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Case Report

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Facial Vein Thrombosis in Head & Neck Squamaous Cell Carcinoma with Review- A Rare Case Report

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ABSTRACT

Introduction: Tumor thrombosis of the head and neck region is a rare occurrence and the majority cases that have been reported are of differentiated thyroid cancers.

Presentation of Case: We discuss a case of a male patient who reported with the complaint of non-healing ulcer on left buccal mucosa which was histopathologically diagnosed as squamous cell carcinoma (SCC). The PET-scan done as a part of initial work up investigations revealed a massive thrombus in the left facial vein. No direct vascular invasion of the tumor into the left facial vein was observed. The patient was aggressively treated with surgery followed by adjuvant chemo-radiation. The patient is disease free since last two years.

Conclusion: Facial vein tumor thrombosis originated from SCC apparently reflects extremely aggressive state of the tumor. Recognition and precaution to this condition is essential for the development of a clinically effective treatment strategy. According to an elaborate literature search, this is first such case to be reported of its kind.

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Introduction

Venous thromboembolism (VTE) is a commonly encountered entity in cancer patients. The association between venous thromboembolism and cancers is well established since historic times. It was first discussed in the 19th century by Trousseau and Bouillaud [1, 2]. It has been estimated that patients with cancer have an approximately four to seven-fold increased risk of VTE compared to those without cancer. Many biological mechanisms have been proposed to explain the increased incidence of thrombosis in cancer patients. All these emphasize that the presence of malignant cells induces a prothrombotic switch of the host hemostatic system, and in turn, the blood clotting activation stimulates tumor growth and dissemination. Apart from these biologic factors, the treatments used for cancers also contribute in creating a hypercoagulable state in the body. In cancer patients, these thrombotic can range from venous or arterial thrombosis to systemic syndromes, such as disseminated intravascular coagulation (DIC) with severe bleeding. Preventing these complications is clinically relevant because they considerably contribute to the morbidity and mortality of such patients [1-4].

Head and heck (H&N) cancer is one of the most common cancers worldwide and in India. It includes oral cavity cancer (lip, tongue, mucosa and gingivae), pharyngeal cancer (oropharynx, nasopharynx, hypopharynx), laryngeal cancer and thyroid cancer. Oral cavity cancer is the most frequently involved location and more than 90% of H&N cancers are squamous cell carcinomas (SCCs). Despite these cancers accounting for considerable numbers, it is difficult to determine the risk of thrombosis due to lack of sufficient evidence in literature. Instead, according to the available literature, it seems that thrombosis risk in head and neck cancer patients is almost negligible [1, 5 & 6].

We discuss a case of a 68 year old male with carcinoma left buccal mucosa, along with review of literature of occurrence of venous thromboembolism in head and neck cancer patients. In the past literature, very few incidents of venous thromboembolisms have been reported the head and neck region particularly in patients diagnosed with Squamous Cell Carcinoma.

Case Report

A sixty eight year old male presented to the outpatient department of a tertiary care hospital in a metro city with the complaint of a non-healing ulcer on left cheek since last 3-4 months. The patient was a resident of a nearby village where he had consulted a private practioner. The patient informed that he first experienced burning

sensation on having hot and spicy food 1 year ago which was followed by development of an ulcer on left cheek. The patient did not pay much attention to it initially and the size of the lesion increased to reach the corner of mouth with associated swelling on face and reduced moth opening. The patient self-medicated with some painkillers and hot fermentation which did not provide any relief. It was then that the patient's family took him to a private practioner in their village who referred him to higher centre post extra-oral and intra-oral examination. At our centre, on extra-oral examination, there was a diffuse swelling on left side of face. Intra-oral examination revealed markedly reduced mouth opening and an ulceroproliferative growth measuring approximately 4.0 cm in greatest dimension involving left buccal mucosa, maxillary and mandibular gingiva-buccal sulci. The lesion was indurated and fixed to the underlying subcutaneous fat, overlying skin was uninvolved. No palpable cervical lymphadenopathy was present. Based on the history and clinical findings a provisional diagnosis of Epithelial Malignancy was made. A punch/ incisional biopsy from the lesion was advised. The patient underwent a punch biopsy with was suggestive of Well differentiated Squamous Cell Carcinoma. After the diagnosis of malignancy, PET-CT was advised to look for any distant metastases. The PET-scan showed a FDG avid soft tissue mass lesion involving left buccal mucosa, upper and lower vestibules of mouth with no cortical erosion of mandible bone. Left facial vein showed mildly FDG avid ill-defined nodular density lateral to the angle of the mandible measuring 3.0 cm. There were such deposits throughout the course of the facial vein involving the masseter muscle and parotid gland. Based on the clinical and radiological findings, it was staged as pT3N0M0 disease. The case was discussed in the tumor board of the hospital where it was planned for surgical resection of primary along with selective neck dissection and excision of the facial vein thrombus followed by adjuvant therapy. The patient was planned for a left composite resection along with left Extended Supra-Omohyoid Neck Dissection (ESOHND). The facial vein along with the thrombotic foci was excised. The resected specimen was submitted for histopathological examination. The specimen included left composite resection - WLE buccal mucosa with marginal mandibulectomy and partial maxillectomy with left ESOHND and excised facial vein. The lesion clinically and radiologically was reaching/ involving both the maxillary and mandibular vestibules warranting resection of the maxilla and mandible bones. The resected primary specimen was sent for intra-operative consultation to the pathology department where the resected margins were found to be adequate (more than 1 cm) and negative for invasive malignancy. The stump of facial vein was submitted for frozen section which was free / uninvolved by tumor. The histopathological examination revealed the primary tumor as Squamous cell carcinoma, conventional with histological grade 1 – well differentiated (Figure 1A, 1B). The pathological TNM staging was pT4aN0 with perineural invasion (PNI) of small and medium sized nerves. The microscopic sections from the excised facial vein specimen showed the entire lumen of facial vein was occluded by tumor deposits of SCC (Figure 2A, 2B). Thereafter, the patient underwent adjuvant chemo-radiation therapy. Patient is under rigorous follow up for last two years (25 months) and is disease free till date (last follow up done 2 months ago).

