

Introduction

Human papillomavirus (HPV) - Related Multiphenotypic Sinonasal Carcinoma (HMSC) is a recently described neoplasm as a provisional entity in the most recent WHO classification of head and neck tumors, it was first identified in 2013 by Bishop et al. followed by an additional expanded cohort in 2017, who first suggested that these tumors have a favorable outcome [1], [2]. To date, more than 70 cases of HMSC have been reported, aiming to gain a better understanding of clinical features and the biology of this rare tumor [3].

Case Report

A 50-year-old female patient was referred to the Head and Neck Surgical Oncology department at King Abdullah Medical City (KAMC) for a painless right cheek swelling gradually progressing over the last 4-months, associated with epiphora, nasal obstruction and rhinorrhea. On physical exam, a painless large round-shaped mass was occupying the right nasolabial fold, approximately 5 × 3 cm in size. On flexible nasolaryngoscopy the left nostril was clear, while there was a complete obstruction of the right nostril with the right lateral nasal wall deviated medially. There was no palpable neck lymph node enlargement.

A Computed Tomography (CT) scan of the paranasal sinuses (PNS) showed enhancing expansile multilocular lytic mass lesion, causing bone remodeling with cortical shell appearance, involving the antero - inferior aspect of right Maxilla and extending to hard palate, right nasal cavity and right maxillary sinus cavity, measuring 3.4 x 3.1 x 5.1cm (TS x AP x CC respectively). (Figure 1). Magnetic Resonance Imaging (MRI) of the paranasal sinuses (PNS) showed in addition to CT finding, the lesion invading the right middle and inferior nasal turbinates obstructing the right nasal cavity, lacrimal sac and Nasolacrimal duct. Other imaging including CT chest/abdomen with contrast were negative. Leading to a clinical stage of T3N0M0.



Fig. 1. CT scan of PNS.

The patient underwent right subtotal maxillectomy with neck dissection and right DCR reconstructed with skin graft and obturator. The resected tumor size was 5.5 cm, surgical cut margins were involved superiorly and laterally to the bone but not the teeth, no necrosis or lymphovascular invasion was detected. Diagnoses of HPV related Multiphenotypic Sinonasal Carcinoma was made. The patient was started on adjuvant chemoradiation therapy (Adjuvant CCRT/ Cisplatin) and finished the course.

After 2 months from the last chemoradiation session, paranasal MRI and CT chest/abdomen had been done, in which paranasal MRI showed a newly developed enhancing and destructive lesion at the left frontal bone, and bilateral mandibular body patchy enhancing which indicates a new onset metastasis. CT scan showed multiple lytic lesions in the left posterior 7th rib, S1 vertebral body and right pubic ramus, after that MSK-Bone scan was done and showed scintigraphic evidence of multiple axial and appendicular active osseous metastasis as correlated with the previous CT scan finding of multiple-site metastasis. The patient was started on Chemotherapy (adjuvant Cisplatin / Docetaxel) and immunotherapy (Cetuximab).

Methods

A comprehensive literature review was conducted using the MEDLINE and EMBASE databases with a primary objective of identifying all documented cases of HMSC in English literature from January 2010 to December 2020 leading to the inclusion of 12 articles for review.

After reviewing the selected articles, data were pooled including 73 cases. Information regarding patient demographics, tumor site, tumor size, treatment modality, and local recurrence was collected and analyzed using SPSS Statistics Software (version 25; IBM).

