# Saudi Journal of Medicine

Abbreviated Key Title: Saudi J Med ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online) Scholars Middle East Publishers, Dubai, United Arab Emirates Journal homepage: https://saudijournals.com

# **Original Research Article**

# Secretory Carcinoma (SC) of the Sinonasal Cavity - A Case Report and Review of Worldwide Reported Cases

Hadi M. Mokarbesh<sup>1\*</sup>, Fatimah H. Dallak<sup>1</sup>, Khalil I. Kariri<sup>1</sup>, Turki M. Hakami<sup>1</sup>, Nehad K. Khawaji<sup>1</sup>, Fatimah Kamili<sup>2</sup>, Shaymaa A. Sadek<sup>3</sup>, Liaqat A. Khan<sup>4</sup>, Aiman Gul<sup>5</sup>, Ibrahim A. Sumaily<sup>1</sup>

**DOI:** 10.36348/sjm.2023.v08i12.008 | **Received:** 03.11.2023 | **Accepted:** 17.12.2023 | **Published:** 30.12.2023

\*Corresponding Author: Hadi M. Mokarbesh

ENT Department, King Fahd Central Hospital, Jazan, Kingdom of Saudi Arabia

## **Abstract**

Background: Numerous malignancies, both benign and malignant is hosted by the sinonasal cavity that poses a diagnostic and therapeutic challenge to otolaryngologist and pathologists. One of the extremely rare neoplasm of the sinonasal cavity is secretory carcinoma (SC), previously called, mammary analogue secretory carcinoma (MASC). Majority of MASCs are localized to the parotid and salivary glands however, it is rarely documented in the sinonasal tract. Herein, we review the reported cases and report a twenty-one-year-old female patient presented to our ear, nose & throat outpatient department of tertiary care center as a polyp in the nasal cavity initially, which was excised on first diagnoses with normal histopathology (H/P). However, a year later she has a recurrence with an invasive course, followed by surgical exploration and confirmed as "Secretory Carcinoma" (SC) on histopathology, immunohistochemistry & genetic confirmation. At twoyears follow-up, the patient has no clinical and radiological signs of recurrence. Aim: this review aims to outline the demographic, clinicopathologic, and confirmatory (radiologic, histopathologic, and immunohistochemistry) findings of the published cases. Methods: PubMed, Google Scholar, and MEDLINE search done with search words such as, secretary carcinoma, sinonasal tract, mammary analogue secretary carcinoma. Results: Total eight case including our case included in this review. The male/female ratio of occurrence of the SC of the sinonasal cavity was 3:5 (34.5:62.5%). Majority of the cases (7/8) reported in middle and old age group except one as reported in a 12 years old child. Equal case distribution among smoker ad non-smoker patients. The common symptoms were nasal obstruction, nasopharyngeal secretions, presence of mass, epistaxis and hyposmia. All cases were characterized by the presence of the ETV6-NTRK3 fusion transcript and / or rearrangement of ETV6 gene. Surgical excision with chemo/radiotherapy was the management considered in majority of the cases with good outcome. Almost all eight cases (100%) has no signs of recurrence both clinical and radiologically at a mean follow-up period of one year. *Conclusion*: Secretary carcinoma of the sinonasal tract is a new entity. More cases / studies are required to know the demographic, clinicopathologic nature, & prognosis of this newly emerging carcinoma.

**Keywords**: Mammary Analogue Secretory Carcinoma (MASC), Secretory Carcinoma (SC), Primary, Sinonasal Cavity, Salivary gland tumors, Immunohistochemistry, Histopathology, Literature review.

Copyright © 2023 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

# Introduction

Mammary analogue secretory carcinoma (MASC) is a rare salivary gland neoplasm that was first reported in 2010 by Skalova *et al.*, [1–4]. MASC is a cancer of the oral cavity and major salivary glands. It has microscopic and immunohistochemical features that are similar to those of secretory carcinoma (SC) of the breast, as well as histologic features that are similar to

those of acinar cell carcinoma (ACC) of the salivary glands [5, 6]. According to recent studies, secretory carcinoma accounts for less than 0.3% of all salivary gland cancers. The majority of these cases were found in the parotid gland, with only a few documented cases in minor salivary glands. It was recently added to the fourth edition of the World Health Organization's (WHO) classification system for head and neck tumors [2-8]. As

<sup>&</sup>lt;sup>1</sup>ENT Department, King Fahd Central Hospital, Jazan, Kingdom of Saudi Arabia

<sup>&</sup>lt;sup>2</sup>Radiology Department, King Fahd Central Hospital, Jazan, Kingdom of Saudi Arabia

<sup>&</sup>lt;sup>3</sup>Consultant Anatomic Pathologist, King Fahd Central Hospital, Jazan, Kingdom of Saudi Arabia

<sup>&</sup>lt;sup>4</sup>General Directorate of Health Jazan, Kingdom of Saudi Arabia

<sup>&</sup>lt;sup>5</sup>Faculty of Medicine, Cairo University, Egypt

mammary analogue secretory carcinoma, recently renamed secretory carcinoma (SC) of salivary glands [7].

