

CASE REPORT

NUT carcinoma in head and neck region: Case report with literature review

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ABSTRACT

Squamous cell carcinoma (SCC) has several variants based on its histopathological features. Nuclear protein in testis (NUT) carcinoma (NC) is a rare and aggressive variant of SCC, previously described exclusively in midline sites. The histopathological features of NC are similar to poorly differentiated carcinoma or undifferentiated carcinoma. Abrupt keratinization in an otherwise undifferentiated carcinoma is an important diagnostic clue. The confirmatory diagnosis is dependent on molecular techniques such as Immunohistochemistry, Fluorescent in situ hybridization technique or RT-PCR to detect mutations in NUT gene. It is most commonly found in middle aged, in lungs and head and neck regions. Since NC features overlap with poorly differentiated and undifferentiated carcinomas, these cases need to be suspected and evaluated for NUT gene mutations thoroughly. Due to their rarity and less known facts, NC cases are required to be reported on large scale.

Here, we report a middle-aged woman with a mass on the forehead diagnosed as NC based on molecular evaluation, with a review of the literature emphasizing the rarity of NUT carcinoma and the importance of careful histopathology as well as immunohistochemistry evaluation.

KEYWORDS: NUT, midline, carcinoma, squamous, head and neck.

INTRODUCTION

Genetic mutations in nuclear protein in testis (NUT) gene result in a rare type of squamous cell carcinoma (SCC) termed initially as NUT midline carcinoma¹. SCC are epithelial neoplasms consisting of several histopathological variants based on clinical and microscopic features. NUT carcinoma (NC) is a rare, aggressive variant of SCC, that was initially described as mediastinal/ thymic malignancy². However, NC has been recently reported in various other sites including lungs, salivary glands, pancreas, bladder, kidneys, soft tissues and bone³.

In comparison with other types of SCC, NC can be found to be the most rare, aggressive and fatal variant. NC is difficult to diagnose based on only hematoxylin and eosin (H&E) stained histopathological findings. It is most of times vaguely diagnosed as poorly differentiated or undifferentiated malignancy with background of loose fibrous stroma, poorly cohesive cells, and areas of haemorrhage, necrosis and neutrophilic infiltrate. The feature indicative of NC includes focally abrupt keratinizing squamous differentiation present in minuscule amount in most of the lesions^{1,2,4,6}. The final diagnosis in-

cluded detection of mutations in NUT gene through immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) method.

The treatment mostly includes surgery and radiotherapy. Chemotherapeutic agents are less likely to be effective in NC and are under clinical trials in recent years.

Here, we report a case of a 42-year-old female that was initially diagnosed as poorly differentiated malignancy and the IHC confirmed NC in the frontal sinus. In addition, we include an extensive review from the literature on NC of the head and neck region, emphasizing the careful histopathology, immunohistochemistry and molecular examinations in poorly differentiated malignancies.

CASE REPORT

A 42-year-old female presented to a medical college with a mass on the forehead, rapidly increasing in size in the previous 2 months. The patient was well oriented and conscious and no other signs and symptoms were reported.

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Figure 1. Clinical image showing a proliferative mass on the forehead extending over bridge of the nose and the right eyebrow.

The clinical examination showed a proliferative mass on the centre of the patient's forehead extending on the bridge of the nose and over the right eyebrow. Due to the mass, there was periorbital edema and difficulty in eye opening (Figure 1). Her routine laboratory investigations were under normal limits except for mild anemia.

The patient underwent imaging investigations, using cerebral contrast enhanced MRI scan, which revealed complete opacifications of both frontal sinuses, with admixed hyperdensities along the anterior aspects of the

frontal sinuses (Figure 2). A heterogeneously enhancing soft tissue mass in the overlying frontal scalp measuring 4.3 cm (cranio-caudally) $\times$ 2.2 (antero-posteriorly) $\times$ 6.1 cm (transverse) was noted. There were marked edematous changes in the bilateral frontal sinus, periorbital and maxillary region. There was evidence of small intracranial extension, with small irregular nodular enhancing soft tissue in the underlying extradural space. The CT scan without contrast done for the purpose of radiation planning was suggestive of midline mass over scalp of size 7.1 $\times$ 3 $\times$ 6.2 cm, mainly in proximity with the frontal bone and bilateral orbits. The tumor was seen eroding the outer cortex of the frontal bone as can be observed in Figure 3. The caudal extent of the tumor was reaching up to the nasal bone, but without the evidence of erosion. It extended intracranially, involving the underlying extradural space in the form of a small nodule. Based on the radiological findings, possibilities of fungal sinusitis and neoplastic lesions were suspected (Figure 2, Figure 3).

