of early diagnosis of maxillary sinus carcinoma, in order to increase chances of survival.

INTRODUCTION

Malignant tumors of the maxillary sinus are rare neoplasms that account for approximately 3% of head and neck cancers and 0.5% of all malignant diseases. The annual incidence of maxillary sinus cancer is 0.5–1.0 case per 100,000 of the population. Squamous cell carcinoma is the most common histologic type, accounting for approximately 70–80% of the cancers [1]. The other histologic types of maxillary sinus cancer include adenoid cystic carcinomas, adenocarcinomas, mucoepidermoid carcinomas, sarcomas, and lymphomas. This disease mainly affects men in their sixth or seventh decade of life. Primary carcinoma of the maxillary antrum is a relatively rare neoplasm and accounts for a small percentage (0.2%) of malignancies in human and constitutes approximately 1.5% of all head and neck malignancies. This includes primary sinonasal neoplasms like squamous cell carcinoma, nasopharyngeal adenocarcinoma, lymphoma, primary sinonasal melanoma, carcinoma of minor salivary gland origin as well as metastatic diseases.

The incidence varies between populations, with more cases reported in Asian countries [2]. Most lesions remain asymptomatic or mimic sinusitis for long periods while the tumor grows to fill the sinus. Hence, diagnosis may not be made until the lesion has perforated through the surrounding bone, and most patients are diagnosed with advanced disease. Smoking and histories of chronic sinusitis are the most common risk factors for maxillary sinus cancer. In addition, occupational exposure to chemical substances, such as formaldehyde, chromium, nickel, and air pollution is associated with an increased risk for malignant tumors of the maxillary sinus. Most patients are diagnosed at an advanced stage with the tumor mass filling the entire antral space and perforating through the surrounding bone. Carcinoma of the maxillary sinus is one of the neoplasms that is difficult to treat and carries a poor prognosis. While optimal treatment patterns, including radiation therapy, conservative surgery and chemotherapy are still under debate, the prognosis remains poor. Radiation therapy, conservative surgery and chemotherapy in a variety of combinations and sequences are considered with a relatively dismal prognosis [3]. Most patients with maxillary sinus cancer have no symptoms in the early stage and, therefore, many of these patients are

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diagnosed in the advanced stage of the disease. The complexity of the anatomy and the proximity of the eyes, brain, and cranial nerves render complete surgical resection difficult, which leads to local recurrence, a major cause of treatment failure. The other issues pertaining to maxillary sinus cancer include the functional aspects of eyesight and the cosmetic aspects of facial contours, which make patients, avoid surgical resection. The standard treatment for maxillary sinus cancer has been surgical resection with or without orbital exenteration, followed by postoperative radiation therapy. However, in the advanced stages, tumor control and survival rate are still considered to be unsatisfactory, with a local control rate of 50–60% and a five-year disease-specific survival rate of 30–50% [4].

Case report

A patient aged 42 year reported to outpatient department of Oral Medicine, Radiology & Diagnosis, Institute of Dental Education & Advance Studies with chief complaint of pain & swelling in right middle one third of face since three months. Swelling extends around the lateral wall of orbit of right eye & right infraorbital margin. (Extra oral photograph not shown as patient did not want his identity to be revealed). Patient gives history of extraction of 16 three months back by a private practitioner seeming it as an odontogenic infection. Swelling subsided for few days after extraction of tooth but again appeared extending up to orbit & nasolabial fold. After 1 month of extraction patient felt choking sensation & went to ENT specialist for opinion. He got radiographic investigations of Panoramic radiograph (Fig 1), PosteroAnterio Mandible & lateral skull (Fig 2) done. Patient was referred to dentist. His past medical history revealed 10/day cigarette smoking habit since 20 years. An eye examination has been performed with attention to the range of extra ocular motion, visual acuity, pupillary response, and signs of globe displacement. An ear examination was included to inspect the tympanic membrane to assess middle ear aeration and to evaluate possible eustachian tube dysfunction or obstruction.

