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Radiation Induced Clear Cell Variant of Acinic Cell Carcinoma in Submandibular Salivary Gland - A Rare Case Report

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Abstract: ***Acinic cell carcinoma (ACC), usually described as a low-grade malignant salivary gland neoplasm thataccounts for about 17% of the tumours with their cell of origin from the acinar cells of the gland. Previous radiation exposure and familial predisposition are documented risk factors for ACC.ACC occurring in the submandibular/ sublingual salivary gland is extremely rare. Clear cells appreciated among the tumour cells population are attributed to physiological and pathological clearing among glandular cells and has been reported in ACC. The proportion of clear cells dominating the cellular population is not a common occurrence. We report one such case diagnosed with involvement of submandibular salivary gland with a previous history of radiation therapy for laryngeal carcinoma 16 years earlier. Histopathological analysis supported the evidence of clear cell variant of Acinic cell carcinoma of submandibular salivary gland, possibly radiation induced.***

Keywords: Radiation Induced Tumours,Salivary Gland Neoplasm, Acinic Cell carcinoma, Submandibular Salivary Gland Tumour, Rare tumours of head and neck

1. Introduction

Radiation science is applied in medicine for diagnostic and therapeutic purposes in both malignancies and non-malignant diseases. The extreme side effect of radiation is the causation of radiation induced malignancies. Radiation activated physical modes of carcinogenesis which induces mutations in an actively dividing cell is proposed as the pathogenesis behind fresh malignancies occurring in those patients treated with radiation therapy for their primaries(1).

Cahan and associates proposed certain criteria to diagnose radiation induced malignancies(2), the modified criteria states that a) Malignancy arises at the irradiation field b) latent period of longer than 4 years have lapsed between earlier treated primary and new tumour c) treated tumour must have been biopsied and proved histologically distinct from current radiation induced malignancy d) tissue in which malignancy arose must have been normal prior to radiation.

Godwin first described ACC by the term “acinar” due to its histological similitude to secretory parenchyma first reported in the parotid gland(3). In previous literature theaggressive nature of the malignancy was highly disputed and classified as an “acinic cell tumour” or “adenoma”. Recent studies elaborated theirnature for repeated recurrence, metastasis and mortality which led to the WHO re-classifying the tumour as a low-grade malignant carcinoma(4).

2. Case Report

A 65 year old male patient presented to the Department of Oral and Maxillofacial Surgery of Rajah Muthiah Dental College and Hospital with a chief complaint of an insidious swelling which gradually increased in size in the left side of neck region for the past 5 months. The swelling was associated with continuous, dull aching and non radiating pain that aggravated on food intake along with hoarseness of voice. The patient gave a history of carcinoma laryngopharynx diagnosed by biopsy under direct laryngoscopy for a mass in right pyriform fossa 15 years back. It was histologically diagnosed as well differentiated squamous cell carcinoma of oropharynx for which the patient had been subjected to 22 cycles of radiation. followed by chemotherapy employing injection cisplatin 50mg by intravenous route andinjection 5FU 500mg by intravenous routein 1unit DNS over 3hrs was administered for the same. Patient gave a positive history of betel nut and gutka chewing for 15 years and had stopped the habit 15 years back during the diagnosis of carcinoma but continued to consume alcohol occasionally.

On clinical examination, the patient had a firm swelling in the left neck region of size 4x3cm extending anteriorly 2cm from parasymphysis region, posteriorly 2cm in front of the angle of mandible, superiorly 2cm below the tragus and inferiorly 2cm below the lower border of mandible upto the anterior triangle of neck. No other palpable regional lymph

nodes were evident. Intraorally, the swelling was bimanually palpable(Fig. 1).

Figure 1: Showing the tumourpre op

Fine needle aspiration cytology was done which revealed, branching cellular clusters of epithelial cells and clear cells, acellular elements including myxomatous and chondroid components were observed. Ultrasonography showed a hypoechoic lesion size(3x3.2cm approx) noted in the left submandibular region and the submandibular gland could not be delineated.

Multi slice CECT of the neck was taken. A well circumscribes, round, soft tissue mass of size 4.3cm x 3.8cm x 4.4cm was noted in the left submandibular region with central low attenuating areas suggestive of necrosis. Peripheral enhancement was noted. Mass effect was exhibited over the adjacent structures with no evidence of bony erosion or invasion of the adjacent structures. With the above findings the tumour was provisionally diagnosed as pleomorphic adenoma(Fig 2.).