Primary clinical examination and evaluation was done in a well renowned medical institute and an incisional biopsy was performed for histopathological diagnosis. Based on the histopathological features, a differential diagnosis of poorly differentiated SCC, sinonasal carcinoma, nasopharyngeal carcinoma and less likely melanoma was given. The patient was referred to our cancer institute for further workup and treatment.

The blocks were submitted to our hospital for review and immunohistochemistry (IHC). Hematoxylin and eosin (H&E) stained sections showed predominant necrotic areas with scattered round to oval tumor cells, showing prominent vesicular nucleoli and clear cytoplasm. Focal areas of squamous differentiation with abrupt kera-

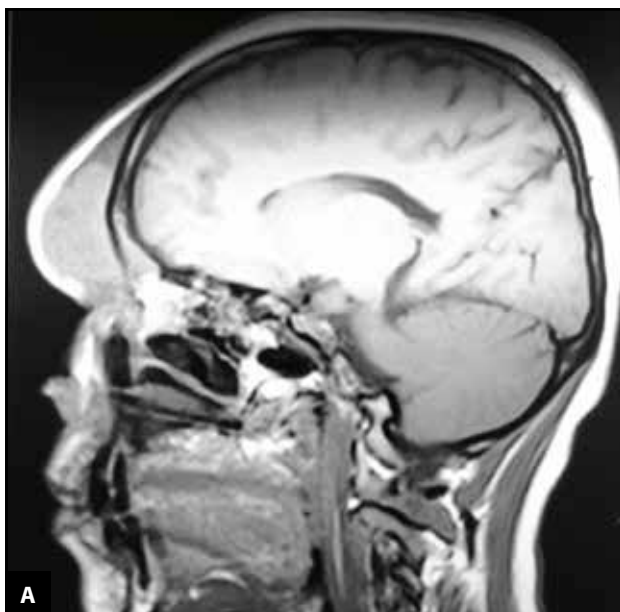


Figure 2. Cerebral MRI with intravenous contrast (A. Sagittal view, B. Axial view) showing a soft tissue mass in the frontal scalp, eroding the outer edge of the frontal sinus.

