ISSN No:-2456-2165

Synchronous Squamous Cell Carcinoma of the Lip and Nasopharyngeal Carcinoma – A Rare Case Report.

M. Guezar[1]* , S. Khalfi[1] , K. Oulabbes[1,2] , S. Badja[3] , D. Kamal[3] F.Z. Farhane[1], Z. Alami[1], T. Bouhafa[1], MN. El Alami Elamine[3] , K. Hassouni[1].

(1) Department of Radiation Oncology, Oncology Hospital, , University Hospital Hassan II, Fez, Morocco
(2) department of Energy, Faculty of Science, Mohammed V University , Rabat, Morocco.
(3) department of maxillo-facial surgery. ENT and CCF, Omar Idrissi Hospital. University Hospital Hassan II, Fez, Morocco
*Corresponding author : M. Guezar[1]

Abstract:- The multiple primary head and neck cancers are becoming more frequent and are the cause of many diagnostic and therapeutic difficulties . Synchronous Nasopharyngeal carcinoma (NPC) and squamous cell carcinoma of the lip (SCCL) is a rare case presentation to be reported in literature.

We report a rare case of synchronous presentation of NPC and SCC of the lip in a 44-years-old male patient with a history of ultraviolet radiation exposure , a poor oral hygiene and poor dietary habits. The patient first presented with a diagnosis of squamous cell carcinoma of the lower lip, the radiological assessment revealed a thickening of the posterior wall of the cavum corresponding of a nasopharyngeal carcinoma that was confirmed by biopsy with histopathological examination. The management consisted of surgical excision of the lip tumor with reconstruction of substance loss and adjuvant external radiotherapy to the tumor bed with concomitant chemoradiotherapy for nasopharyngeal carcinoma with a follow up of 24 months, without local relapse or remote metastases.

Keywords:- *Synchronous Carcinoma, Head and Neck Multiple Cancers, Epstein Barr Virus, Field Cancerization.*

I. INTRODUCTION

Head and neck cancers are the ninth leading cause of cancer worldwide, with high mortality rates in developing countries, these tumors are biologically aggressive, locally and remotely with early development of lymph node metastases and secondary locations. [1] The multiple primary cancers of this entity are becoming more frequent and are the cause of many diagnostic and therapeutic difficulties with a profound impact on long term survival, particularly of patients with early disease.[1-2]

Multiple primary tumors can be Synchronous or metachronous : synchronous carcinomas are evolving at the same time or within a period of 6 months after the diagnosis of the first lesion, after this period they are considered metachronal cancers. [4]

Along the same lines, Warren S, Gates O. [3] defined the criteria for identifying synchronous tumors: (1) all tumors must be histologically malignant; (2) all must be distinct masses separated by normal tissue (at least 2 cm); and (3) the possibility that tumors may be metastatic must be histologically excluded.

II. CASE REPORT

We report the case of a male patient, 44 years old of Moroccan nationality, without notable pathological history, in particular no notion of active smoking or alcohol consumption, farmer by profession, its history of the disease dates back to one year before its admission by the appearance of a mass of the lower lip gradually increasing in volume, painless, what motivated him to consult. The clinical examination found a patient in good general condition, WHO at 0, the ENT examination found an ulcerated mass of the lower lip measuring 1,5 cm, normal oral opening, poor oral condition, free oropharynx, examination of the lymph nodes did not find any cervical-supraclavicular lymphadenopathy. The rest of the somatic examination was without particularity.

The locoregional extension assessment made by a cervical facial scan showed an hypodense cutaneous and subcutaneous tissue lesion of the lower lip measuring 30x13 mm lateralized to the right, raised weakly, without bone lesion .It also revealed a thickening of the posterior wall of the cavum containing hypodense areas, more marked on the left side extended at the homolateral choana and para-pharyngeal fat, without bone lysis, bilateral cervical nodes of small infracentimetric axes. Figure 1.

Nasofibroscopy found a filling of the posterior wall of the cavum, biopsy objectified undifferentiated nasopharyngeal carcinoma (UCNT).