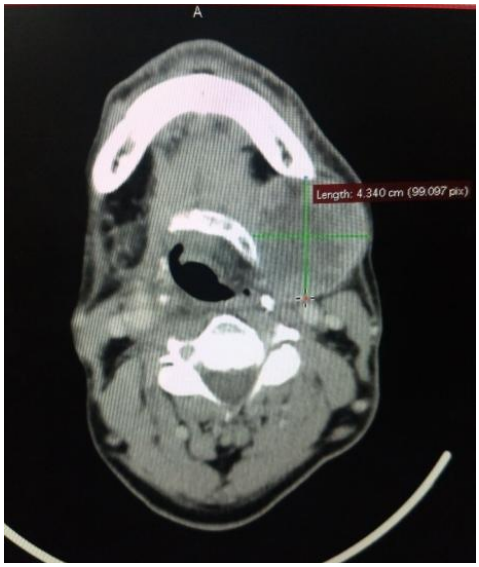

Figure 2: Showing CECT Scan

Excisional biopsy of the tumour mass was planned and executed under general anaesthesia(Fig 2,3). The tumour was excised as a whole and sent for histopathological examination . Aromovac drain was placed and secured using 3-0 silk. Layered closure was done using 3-0 vicryl and skin staples. The post operative recovery period was uneventful.

Figure 3: Exposure of tumour

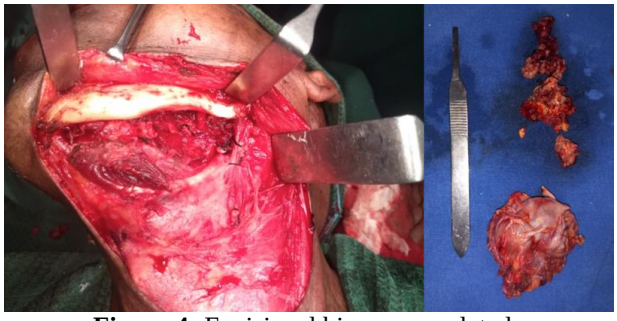

Figure 4: Excisional biopsy completed

Post operative biopsy report revealed circumscribed islands of clear cells with pale staining nuclei and dispersed chromatin and ductal cells with granular cytoplasm and hyperchromatic nuclei. Most islands showed areas of hyalinisation and focal areas of haemorrhage(Fig. 5,6). The case was finally diagnosed as clear cell variant of acinic cell adenocarcinoma.

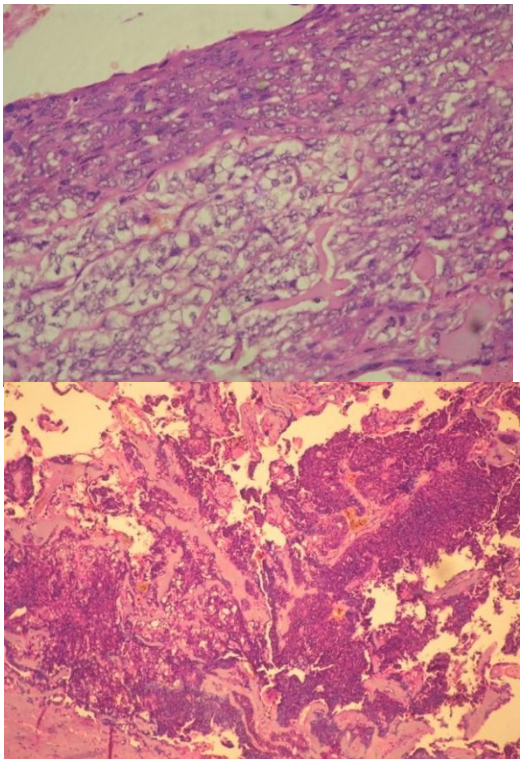

Figure 5 & 6: Showing the histopathology picture of ACC

Patient was reviewed for past 1 year and except for altered sensation in the anterior part of the left side of the tongue the patient was normal and had no other complaints.

3. Discussion

Though previous radiation exposure is a well known risk factor for salivary gland malignancies, there are limited documentation on the same owing to their occurrence of just 6-8% in the head and neck region[4,5]. The most common documented malignancy being mucoepidermoid carcinoma followed by adenocarcinomas.