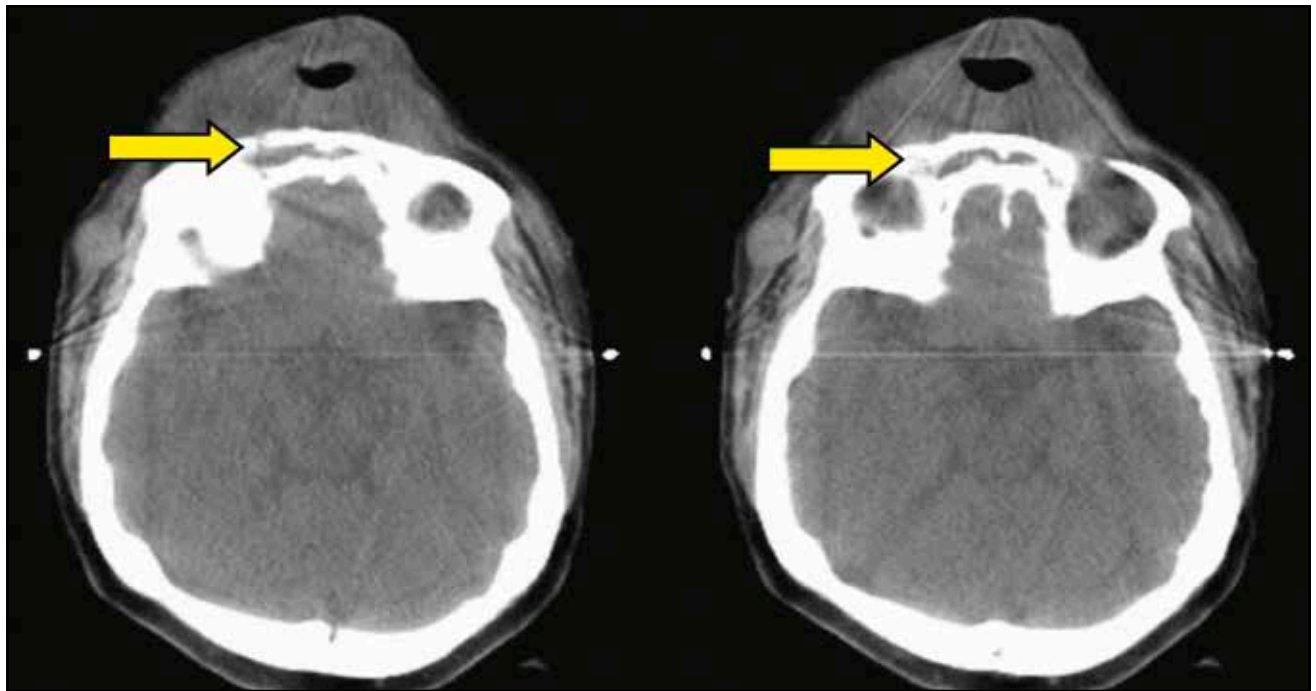


Figure 3. Cranio-facial CT scan without contrast showing erosion in the right frontal sinus.

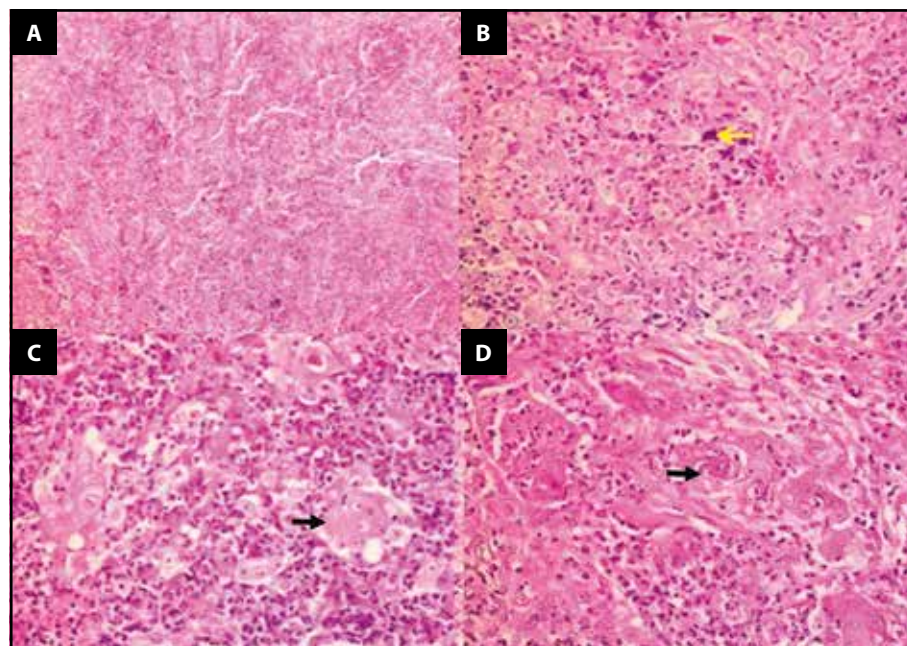


Figure 4. Microscopic images from the tumour showing **A)** tumor cells arranged in clusters, **B)** tumor cell clusters with vesicular nuclei, prominent nucleolus and increased mitosis (yellow arrow), **C)** and **D)** loosely arranged tumor clusters with abrupt keratinization (black arrow) and many admixed polymorphs [H&E: **A).** $\times 100$; **B), C)** and **D)** $\times 400$].

tinization were noted hinting for carcinomatous neoplasm. The intervening stroma showed extensive infiltration of neutrophils, lymphocytes and eosinophils. Based on these features, preliminary suggestions consisted of similar differentials. However, abrupt keratinization made us suspect NUT carcinoma as an addition to the list

(Figure 4). Thus, a panel of immunohistochemistry markers was run for determining the definitive diagnosis. The tumor cells expressed CK (cytokeratin), EMA (epithelial membrane antigen), p63, p40 and p16 (Figure 5). The cells were negative for LCA (leukocyte common antigen), CK7, CK20, CD117 and EBV LMP (*Epstein-Barr* virus-encoded la-