Intraoral inspection of the hard palate, gingiva, and anterior maxillary wall were also assessed for fullness, signifying an expanding mass within the maxillary sinus. Mandibular excursion was assessed for trismus, a possible sign of pterygoid musculature invasion. Cranial nerves were tested with particular attention to nerves I through VI along with a general neurologic evaluation. A thorough neck examination was performed to evaluate for palpable lymph node metastases. Clinical examination showed a moderately firm soft-tissue swelling in the area of right maxillary buccal sulcus & right half of dorsum of hard palate extending to maximum dimension measuring 3 cm (Fig 3). The lesion was mildly painful to palpation. Some purulent drainage was obtained. This soft tissue was submitted for histopathologic examination. Imaging studies Computed tomography (CT) was advised as it prove to be an essential component in the diagnosis, staging, and follow-up of sinonasal malignancies. CT reveals an enhancing soft tissue density mass in right maxillary sinus infiltrating anterior, medial, lateral & posterior wall, roof and floor of maxillary sinus (Fig 4). Medially it is extending into nasal cavity & posterior ethmoidal sinuses. Rest of visualized paranasal sinuses is well aerated. No evidence of mucosal thickening or air fluid level is seen. Visualized upper digestive tract, part of mandible & bilateral temporomandibular joints, mastoids, bony orbits, globes, extra ocular muscles, optic nerves & retro bulbar fat appear normal. Hypertrophy of inferior nasal turbinates & nasal septum is deviated with convexity towards left side is appreciable. Histopathologic examination reveals lesion as well differentiated squamous cell carcinoma. Considering the median time from onset of symptoms until diagnosis, which is about three months, it took a long time for our patient to be diagnosed. Indeed, it has been stated that diagnosis of sinus malignancies is difficult to obtain, due to the air filled nature and deep position of structures involved. Hence, our case strongly emphasizes that misdiagnosis is crucially responsible for diagnosis delay, and efforts should be made to avoid it. The patient was referred to oncologist for further management.

Figure 1. (Panoramic radiograph revealing extracted 16 with disruption in continuity of right maxillary antrum taken at a private clinic)

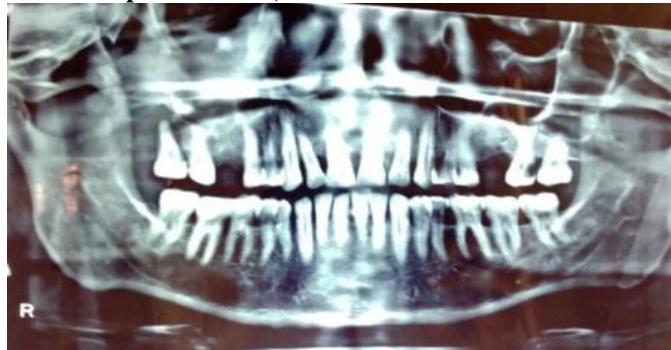


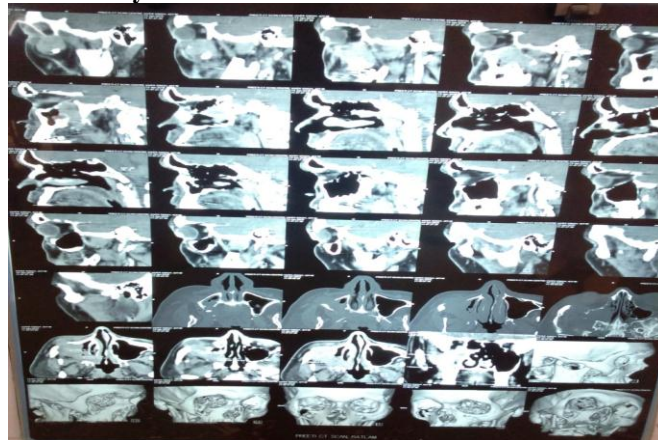
Figure 2. (Posteroanterior mandible & lateral skull of patient advised by ENT specialist)



Figure 3. Intraoral picture of expansile lesion of tumor of Right maxillary antrum (Courtesy: Outpatient department of Oral Medicine, Diagnosis & Radiology, Institute of Dental Education & Advance Studies, Gwalior)



Figure 4. Three dimensional CT reveals an enhancing soft tissue density mass in right maxillary sinus infiltrating anterior, medial, lateral & posterior wall, roof and floor of maxillary sinus