The remote extension assessment: was completed by a thoraco-abdominal-pelvic scan and bone scintigraphy that did not find any secondary locations.

ISSN No:-2456-2165

According to the TNM classification our patient was classified for his lip tumor: T2N0M0 and T2N0M0 for its cavum tumor.

The decision of the multidisciplinary reconcertation staff was to do a surgical excision of the lip tumor with reconstruction and a concurrent chemo-radiotherapy for the NPC.

Fig 1 : CT-scan in axial plane showing a tumoral mass of the left side of the posterior wall of the nasopharynx.

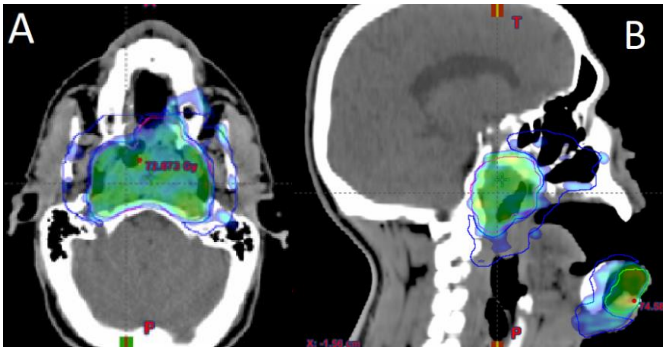

Fig 2 : Axial (A) , and sagittal (B) planes showing dose distribution at PTV 66 and 70 Gy.

The surgical procedure consisted of four stages: first stage: cross-over at the level of the labial groove, at the level of the mucosa with supported curettage of the mandible , second stage: bilateral functional lymph node dissection : I II III, 3rd time: excision of the tumor of the lower lip with margins of safety of 1 cm, 4th time: repair by a flap of the large right pectoral of the loss of labial substance. histopathological examinations of the surgical piece found a well differentiated squamous cell carcinoma mature and infiltrating, but the lower and deep limits were insufficient: 3 mm of the lower limit and 1 mm of the deep limit, the bilateral functional lymph node dissection was negative .

The management was supplemented with adjuvant radiation therapy on the tumor bed at a total dose of 66 Gy due to insufficient limits and concurrent chemo-radiotherapy at a total dose of 70 Gy/35 fractions to nasopharynx , microscopic extent (63Gy) and enlarged neck lymph nodes (56 Gy) with weekly cisplatin 50mg/m² . The technique used was conformational intensity modulated radiotherapy with a two-years of follow-up.

III. DISCUSSION :

The incidence of multiple primary head and neck carcinoma tumors is relatively high (2-3% per year) [4]

The frequency of synchronous and metachronal carcinomas in the mucous membranes of the head and neck, ranges from 8% to 21%[4]. The most common synchronous malignancies found in this area are those of the lung, and esophagus, reflecting the commonality of risk factors for these diseases. The synchronous occurrence of head and neck SCC and NPC is, on the other hand, much rarer.[5] The case reported in our study correspond to two synchronous ENT cancers.

To explain the clonal relationship between multiple primary tumors of the oral cavity, Slaughter et al. [6] proposed the “field cancerization” theory. where multiple tumors could originate independently in an area of the epithelium preconditioned to cancer development by long-term exposure to carcinogens of the head and neck.

In a study reported by F. Cianfriglia [7] the incidence rate of Second Primary Tumors (SPT) was 14%: 39% arose in the oral cavity, and 7% in the lip. The most common histological type was squamous cell carcinoma with 96%. 40% of the new cancers were synchronous and 60% were metachronous. 90% of patients with synchronous squamous cell carcinomas were over 40 years of age, which correlate with our patient.

Men were more frequent than women among both the synchronous and metachronous tumors in earlier reports. A 100% male predominance was reported in a study in patients with synchronous squamous cell carcinomas of the head and neck [4]

Our patient had two cancers of different histology: squamous cell carcinoma of the lip and undifferentiated nasopharyngeal carcinoma.

The risk factors for lip cancer are mainly smoking, alcohol consumption and ultraviolet radiation exposure which is the most common factor for lip cancer especially the lower lip [8] which is consistent with our patient’s occupation (farmer). Note that our patient had no toxic habits, especially no smoking or alcoholism

Poor oral hygiene with a high bacterial load in the mouth, present important risk factors [8], our patient had poor oral condition.