In studies by Shore-freedman et al, the first cases were diagnosed 5 years after radiation therapy and incidence of secondary salivary gland malignancies increased upto 25 years post radiation treatment[6].Carcinomas and leukemias are frequently encountered in organs subjected to low dose radiation and at distant sites from focus of radiation; whereas sarcomas are principallyevidenced to arise from tissues receiving high dose radiation and in close relationship to radiation fields[7].

Non-therapeutic scatter dose to tissues at a distance from the primary treatment volume has been postulated to be the reason of radiation induced malignancies arising in these areas because of low-dose effects and are mainly carcinomas[8].Intensity-modulated radiation therapy (IMRT) involves more fields for treatment; as a consequence, a larger volume of normal tissue is exposed to lower doses. In addition, IMRT requires longer beam-on time, which results in increase in the number of monitor units. Both factors are associated with increased integral dose, which tends to increase the risk of secondary malignancies[9].

Zablotskaet al, reported an increase in risk of squamous cell carcinoma and adenocarcinoma after radiation therapy for well differentiated carcinoma involving the oesophagus. Genetic alterations and genomic injury are proposed mechanisms for radiation-induced tumorigenesis in normal tissues[10]. Best et al in their genome wide association studies (GWASs) have elaborated the identification of significant predictors of cancer susceptibility in patients earlier treated for carcinomas[11]. The mechanism of RIM in non-target tissues may be attributed to chromosomal abnormalities after exposure which is termed as by-stander effect.

In a series of 54 cases exclusively involving minor salivary glands by Zhou et al 81% were found to be malignant the treatment policy for benign tumors was simple tumor excision, while that for malignant tumors was surgery combined with pre- or post-operative radiation therapy. Complete surgical resection of tumor masses and tumor free margin was vital for successful treatment[12].

Lombardi et al, in their study state that the most debated issues in major glands is the extent of surgery due to involvement of facial nerve while in minor salivary gland malignant tumorsconversely, surgical planning is influenced by the specific pattern of growth of the different neoplasms as well as the site of origin of the lesion[13]. The treatment of the neck both therapeutic and elective and reconstructive strategy after ablative surgery, are of pivotal importance in management.

Treatment strategies for submandibular-minor salivary gland malignant tumors are as stated, exclusive surgery for low grade and early detected primary tumors, whereas higher stages and high-grade tumors, or histologic risk-factors associated tumours like, positive microscopic margins and peri-neural involvement are successfully managed with combination of surgery and radiation therapy. Inadequate primary excision is noted in one-third of the treated sub-mandibular salivary gland cases with submandibulectomy and 20% of the cases report recurrence of the tumour and secondary surgeries inreferral centers[14,15].

The clinical grading but also histologic sub-type of the tumour majorly may influence the treatment planning. The most common malignant tumor of the submandibular gland is adenocarcinomas which involve 44% of sub-mandibular gland malignancies[16].For its biological behavior, it may be necessary to extend the resection to surrounding structures such as nerves (lingual, hypoglossal) and muscles (digastric, mylohyoid, hyoglossus, stylohyoid). In locally advanced submandibular Adenocarcinoma, the mandible should be very accurately evaluated in the preoperative setting since the tumor can infiltrate the inferior alveolar canal through retrograde- anterograde perineural spread to the Spixforamen[17,18].

Wide and sometimes contralateral extension through subperiostealspread should be considered. Furthermore, the prevalence of neck metastasis in submandibular Adenocarcinoma is significantly higher thanwhat reported for the parotid: Bosch et al, suggested that thiscould be related to direct extension of the tumor from the gland to adjacent nodes or from infiltrated surrounding soft tissues, rather than by classic embolic metastasis[19].Vander Poorten et al. suggested that, when dealing with amalignant tumor of the submandibular gland without clinical evidence of nodal metastases, the minimal procedure should be a selective neck dissection[20].

In conclusion, salivary gland malignancy post-radiation induced can arise almost anywhere in the head and neck area. The possibility of a malignancy to arise in a previously irradiated site should always be anticipated. As such resectability, functional implications of the resection, and the reconstructive needs depend on the anatomical site wherethe tumor arises, the locoregional extent and the tumor histology.

