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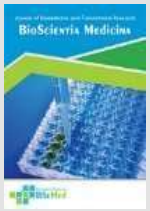

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The Profile of Sinonasal Tumors with Orbital Involvement in Dr. M. Djamil General Hospital, Padang, Indonesia: A 10-Year Overview

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A B S T R A C T

Background: Sinonasal tumors are rare tumors, either malignant or benign, that vary greatly based on the origin and primary tumor location in the sinonasal tract. The close anatomical relationship between the sinonasal tract and the orbital cavity makes orbital involvement very common (50%-80%) in sinonasal tumors, and this indicates a negative prognostic factor in sinonasal malignancy. The purpose of this study is to demonstrate the profile of sinonasal tumors with orbital involvement in our center. **Methods:** Retrospective study from oncology subdivision files and medical records from January 2011 – December 2020. Collected data including age, gender, the clinical manifestations of orbital involvement, primary location, histopathology, and management of sinonasal tumors. **Results:** There were 35 patients examined by the oncology subdivision either directly came or consulted from the ENT department, consisting of 18 (51.4%) males and 17 (48.6%) females. The age of patients ranged from 11 to 83 years old. with the most common age groups being 41-50 and 51-60 (25.7% in each age group). The majority of the patients (77.1%) had presented with proptosis. Maxillary sinus was the most common (45.7%) primary site of tumors, and squamous cell carcinoma was the most common (51.4%) histopathology found. Most of the patients (37.1%) were treated with a combination of chemotherapy and radiotherapy. **Conclusion:** Orbital involvement commonly occurs in malignant sinonasal tumors with proptosis as a major clinical presentation. A combination of chemotherapy and radiotherapy was the most common practice management because the tumors were unresectable at the time of presentation.

1. Introduction

Nasal and paranasal sinus (sinonasal) tumors are rarely found tumors, representing only 1% of all malignancies and 5-10% of head and neck tumors. More than 80% of sinonasal tumors are of epithelial origin, while the remainder are of cartilage and soft-tissue origin. Twenty-five percent of sinonasal tumors are benign, and 75% of them are malignant. Squamous cell carcinoma (SCC) is the most common pathology in sinonasal tumors, accounting for 50% of malignant sinonasal tumors. Most sinonasal tumors are found in people aged 50-60 years and are more common in men with an estimated male-to-female ratio of 2:1.[1-3] The early stage of sinonasal tumors usually have non-specific symptoms and are often misdiagnosed as milder diseases, such as rhinosinusitis. As a result, the diagnosis is often delayed until the diseases become more advanced due to the tumor invasion into the surrounding structures. There is frequent orbital involvement in the sinonasal tumors due to the anatomical relationship between the sinonasal tracts and the orbits. Orbital involvement was found in 50-80% of sinonasal tumor cases, which is a poor prognostic factor in sinonasal malignancies.[4-7] A study by Alabi et al. in Nigeria showed that 41% of malignant sinonasal tumors presented first to the ophthalmologist with a complaint of proptosis with visual impairment and/or facial asymmetry without

prominent rhinology symptoms. This showed that ophthalmologists had a significant contribution to the detection and diagnosis of sinonasal tumors.[8]

Diagnosis of sinonasal tumors with orbital involvement is made through detailed history taking, physical examinations, and imaging, such as CT-Scan and MRI. A histopathology examination is needed for the definitive diagnosis. Orbital involvement may occur due to direct bone macroscopic erosion or microscopic neurovascular invasion. Ocular involvement signs and symptoms include proptosis, visual impairment, limited movement of extraocular muscles, diplopia, and epiphora. [2,5,9] Management of sinonasal tumors with orbital involvement could be done using various approaches, including surgery, radiotherapy, chemotherapy, or a combination of those treatment modalities. The choice of treatment modalities depends on whether the tumor is malignant or benign and the stage of the tumor.[1,2,5] Because there is limited literature regarding sinonasal tumor cases with orbital involvement and no study reviewed such cases in Dr. M. Djamil General Hospital Padang over the last ten years period, we were encouraged to conduct a study regarding the profile of sinonasal tumors with orbital involvement found in Dr. M. Djamil General Hospital Padang from January 2011 until December 2020.

2. Methods

This retrospective descriptive study involved a sinonasal tumor patient with orbital involvement in Dr. M. Djamil General Hospital Padang. All patients met the inclusion and exclusion criteria and were chosen using the total sampling method, resulting in a total of 35 patients. The inclusion criteria of this study were outpatients at the oncologic division of the ophthalmology polyclinic (who came directly or consulted from the ENT department) and inpatients at the ophthalmology ward or consulted from the ENT ward who were diagnosed with sinonasal tumors with orbital involvement based on ophthalmology examinations and diagnostic tests (CT-Scan and histopathology examination) with complete medical record data from January 2011 until December 2020. The exclusion criteria were patients with sinonasal tumors with orbital involvement that were not primary tumors of sinonasal tissue.