Results

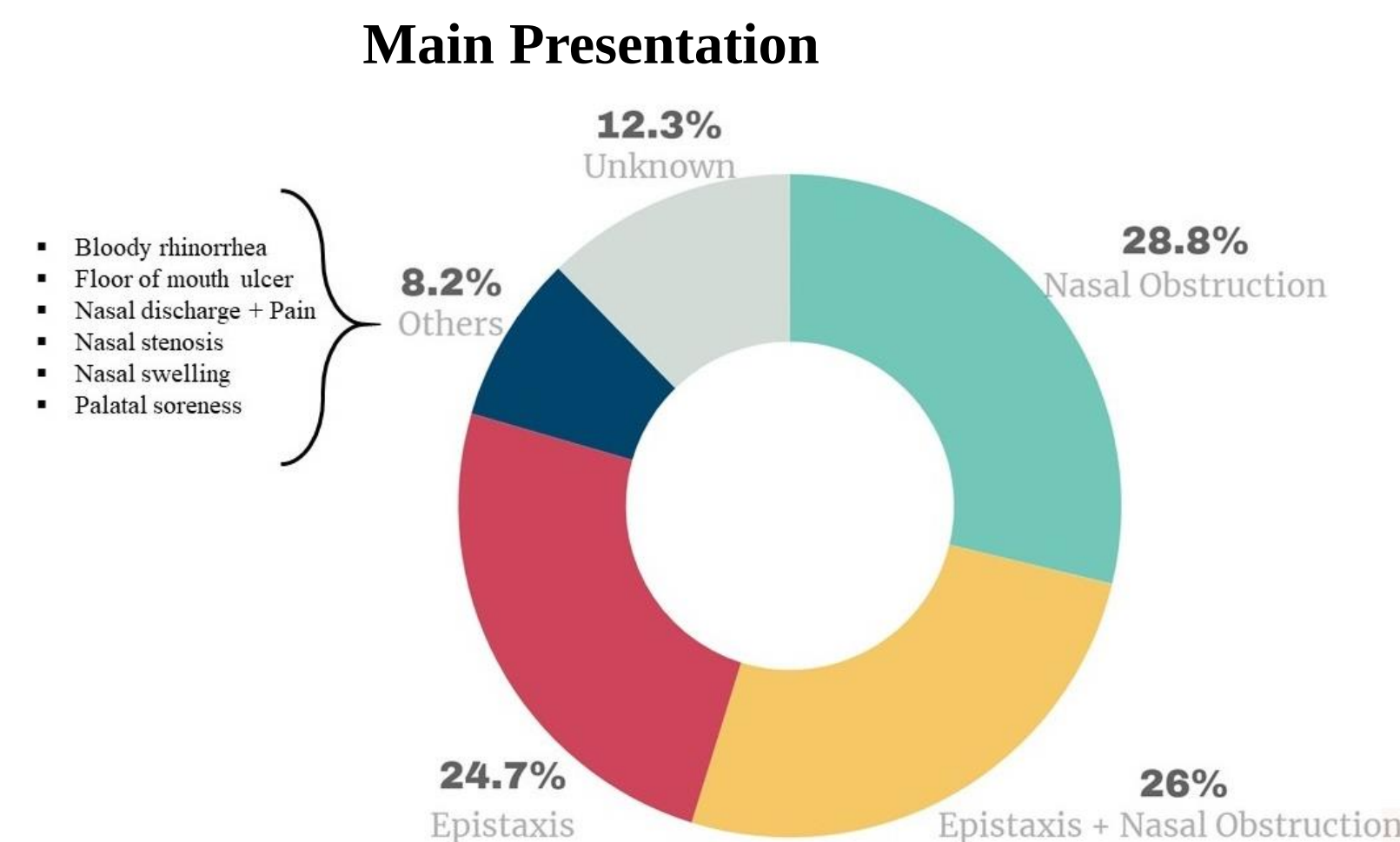


TABLE 1 | Relation between the outcome and type of treatment.

Variables	DM	LR	LR + DM	NED	Unknown
Surgery	1 (1.4%)	5 (6.8%)	1 (1.4%)	6 (54.5%)	3 (4.1%)
Surgery + Chemotherapy	1 (1.4%)	-	-	-	-
Surgery + Radiotherapy	1 (1.4%)	5 (6.8%)	1 (1.4%)	4 (36.4%)	-
Surgery + Radiotherapy + Chemotherapy	-	-	-	1 (9.1%)	-
Radiotherapy	-	-	-	-	1 (1.4%)
Radiotherapy + Chemotherapy	-	1 (1.4%)	-	-	-
Unknown	-	2 (2.7%)	-	-	10 (13.7%)
Total (n, %)	3 (4.1%)	13 (17.8%)	2 (2.7%)	11 (100%)	14 (19.2%)

DM Distant Metastasis, **LR** Local Recurrence, **NED** No Evidence of Disease.

On post-operative follow-up, 40 cases (54.8%) reported disease-free survival, however after exclusion of cases with follow-up period less than 23 months, only 11 cases (15%) were left, which is insufficient for illustrating a long-term prognosis.

Discussion

The principal clinical manifestation is epistaxis and nasal obstruction, one case has been reported to date with distant metastasis to orbital and intracranial extension at initial presentation, the patient underwent surgical resection of the tumor with adjuvant radiotherapy, and the patient died 11 months post surgically [4]. HMSC appears to have a relatively indolent prognosis, with frequent local recurrence (up to 20%). Most HMSC local recurrences occurred between 24 to 60 month after the treatment, and no recurrences occurred before 23 months, but two cases reported late recurrence at 130 and 192 months [5],[6]. Another case developed a second recurrence after 348 months [1]. The follow-up period for local recurrence group showed a significant P value of less than 0.05 (Table 2), which indicates the possibility of late tumor recurrence, and thus the importance of long-term and possibly life-long surveillance.

Four reported cases in the literature progressed to distal metastasis, two of those developed additional local recurrence. The fifth case, which is ours, presented just after 6 months with early and progressive multiple sites metastasis despite the patient undergoing through gross total resection and adjuvant chemoradiotherapy. Our case considered the first presented with such early and aggressive metastasis, which indicates a possibility of disease aggression, and highlight the need to accordingly stratify patients to determine the need for adjuvant therapy .