#### **CASE REPORT**

A 21-year-old female presented to ear, nose and throat (ENT) clinic in April 2018 with a right-side nasal obstruction. On clinical examination, right sided nasal polypoidal mass, red in color, not bleeding on touch was found (Fig-1).



Fig. 1: Endoscopic nasal exam (right sided nasal polypoidal mass, red in color, not bleeding on touch)

Computed Tomography (CT) scan, Pre and Post Contrast demonstrate right posterior nasal soft tissue mass (white arrows) isointense to hyperintense signal on T1, hypo-intense in T1and shows enhanced in postcontrast image. It's infiltrating the right medial and inferior turbinate causing obstruction of the nasal ostium and extending to the right hemisinus, superiorly to the sphenoid sinus and the sphenopalatine fossa, (Fig.2a, 2b).

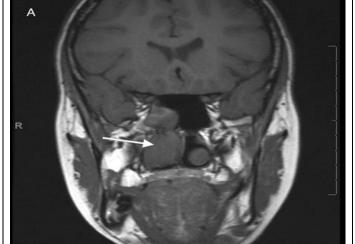


Fig. 2a: Coronal T1

D

Fig. 2b: Axial T1

Fig-(2a) Coronal T1, pre-contrast and (2b) Axial T1, post-contrast demonstrates right posterior nasal soft tissue mass (white arrows) hypo-intense in T1 and shows enhanced in post-contrast image. It's infiltrating the right medial and inferior turbinate causing obstruction of the nasal ostium and extending to the right hemisinus, superiorly to the sphenoid sinus and the sphenopalatine fossa.

In March 2020, the patient presented with the same complaint although she did an operation a year ago and she was advised to do a CT scan with a clinical follow-up. In May 2021 she was complaining of nasal obstruction with nasal discharge, headache, hyposmia, and nasal bleeding. Examination showed that she was conscious, alert, oriented, and vitally stable, then an operation was planned for her the next day.

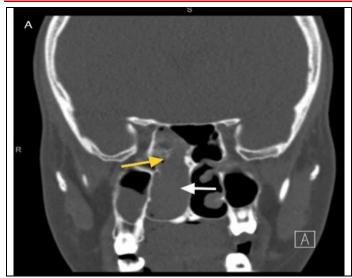


Fig. 3a: Coronal view- bone window

Fig-3a & 3b: Coronal and Axial non-enhanced CT scan shows complete opacification of the right nasal cavity with thick hyperdense secretion extended to sphenoidal sinus (white arrows), associated with sphenoidal sinus erosion best demonstrated on bone window (yellow arrow). Incidental findings: Evidence of right maxillary sinusitis.

The operation was performed on 17 May 2021 and right nasal polyp excision was done and consequently sent to laboratory. The microscopic examination for the excisional polyp showed well demarcated but focally infiltrative neoplasm with lobulated growth composed of a mixture of macrocytic, microcytic, and solid areas. The tumor cells are relatively monomorphic epithelioid cells with a moderate amount of vacuolated eosinophilic cytoplasm, and a central round nucleus with a small nucleolus and rare mitotic activity. The cystic spaces contained intraluminal colloid eosinophilic like secretions (Fig.3a). immunohistochemistry profile was described as tumor cells diffusely and strongly positive for S100 protein, CK7 and gross cystic disease fluid protein 15 (GCDFP15), which was focally positive. Other markers, such as transcription termination factor 1 (TTF1), thyroglobulin, SMA, P63, Calponin and DOG1 were negative and the mitotic (Ki67) index was About 5%. Genetic findings are characterized by the rearrangement of the ETV6 gene by FISH and/or the presence of the ETV6-NTRK3 fusion transcript. The morphological, immunohistochemical, and genetic workup features are consistent with secretory carcinoma (SC).



Fig. 3b: Axial view - bone window

The patient was seen after the operation on the next day and she was stable and discharged with medication to be seen after two weeks for follow-up. Two weeks later, in June 2021, she was admitted for another operation for the excision of the nasal tumor, and the microscopic examination for the excised part showed multiple fragmented tissues with normal covering pseudostratified epithelium, and submucosal mucous secreting glands (Fig.3b). Underlying cartilage and all surgical margins are free from malignancy. The immunohistochemistry profile was negative S100 and Ck7.

