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Case Report

Adjuvant Radiation Therapy in Nut Carcinoma of Parotid Gland - Rare Case Scenario

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Abstract

Tumors of salivary glands accounts to 3-4% of all head and neck neoplasms. The most common site of tumors among salivary glands is parotid and it accounts to 70% (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). In parotid gland tumors, both children and adult are the most common malignant subtype and it is Mucoepidermoid carcinoma (MEC) (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). Nuclear protein in testis (NUT) germline carcinomas represents a rare subset of highly aggressive and poorly differentiated epithelial neoplasms. It occurs due to the rearrangement of the NUT gene and it also occur in the aero-digestive tract, particularly in the sinonasal region and mediastinum (50%). It is initially described as mediastinal (midline) malignancy (French et al., 2003; Kubonishi et al., 1991). It affects mainly young adults but the age range varies greatly from the new-born to the elderly. Diagnosis of salivary gland NUT carcinoma is only feasible if NUT Carcinoma is included in the differential diagnosis, NUT IHC and or molecular testing should be performed (NUT Carcinoma of the Salivary Glands, 2018). In this article, we discussed our experience on treating a case with NUT-associated salivary gland carcinoma of right parotid gland with surgery followed by adjuvant radiotherapy. Patient is on regular follow up and remains free of the disease six months after his initial diagnosis and we concluded IHC for NUT to be done for diagnosis and on controversy, Genetic testing should be done for more accurate diagnosis.

Keywords: Midline carcinoma, NUT carcinoma, Poorly differentiated carcinoma, Salivary glands carcinoma, Squamous cell carcinoma

INTRODUCTION

Tumors of salivary glands accounts for 0.4% of all cancers, 3-4% of all head and neck neoplasms. The most common site of tumors among salivary glands is the parotid and it accounts to 70% (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). Approximately, 25% of parotid, 43% of submandibular and 65% of minor salivary glands tumors are malignant (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). Benign tumors are more common in young age and malignant tumors occurs at mean age group of 50 years, 2-3% of neoplasms occurs in children. In 2005, WHO classified major salivary gland tumors as 24 subtypes histologically (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). In parotid gland tumors, both in children and adult are the most common malignant subtype and it is mucoepidermoid carcinoma (MEC). Histologically, most common sub-type being adenoid cystic carcinoma (27%) are the most

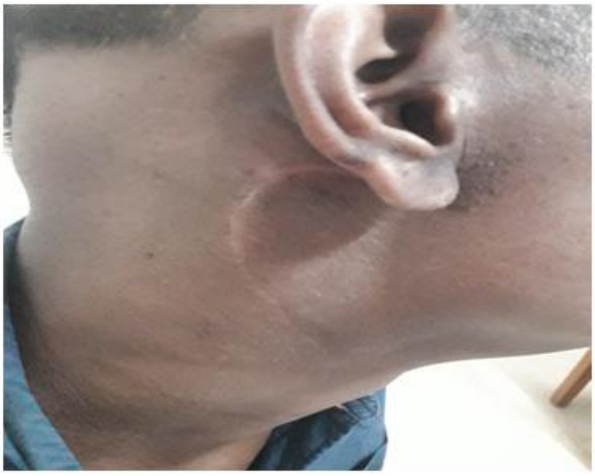


Figure 1. POST Radiation site -Courtesy Mr. Vignesh

common in minor salivary glands (Perez and Brady's principles and practice of radiation oncology/ editors, Edward Halperin et al-6th edition). NUT germline carcinomas represents a rare subset of highly aggressive and poorly differentiated epithelial neoplasms and it occurs due to rearrangement of the NUT genet (15;19) (q13;p13.1), which is commonly fused to BRD4 to form the BRD4-NUT oncogene which blocks epithelial differentiation through chromatin binding and it exhibit fast growth and distant metastasis (French et al., 2003; Kubonishi et al., 1991). Majority occurs in the aero-digestive tract, particularly the sinonasal region and mediastinum (50%), initially described as mediastinal (midline) malignancy. Rarely it has risen in bone, bladder, abdominal retroperitoneum, pancreas and salivary glands. It affects mainly young adults but the age range varies greatly from the new-born to the elderly (First evidence of treatment efficacy in metastatic carcinoma of the parotid gland with BRD4/NUT translocation (2015). Through review of literature uncovered till now, ten cases of NUT carcinoma possibly of salivary gland origin (Case reports). This article shares the experience on treating a case of NUT-associated salivary gland carcinoma of right parotid gland in an adolescent male with surgery followed by adjuvant radiotherapy.