DISCUSSION

Maxillary sinus carcinomas are rare, comprising 0.2–0.8% of neoplasms, 3% of head and neck carcinomas, and 80% of all cases of paranasal sinus tumors [5]. The most commonly affected paranasal sinus is the maxillary sinus. The majority of tumors occurring in the maxillary antrum are of epithelial origin and epidermoid carcinomas correspond to more than 80% of all cases of malignant neoplasms, the adenocystic carcinoma being the second more frequent of them. The majority of patients present with an advanced stage of the disease at the first symptoms presentation. Signs that should alert the clinician to the possibility of a malignant tumour include paresthesia, radiographic evidence of irregular bone resorption and localized irregular widening of the periodontal ligament. Of these, altered sensation (paresthesia) is an especially ominous sign. Although paresthesia can be related to nerve damage secondary to previous surgical procedures, metabolic disorders or infection, it is mandatory that the possibility of a malignant neoplasm be ruled out in all patients presenting with paresthesia [6]. Additional symptoms that are commonly noted with involvement of the sinonasal complex include maxillary swelling, epistaxis, nasal obstruction or discharge, diplopia and proptosis. When these classic signs are not present, the possibility of a malignant tumour may be overlooked. The fact that bony destruction not evident on initial panoramic evaluation should remind the clinician of the limitations of this form of radiographic examination. Although destruction of maxillary sinus walls, especially the inferior antral wall, can be identified by panoramic radiography in many advanced cases of maxillary sinus malignancies. This imaging modality may not show evidence of early bone destruction. Panoramic radiography is usually made use of by the majority of clinicians for the diagnosis of antral carcinoma. While it is adequate to identify destruction of the boundaries of maxillary antrum particularly the

inferior antral wall, this imaging modality has got its own limitations when it comes to showing evidence of early bone destruction. CT and magnetic resonance imaging (MRI) are the tools of choice in such situations [7].

Invasion of structures beyond the site of origin is best characterized by CT and MRI studies. The computerized tomogram provides more details of bone invasion than magnetic resonance imaging. On CT studies all of the cases present as soft tissue masses in the maxillary sinus cavity, with 70% to 90% of cases evidencing bony destruction. CT provides more details of bone involvement than MRI. At MRI, these tumors present middle signal intensity on T1-weighted images and high intensity signal on T2-weighted images, and this method is of help in the evaluation of the posterior cranial fossa, orbit, and perineural/perivascular dissemination, besides allowing the differentiation between retained secretions and neoplastic tissue. Usually, CT and MRI may be complementary in the staging of paranasal sinus tumors, according to Loevner & Sonners [8]. Malignancies involving the maxillary sinus are usually diagnosed in the advanced stages and so determining its primary locale of origin can be difficult. Because of the non-specific symptoms, maxillary sinus carcinomas tend to remain localized for a long time before they get diagnosed resulting in inadvertent involvement of adjacent structures and delay in treatment planning. Malignant neoplasms of the maxillary antrum can be in a fairly advanced stage when the patient first reports before the clinician, even though the duration of symptoms may be less. The tumor is usually more extensive than what the clinical examination suggests and conventional radiography is insufficient to note the extent of the invasion. In this context, CT scan and MRI are valuable aids to know the extent of tumor spread and should be used more frequently. CT is the examination of choice in both primary sinonasal neoplasms (e.g., squamous cell