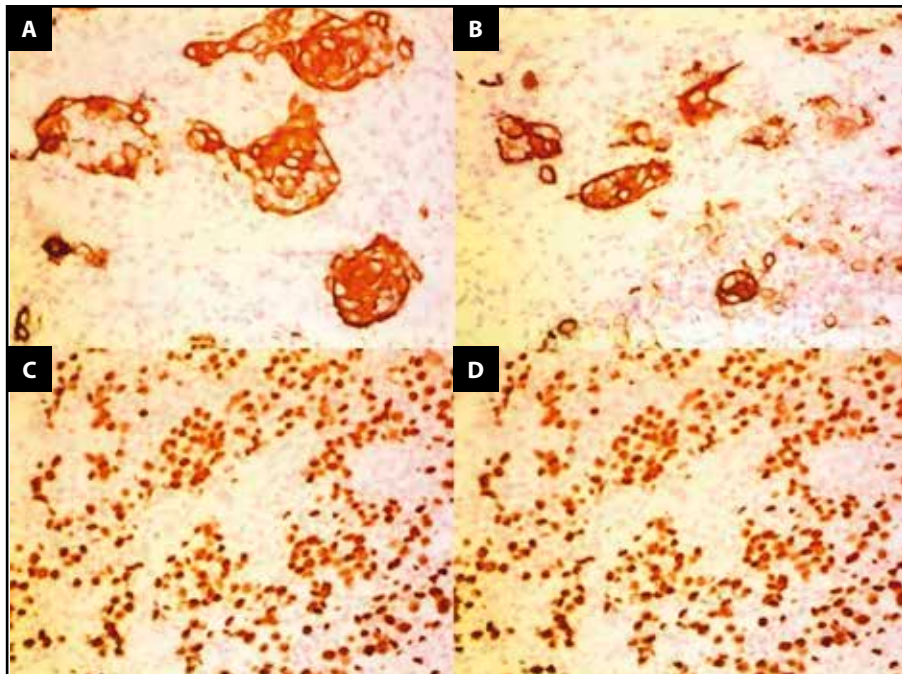


Figure 5. Immunohistochemistry images – The tumor cells expressed CK (A), EMA (B), and showed nuclear expression of p63 (C) and p40 (D) (IHC: A, B, C & D x400).

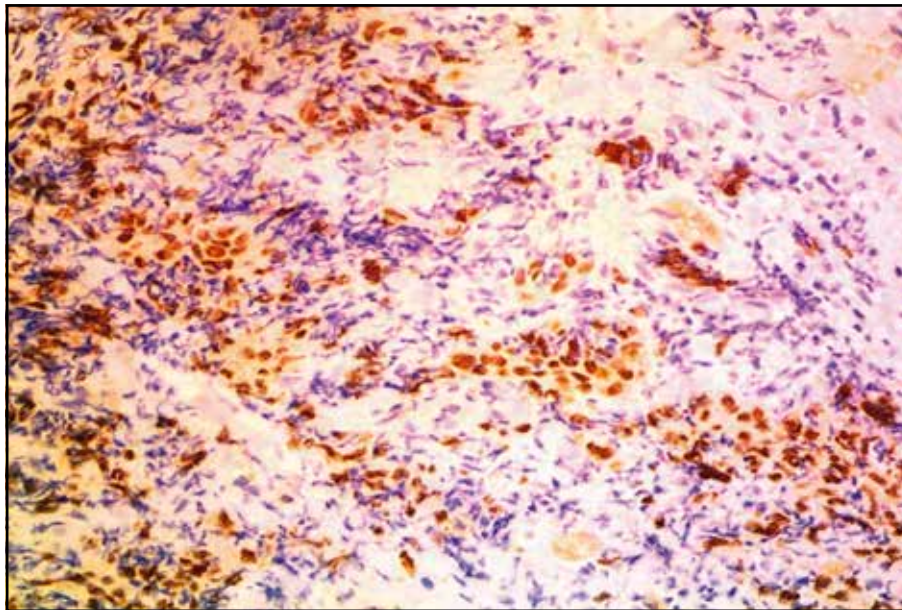


Figure 6. The tumor cells showed bright nuclear expression with NUT antibody [IHC- x400].

tent membrane protein). Considering the presence of abrupt keratinisation and strong positivity for epithelial IHC markers, we added NUT marker in the panel. It showed a bright nuclear expression in the tumor cells, confirming the diagnosis of NUT carcinoma (Figure 6).

The patient was planned for surgery and radiotherapy, but she succumbed within a week before the therapeutic commencement.

DISCUSSIONS

NUT midline carcinoma was originally found in midline sites of the body, but in recent years, it is also found in other sites and thus it has been renamed NUT carcinoma. It is a rare, aggressive variant of SCC that is genetically defined and diagnosed. Shiota et al.⁷ were the first ones to unleash the mutation of NUT gene in post-

meiotic spermatogenic germ cells causing recruitment of p300/ CBP to enhance the acetylation of H4K5 and H4K8 histone. This recruitment led to histone-to-protamine replacement, causing the malignancy. The characteristic genetic mutation is fusion of NUT at 15q14 with BRD4 on 19q13, resulting in the transformation of BRD4-NUT oncogene or sometimes BRD3-NUT formation¹⁻⁸.