Case Report

An apparently healthy 25 years old male with no comorbid was evaluated for swelling in right side face for 2 months duration which is insidious in onset. It gradually increased in size with pain in swelling for over 10 days. He had no fever or oral discharge. No other significant past history, treatment history or family history. Examination and investigation was done at private non oncological center in local place and the results showed poorly differentiated neoplasm. He underwent total parotidectomy with removal of cervical lymph nodes in November, 2019 in same hospital. Intraoperatively, cystic swelling of 4x3cm lesion in superficial lobe of parotid with inflammation was noted. Both lobes were removed and facial nerve was preserved. Post-operative histopath-ology reported a poorly differentiated mucoepi-dermoid carcinoma and in cervical node suggests poorly differentiated squamous cell carcinoma. Then he was referred to our institute for further management. Here on clinical examination, no abnormality detected in oral cavity or right parotid bed. Scar was healthy. No significant neck nodes present (Figure 1). House backmann Grade II facial nerve Palsy was there. MRI of parotid region done showed only post-operative changes. Chest X ray done was normal. Slide review done here suggested poorly differentiated malignant tumour, infiltrating small typical cells exhibiting scanty cytoplasm and hyperchromatic vesicular nuclei with prominent nucleoi. Focal keratin pearls were seen. Further Immunohistochemistry (IHC) was done. IHC NUT, Keratin, p40 showed diffused positive reaction with ki67 80%. IHC Vimentin, Synaptophysin, CD 99,CD34 showed negative reaction. Taking morphology, IHC reaction into consideration, features suggestion of NUT associated carcinoma of parotid gland (Figure 2). Further PET CT done showed thickening with fat stranding in the operated site with no other increased metabolic activity. It was diagnosed as a case of non metastatic NUT associated carcinoma of right parotid gland pT2Nx. It was discussed in forum and planned for adjuvant radiotherapy and close follow up. Chemotherapy was not considered as there was no definite role. He was treated with 6Mv x ray beam therapy to post-operative site and right side of neck using intensity modulated radiotherapy technique (IMRT). Planned PTV receives TD 60Gy (200cGy in 30 fractions) for 5 days in a week for 6 weeks, maintaining OAR constraints in January 2020. Patient was on regular follow up and remains free of disease 6 months after his

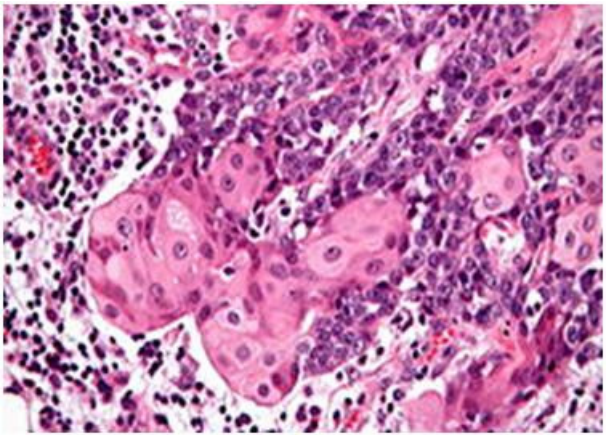


Figure 2. NUT associated carcinoma-very high mag (WC)