References

[1] Singh GK, Yadav V, Singh P, Bhowmik KT. Radiation-Induced Malignancies Making Radiotherapy a “Two-Edged Sword”: A Review of Literature. World journal of oncology. 2017 Feb;8(1):1.
[2] Pope T, Bloem HL, Beltran J, Morrison WB, Wilson DJ. Musculoskeletal imaging. Elsevier Health Sciences; 2014 Oct 21.
[3] Godwin JT, Foote Jr FW, Frazell EL. Acinic cell adenocarcinoma of the parotid gland: report of twenty-

seven cases. The American journal of pathology. 1954 Jun;30(3):465.
[4] Al-Zaher N, Obeid A, Al-Salam S, Al-Kayyali BS. Acinic cell carcinoma of the salivary glands: a literature review. Hematology/oncology and stem cell therapy. 2009 Jan 1;2(1):259-64.
[5] Metayer C, Lynch CF, Clarke EA, Glimelius B, Storm H, Pukkala E, Joensuu T, Van Leeuwen FE, van't Veer MB, Curtis RE, Holowaty EJ. Second cancers among long-term survivors of Hodgkin's disease diagnosed in childhood and adolescence. Journal of Clinical Oncology. 2000 Jun 12;18(12):2435-43.
[6] Shore-Freedman E, Abrahams C, Recant W, Schneider AB. Neurilemomas and salivary gland tumors of the head and neck following childhood irradiation. Cancer. 1983 Jun 15;51(12):2159-63.
[7] Hall EJ, Wuu CS. Radiation-induced second cancers: the impact of 3D-CRT and IMRT. Int J Radiat Oncol Biol Phys. 2003;56(1):83-88
[8] Dorr W, Herrmann T. Second primary tumors after radio- therapy for malignancies. Treatment-related parameters. StrahlentherOnkol. 2002;178(7):357-362.
[9] Hall EJ. Intensity-modulated radiation therapy, protons, and the risk of second cancers. Int J Radiat Oncol Biol Phys. 2006;65(1):1-7.
[10] Zablotska LB, Chak A, Das A, Neugut AI. Increased risk of squamous cell esophageal cancer after adjuvant radiation therapy for primary breast cancer. Am J Epidemiol. 2005;161(4):330-337.
[11] Best T, Li D, Skol AD, Kirchhoff T, Jackson SA, Yasui Y, Bhatia S, et al. Variants at 6q21 implicate PRDM1 in the etiology of therapy-induced second malignancies after Hodgkin's lymphoma. Nat Med. 2011;17(8):941-943.
[12] Shuryak I, Sachs RK, Brenner DJ. Biophysical models of radiation bystander effects: 1. Spatial effects in three- dimensional tissues. Radiat Res. 2007; 168(6):741-749.
[13] Zhou L, Chen X, Huang W, Li K, Zhang X, Wang W. Surgical management of minor salivary gland tumors. Lin chuanger bi yanhoutoujingwaikezazhi= Journal of clinical otorhinolaryngology, head, and neck surgery. 2007 Nov;21(21):963-5.
[14] Lombardi D, McGurk M, Vander Poorten V, Guzzo M, Accorona R, Rampinelli V, Nicolai P. Surgical treatment of salivary malignant tumors. Oral oncology. 2017 Feb 1;65:102-13.
[15] Gallina E, Gallo O, Boccuzzi S, Paradiso P. Analysis of 185 submandibular glands excisions. Acta Otorhinolaryngol Belgium 1990;44:7–10.
[16] Klussmann JP, Ponert T, Mueller RP, Dienes HP, Guntinas-Lichius O. Patterns of lymph node spread and its influence on outcome in resectable parotid cancer. Eur J Surg Oncol 2008;34:932–7.
[17] Vander Poorten VLM, Balm AJM, Hilgers FJM, Tan IB, Loftus-Coll BM, KeusRB,et al. Prognostic factors for long term results of the treatment of patients withmalignant submandibular gland tumors. Cancer 1999;85:2255–64.
[18] Rinaldo A, Ferlito A, Pellitteri PK, Robbins KT, Shaha AR, Bradley PJ, et al. Management of malignant submandibular gland tumors. Acta Otolaryngol2003; 123:896–904.
[19] Bosch A, Brandenburg JH, Gilchrist KW. Lymph node metastases in adenoid cystic carcinoma of the submaxillary gland. Cancer 1980;45:2872–7.
[20] Loh KS, Barker E, Bruch G, O'Sullivan B, Brown DH, Goldstein DP, et al. Prognostic factors in malignancy of the minor salivary glands. Head Neck 2009;31:58–63.