carcinoma, nasopharyngeal carcinoma, lymphoma, esthesioneuroblastoma, primary sinonasal melanoma and adenocarcinoma of minor salivary gland origin) and metastatic disease [9]. Sinonasal malignancies are very difficult tumors to treat and traditionally have been associated with a poor prognosis. One reason for these poor outcomes is the close anatomic proximity of the nasal cavity and paranasal sinuses to vital structures such as the skull base, brain, orbit and carotid artery. This complex location makes complete surgical resection of sinonasal tumors a challenging and sometimes impossible task. In addition, tumors of the paranasal sinuses and nasal cavity tend to be asymptomatic at early stages, appearing more frequently at late stages once extensive local invasion has occurred. The unfortunate combination of complex surrounding anatomy with late, advanced stage presentation therefore leads to the frequent local recurrence and subsequent poor outcome associated with sinonasal malignancies [10]. The clinical presentation of carcinoma of the maxillary sinus can be highly variable. Approximately, 40-60% of the cases exhibit facial asymmetry, oral cavity swelling and tumor extension medially to the nose, superiorly to orbit and ethmoidal sinus and anterolateral extension to soft tissues and cheek. Inferiorly growing tumors can involve the maxillary sinus floor, dental alveolus and palate whereas posteriorly growing tumor may reach the pterygopalatine fossa and pterygoid muscles. Through the pterygoid fossa, they may superiorly extend towards the orbital fissure and the cavernous sinus. There is also the possibility of small sized tumors getting wrongly diagnosed for chronic sinusitis, nasal polyp, lacrimal duct obstruction, or even cranial arteritis etc [11]. Pathologies involving the sinonasal complex usually manifest as maxillary swelling, epistaxis, nasal obstruction or discharge, diplopia and proptosis of the eye. In the early stages of the disease, symptoms may be totally absent. Another practical problem that makes an early detection difficult is that, symptoms if present are not specific. Blocked sinuses that do not clear, headaches, pain in the sinus areas on either sides of the nose, runny nose, nosebleeds, lump or sore inside the nose that does not heal, swelling on the face or roof of the mouth, numbness of cheeks, pain in the upper teeth, loose teeth, dentures that no longer fit well, swelling or other difficulties with the eyes. The common symptoms associated with antral carcinoma are pain (59%), followed by oral symptoms (40%), facial swelling (38%), nasal obstruction (35%) and epistaxis (25%). In the absence of these physical signs, the clinician may overlook the possibility of a malignant disease [12]. Sinonasal cancers are rare, comprising approximately 5% of head and neck cancers, and less than 1% of all malignancies. These sinuses are normally lined by thin, flat cells called squamous cells. The abnormal division of these cells results in squamous cell carcinoma. The following conditions may predispose a person to increased risk of developing a maxillary sinus cancer. Exposure to certain

workplace chemicals or dust, work in furniture-making, work in sawmill, carpentry, shoemaking, metal-plating, flour mill or bakery work, being male, age more than 40 years, smoking; tobacco use, chronic sinusitis. Treating maxillary sinus cancer is challenging because of the proximity of critical structures, such as the eye and the brain, which preclude wide surgical excision and high-dose radiotherapy. These difficulties with maxillary cancer treatment are linked to the complex anatomy of the paranasal sinus region, and a propensity for late presentation due to the absence of symptoms in an early stage of disease. The clinical course is indolent at most and a substantial number of patients have advanced disease at the time of diagnosis. Combined-modality therapy consisting of surgery and radiotherapy with or without intra arterial chemotherapy is generally used for the treatment. Although epidemiologic, incidence, and survival trends have been studied extensively for maxillary sinus squamous cell carcinoma, far less is known about metastasis. Diagnosis most often occurs at an advanced stage due to nonspecific symptoms early in disease, with over 80% of patients reportedly presenting with at least stage T3 disease. Local recurrence has proven to be the primary impediment to the treatment of maxillary squamous cell carcinoma, highlighting the importance of local control. Traditionally, lymph node involvement at the time of diagnosis of maxillary sinus malignancies has been considered rare due to limited lymphatic drainage. However, maxillary squamous cell carcinoma has been demonstrated to have a higher incidence of nodal involvement upon diagnosis [13]. The topographic distribution of lymph node metastasis in the neck usually is dependent on the tumor site, contiguity and high number of capillaries. Patients with tumor extension to the nasopharynx and oral cavity present a higher incidence of cervical metastases than in other regions. St. Pierre and Baker have emphasized the worst prognosis when associated with lymph node metastasis [14]. Distant metastasis incidence usually is low in cases of epidermoid carcinoma of the maxillary sinus and is more frequent in the poorly differentiated subtype. Frequently, adenocystic carcinoma distant metastases occur tardively. Lungs and bones are the sites most frequently affected. With lack of clear evidence strongly supporting optimal treatment employed in maxillary sinus squamous cell carcinoma, especially in the absence of neck metastasis, a population-based study reflecting the metastatic tendency and clinical approach to different stages of maxillary SCC could prove valuable to otolaryngologists in establishing adequate guidelines for therapy [15]. In the vast majority of cases, clinical examination of patients presenting with pain and swelling of the jaws will reveal lesions of dental etiology, most commonly related to pulpal or periodontal pathology. However, when faced with such a situation, the dental practitioner must consider the possibility of a non odontogenic cause. When formulating a differential diagnosis for a swelling in proximity to the jaws, it is often