The role of HPV: oral infection with HPV 16 was more described as a risk factor for oropharyngeal cancers [9] The expression of oncogene HPV E6 and E7 inactivates the tumor suppressive protein p53 and pRb resulting in genomic instability as well as the development of cancers. But the HPV research in non-oropharyngeal cancers is not recommended in routine. [9,10,11]

The incidence of nasopharyngeal carcinoma is highly variable worldwide (generally <1/100000), its frequency is more pronounced in South East Asia which corresponds to the highest incidence area (10–35/100,000 person years) North Africa is noted like an intermediate incidence area (1–10/100,000 person-years). [12]

NPC has a complex interaction of genetic, viral (Epstein Barr Virus), environmental and dietary factors ; Genetic factors are defined by the existence of family cases: Deletion 3p21 , Specific HLA profiles (HLA-A2: Chinese, HLA-B5: North Africa). The EBV is an important risk factor : viral DNA and expression of EBV genes in tumor cells are found in 75% of cases especially for UCNT. [12-1-13]

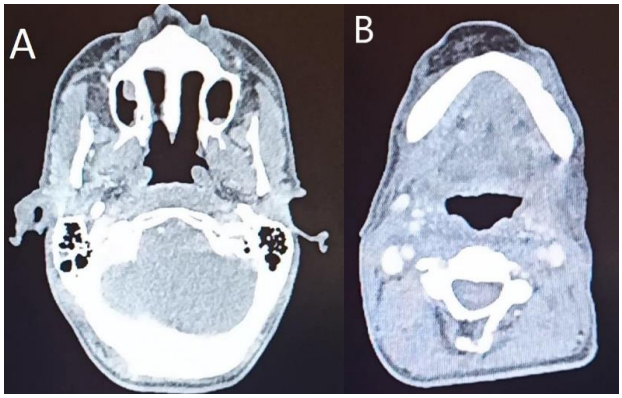

Fig 3 : control scanner 2 years after completion of radiotherapy in coronal (A) and axial (B) planes

A : Rigid appearance of the cavum without mass or pathological contrast.
B : Absence of mass syndrome or pathological contrast at the lower lip.

Fig 4 : clinical image 24 months after completion of treatment showing a poor aesthetic result with lower lip fistula

Environmental and dietary factors such as salted fish, smoked volatile, hot spices, Chinese herbs and certain preserved foods (rich in dimethylnitrosamine which is toxic to the aerodigestive tract). Alcohol and tobacco have controversial role. [12]

In this light a complete initial assessment of each apparently isolated cancer is needed to avoid missing a second metachronal or synchronous cancer.

The multiple cancers pose many problems of management, so It is important to conserve certain therapeutic methods such as radiotherapy to second primitive cancers [6,7]. Our patient was treated by surgery for its lip tumor which is the gold standard in the treatment of these cancers, the use of adjuvant treatment by radiotherapy was essential because of insufficient surgical limits. On the other hand, the NPC was treated with concurrent chemo-radiotherapy. The double synchronous location in this region has caused us some difficulties in optimizing doses of radiotherapy because of the proximity of the organs at risk. Fig 2 : A,B.

Our patient received optimal treatment thanks to the good management of the therapeutic arsenal and the means we have at our disposal, such as the radiotherapy technique used, which was conformational intensity modulated radiotherapy. This allowed an event-free survival of 24-month of follow up. Fig 3 : A,B.

The aesthetic result was not satisfactory especially after the recent occurrence of a fistula that was infected. On the other hand The functional result was good, The patient can speak normally and eat with a mild salivary incontinence. Fig.4 : A, B

IV. CONCLUSION

Synchronous presentation of the NPC and SCC of the lip is rare. We report this case, not only for its rarity but also in order to be acquainted with this coexistence especially in countries with a high incidence of nasopharyngeal cancer and also to focus on the initial assessment of the first cancer that needs to be further developed, especially in patient of NPC with history of cigarette smoking and/or poor dietary habits for better diagnostic and therapeutic management. On the other hand second primary cancers of the head and neck either synchronous or metachronous have a poor survival.