The variables of this study were age, gender, signs and symptoms of orbital involvement, tumor location, histopathology result, and the treatment of sinonasal tumors with orbital involvement. Age was defined as the patient's lifespan (from born until diagnosed and getting treatment for the sinonasal tumor). Gender was defined as anatomical and biological differences that classified as male and female. Signs and symptoms of orbital involvement were all subjective and objective findings on history taking and ophthalmology examination. The primary tumor location was the location of the sinonasal tumor origin based on the CT-Scan image. Histopathology result was defined as the morphology of neoplastic cells found in tumor tissue samples based on histopathology examination in the Pathology Laboratory. Treatment of sinonasal tumors was a treatment modality given to the patients. Sinonasal tumors with orbital involvement were tumors of the nasal cavity and paranasal sinuses that disrupt the integrity of the orbital tissue by compression, local destruction, and suppression of the orbital wall and contents, resulting in impairment of normal orbital function.[1,10,11] Data from this study were tabulated and presented descriptively as frequency distribution for each variable.

3. Results

There was a total of 35 patients in this study. The distribution of age and gender characteristics of the patients is shown in Table 1. The most common age groups in this study were 41-50 years old and 51-60 years old, accounting for 25.7% of cases each. Based on gender, the number of male and female patients was comparable, with 18 (51.4%) and 17 (48.6%) patients, respectively. Thus, the male-to-female ratio in this study was 1.1:1. The signs and symptoms of orbital involvement in sinonasal tumor patients are shown in Table 2. The majority of sinonasal tumors

with orbital involvement patients had more than one sign and symptom suggesting an orbital involvement. Proptosis was the most common clinical manifestation, affecting 27 patients (77.1%). Other clinical manifestations of orbital involvement that were also commonly found were limited ocular movement in 23 patients (65%) and visual impairment in 21 patients (60%). The least common clinical manifestation of orbital involvement was epiphora, found only in 8 patients (22.8%) in this study. The location of the primary tumor in this study is shown in Table 3. Based on diagnostic imaging (CT-Scan) results, most sinonasal tumors originate from the maxillary sinus (45.7%) and nasal cavity (37.1%). Meanwhile, the least sinonasal tumors were found to originate from the sphenoid sinus and frontal sinus, accounting for 2.8% of cases each. The histopathology type of sinonasal tumors is shown in Table 4. Sinonasal tumors with orbital involvement are usually malignant tumors. The most common malignant histopathology types found in this study were squamous cell carcinoma in 18 cases (51.4%) and sinonasal undifferentiated carcinomas (SNUCs) in 5 cases (14.3%). Non-Hodgkin lymphoma and adenoid cystic carcinoma were the least malignant histopathology type, with 2 cases (5.7%) each. The majority of benign sinonasal tumors were exophytic papillomas, with 2 cases (5.7%) found. Other benign histopathology types found were trabecular ossifying fibroma, inverted papilloma, and fibroma, accounting for 1 case (2.8%) each. Table 5 shows the treatment modalities for the management of sinonasal tumors with orbital involvement in this study. According to Table 5, the most common treatment modality was the combination of chemotherapy and radiotherapy (chemoradiation), which was used for 13 cases (37.1%) of this study. The treatment modality involving the Oncologic Division of the Ophthalmology Department was maxillectomy with exenteration performed in 10 cases (28.6%). The least used treatment modality in this study was chemotherapy alone, which was performed only in two patients (5.7%).

Table 1. Distribution by age and gender characteristics.

Age group (years)	**Gender**		**Total**
	Male (people)	**Female (people)**	
0-10	0 (0%)	0 (0%)	0 (0%)
11-20	0 (0%)	2 (5.7%)	2 (5.7%)
21-30	1 (2.8%)	0 (0%)	1 (2.8%)
31-40	5 (14.3%)	0 (0%)	5 (14.3%)
41-50	4 (11.4%)	5 (14.3%)	9 (25.7%)
51-60	3 (8.6%)	6 (17.1%)	9 (25.7%)
61-70	4 (11.4%)	4 (11.4%)	8 (22.8%)
71-80	0 (0%)	0 (0%)	0 (0%)
81-90	1 (2.8%)	0 (0%)	1 (2.8%)
Total	**18 (51.4%)**	**17 (48.6%)**	**35 (100%)**

Table 2. Distribution of signs and symptoms of orbital involvement in sinonasal tumor.

Clinical signs and symptoms	**Total (people)**	**Percentages**
Proptosis	27	77.1%
Limited ocular movement	23	65 %
Visual impairment	21	60%
Diplopia	10	28.6%
Epiphora	8	22.8%

Table 3. Distribution of primary sinonasal tumor location.