helpful to determine first, by radiographic examination, whether the enlargement originates primarily in bone or in the extra osseous soft tissue. Common intraosseous expansile radiolucent lesions would include central giant-cell granulomas, developmental odontogenic cysts (e.g., dentigerous cyst, odontogenic keratocyst), as well as odontogenic tumours (e.g., ameloblastoma). When faced with an expansile radiopaque or mixed radiopaque–radiolucent intraosseous lesion, the practitioner should also consider the possibility of a benign fibro-osseous lesion. An infection of odontogenic origin is the most common cause of a soft tissue swelling of the maxillary buccal vestibule. Less common reactive or neoplastic lesions of connective tissue origin, such as inflammatory myofibroblastic tumor, nodular fasciitis, myofibroma and desmoplastic fibroma should also be included in the differential diagnosis.

Finally, the possibility of a malignant neoplasm of the maxillary antrum, although uncommon, should be considered [16].

Biopsy:

Once the site of the tumor is identified, tissue diagnosis is required. A fundamental principle is to obtain representative tissue by the least invasive method possible. An optimal procedure for biopsy of sinonasal malignancies is endoscopic approach through the nares. This approach offers several advantages, including excellent visualization, low morbidity, and minimal alteration of the tumor and its surrounding structures. Even small, lateral tumors within the maxillary sinus may be accessible with the creation of a middle meatal antrostomy, visualization with a 30° or 70° endoscope, and biopsy using a long, curved giraffe instrument. However, an endoscopic approach is not used for either debulking or an attempted resection of the tumor. When the tumor presented itself at the nasal vestibule, punch biopsy in the office was considered [17]. However, it is important to ensure by clinical examination that the mass is neither contiguous with the cerebrospinal fluid space nor highly vascular. If the mass compresses easily or appears vascular, further imaging should be obtained prior to biopsy. In cases where a maxillary sinus tumor is not accessible transnasally with the endoscope, a canine fossa puncture is combined with endoscopic visualization and biopsy. Open biopsy is rarely necessary for poorly accessible tumors, through either the Caldwell-Luc approach or an external ethmoidectomy (Lynch) incision. Biopsy confirmed the presence of a malignant tumor of the maxillary sinus. Immunohistochemistry is an important tool that can be valuable in reaching a diagnosis in such a situation. It uses specific antibodies to stain conventionally prepared tissue sections. The antibodies recognize specific antigens expressed by different tumors, depending on their cell of origin [18].

Management: The most effective barrier against tumors propagation is the integrity of the periosteum that is particularly more resistant in two critical areas: the skull base and orbit. The surgery/postoperative radiotherapy combination results in survival rates higher than those for radiotherapy alone. Tumors causing skull base destruction or involving the internal carotid artery are irresectable. In these cases, even with combined surgery and post-surgical radiotherapy, they do not present a good prognosis, so this method is preferable for patients who have developed distant metastases. Radiotherapy is accepted as a palliative method in inoperable cases. Some authors have recommended an aggressive treatment for patients with metastatic disease. The poor prognosis of maxillary sinus carcinoma may be due to the delayed detection of extensive tumors and the impossibility of a complete surgical. The five year survival rate ranges between 20% and 40% [19]. Ohngren has divided the maxillary antrum into posterosuperior and anteroinferior segments, drawing a line from the mandible angle on the profile face image, and has suggested that a tumor confined to the anteroinferior portion could present a better prognosis. Patients with perineural invasion had an unfavourable prognosis. However, an appropriate treatment strategy in terms of surgical procedure, radiotherapy methods and their sequence is still a matter of controversy. Local control is a particularly difficult problem, with the majority of failures occurring at the primary site. Surgical removal of the tumor with postoperative radiation therapy remains the standard of care for resectable lesions. Improved reconstructive techniques including micro vascular free flaps and prosthetic obturators have significantly decreased the functional and cosmetic morbidity from aggressive surgical resection. The type of surgical resection required for tumors of the maxillary sinuses is dictated by each lesion's anatomic location and sites of extension. Tumors originating in the maxillary sinus are removed by some form of maxillectomy. Intraoral mucosal incisions can be made on the hard palate and extended into the gingival-buccal sulcus, allowing elevation of the cheek soft tissues off the anterior maxillary wall. Osteotomies along the inferior maxilla are then made with a high-speed power saw and osteotome [20]. Larger tumors of the maxillary sinus are resected by subtotal maxillectomy, a procedure removing at least two walls of the sinus including a portion of the hard palate [21]. The tumor location determines the particular subtotal variant that is appropriate. Orbital exenteration is included in few cases of total maxillectomy. The optimum management of carcinoma arising in the maxillary sinus remains undefined. Therapeutic approaches include surgery, radiation and systemic and topical chemotherapy in a variety of combinations and sequences. Maxillary sinus malignancies have a poor prognosis, with the five-year cause-specific survival rate being 43%.