NC consists of fusion between NUTM1 with BRD4 (Bromodomain containing protein 4) to form BRD4-NUTM1 oncogene or may also fuse with various other genes such as BRD3, Nuclear receptor Binding SET Domain Protein 3 (NSD3), Zinc Finger Protein 532 (ZNF532), Capicua transcriptional repressor (CTC) and other yet to be discovered genes¹. The usual fusion partner for NUT includes BRD4, BRD3 and sometimes NSD3^{9,10}. However, Alekseyenko et al. revealed ZNF532 chromatin factor could interact with BRD4-NUT complex to form ZNF532-NUT¹¹. Lee et al. confirmed no other genes except BRD3 or BRD4-NUT were affected, causing NC¹². BRD4-NUT prevented the differentiation of NC by maintaining the expression of MYC gene. Aggressiveness of NC is because of the ability of BRD4-NUT to fill the MYC gene region and other genes^{13,14}.

A characteristic and diagnostic feature of NC includes genetic mutations on 15q14 chromosome to form BRD4-NUT oncogene responsible for the formation of NC. The reason for these mutations is not detected till date to be in association with any environmental, familial or microbial causes and, thus, it is an area to be explored further. The diagnosis is finalized only after the genetic detection of BRD4-NUT mutation. This mutation can be identified by protein evaluation through immunohistochemistry or other genetic detection methods, such as FISH and RT-PCR. In the presented case, IHC evaluation was done, and the epithelial islands showed nuclear expression for NUT to confirm the diagnosis of NC^{1-6,8}.

The oncogene is responsible for NC that may only be treated by targeting this gene formed. NC was mostly found in children and young adults initially; the age range has increased to vary between 1st to 8th decades of life. NC equally affects both genders. The present case reported was in her 4th decade. NC was originally depicted to be a midline carcinoma. This case is in the forehead frontal region that fits to the midline entity of the earlier term. However, in recent years, researchers have reported cases involving sites other than midline organs including lungs, salivary glands, thigh, pancreas, liver and kidneys^{1-6,8}.

Most common symptoms include tumoral mass that may increase in size rapidly, pain, involvement of adjacent bone and organs and also regional and distant metastases^{4,6}. In our case, the lesion presented as a rapidly growing mass and involved the frontal sinus and surrounding bone from the forehead skin region. It also involved the extradural space intracranially, thus showing local destruction. The mass caused infraorbital

edema. Based on the examination and most common clinical findings, such cases are usually diagnosed as neoplasms. In the current case, the clinical diagnosis was given as malignant neoplasm due to the clinical presentation as fungating mass rapidly increasing in size over a short period.

Imaging findings (CT scan or MRI) reveal mostly varying soft tissue densities, bone lesion findings which can vary from erosions to complete involvement. Regional and distant metastases are the common findings^{1-6,8}. Radiological findings of the current case included MRI and CT scan revealing radio-opacities, multiple bone erosions, bone marrow edema with admixed hyperdensities over the frontal sinuses. Hence, radiological differentials offered in the present case were malignancy and fungal sinusitis.

Histological features of NC are those of poorly differentiated or undifferentiated malignancies showing poorly distinguished cells with few nests, islands or sheets of epithelial cells consisting of abrupt keratinization that is an alarming feature of NC. Epithelial cells may show nuclear and cytoplasmic pleomorphism with prominent nucleoli⁸. In the current case, the histopathological picture showed uniform, loosely arranged, poorly differentiated large ovoid cells having vesicular nuclei and prominent nucleoli. There was a noticeable mixture of polymorphs. Based on the microscopic findings, the diagnosis initially given was poorly differentiated malignancy with a differential of undifferentiated sinonasal carcinoma, high-grade non-Hodgkin lymphoma and poorly differentiated sinonasal carcinoma. On careful review of H&E slides, we could notice abrupt keratinization and hence we considered NC in the differential⁸. IHC confirmed the diagnosis of NC.