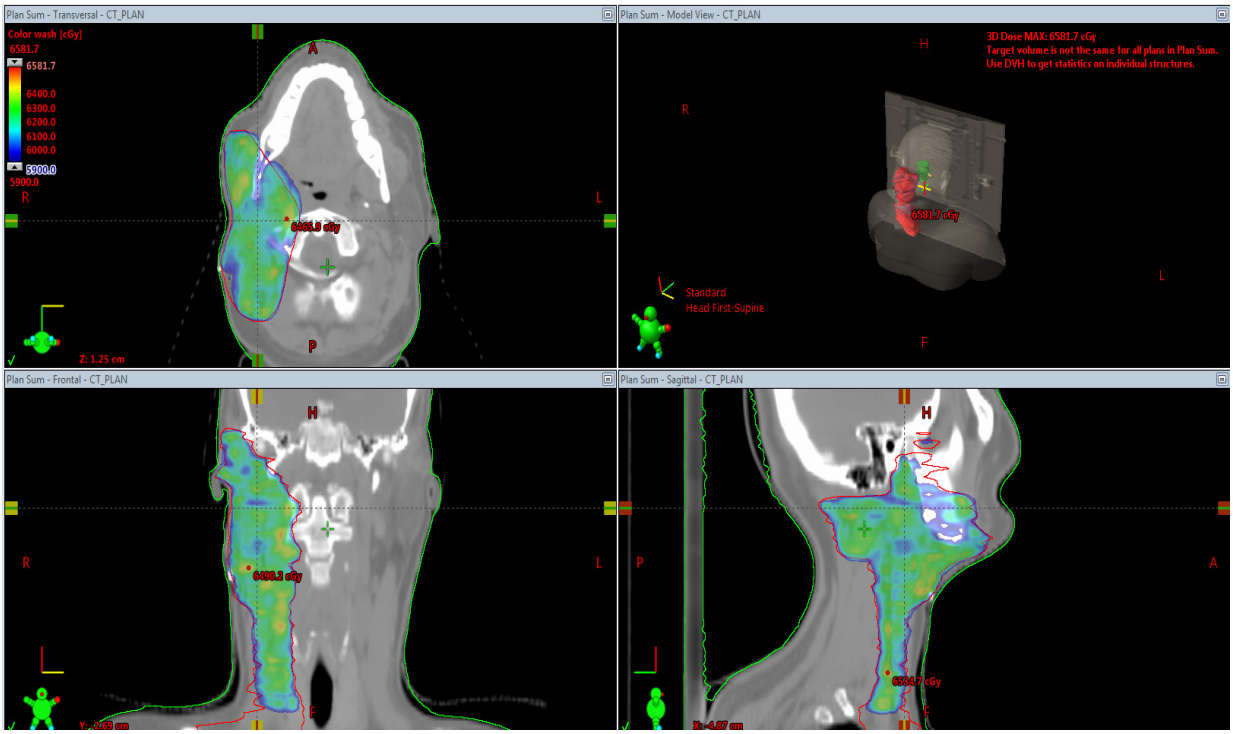
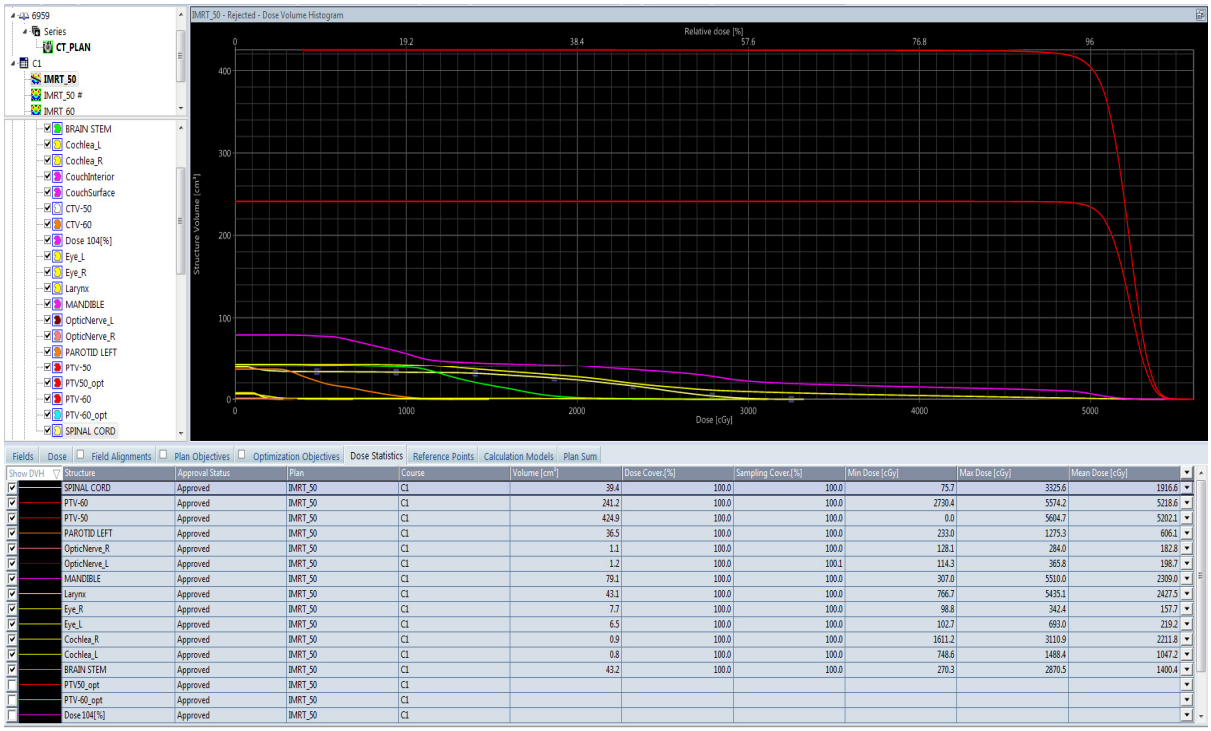