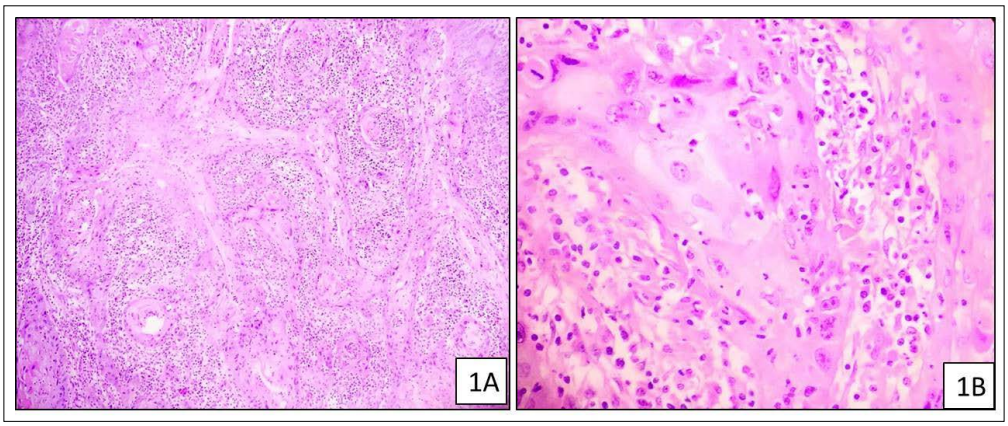

Figure 1

A-Photomicrogrpah showing conventional squamous cell carcinoma (HE-100x)
B-Photmicrograph showing the high power of malignant squamous epithelial cells (HE-400x)

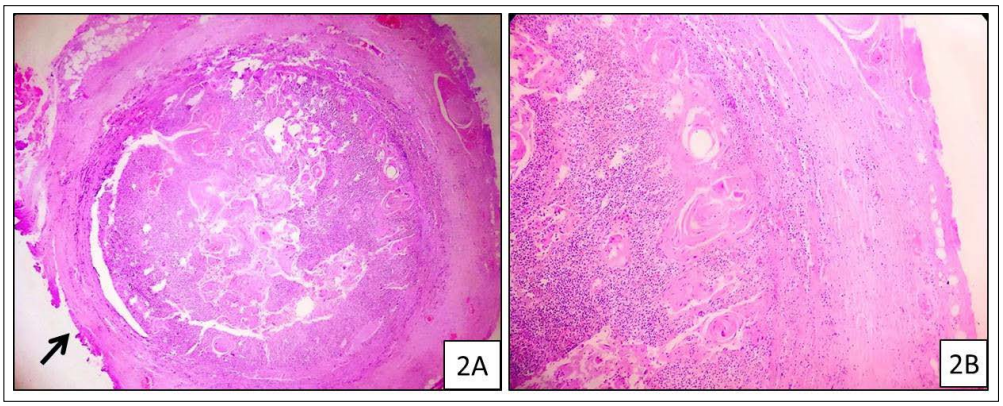

Figure 2

A-Photomicrograph showing the intact facial vein wall and the lumen occluded by tumor (HE-40x)
B-Photomicrograph showing the tumor attached to wall of facial vein (HE-100x)