We came across very few cases in our review of previous literature. Giridhar et al., in 2018, published an extensive report of systematic review that included cases of NC with the most common site of lungs (35.3%) followed by head and neck sites (35%)¹⁵. Table 1 includes previously reported cases of NUT carcinoma in the head and neck. On reviewing the literature, so far 39 cases of NC have been reported in the head and neck region. In the head and neck region, the most common site identified is the nasal cavity, followed by sinus cavities. Few cases originated in the oral cavity and salivary gland^{1,2,16,17}. The cases in our review were mostly of middle-aged, only 3 cases were found in young individuals^{16,18,19}.

Overall, 26 cases of NC have been reported in the Indian literature at various sites. Of these, 21 cases of NC have been reported in the head and neck region. These authors observed that the nasal cavity and sinuses are the most common sites in middle-aged individuals with poor survival rates of few months^{15,16,18-26}.

Treatment protocol for NC majorly includes surgical approach and radiotherapy. In the present case, the patient had already reported 5 months late due to lockdown pertaining to COVID-19 and was lost before starting any treatment protocol, within 1 week after the diagnosis.

Table 1. Published case reports of NUT carcinoma of the head and neck region.

Author and publication year	Cases	Site	Age/Sex	Clinical features/ Presentation	Radiological features	Provisional diagnosis	Treatment	Survival
Vakani et al, 2020 ²¹	1	Right sphenoid sinus	44yr/ M	Headache, dizziness, mild proptosis	Soft tissue density and erosions involving multiple bones	Neoplastic lesion	NM	NM
Hsieh et al, 2011 ⁶	1	Left paranasal sinus	54yr/ F	Diplopia of 2 months, left eye blindness, ptosis, absent light reflex, limited range of motion	MRI – tumor mass in the paranasal sinus	Tumor	NM	NM
Mills et al, 2014 ⁴	1	Right side neck	23yr/ M	Neck mass with sore throat, tongue swelling	MDCT - irregular margined mass involving the hypopharynx FDG-PET – multiple ground glass densities	-	Chemoradiation	3 months
Aqaimy et al, 2018 ²	3	Salivary gland	39yr/ F	Rapidly enlarging right parotid gland and lymphadenopathy	After 3 months metastasis to multiple bones	High-grade mucoepidermoid carcinoma	Excision and chemoradiotherapy	Metastasis after 3 months and died 4 months after primary surgery
			35yr/ M	Infiltrative Parotid mass	-	-	Total parotidectomy and neck dissection and chemotherapy	Multiple bone metastases 3 months postoperatively
			55yr/ F	Right parotid mass	-	-	Excision and neck dissection + chemotherapy and radiotherapy	Metastasis after 6 months and death 7 months after primary surgery
Kakkar et al, 2018 ¹⁸	5	Sinonasal and orbital	30yr/ M	Proptosis	-	Poorly differentiated SCC	-	-
		Left nasal cavity	31yr/ F	Nasal obstruction, proptosis and epistaxis	Large mass in the left nasal cavity, and involving multiple bones	Poorly differentiated carcinoma	Excision, chemotherapy	Died within 2 months of treatment
		Right nasal cavity	25yr/ M	Nasal obstruction and epistaxis for 1 month	-	Undifferentiated carcinoma	NA	NA
		Nasal mass	10yr/ F	Watery left eye with nasolacrimal duct blockage. 2nd time - Swelling over the medial canthus of the same side	2nd time CT – friable mass filling the left nasal cavity	Sebaceous carcinoma	Surgery and radiotherapy	NA
		Left nasal cavity	30yr/ F	Nasal obstruction and diminished vision	Endoscopy – polypoidal mass in the middle meatus of the left nasal cavity	Undifferentiated carcinoma	NM	NM