Figure 3. Isodose volume with colour wash of dose Distribution



Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [cGy]	Max Dose [cGy]	Mean Dose [cGy]
SPINAL CORD	Approved	IMRT_50	C1	39.4	100.0	100.0	75.7	3325.6	1916.6
PTV-60	Approved	IMRT_50	C1	241.2	100.0	100.0	2730.4	5574.2	5218.6
PTV-50	Approved	IMRT_50	C1	424.9	100.0	100.0	0.0	5604.7	5202.1
PAROTID LEFT	Approved	IMRT_50	C1	36.5	100.0	100.0	233.0	1275.3	606.1
OpticNerve_R	Approved	IMRT_50	C1	1.1	100.0	100.0	128.1	284.0	182.8
OpticNerve_L	Approved	IMRT_50	C1	1.2	100.0	100.1	114.3	365.8	198.7
MANDIBLE	Approved	IMRT_50	C1	79.1	100.0	100.0	307.0	5510.0	2309.0
Larynx	Approved	IMRT_50	C1	43.1	100.0	100.0	766.7	5435.1	2427.5
Eye_R	Approved	IMRT_50	C1	7.7	100.0	100.0	98.8	342.4	157.7
Eye_L	Approved	IMRT_50	C1	6.5	100.0	100.0	102.7	693.0	219.2
Cochlea_R	Approved	IMRT_50	C1	0.9	100.0	100.0	1611.2	3110.9	2211.8
Cochlea_L	Approved	IMRT_50	C1	0.8	100.0	100.0	748.6	1488.4	1047.2
BRAIN STEM	Approved	IMRT_50	C1	43.2	100.0	100.0	270.3	2870.5	1400.4
PTV50_opt	Approved	IMRT_50	C1						
PTV-60_opt	Approved	IMRT_50	C1						
Dose 104[%]	Approved	IMRT_50	C1						

Figure 4. Dose volume Histogram and Organ at risk dose constraints

initial diagnosis. Dose distribution and dose volume histogram graph are shown in Figure 3,4

DISCUSSION

Nuclear protein in testis (NUT) carcinomas is a poorly differentiated carcinomas of the salivary gland and it represents the diagnostic challenges and usually portend poor prognosis. Such tumors frequently exhibit high-grade anaplasia, increased mitoses and necrosis (NUT Gene Rearrangement in a Poorly-differentiated Carcinoma of the Submandibular Gland (2010). Since histologic features are that of a poorly differentiated carcinoma, NUT carcinoma is often misdiagnosed mainly due to the superficial similarity of this neoplasm to conventional squamous cell carcinoma (SCC) or other poorly differentiated. Thus, diagnosis of salivary gland NUT carcinoma is only feasible if NUT Carcinoma is included in the differential diagnosis, NUT IHC and/or molecular testing performed (NUT Carcinoma of the Salivary Glands, 2018). Review of current literature shows that NUT carcinoma commonly occurs in young adults with median age group of 21 years and there is no gender predilection (NUT Carcinoma of the Salivary Glands, 2018). Thus, it is recommended to include NUT IHC in the workup of undifferentiated carcinomas and it is considered sufficient for diagnosis based on the high specificity (almost 100%) and sensitivity (87%) of the antibody (NUT Carcinoma of the Salivary Glands, 2018; Stelow and French, 2009; Bishop and Westra, 2012; Haack et al., 2009). However Genetic testing for rearrangements is recommended for better understanding and characterization of this rare aggressive disease (First evidence of treatment efficacy in metastatic carcinoma of the parotid gland with BRD4/NUT translocation, 2015; NUT Gene Rearrangement in a Poorly-differentiated Carcinoma of the Submandibular Gland, 2010; NUT Carcinoma of the Salivary Glands, 2018). As NUT gene with negative BRD3/BRD4 signals, classifying this salivary gland tumor as a ‘‘NUT-variant’’ carcinoma, shows better survival than positive BRD4-NUT translocation in review (NUT Gene Rearrangement in a poorly-differentiated carcinoma of the submandibular gland (2010).

CONCLUSION

NUT associated carcinoma should be included in differential diagnosis of poorly differentiated salivary gland carcinomas particularly in cases of poorly differentiated SCC (especially in children and adult age group). IHC for NUT should be done for diagnosis and on controversy, genetic testing should be done for more accurate diagnosis. Adjuvant radiotherapy is a must to be indicated in all stage for better local control. In metastatic setting, in literature chemotherapy (including platinum, alkylating agents, taxanes or anthracycline-based regimens) is considered, but no durable responses (NUT

Gene Rearrangement in a Poorly-differentiated carcinoma of the submandibular gland (2010).

Consideration

In poorly differentiated tumors, BRD4-NUT positive and NUT-variant carcinomas lack in distinguishing histological or immunohistochemical feature. It can diagnose only by genetic testing. In our case, genetic testing was not done as IHC NUT itself was positive and also have logistic issue. Genetic testing would have been done and it may helped for accurate categorization, treatment and in follow up.

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