# The Histopathology of the Specimen Shows:

Gross appearance: The specimen was received as multiple pieces of soft, tan-to-grey tissue collectively measuring 3x2x1cm

#### **Microscopic Findings (Fig-4a-d):**

Sections revealed a well-demarcated but focally infiltrative neoplasm with lobulated growth composed of mixture of macrocytic, microcystic and solid areas. The tumor cells are monomorphic and exhibit moderate amounts of vacuolated eosinophilic cytoplasm, central round nuclei and rare mitotic activity. The cystic spaces contain intraluminal colloid-like material which is PAS positive and diastase-resistant. The tumor cells are diffusely and strongly positive for cytokeratin-7 and S100, while they are focally positive for GCDFP15 and negative for TTF1, Thyroglobulin, SMA, Calponin and DOG1. The combination of morphologic features along with special stain findings and immune-profile lead to diagnosis establishment and exclusion of other mimics within the differential diagnosis.

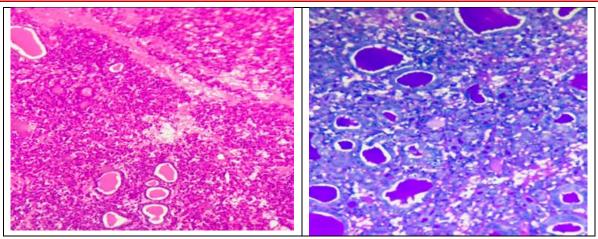


Fig. 4a: H&E stain

Fig. 4b: H&E stain

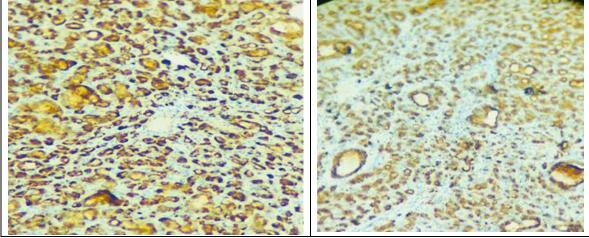


Fig. 4c- PAS stain

Fig. 4d: PAS stain

Figure-3 (a & b): H & E - stained section of secretory carcinoma showing mixture of macro and microcystic and solid areas with colloid-like material in some spaces (3a), PAS special stain demonstrating PAS-positive secretory material (3b), S100 (3c) and CK7(3d) immunostains are diffusely and strongly positive.

The follow-up course in the last six months' period for the patient remains un-eventful with four consecutive follow-ups in the otolaryngology outpatient clinic and radiotherapy clinics with no signs and symptoms of recurrence as evident by clinical and radiological evaluation (Fig-5a, b)

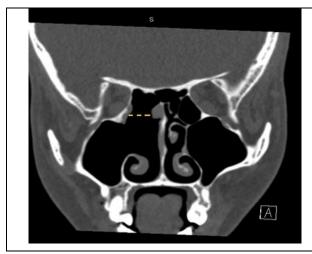


Fig-5a: Coronal view - bone window (post-operative)

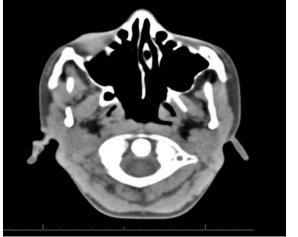


Fig-5b: Axial view - bone window (post-operative)

Fig-5a and 5b Bone window CT (Postoperative) shows no evidence of recurrence and confirmed the good reconstruction results obtained.

The patient was followed in the otolaryngology clinic. Last visit was two years' post-surgical

intervention. Clinically there is no evidence of recurrence with normal looking mucosa on endoscopic evaluation (Fig.6).

The patient's events time line is graphically presented in figure-7.

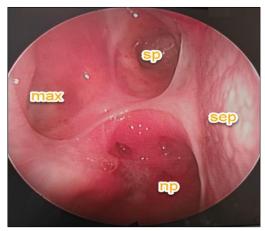


Fig. 6: Endoscopic view of the tumor site after 2 years of excision with complete mucosa normalization and no signs of recurrence.