Discussion

Thromboembolisms have been always associated with cancers, although its incidence in head and neck cancers is not well established yet. The head and neck region veins are rare sites for thrombosis; however, venous thrombosis without an obvious cause may be the initial manifestation of an occult malignancy. Haen et al. did an extensive review of literature to assess the risk of venous thromboembolism (VTE) associated with H&N cancer. In their review they concluded that there is a very low thrombosis risk associated with H&N cancer (Table 1). A myriad of clinical risk factors, i.e., patient-related or cancer-specific, concur to the activation of blood coagulation and importantly contribute to the thrombotic risk of cancer patients. all HN cancers have similar biological risk factors and disturbed balance of hoemostatic system leading to thrombotic complications as for other cancers. These risk factors include the following: a) Strong expression of procoagulant proteins – Tissue Factor (TF), Cancer Procoagulant, Factor VII); amongst these TF is best studied and induces changes in stromal cells of the 'tumor niche'; b) Modified thrombosis/fibrinolysis mechanisms; c) Tumor-shed procoagulant microparticles- possibly lead to development of Disseminated Intravascular Coagulation (DIC) like syndrome; d) Procoagulant cytokines [1-3]. Thrombus in the head and neck region has been reported majorly in cases of differentiated thyroid carcinoma origin- probably due to increased incidence of hematogenous metastases in these type of cancers especially follicular carcinoma thyroid. It is conjectured that these extravasated tumor cells form tumor thrombus in their circulating veins, including the IJV and innominate veins. However, no case of an IJV thrombus due to any other type of HN cancer has been reported in past literature. Tecker AM et al (2008) reported a case of a patient with cutaneous SCC (dorsum of nose and temple) who developed tumor thrombus in the facial vein in association with tumor recurrence [4]. These authors proposed that the thrombus developed by direct vascular invasion of the facial vein [4]. Wakasaki T et al, reported two cases of IJV tumor thrombosis originating from squamous cell carcinoma (SCC) believed to be the first such case report in literature. One of the cases was a Supraglottic SCC and other was SCC of the thyroid gland. They speculated that may be the SCC tumor cells are less likely to aggregate in the vein than thyroid cancer cells. These authors proposed that the presence of tumor thrombus is directly associated with increased risk of local recurrence and distant metastases and decreased disease free survival and overall survival. In the article by Wakasaki et al, the patient survived less than one year post surgery [2, 4-6]. In our case, there was no direct invasion of the facial vein by the tumor similar to the findings in the study by Wakasaki T. Our patient is under strict vigilant follow up both clinically and radiologically every alternate month and is disease free till date.

First Author	Year	Study Design	Population	Number of Patient	Median Follow-up	Number and per Centage of VTE in H&N Cancer
Innis	2009	Retrospective review study	Patients following otolaryngological surgery with and without malignancy	6122	5 years	5 VTE/542–0.92%
Hennessey	2012	Retrospective cross sectional study	Patients following H&N cancer surgery	93,663	5 years	1860 VTE /93663–2%
Thai	2013	Retrospective review study	Patients following a > 4h00 H&N cancer surgery	134	2 years	2 (confirmed-8 (suspected) VTE/134–1.4–5.8%
Gavriel	2013	Retrospective cohort study	Patients following a H&N cancer surgery, with and without chemoprophylaxis	1018	5 years	0 VTE/1018–0% (both cohort)
Clayburgh	2013	Prospective cohort study	Patients following H&N cancer surgery	100	1 month	8 VTE /100–8%
Lodders	2015	Retrospective cohort study	Patients following oral cavity cancer surgery	233	5 years	1 VTE/233–0.41%
Ali	2015	Retrospective cohort study	Patients following H&N cancer surgery	413	8 years	12 VTE/413–2.9%
Kakei	2016	Retrospective descriptive study	Patients following oral cavity cancer surgery with simultaneous reconstruction	133	7 years	35 VTE/133–26.3%
Wang	2017	Retrospective descriptive study	Patients following oral cavity and maxillary cancer surgery	9724	4 years	14 VTE/9724–0.14%

Table 1: Incidence of VTE in patients with H&N cancer following treatment (surgery), an analysis of specific studies (Table reprinted from Haen et al.) [2].

Role of adjuvant therapy has been controversial with some authors reporting no or little effect of adjuvant treatments while others showing increased disease free survival or mortality with addition of adjuvant therapy after surgery. Previous researchers have anticipated that the presence of a thrombus in IJV/ facial vein apparently reflects extremely aggressive behaviour of tumor with a high risk for distant metastases and recurrences. In our case, the facial vein thrombus was well detected during the initial investigation work up and till date the patient has developed no distant metastases or recurrences in last two years. To the best of our knowledge, this is the first such reported case of SCC of left buccal mucosa with facial vein thrombus in the past literature [1-6].

Conclusion

Venous thromboembolisms in a facial vein in a case of SCC of oral cavity are extremely rare. SCC tumor thrombus in the facial vein apparently reflects extremely aggressive property of tumor with a high risk of distant metastases and recurrences. Thus, early and accurate diagnosis is very important in preventing debilitating complications and decreased life expectancy/ quality of life of patients. Therefore, aggressive and prompt treatment approaches can prove to be life-saving in such patients.

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