Location of the primary tumor	Total (people)	Percentages
Maxillary sinus	16	45.7%
Nasal cavity	13	37.1%
Ethmoid sinus	4	11.4%
Sphenoid sinus	1	2.8%
Frontal sinus	1	2.8%
Total	**35**	**100%**

Table 4. Distribution of histopathology types of sinonasal tumor.

Histopathology type	Total (people)	Percentages
Squamous cell carcinoma	18	51.4%
Sinonasal undifferentiated carcinomas	5	14.3%
Transitional cell carcinoma	3	8.6%
Non-Hodgkin lymphoma	2	5.7%
Adenoid cystic carcinoma	2	5.7%
Exophytic papilloma	2	5.7%
Trabecular ossifying fibroma	1	2.8%
Inverted papilloma	1	2.8%
Fibroma	1	2.8%
Total	**35**	**100%**

Table 5. Distribution of treatment modalities for sinonasal tumors with orbital involvement.

Treatment modalities	Total (people)	Percentages
Chemotherapy and radiotherapy	13	37.1%
Maxillectomy and exenteration	10	28.6%
Radiotherapy	4	11.4%
Maxillectomy	3	8.6%
Endoscopic tumor extirpation	3	8.6%
Chemotherapy	2	5.7%
Total	**35**	**100%**

4. Discussion

There was a total of 53 cases of sinonasal tumors with orbital involvement found in the Oncologic Division of Ophthalmology Department in Dr. M. Djamil General Hospital Padang from January 2011 until December 2020, but only 35 of them were eligible based on the inclusion and exclusion criteria of this study. Out of 35 eligible patients, only 9 (25.7%) of them (25.7%) presented directly to the Ophthalmology polyclinic, while the remaining 26 (74.3%) patients were consulted by the ENT department.

There was a considerably wide age range in this study that consisted of patients aged from 11 to 83 years old. In general, the most common age group found was 41-50 and 51-60 years consisting of 9 (25.7%) patients each. This study did not classify the age group according to the histopathological type of sinonasal tumors (benign or malignant). Shirazi et al. conducted a study regarding the sinonasal tumors spectrum in North India over 10 years, and they also found a wide age group range from 0-10 years to 81-90 years, and the malignant sinonasal tumors were most commonly found in the younger age group which was 21-30 years.[12]

The number of male patients was slightly higher than that of female patients in this study, with a male-to-female ratio of 1.1:1. Shirazi et al. found a similar male-to-female ratio of 1.2:1 for malignant sinonasal

tumors, while there was a male preponderance found for benign sinonasal tumors with a male-to-female ratio of 3:1. Several studies stated that there was a tendency for men to suffer from sinonasal tumors more than women with a male-to-female ratio of 2:1. On the other hand, Alabi et al. in Nigeria found that there were fewer male patients compared to female patients with a male-to-female ratio of 1:1.2. Thus, the tendency of specific genders to suffer sinonasal tumors remains uncertain because it also may be affected by a different type of sinonasal tumors and occupational exposure in various countries.[2,8,12]

In this study, clinical manifestations of orbital involvement in sinonasal tumors mostly were proptosis (77.1%), followed by limited ocular movement (65%), visual impairment (60%), diplopia (28.6%), and epiphora (22.8%). Generally, there was more than one sign and symptom of ocular involvement in each sinonasal tumor patient. The direction of proptosis is an important clue for a mass location that causes a space-occupying mass effect on the orbital cavity. A primary tumor located in the maxillary sinus usually causes non-axial proptosis with superior displacement of the globe, while a primary tumor originating from the ethmoid sinus will cause non-axial proptosis with an inferolateral displacement of the globe. This space-occupying mass effect may also interfere with the optical nerve, resulting in visual impairment. The other mechanisms for visual impairment in sinonasal tumors are peritumoral inflammation reaction and direct infiltration of tumor cells to the optical nerve. Limited eye movement may occur due to mechanical restriction due to tumor mass effect or paralysis of the cranial nerve that innervates the extraocular muscles. This limitation of eye movement then will cause diplopia. Epiphora was commonly found in a tumor located in the nasal cavity because an enlarged tumor mass in the nasal cavity will obstruct the nasolacrimal ducts, interfering with tear drainage. Thus, it can be concluded that clinical signs and symptoms of sinonasal tumors are related to the location of the primary tumor and its extension. Consistent with our study, Chu et al. also found that the most common manifestations of orbital involvement in sinonasal tumors were proptosis (35.5%), followed by visual impairment and diplopia (21.6%). Alabi et al. also showed that 41% of sinonasal tumor patients presented first to the ophthalmologist with a complaint of proptosis with visual impairment and/or facial asymmetry without prominent rhinology symptoms.[3,8,9,13]