REFERENCES

[1]. Bhawna Gupta , Newell W. Johnson , Narinder Kumar. Global Epidemiology of Head and Neck Cancers: A Continuing Challenge. Oncology , June 1, 2016 , DOI: 10.1159/000446117
[2]. Krishnatreya M, Rahman T , Kataki AC, Das A , Das AK , Lahkar K. Synchronous primary cancers of the head and neck region and upper aero digestive tract: Defining high risk patients. Indian Journal of Cancer | October–December 2013.
[3]. Warren S, Gates O. Multiple primary malignant tumors: A survey of the literature and a statistical study. Am J Cancer 1932;16:1358 414.
[4]. Kiran Kumar, Devi Charan Shetty, Vijay Wadhwan, Prashanth Gupta. Synchronous oral squamous cell carcinomas with unusual histopathological feature.

Journal of Oral and Maxillofacial Pathology Vol. 16 Issue 3 Sep - Dec 2012

[5]. Krishnatreya M, Rahman T , Kataki AC, Das A , Das AK , Lahkar K. Synchronous primary cancers of the head and neck region and upper aero digestive tract: Defining high risk patients. Indian Journal of Cancer | October–December 2013 | Volume 50 | Issue 4

[6]. SLAUGHTER DP, SOUTHWICK HW, SMEJKAL W. Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer. 1953 Sep;6(5):963-8. doi: 10.1002/1097-0142(195309)6:5<963::aid-cncr2820060515>3.0.co;2-q. PMID: 13094644.

[7]. Cianfriglia F, Di Gregorio DA, Manieri A. Multiple primary tumours in patients with oral squamous cell carcinoma. Oral Oncol. 1999 Mar;35(2):157-63. doi: 10.1016/s1368-8375(98)00105-5. PMID: 10435150.

[8]. Gupta B, Johnson NW, Kumar N. Global Epidemiology of Head and Neck Cancers: A Continuing Challenge. Oncology. 2016;91(1):13-23. doi: 10.1159/000446117. Epub 2016 Jun 1. PMID: 27245686.

[9]. Gillison ML, Koch WM, Capone RB, Spafford M, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst. 2000 May 3;92(9):709-20. doi: 10.1093/jnci/92.9.709. PMID: 10793107.

[10]. Schiffman M, Doorbar J, Wentzensen N, de Sanjosé S, Fakhry C, Monk BJ, Stanley MA, Franceschi S. Carcinogenic human papillomavirus infection. Nat Rev Dis Primers. 2016 Dec 1;2:16086. doi: 10.1038/nrdp.2016.86. PMID: 27905473.

[11]. Fakhry C, Lacchetti C, Rooper LM, Jordan RC, Rischin D, Sturgis EM, Bell D, Lingen MW, Harichand-Herdt S, Thibo J, Zevallos J, Perez-Ordonez B. Human Papillomavirus Testing in Head and Neck Carcinomas: ASCO Clinical Practice Guideline Endorsement of the College of American Pathologists Guideline. J Clin Oncol. 2018 Nov 1;36(31):3152-3161. doi: 10.1200/JCO.18.00684.

[12]. Sanjeet Kumar Mandal, Thoudem Tomcha Singh , Takhenchangbam Dhaneshor Sharma , Venkatesan Amrithalingam, and Pamu Chukey Rai. Synchronous Presentation of Nasopharyngeal and Hepatocellular Carcinoma- A Rare Case Report , Ann Clin Pathol 4(4): 1077 (2016)

[13]. Banko AV, Lazarevic IB, Folic MM, Djukic VB, Cirkovic AM, Karalic DZ, Cupic MD, Jovanovic TP. Characterization of the Variability of Epstein-Barr Virus Genes in Nasopharyngeal Biopsies: Potential Predictors for Carcinoma Progression. PLoS One. 2016 Apr 12;11(4):e0153498. doi: 10.1371/journal.pone.0153498. PMID: 27071030; PMCID: PMC4829223.