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SYNCHRONOUS MAXILLO-MANDIBULAR SECOND PRIMARY TUMORS IN A PATIENT TREATED FOR CARCINOMA CERVIX - ROLE OF FIELD CANCERIZATION

Oncology

Varsha Haridas Upadya — Assistant Professor, Department of Oral & Maxillofacial Surgery, Yenepoya Dental College & Hospital, Mangalore

Rohan Shetty — Assistant Professor, Department of Surgical Oncology, Yenepoya Medical College & Hospital, Mangalore

Julie Jacob — Post graduate, Department of Oral & Maxillofacial Surgery, Yenepoya Dental College & Hospital, Mangalore

Syed Mohammed Miqdad — Assistant Professor, Department of Oral Pathology, Yenepoya Dental College & Hospital, Mangalore

Saini Mondal — Post graduate, Department of Oral Pathology, Yenepoya Dental College & Hospital, Mangalore

ABSTRACT

There has been no significant improvement in the long term survival of patients with head and neck cancer in the past few decades despite advances in therapy. An important reason for this is the development of second primary tumors (SPTs) [1]. Apart from loco-regional failure and distant metastasis, SPTs are the major cause of death in patients with head and neck squamous cell carcinoma (HNSCC). Apart from the classic tobacco/alcohol-associated HNSCC, the human papillomavirus (HPV) has emerged as a distinct risk factor for oropharyngeal SCC in recent times, suggesting that there may be distinct patterns of synchronous SPTs [2]. We present a rare case of oral SCC involving extraction sockets of both maxilla and mandible, occurring as synchronous SPTs in a patient treated for SCC of the cervix. The mandibular lesion was initially misdiagnosed as an unhealed socket. The paper highlights the importance of early screening for SPTs during the time of diagnosis of the index cancer as these lesions are more aggressive & metastasize early.

KEYWORDS

oral squamous cell carcinoma, synchronous, second primary tumor, extraction socket, carcinoma cervix.

INTRODUCTION

Patients with HNSCC are at a higher risk of developing SPTs, which are the leading cause of death in survivors [2]. Despite multimodal therapy with surgery and radiotherapy, augmented by induction chemotherapy, local/regional recurrence is seen in 30-50%, distant metastasis in 20-30% and second primaries in 10-40% of patients [3].
The field cancerization theory was proposed to explain the development of multiple primary tumors and locally recurrent cancer. However, recent molecular studies now support the alternative theory of a common clonal origin [4]. Field cancerization is known to occur in the head and neck (oral cavity, oropharynx, and larynx), cervix, lung, vulva, esophagus, breast, skin, colon and bladder [5].

We report a case of synchronous primaries of the maxillary & mandibular alveolus in a patient with a previous history of carcinoma of the cervix.

CASE REPORT

A 64-year old female patient reported with a chief complaint of pain in the upper and lower right posterior region of the jaws since 2 months following extraction of a right upper posterior tooth. Pain was dull, intermittent and mild in nature, radiated to the forehead and was associated with disturbed sleep. Ten days ago she underwent extraction of a right lower posterior tooth due to mobility.

The patient was a known hypertensive and diabetic and was under medication. Two years ago, she was diagnosed with carcinoma of the cervix. At that time, a PET CT scan was performed which revealed a heterogeneously enhancing mass in the vaginal vault and upper vaginal canal with no significant pelvic lymphadenopathy, distant metastasis or orofacial hotspots. She underwent surgery followed by chemotherapy and radiotherapy and was under follow-up for the same with no signs of recurrence.

She had chewed betel quid (3-4 times/day) for a year and had discontinued the habit 2 years ago.

An ulceroproliferative growth of size 4x2 cm was present over the extraction site of 17 extending buccally up to 15 and palatally upto 14 (Fig 1). The lesion had ill-defined borders, was firm, and tender on palpation. A single mobile right submandibular lymph node was palpable. The extraction socket of 46 had incompletely healed and bled easily on probing

Fig 1: Ulceroproliferative growth measuring 4x2 cm over the extraction site of 17 extending buccally up to 15 and palatally upto 14

CT revealed a soft tissue attenuating, heterogeneously enhancing lesion in the right upper gingiva with erosion of the alveolar ridge, suggestive of neoplasm (Fig 2). Heterogenously enhancing submandibular lymph nodes were noted bilaterally. The tumour was staged as T2 N2C MX..