## Case Timeline (Fig-7)

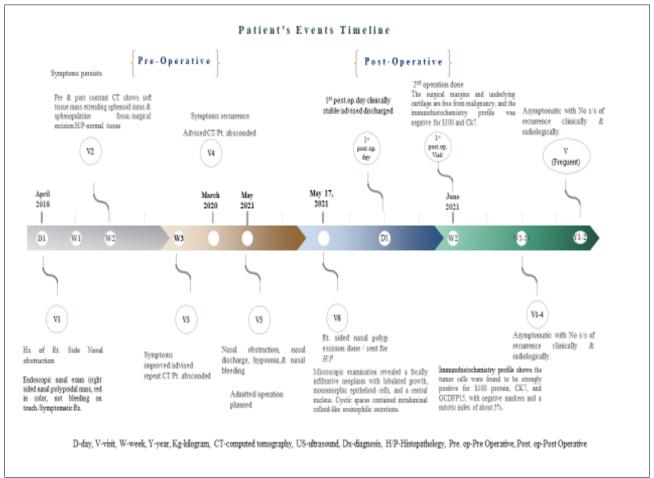


Fig. 7

			1		Table	1: Demog	raphics / Cli	nical Eva	luation of Repor	ted C	ases		
Author (s)	Publ. Year	Country	Gender	Age	Smoking History	Past Med. History	Present Med. History	Site	Examination (Inspection / Palpation)	Size	TNM Stage	Management	Follow-up / Recurrence
o Cases)	2018	Denmark	Ţ	51Y	Non-smoker	Hx of breast cancer	Intermittent tenderness / retro- bulbar pain / forehead discomfort (occasional)	Rt. sided nasal septum	Rt. sided nasal polypoidal mass Examination (Inspection / Palpation)	$1.5 \times 1.5 \times 0.4 \text{ cm}$	T1N0M0	Surgical Excision + chemotherapy	At 14-years follow-up (last). No signs of recurrence both clinically and radiologically
Martina et al <sup>18</sup> . (Two Cases)	2018	Denmark	Ĭ	65Y	Non-smoker	Unremarkable except pleomorphic adenoma of the palate 5y past.	Rt. sided nasal obstruction / nasopharyngeal secretion / retro-bulbar pain (occasional)	Rt. sided nasal cavity / nasopharyngeal extension	Rt. sided nasal polypoidal mass	4 x 4 x 1.5 cm	T2NxM0	Surgical Excision of the mass including the middle turbinate along with maxillary sinus antrostomy, right ethmoidectomy, and partial resection of the nasal septum. + chemotherapy	At Four-years follow-up (last).  No signs of recurrence both clinically and radiologically
Xu et al <sup>19</sup> (Case)	2018	NSA	M	Y 19	25 pack-year history of smoking (farmer)	Un-remarkable	Mass found- (P. Hx description -NA)	Lt. maxillary sinus	Lt. sided maxillary sinus solid mass	4.2 cm		Left maxillectomy, orbital reconstruction, fibular free flap reconstruction, maxilla reconstruction with vincryl mesh, free bone graft, and skin graft. + chemotherapy	At Eight-months follow-up (last). No signs of recurrence both clinically and radiologically
Willis et al <sup>20</sup> . (Case)	2021	Canada	M	39 Y	25 pack-year history of smoking and daily cannabis use	Chronic rhinosinusitis	Lt. nasal obstruction & chronic rhinosinusitis	Left nasal (Maxillary & Ethmoid sinuses)	An erythematous, lobulated mass was observed from the middle turbinate, extending to the lateral nasal wall, posterior nasal choanae, and sphenoid rostrum.	Large (size not specified)		Functional endoscopic sinus surgery (FEES).  2 <sup>nd</sup> resection with medial maxillectomy at 3months interval.	At One-year follow-up (last). No signs of recurrence both clinically and radiologically

Present Case	Klubíčková et al <sup>22</sup> .		Cardoni et al <sup>21</sup> .	Author (s)	
2023	2023	2023	2023	Publ. Year	
Saudi Arabia	Czech Republic	Czech Republic	Italy	Country	
	M	F	F	Gender	Ta
21Y	39 Y	39 Y	12 Y	Age	ble 2:
Non-smoker	NA	NA	Not Sig.	Smoking	Den
Not significant	Not significant	Not significant	Acute onset	Past Med. History	nograp
Painless mass / nasal obstruction / hyposmia / bleeding	Hx. of Epistaxis	Nasal obstruction	Rt. cheekbone large disfiguring mass-recent onset	Present Med. History	hics / Clin
Right nasal (Maxillary & Ethmoid sinuses)	Lt. nasal cavity	Lt. maxillary sinus/ nasal cavity	Rt. Maxillary Sinus	Site	ical Ev
A soft palpable red mass, not bleeding on touch.	A soft mass in the Lt. nasal cavity	Lt. maxillary sinus/ nasal cavity/ Lt. orbital infiltration	large mass (disfiguring) of the right cheekbone	Examination (Inspection / Palpation)	aluation of
x 2 x 1 cm	18 mm		62 x 48 mm	Size	Repo
		сТ4а		TNM Stage	rted
Surgical Excision + RT	Surgical resection (ethmoidectomy) + RT	1st instance chemotherapy Followed by Surgical resection (conservative)	Surgical Excision + chemotherapy  2 <sup>nd</sup> resection for a possible remnant of cancer in the ethmoid region, without dissecting any lymph nodes. (H/P-normal)	Management	Cases (Cont):
At two years' follow-up. No signs of recurrence both clinically and radiologically	At seventeen months' follow- up. No signs of disease recurrence.	Still under follow-up	Still under follow-up (last). No signs of recurrence both clinically and radiologically	Follow-up / Recurrence	