Being a recently recognized entity with a limited number of reported cases, optimal treatment guidelines are not established. The consensus in the literature for HMSC has suggested surgery with close monitoring as the primary treatment modality[3],[2]. Adjuvant radiotherapy have been applied with many patients with varied outcomes, it is routinely indicated in cases with involved margins considering local recurrences are not rare. However, in cases of clear margins the role of radiotherapy remains unclear. One recent study suggested that the addition of adjuvant RT may not impact long term survival but may increase the disease-free interval, as its effect on the disease-free interval approached statistical significance despite the small number of cases included in analysis [7].

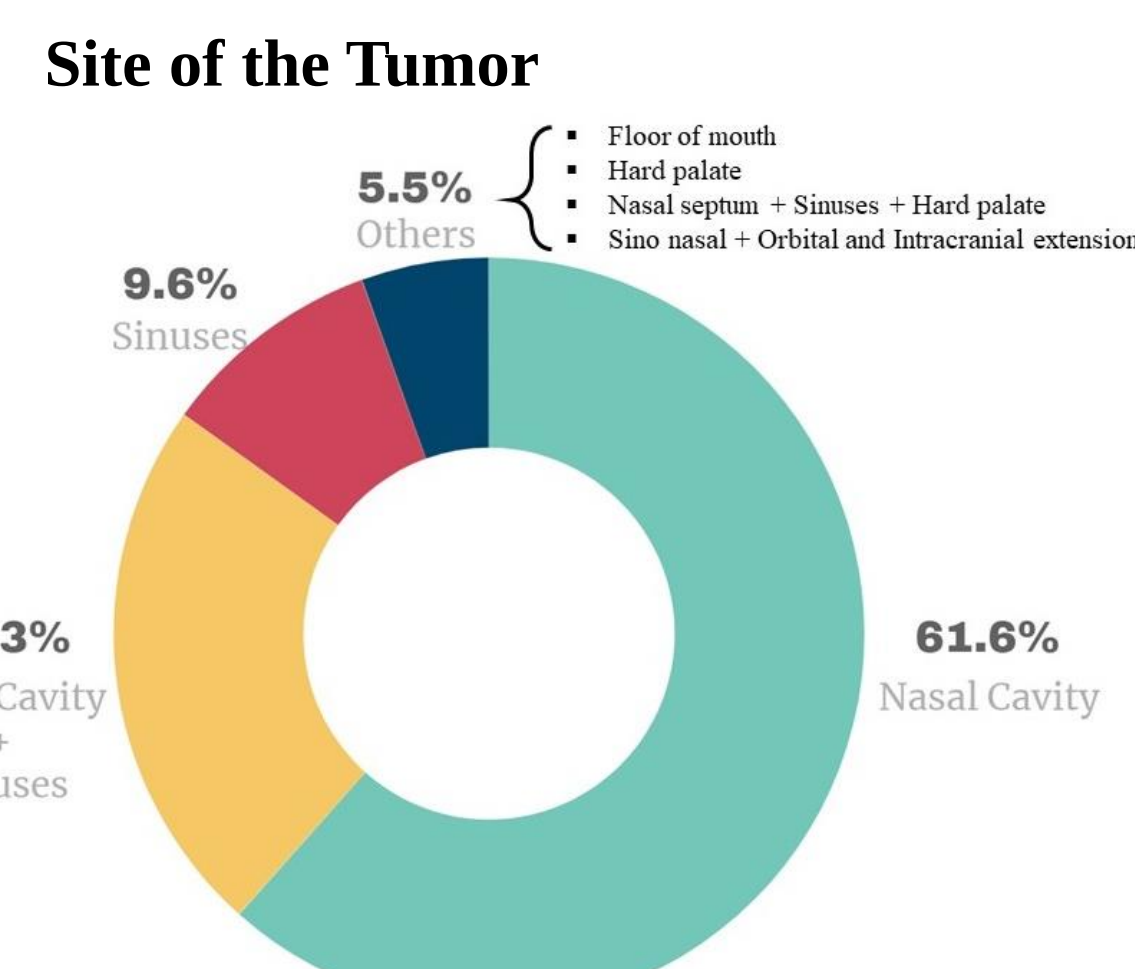


TABLE 2 | Relation between the outcome and disease-free interval.

Variables	(n, %)	Site of DM	Mean of disease-free interval (months)	P value
DM	3 (100%)	- Lung - Lung + Liver - Frontal bone, Mandible, Symphysis pubis - Vertebral body, Rib.	23.50	.014
LR	13 (100%)		61.30	.001
LR + DM	2 (100%)	- Lung - Lung + Finger	36	.000
NED	11 (100%)		54.8	.004

DM Distant Metastasis, **LR** Local Recurrence, **NED** No Evidence of Disease.

Conclusion

Human Papillomavirus (HPV) - Related Multiphenotypic Sinonasal Carcinoma (HMSC) has an indolent course, thus, maximising treatment by multimodalities may increase the survival rate but doesn't prevent metastasis. There is no evidence that supports neck dissection even in locally advance stage tumor. However, negative margin is a key role for decreasing local recurrence rate, with post-operative close observation and long term follow up. Further study and investigation are needed.

References

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