The most common locations of the primary sinonasal tumor cases were the maxillary sinus, nasal cavity, and ethmoid sinus. The largest percentage of primary tumor locations in this study were maxillary sinus and nasal cavities, which were 35.7% and 37.1% of cases, respectively. Four patients (11.4%) had primary sinonasal tumors located in the ethmoid sinus, and only 1 patient (2.8%) had sinonasal tumors originating from the frontal sinus. The literature stated that the majority of sinonasal tumors originate in the maxillary sinus (60%), followed by the nasal cavity (20-30%) and ethmoid sinus (10-15%). In line with our study, Shirazi et al. also found that the maxillary sinus was the most common location of sinonasal tumors, accounting for 62% of cases. The manifestations of orbital involvement may vary according to the location of the sinonasal tumor. The tumor of the infrastructures of the maxillary sinus usually may expand to the oral cavity, nasal cavity, and soft tissue of the cheek. Meanwhile, a primary tumor of the supra-structure tends to extend to pterygomaxillary space, infratemporal fossa, orbits, and anterior cranial fossa. Primary tumor originates from the nasal cavity and may extend to the hard palate, maxillary antrum, or orbits. The primary tumor originates from the ethmoid sinus and may extend to the sphenoid sinus, orbits, nasal cavity, antrum or maxillary, and nasopharynx. Due to their anatomical locations, a tumor originating from the frontal and sphenoid sinus rarely extends to the orbits but often extends intracranially.[1,5,9,12]

Squamous cell carcinoma is the most common type of malignant tumor found in the sinonasal area, contributing to 50% of cases. The majority of benign

sinonasal tumors are exophytic papillomas, with an incidence of 0.5% to 4% of all sinonasal tumor cases. Alabi et al., in their study, showed that most malignant sinonasal tumors were squamous cell carcinoma (60%) and adenocarcinoma (18.2%). Similarly, Shirazi et al. also found that squamous cell carcinoma (40.6%) was the most common histopathology type in malignant sinonasal tumors cases, and the most common histopathology found in benign sinonasal tumors was Schneiderian papilloma (7.1%). According to the histology examination, the histopathology type of sinonasal tumors with orbital involvement dominated by malignant sinonasal tumors, including squamous cell carcinoma with 18 cases (51.4%), sinonasal undifferentiated carcinomas with 5 cases (14.3%), transitional cell carcinoma with 3 cases (8.6%), and non-Hodgkin lymphoma as well as adenoid cystic carcinoma with 2 cases (5.7%) each. Benign sinonasal tumors found in this study were exophytic papilloma with 2 cases (5.7%), trabecular ossifying fibroma, and fibroma with 1 case (2.8%) each.[1,2,9,12]

Management of sinonasal tumors with orbital involvement depends on malignancy and the stage of the tumor. The treatment modalities used in this study for benign sinonasal tumors were endoscopic tumor extirpation in 3 patients and maxillectomy in 2 patients. The majority of malignant sinonasal tumors with orbital involvement in this study were managed using a combination of chemotherapy and radiotherapy (37.1%), followed by maxillectomy and exenteration (28.6%). Radiotherapy alone was used in 4 patients (11.4%), while chemotherapy alone was used in 2 patients (5.7%). Only 1 patient with malignant sinonasal tumors had maxillectomy. Orbital involvement in patients with malignant sinonasal tumors indicates that the tumor has reached stage ≥ III. Surgery may be indicated in malignant sinonasal tumors up to stage III and IVA, accompanied by additional surgical procedures (such as neck dissection) if there is cervical lymph node involvement or preoperative chemotherapy for reducing the tumor size. In more advanced-stage tumors with intracranial extension, a combination of chemotherapy and radiotherapy is the treatment of choice because the tumor is not resectable. Non-surgical treatment of sinonasal tumors may also be indicated in tumors originating from sphenoid sinus and tumors with adenoid cystic carcinoma type. Consistent with our study, Alabi et al. showed that a combination of chemotherapy and radiotherapy was the most common treatment modality used for patients with sinonasal malignancies, accounting for 45.5% of all malignant sinonasal tumors.[5,8,10,11]

5. Conclusion

Sinonasal tumors with orbital involvement are commonly found in patients aged 41-50 years and 51-60 years with a comparable male-to-female ratio. The most common clinical manifestations of sinonasal tumors with orbital involvement found were proptosis and limited ocular movement. The majority of sinonasal tumors with orbital involvement originate from the maxillary sinus and nasal cavity. These tumors are dominated by malignant tumors, with squamous cell carcinoma as the most common malignant sinonasal tumor type. Most malignant sinonasal tumors with orbital involvement were managed with a non-surgical approach using a combination of chemotherapy and radiotherapy because the tumor was already unresectable at the time of diagnosis.

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