	Pre-operative		Post-operative (Follow-up)		
	CT / MRI				
	Findings	Extension/Infiltration	Findings	Extension/ Infiltration	
Martina <i>et al.</i> , [18].	Rt. sided nasal polypoidal mass		No signs of recurrence	None	
	Rt. sided nasal polypoidal mass	CT scan revealed a mass in the right nasal cavity, extending into the nasopharynx.	No signs of recurrence	None	
Xu <i>et al</i> ., [19].	Lt. maxillary sinus mass	CT scan revealed soft tissue density in the left maxillary sinus	No signs of recurrence	None	
Willis <i>et al.</i> , [20].	Lt. sided post. nasal soft tissue mass	CT scan revealed soft tissue density in the left maxillary sinus, extending through the ethmoid sinus and posterior nasal cavity.	No signs of recurrence	None	
Cardoni <i>et al.</i> , [21].	Mass at Rt. Maxillary sinus	CT scan revealed a large mass (62 mm × 48 mm) obliterating the maxillary sinus was seen having osteolytic appearance and uneven post-contrast enhancement.	No signs of recurrence	None	

Klubíčková et al., [22].	Mass at Rt. Maxillary sinus extending to the Lt. orbital cavity.	CT scan revealed the tumor filled the left maxillary sinus, extended into the nasal cavity, and infiltrated in to the orbit.	No signs of recurrence (Under follow-up)	
		A mass in the left nasal cavity, measuring 18 mm in the greatest dimension		
Present Case	Rt. sided post. nasal soft tissue mass.	CT scan revealed mas (3 x 2 x 1 cm), at Rt. medial & inferior turbinate / obstructing ostium extending to Rt. hemisinus, sphenoid sinus & sphenopalatine fossa superiorly.	No signs of recurrence / good reconstruction	None

Table 4: Confirmatory Assessment (Histopathology)

Author (s)	Table 4: Confirmatory Assessment (Histopathology)  Microscopic Examination	Mitotic
rumor (s)	Wicroscopic Examination	Index
		(Ki67)
Martina et	The tumor was un-encapsulated, exhibiting tubular, papillary, and microcystic growth	MIB1
al., [18].	patterns with invasive margins and low-grade nuclei. It contained abundant eosinophilic	5%
<i>ui.</i> , [10].	homogenous extracellular periodic acid-Schiff with diastase-positive material.	(Low)
	Un-encapsulated and composed of tubular, papillary, and microcystic growth patterns with	MIB1
	invasive margins with low-grade vesicular and round to oval nuclei with fine, granular	40%
	chromatin. Abundant eosinophilic homogenous extracellular periodic acid-Schiff with	(High)
	diastase–positive material was present / composed of solid microcystic growth patterns, in	(IIIgII)
	places divided by thick hyalinized fibrous septa with focal necrotic areas.	
Xu et al.,	The tumor was infiltrative, with acinar, tubular, and microcystic growth patterns. It had	
[19].	dense eosinophilic secretions, vesicular chromatin-filled nuclei, and eosinophilic granular	
[17].	to clear vacuolated cytoplasm, with higher grade component with solid growth, nucleoli,	
	and nuclear pleomorphism.	
	10 per 10 high power fields (High grade transformation)	
Willis et al.,	The biopsy specimens revealed multiple adenocarcinoma fragments with a cribriform	
[20].	growth pattern, confluent tumor necrosis, eosinophilic to slightly vacuolated cytoplasm,	
[].	mild nuclear pleomorphism, and abundant mucin production. greater degree of cytologic	
	atypia and necrosis.	
Cardoni et	The biopsy revealed vacuolated eosinophilic cytoplasm, high nuclear/cytoplasmic ratio,	60%
al., [21].	dense chromatin, and luminal secretion positive for PAS and PAS-D. Cells were growing	(High)
	in papillary and tubular/follicular forms, with high mitotic index, necrosis, and peri-neural	
	invasion foci.	
Klubíčková	The tumors, primarily in hypercellular solid and dense cribriform nests, grew extensively	42%
et al., [22].	in the nasal cavity's submucosa. Minor sections had high-grade cytological characteristics,	(High)
	clustering large nuclei with prominent eosinophilic nucleoli, and mild to moderate pale	
	eosinophilic cytoplasm. 26 mitotic figures / 2.4mm <sup>2</sup> High grade.	
	The tumors penetrated the nasal cavity's submucosa, exhibiting high-grade features in	51%
	dense cribriform nests with central necrosis, large nuclei, prominent eosinophilic nucleoli,	(High)
	clear cytoplasmic vacuoles, and stromal chronic inflammation in abluminal cells. 17	
	mitotic figures / 2.4mm <sup>2 -</sup> High grade.	
Present Case	Well demarcated but focally infiltrative neoplasm with lobulated growth composed of a	5%
	mixture of macrocytic, microcytic, and solid areas. Tumor cells are monomorphic	(Low)
	epithelioid cells with a central round small nucleus, and rare mitotic activity, with cystic	
	spaces containing intraluminal colloid-like eosinophilic secretions.	