Lee et al, 2020 ²⁰	4	Right maxillary sinus	60yr/ F	2 nd time - skin defect and crust at the right nasofacial angle. 2 cm ulcerative lesion on the right hard palate	CT and MRI: soft tissue mass in the right maxillary sinus and nasal cavity	Poorly differentiated squamous cell carcinoma	Not done	Died in 1 year
		Left ethmoid sinus	45yr/ F	NM	CT: enhancing mass filling the nasal cavity	Poorly differentiated squamous cell carcinoma	Resection CCRT	NA
		Right ethmoid sinus	42yr/ M	Right periorbital swelling, eyelid edema, forehead skin numbness	CT and MRI: large necrotic mass in the right ethmoidal sinus and nasal cavity	Poorly differentiated carcinoma	Chemotherapy	NA
		Right ethmoid sinus	29yr/ M	NM	CT and MRI: high density mass-like lesion	Poorly differentiated carcinoma	Not done	NA
Magalhães et al, 2016 ¹⁶	1	Tongue dorsum	8yr/ F	Asymptomatic lymphadenomegaly, anorexia, dysphagia, weight loss	-	Poorly differentiated malignant neoplasm	Surgery, chemotherapy, radiotherapy	Died 8 months after the diagnosis
Minato et al, 2018 ¹⁹	4	Left nasal cavity, ethmoidal sinus, nasopharynx	56yr/ F	Nasal congestion and epistaxis	-	-	Chemoradiation	10 months
		Frontal sinus	66yr/ F	Subcutaneous mass	-	-	Chemoradiation	13 months
		Right nasal cavity, right maxillary and ethmoidal sinus	18yr/ F	Epistaxis and pain	-	-	Chemoradiation	Alive with disease at 12 months
		Bilateral nasal cavity and maxillary sinus	9m/ M	Swelling of the lacrimal sac and upper palpebrae	-	-	Chemoradiation	15 months
Saik et al, 2021 ²²	1	Left parotid lump	34yr/ F	Parotid lump – post partum	Well defined solitary mass	High-grade neuroendocrine carcinoma	Surgery	Died within 6 months after diagnosis
					Recurrent tumor: Same site single mass at surgical site		Recurrent tumor: Surgery, chemotherapy and radiotherapy	

Zhou et al, 2020 ¹	5 (3 cases of head and neck site)	Right orbit	59yr/ F	Mass in the right orbit	MRI: 1 cm infiltrative mass in the orbit	NM	No treatment	Died 4 months after diagnosis
		Larynx	35yr/ F	Dyspnea and dysphagia	NM	-	Chemotherapy	Died 9 months after
		Left maxillary gingiva	38yr/ F	Mass on the gingiva	2cm×1.5cm ovoid transparent shadow at the tooth apex surrounded by poorly defined borders	-	Surgery	AWD
Lee et al, 2017 ¹²	2 (1 head and neck case)	Sinonasal and intrathoracic	34yr/ M	Sinonasal and intrathoracic	-	-	Chemotherapy	Death in 4 months
Elkhatib et al, 2019 ²⁷	1	Sella	47yr/ F	Headaches and frontal sinus pressure	MRI shows 2.6x1.7 cm mass centered in the sella, extending to the pituitary infundibulum, laterally to the cavernous sinuses, bilaterally to the carotid arteries and anteriorly into the bilateral sphenoid sinuses	Melanoma	Chemotherapy and radiotherapy	Death after 5 months
Albrecht et al, 2019 ²⁸	1	Sphenoidal sinus	48yr/ M	Cephalgia, oculomotor nerve palsy, with consequent double vision, exophthalmos and ptosis	Soft tissue mass in the left sphenoidal sinus	-	Surgery, chemotherapy and radiotherapy	Free of disease at the 6-month follow-up
Klijaneinko et al, 2016 ²⁹	2	Sinonasal	20yr/ M	-	-	Esthesioneurocytoma Poorly differentiated carcinoma	Surgery, chemotherapy and radiotherapy	Recurrence and death after 8 months
Arimizu et al, 2018 ³⁰	1	Parotid Left nasal cavity	21yr/ F 49yr/ M	- Epistaxis and pain in the left eye	Mass invading the left maxillary sinus and the left frontal sinus. Bone metastases in the left ilium.	High-grade lymphoma	Radiotherapy	Death after 2 months
Seim et al, 2017 ³¹	1	Oral cavity	26yr/ M	Neck pain, swelling, otalgia and reduced oral intake	Mass involving the right oral cavity with involvement of the lymph nodes	Undifferentiated carcinoma of the salivary gland	Surgery and chemotherapy	Death after 4 months
Oliveria et al, 2019 ³²	1	Maxillary sinus	42yr/ M	Productive cough, facial pain and rhinorrhea	Expansive irregular heterogenous lesion on the left maxillary sinus and the left orbit apex with intracranial extension through the inferior orbital fissure	Poorly differentiated squamous cell carcinoma	Chemotherapy and radiotherapy	Death after 2 months