Advanced T stage, regional and distant metastasis are highly predictive of poor prognosis. One of four different treatment modalities, including intra-arterial (IA)-Induction chemotherapy (ICT), intravenous (IV)-ICT, concurrent chemo radiation therapy (CCRT), and surgical resection. Treatment modality is selected as a primary treatment based on the TNM stage, performance status, age, and co-morbidity. Super selective IA infusion of chemotherapeutic drugs attempted via a series of processes. Cisplatin (100 mg/m²) can be administered via a micro catheter into the internal maxillary artery over two hours on day 1, and then 5-FU (1000 mg/m²/day) is continuously infused from day 1 to day 5 over 120 hours through the IV route. A standard hydration and mannitol diuresis regimen is applied. The entire procedure is repeated 2–3 times every 3–4 weeks. The IV-ICT is performed 2–3 times every four weeks as well [22]. All patients receiving ICT are re-evaluated for tumor response with CT and/or MRI at least 4–6 weeks after the completion of ICT. The decision to perform surgery after ICT is based on the tumor response. The chemotherapeutic agent used in the CCRT group is cisplatin. During radiation therapy, cisplatin (30 mg/m²) is administered by a weekly schedule on days 1, 8, 15, 22, 29, 36, 43, and 50, or cisplatin (100 mg/m²) is administered every 3 weeks on days 1, 22, and 43. All patients treated with CCRT are evaluated for tumor response, and then the next treatment modality, surgical resection or salvage chemotherapy, was determined. The periodic follow-up is done at least 6–8 weeks after the completion of radiation therapy. Three-dimensional conformal radiation therapy (3DCRT) is applied as an external radiation therapy technique. The total dose of 55–60 Gy with 1.8–2.0 Gy daily fractions five times per week is given to the clinical target volume (CTV) in postoperative adjuvant radiation therapy. In the case of CCRT, the total dose of 70–75 Gy in 35–40 fractions is given with a shrinking-field technique; 50 Gy

is given to the CTV with daily fractions of 1.8 Gy five times per week, and followed by 20–25 Gy to the gross tumor volume (GTV) [23].

CONCLUSION

The accurate analysis of the tumor local extent and dissemination allowed by CT and MRI plays a significant role in the surgical planning, also influencing the therapeutic conduct and prognosis. Biopsy of the lesion confirmed the clinical suspicion of a rare malignant tumor of maxillary sinus origin. Clinicians should be aware that the clinical signs and symptoms that might lead one to suspect a malignancy might be relatively nonspecific, potentially leading to a delay in diagnosis. Therefore, it is important for the dental practitioner to maintain a high index of suspicion to allow for early recognition and referral of these patients. Close follow-up is required in all cases involving swellings of the head and neck. In the presence of ominous signs, such as pain and swelling with associated paresthesia, or if conventional therapy fails to resolve the swelling rapidly, prompt referral for biopsy and advanced imaging techniques, such as computed tomography, is mandatory. Carcinoma of the maxillary antrum can present itself as a diagnostic challenge to the general dental practitioner and can occasionally complicate the outcome of routine dental treatment. Patients presenting with pain and swelling of jaws, when examined clinically will reveal lesions of dental origin, of either pulpal or periodontal pathology. However the dentist must always consider the possibility of non-dental causes for common complaints like pain and mobility of teeth especially of the upper jaw. An early diagnosis can be made possible by increasing the awareness of the people regarding the symptomatology and encouraging them to seek medical attention at the beginning in order to increase chances of survival and to reduce morbidity.

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