**Table 5: Confirmatory Assessment (Immunohistochemistry)** 

	AUTH	AUTHORS						
	Martina	a et al.,	Xu et al.,	Willis et al.,	Cardoni et al.,	Klubíčková	et al.,	Present
	[18].		[19].	[20].	[21].	[22].		Case
CASES	1	2	3	4	5	6	7	8
MARKERS								
AR						(-)	(-)	
Calponin				(-)				(-)
CDX2	(-)	(-)		(-)			(-)	
CK7	(+)	(+)	(+)	(+)	(+)	(+)	(+)	
CK8						F*(+)		

CK14							(+)	
CK17								
CK18						(+)	(+)	
CK19				(+)		(+)	(+)	
CK20	(-)	(-)		(-)				
CK					(+)			
(AE1/AE3)								
CK5/6				(-)		(-)	(-)	
DOG1		(-)				F*(+)	(-)	(-)
EMA					(+)			
GATA1								
GATA3		(+)		(+)		(+) W*	(+)	
GCDFP15	F*(+)	(+)	(+)	(+)	(-)			(+)
		EM*						
Her2						(-)	(-)	
Mammaglobin	(+)	F*(+)	(+)			(-)	(-)	
MUC						(-)	(+)	
NOR1							(-)	
Pan Trk	(+)	(+)				(+)	(+)	
p16							(-)	
P40						F*(+)	(+)	
P63	(-)	(-)			(-)	F*(+)	(+)	(-)
S100	(+)	F*(+)	(+)	(+)	(+)		(+)	(+)
SALL4						(-)		
SATB2	(-)	(-)						
SOX10	(+)	(+)			(+)	(+)	(+)	
SMA					(-)	(-)	(-)	(-)
Stat5		(+)						
Stat6								(-)
TTF1				(-)		(-)		
Thyroglobulin								(-)
Vimentin				(+)	(+)			

**Table 6: Confirmatory Assessment (Genetic Findings)** 

Author (s)	Cases	Positive for			
Martina <i>et al.</i> , [18].	Case-1	Characterized by the presence of the ETV6-NTRK3 fusion transcript and / or rearrangement of ETV6 gene by FISH			
[10].	Case-2	Characterized by the presence of the ETV6-NTRK3 fusion transcript and / or rearrangement of ETV6 gene by FISH			
Xu et al., [19].	Case	ETV6 rearrangement was shown by fluorescence in-situ hybridization (FISH) with a commercial ETV6 break apart probe.			
Willis <i>et al.</i> , [20].	Case	Positive for rearrangement of the ETV6 (12p13) locus in 92% of 100 interphase cells analyzed.			
Cardoni <i>et al.</i> , [21].	Case	Characterized by the presence of the ETV6 (exon-5) -NTRK3 (exon-15) fusion transcript and / or rearrangement of ETV6 gene			
Klubíčková <i>et</i> al., [22].	Case-1	RNA-sequencing revealed an identical ETV6::NTRK3 fusion involving exon 5 of the ETV6 gene and exon 15 of the NTRK3 gene.			
	Case-2	RNA-sequencing revealed an identical ETV6::NTRK3 fusion involving exon 5 of the ETV6 gene and exon 15 of the NTRK3 gene.			
Present Case	Case	Characterized by the rearrangement of the ETV6 gene by FISH and/or the presence of the ETV6-NTRK3 fusion transcript.			

## **DISCUSSION**

Mammary gland analogue Secretory carcinoma is a newly discovered kind of salivary gland carcinoma. This disease is rare and can affect children and adolescents [9, 10]. Adult individuals are most likely to develop secretory carcinoma of the salivary gland (SC).

The youngest case reported was a 5-year-old girl from the United States, while the oldest was an 87-year-old woman from Australia [9-12]. Several researches have been published that detailed clinical, histologic, and immunohistochemical characteristics of MASC <sup>13</sup>. Up to date, there have been over 100 cases of MASC recorded

in the literature, with the parotid gland being the most common site of occurrence [11].

Although the majority of SCs affect the major salivary glands, yet about 30% of them can develop in minor salivary glands, and mostly in the oral cavity. SCs in the sinonasal tract appear to be rare, however, there have been some recorded cases [11-16]. Cardoni et al., [21], reported a 12-year-old female child with large mass at Rt. Check which then turned as SC of the Rt. Maxillary sinus with good prognosis. Other reported cases including our case were in the middle and old age patients.

SCs are slow-growing tumors that are discovered incidentally during a physical examination [9]. The most common Presentation of MASC is a slowly growing painless nodule. Pain, skin infiltration, ulceration, cervical lymphadenopathy, and facial nerve involvement are some of the other reported symptoms [11]. The commonly reported symptom among the reported cases included in this review were, nasal obstruction, nasopharyngeal secretions, presence of mass, epistaxis and hyposmia. The demographic and clinical evaluations of the included cases is given in Table-1.

Imaging has only been described in a small number of cases, thus, relying on imaging as a diagnostic modality has not been well reported. Radiological such as CT/MRI helps in the severity and extension/invasion of the disease as seen in almost all patients of the present review. Imaging details for the included cases are presented in Table-2.

To date, the only definitive approach to diagnose MASC is excisional biopsy of the mass followed by further histological investigation 11. Histopathological confirmation done for all eight patients as given in Table-3.