D'Souza et al, 2015 ³³	1	Nasal cavity	32yr/ F	Nasal congestion and rhinorrhea for 6 months. Epistaxis and sinus pressure, swelling around the right eye. Extension into the right orbit causing exophthalmos in the right eye.	Right nasal mass extending into adjacent paranasal sinuses.	-	Surgery, chemotherapy and radiotherapy	-
Ding et al, 2019 ³⁴	1	Right eye	60yr/ F	Pain in the right eye	Mass in the right orbit involving the right maxillary sinus and ethmoid sinuses	-	Surgery, chemotherapy and radiotherapy	Survival of 15 months
Maher et al, 2015 ³⁵	1	Right mandible	17yr/ F	Fever, weight loss, generalized bone pain, right mandibular swelling and shortness of breath	Large destructive lesion in the right mandible and compression fracture at T8 with abdominal and mediastinal lymphadenopathy	Round cell malignant neoplasm	Chemotherapy and radiotherapy	Death in 10 months
Storck et al, 2017 ³⁶	2	Sublingual gland	9yr/ M	Fever, vomiting and indigestion	Sublingual lesion with lymph node involvement	Lymphoma and small cell poorly differentiated blastoma	Surgery, chemotherapy and radiotherapy	Survival for more than 6 years
Wei et al, 2022 ¹⁷	1	Nasal cavity	60yr/ F	Nasal pain, nasal congestion with masses in the right nasal sinus and frontal sinus	Mass in the masseter muscle measuring 1.3 x 3 cm	Strept throat	Surgery, chemotherapy and radiotherapy	Disease free, survival for 8 months
Andreasen et al, 2016 ³⁷	1	Sublingual gland	40yr/ F	Swelling and meal related pain in the right sublingual region for 1 month	Heterogeneously enhancing soft tissue lesion	Allergic rhinitis	Surgery and radiotherapy	Survival of 5 months
					Well circumscribed contrast enhancing sublingual gland mass with necrotic centre	Poorly differentiated squamous cell carcinoma with basaloid differentiation	Surgery, chemotherapy and radiotherapy	Survival of 5 and a half months

NA - not available; NM - Not mentioned; AWD - Alive with disease.

The chemotherapeutic agent targeting BRD4 and BRD3 Bromodomain inhibitors is under development in recent times. Surgery and radiotherapy in NC are both independent factors that are found to be effective in NC and are most effective when started early. Numerous chemotherapeutic agents are being used in recent times. Drugs used for treatment of NC include cisplatin, carboplatin, cyclophosphamide, etoposide, doxorubicin, actinomycin D, vinorelbine, vinblastine, paclitaxel, docetaxel, 5-fluorouracil, S1, bleomycin, vincristine, ifosfamide, gemcitabine and BETis. These drugs are used experimentally as a single drug or in combinations¹³. In two case reports, the NC was treated as a sarcoma with comprehensive protocol due to its aggressive behaviour. The patients showed a favourable overall survival rate of 6 to 13 years. However, due to the fact that NC is underdiagnosed, standardized guidelines on its treatment modalities are not yet available^{36,38}. BET inhibitors are used in targeted therapies, showing a significant reduction in the tumour size and disease intensity. However, the studies have showed eventual development of resistance and relapse.

Due to unavailability of IHC markers and FISH probes for NUT gene in various laboratories and centres, the disease has been mostly reported as poorly differentiated or undifferentiated malignant neoplasm and due to under-reporting, the entity lacks enough clinical, pathological, therapeutic and prognostic data^{1-4,8}.

NC is an extremely fatal disease with the poor prognosis of survival rate ranging from few months to 2 years. Due to lack of definitive treatment protocol, the prognosis of the malignancy is very poor.

CONCLUSIONS

NUT midline carcinoma, a variant of squamous cell carcinoma, is a rare and aggressive neoplasm. Diagnostic and therapeutic challenges contribute to the poor prognosis of this malignancy. Poorly differentiated carcinoma with abrupt keratinization at few places in the entire lesion is the major morphological indicator for NUT carcinoma and needs to be further evaluated. The lesion can be diagnosed only through Immunohistochemistry and other molecular techniques such as PCR and FISH.

Previously, the entity was noted in the midline organs. However, recently, the lesions have been detected at other sites in the body. Very few cases have been reported in the head and neck region in the Indian literature. In our review, seven Indian researchers reported NUT carcinoma cases associated with head and neck sites. The most common site in the literature is the nasal cavity and thus, lesions at this site need a thorough evaluation for NC. Although several cases of NUT carcinoma have been reported overall, it is still a less known entity amongst Indian clinicians and needs to be diagnosed and reported at a larger scale.

The poor prognostic outcome and less established treatment protocols for the same condition makes further reporting and research on this entity necessary. Further reports including clinical, radiological, histological and prognostic behaviour of the lesion might aid in the development and administration of new definitive treatment protocols for NUT carcinoma.

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