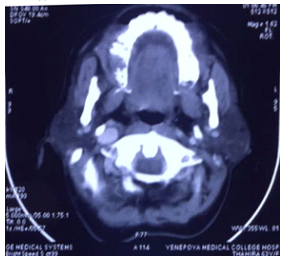

Fig 2: CT revealing a soft tissue attenuating, heterogeneously enhancing lesion in the right upper gingiva with erosion of the alveolar ridge, suggestive of neoplasm.

Incisional biopsies of the lesion were performed which showed dysplastic parakeratinized stratified squamous epithelium. The connective tissue stroma showed dense collagen fibers with plasma cells and lymphocyte infiltration. Keratin pearls, mitotic figures and individual cell keratinization were seen. The features were suggestive of well differentiated squamous cell carcinoma.

When the patient was recalled a week later, an endophytic growth of size 3x2cm was seen involving the extraction socket of 46 with loss of alveolar ridge height (Fig 3). The lesion was inflammed with ill-defined borders and was tender on palpation. The adjacent teeth were grade 1 mobile. An incisional biopsy was performed which was reported as SCC with early invasion with dysplastic epithelium showing basilar hyperplasia, loss of basal cell polarity, cellular pleomorphism, increased nuclear cytoplasmic ratio, nuclear hyperchromatism and individual cell keratinization. CBCT revealed irregular bone loss between 45 to 48.

Fig 3: Endophytic growth of size 3x2cm was seen involving the extraction socket of 46 with loss of alveolar ridge height

A bite excision with MRND was performed. Ipsilateral level 1- 5 and contralateral level 1a lymph nodes were resected. The defect was closed using a masseter flap. An obturator was placed to close the resultant oroantral communication.

The post-resection specimens of the maxillary and mandibular lesions showed moderately differentiated squamous cell carcinoma with tumor infiltrating the underlying submucosa, skeletal muscle and bone. Four out of the ten lymph nodes isolated, showed metastasis with extracapsular spread. P16 immunohistochemistry was negative.

The patient received 66Gy in 33 fractions (2Gy per fraction, 5 fractions per week) by IMRT technique along with 5 cycles of injection Cisplatin.

Six months later the patient presented with chemosis of the right eye and upper eyelid ptosis. Intraoral examination was not possible due to severe trismus. MRI revealed local recurrence with infiltration into the retroantral fat pad, temporalis and masseter muscle as well as extension into the pterygopalatine fossa and intraorbital region through the inferior orbital fissure. The patient was advised palliative care.

DISCUSSION

SPTs occurring simultaneously or within 6 months of the index tumor are termed synchronous, but often they occur after 6 months and are termed as metachronous [1]. Criteria for the diagnosis of SPTs was suggested by Warren and Gates and Moertel [1]

In the most commonly referred to "classical view," of the field cancerization theory [6], large areas of the tissue are affected by long-term exposure to carcinogens. Genetically unrelated multifocal carcinomas can develop in this preconditioned epithelium, as a result of independent mutations [7]. In the "alternative view" or "clonal theory," a single cell transforms and produces a large extended premalignant field by clonal expansion and gradual replacement of normal mucosa. Two separate tumors of the same clonal origin can develop in this field of various subclones by accumulation of additional genetic alterations [8].

Reports of metastatic spread to the oral cavity in patients with cervix cancer have been reported. High risk Human Papilloma Virus (HR-HPV), particularly type 16 & 18, play a significant role in OSSC & cervical carcinoma. P16, a cell cycle inhibitor has been considered as a surrogate marker for HR-HPV since p16 is over expressed in these lesions [9]. However, in our case, since P16 immunohistochemistry was negative and the alveolar lesions were of mucosal origin, the lesions were considered as second primaries rather than metastases of the cervix carcinoma. The synchronous intraoral lesions were probably a result of field cancerization attributed to betel quid chewing. A study by Liao CT et al concluded that betel quid chewers showed a significantly higher incidence of 5-year SPTs and local recurrences compared to non-chewers [10].

Whether SPTs arise due to lateral spread of clones or multiple foci of independent alterations, has no bearing on the medical and surgical management at present. Altered clonal patches that are grossly undetectable and are beyond the initial scope of surgical excision, may be indications for aggressive therapy, including chemoprevention or radiotherapy [1]. SPTs are a major problem in head and neck carcinomas as their development decreases the 5-year survival by 18-30% and hence early detection of these lesions is important as they are usually more aggressive, more treatment resistant, and metastasize early[1]. In this case the mandibular lesion was initially misdiagnosed to be an incompletely healed socket and hence we advocate a detailed clinical examination and a careful look out for SPTs in patients with habit related SCC.

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