MASC has a lobulated development pattern and is frequently formed of microcystic, tubular, and solid structures with copious eosinophilic homogenous or bubbly secretions. And commonly positive for GCDFPmammaglobin, S100, and immunophenotypically, but negative for DOG1 [14-17]. The immunohistochemistry of the included patients is presented in Table-4

Surgical excision is the most common treatment for SC as seen in almost all eight cases included in this review. Despite the lack of evidence on treatments and outcomes, SC appears to be a low-grade malignant tumor with a good prognosis. However, in a significant number of cases, recurrences and local tumor metastases have previously been reported [12]. Almost all eight cases (8/8-100%) show good prognosis with no signs of recurrence both clinically and radiologically at a mean follow-up interval of one year.

## **CONCLUSION**

Secretory Carcinoma (SC) is a newly discovered kind of salivary gland carcinoma that appears as a slow-growing, painless nodule. It has been documented in a number of sub-sites of the head and neck and rarely in sinonasal cavity. It poses a diagnostic challenge both for otolaryngologists and pathologists. A definitive diagnosis is made by excisional biopsy of the mass followed by histopathological analysis. This review highlights the notion that more cases / studies are required to know the demographic, clinicopathologic nature, & prognosis of this newly emerging carcinoma.

**Conflict of Interest:** The authors declare, that they have no conflict of interest to declare.

Funding: This research work did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

## **Author's Contributions**

Conception and design: Dr Hadi M. Mukarbesh, Dr Ibrahim A. Sumaily.

Collection and assembly of data: Dr Fatimah Dallak, Dr Turki M. Hakami, Dr Khalil I. Kariri.

Analysis and interpretation of the data: Dr Liaqat A. Khan, Dr Fatimah Dallak.

Histopathology Reporting: Dr Shaymaa A. Sadek.

Radiology reporting: Dr Fatimah Kamly

Drafting of the article: Dr Nehad K. Khawaji, Dr Fatimah

Dallak, Dr Aiman Gul, Dr Liaqat A. Khan.

Critical revision of the manuscript: Dr Hadi M. Mokarbesh.

Final approval and guarantor of the article: Dr Hadi M. Mokarbesh, Dr Ibrahim A. Sumaily.

### **Abbreviations**

Abbr.	Description	Abbr.	Description
SC	Secretory Carcinoma	FISH	Fluorescence in situ
MASC	Mammary Analogue Secretory Carcinoma	GCDFP-15	Gross Cystic Disease Fluid Protein-15
DOG-1	Discovered on DIST-1	SMA	Smooth Muscle Actin
GCDFP-15	Gross Cystic Disease Fluid Protein-15	TRK	Tropomyosin receptor kinase
CK7	Cytokeratin-7	EMA	Epithelial membrane antigen
PAS-positive	Periodic Acid-Schiff	HPF	High power field
TTF-1	Transcription Termination Factor-1	PCR	Protein chain reaction

CT	Computed Tomography	MRI	Magnetic resonance imaging
WHO	World Health Organization		
Rt.	Right		
Lt.	Left		
RT	Radiotherapy		
M	Male		
F	Female		
+ve	Positive		
-ve	Negative		
NA	Not available		

## **REFERENCES**

- Skálová, A., Vanecek, T., Sima, R., Laco, J., Weinreb, I., Perez-Ordonez, B., ... & Michal, M. (2010). Mammary analogue secretory carcinoma of salivary glands, containing the ETV6-NTRK3 fusion gene: a hitherto undescribed salivary gland tumor entity. The American journal of surgical pathology, 34(5), 599-608.
- Takano, H., Fukuda, M., Hatakeyama, S., Konno, Y., Yamazaki, M., Igarashi, H., ... & Yoshioka, T. (2021). A case of secretory carcinoma of the minor salivary gland in the buccal mucosa. *Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology*, 33(2), 136-140.
- 3. Boliere, C., Murphy, J., Qaisi, M., Manosca, F., & Fung, H. (2019). Mammary Analogue Secretory Carcinoma of the Palate: Case Report and Review of the Literature. *Case Rep. Dent*, 1–6.
- Venkat, S., Fitzpatrick, S., Drew, P. A., Bhattacharyya, I., Cohen, D. M., & Islam, M. N. (2021). Secretory carcinoma of the oral cavity: a retrospective case series with review of literature. *Head and Neck Pathology*, 15, 893-904.
- 5. Willis, K., Bullock, M., & Rigby, M. H. (2021). A case report of surgical resection of secretory carcinoma in the maxillary and ethmoid sinus. *International Journal of Surgery Case Reports*, 81, 105750.
- 6. Gaopande, V. L., Kulkarni, M. M., Khandeparkar, S. G., & Joshi, A. R. (2017). Mammary analog secretory carcinoma parotid gland: Case report of a recently described tumor with review of literature. *Asian Journal of Oncology*, *3*(02), 139-143.
- Seethala, R. R., & Stenman, G. (2017). Update from the 4th edition of the World Health Organization classification of head and neck tumours: tumors of the salivary gland. *Head and neck pathology*, 11, 55-67.
- 8. Salat, H., Mumtaz, R., Ikram, M., & Din, N. U. (2015). Mammary analogue secretory carcinoma of the parotid gland: a third world country perspective—a case series. *Case reports in otolaryngology*, 2015.
- Simon, C. T., McHugh, J. B., Rabah, R., & Heider, A. (2021). Secretory Carcinoma in Children and Young Adults: A Case Series. *Pediatr. Dev. Pathol.* 109352662110469. doi:10.1177/10935266211046996.
- 10. Sethi, R., Kozin, E., Remenschneider, A., Meier, J., VanderLaan, P., Faquin, W., ... & Frankenthaler, R.

- (2014). Mammary analogue secretory carcinoma: update on a new diagnosis of salivary gland malignancy. *The Laryngoscope*, 124(1), 188-195.
- 11. Tjahjono, R., Chin, R., & Iqbal, F. (2018). Mammary analogue secretory carcinoma of the parotid gland: a case report. *Otolaryngology Case Reports*, 6, 7-9.
- Alves, L. D. B., de Melo, A. C., Farinha, T. A., de Lima Araujo, L. H., de Souza Thiago, L., Dias, F. L., ... & Goldemberg, D. C. (2021). A systematic review of secretory carcinoma of the salivary gland: where are we?. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 132(4), e143-e152.
- Skálová, A., Vanecek, T., Simpson, R. H., Laco, J., Majewska, H., Baneckova, M., ... & Michal, M. (2016). Mammary analogue secretory carcinoma of salivary glands. *The American Journal of Surgical Pathology*, 40(1), 3-13.
- 14. Xu, B., Aryeequaye, R., Wang, L., & Katabi, N. (2018). Sinonasal secretory carcinoma of salivary gland with high grade transformation: a case report of this under-recognized diagnostic entity with prognostic and therapeutic implications. *Head and Neck Pathology*, 12, 274-278.
- 15. Wu, B., Loh, T. K. S., Vanecek, T., Michal, M., & Petersson, F. (2020). (mammary analogue) secretory carcinoma of the nasal cavity: report of a rare case with p63 and DOG1 expression and uncommon exon 4–exon 14 ETV6-NTRK3 fusion diagnosed with next generation sequencing. *Head and Neck Pathology*, 14, 542-549.
- 16. Majewska, H., Skálová, A., Stodulski, D., Klimková, A., Steiner, P., Stankiewicz, C., & Biernat, W. (2015). Mammary analogue secretory carcinoma of salivary glands: a new entity associated with ETV6 gene rearrangement. Virchows Archiv, 466, 245-254.
- 17. Skalova, A. (2013). Mammary analogue secretory carcinoma of salivary gland origin: an update and expanded morphologic and immunohistochemical spectrum of recently described entity. *Head and Neck Pathology*, 7, 30-36.
- 18. Baneckova, M., Agaimy, A., Andreasen, S., Vanecek, T., Steiner, P., Slouka, D., ... & Skálová, A. (2018). Mammary analog secretory carcinoma of the nasal cavity: characterization of 2 cases and their distinction from other low-grade sinonasal adenocarcinomas. The American Journal of

- Surgical Pathology, 42(6), 735-743. DOI:10.1097/PAS.000000000001048.
- 19. Xu, B., Aryeequaye, R., Wang, L., & Katabi, N. (2018). Sinonasal secretory carcinoma of salivary gland with high grade transformation: a case report of this under-recognized diagnostic entity with prognostic and therapeutic implications. *Head and Neck Pathology*, 12, 274-278.
- 20. Willis, K., Bullock, M., & Rigby, M. H. (2021). A case report of surgical resection of secretory carcinoma in the maxillary and ethmoid sinus. *International Journal of Surgery Case Reports*, 81, 105750. https://doi.org/10.1016/j.ijscr.2021.105750.
- Cardoni, A., De Vito, R., Milano, G. M., De Pasquale, M. D., & Alaggio, R. (2023). A Pediatric Case of High-Grade Secretory Carcinoma of the Maxillary Sinus With ETV6:: NTRK3 Gene Fusion, Therapeutic Implications, and Review of the Literature. *Pediatric and Developmental Pathology*, 26(1), 59-64. doi:10.1177/10935266221138706.
- Klubíčková, N., Mosaieby, E., Ptáková, N., Trinquet, A., Laé, M., Costes-Martineau, V., & Skálová, A. (2023). High-grade non-intestinal type sinonasal adenocarcinoma with ETV6:: NTRK3 fusion, distinct from secretory carcinoma by immunoprofile and morphology. *Virchows Archiv*, 483(2), 187-195. https://doi.org/10.1007/s00428-023-03587-6.