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Review

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Vertebral metastases from oral squamous cell carcinoma of the buccal mucosa – report of a case and review of literature.

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Introduction: Oral squamous cell carcinoma (OSCC) is the most common head neck malignancy having a propensity for loco-regional spread. Hematogenous spread is rare with only a few existing reports in the literature.

Case report and Methods: Here we present a case of 55 year old mail with squamous cell carcinoma of the buccal mucosa with metastasis to vertebrae with a review of the literature on osseous metastases from OSCC.

Conclusions: With improved loco-regional control of the primary disease now possible with newer treatment modalities, more and more cases of distant metastasis from OSCC are being detected. Most frequently reported sites of metastasis from OSCC include lung, bone, liver, adrenals, heart, and kidney.

Introduction

Squamous cell carcinoma (SCC) is the most common malignant neoplasm of the oral cavity and represents about 90% of all oral malignancies [1]. Oral squamous cell carcinoma (OSCC) has traditionally been considered a loco-regional disease, with distant metastasis from primary site being rare. Distant metastatic spread from OSCC is thought to be by the hematogenous route either from the primary site or from the cervical lymph nodes that have been infiltrated by the oral squamous cell carcinoma. Crile reported an incidence of 1% for the distant metastasis from 4500 cases of head and neck squamous cell carcinomas (HNSCC) reviewed by him [2]. He stated that "the collar of lymphatics about the neck forms an almost impassable barrier through which cancer rarely penetrates" signifying the rarity of hematogenous spread [3]. Subsequent studies have shown the incidence of distant metastases to be much higher. Many investigators have reported the incidence of clinically detected distant metastases in squamous cell cancer of the head and neck, ranging from 11 to 23 percent [4-7]. The prevalence of distant metastases at autopsy (37–57%) is much higher than in clinical studies [4, 8-18].

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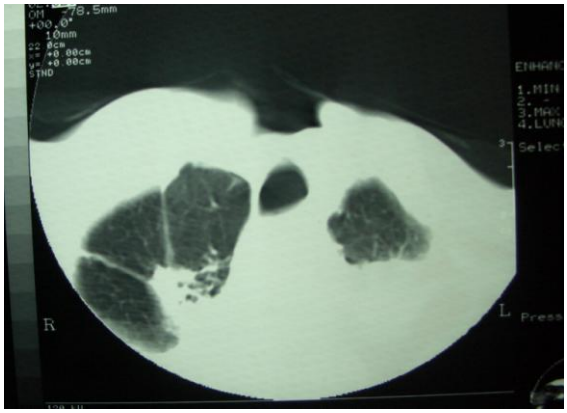

Figure 1: Computerized tomography of the chest showing pulmonary tuberculosis

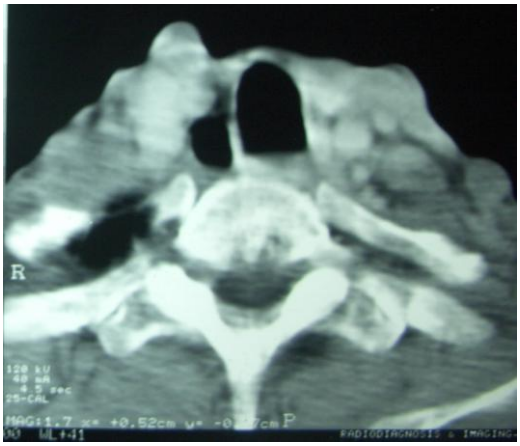

Figure 2: CT scan of the neck showing metastasis to the cervical vertebra

Most frequent sites of metastasis from cancer of the oral cavity include lung, bone and bone marrow, liver, adrenal, heart, mediastinum, skin, and kidney [4, 12, 16, 19-21]. Osseous involvement has been reported with varying frequencies and almost always second only to pulmonary involvement [22]. Here we present a case of squamous cell carcinoma of buccal mucosa which showed metastases to vertebrae and review the literature on distant bone metastases in OSCC.

Case report

A 55 year old male presented with a painful, non-healing ulcer on the left side of cheek noticed 3 months back. He was habituated to chewing pan with betel nut, tobacco and lime and keeping the quid in the buccal sulcus. On clinical examination an 3.5 X 3.0 cm ulceroproliferative lesion was found on the left buccal mucosa, extending from canine to retromolar trigone posteriorly and from lower gingivobuccal sulcus to superior gingivobuccal sulcus. He had clinically palpable lymph nodes of 0.5 X 0.5cm size at level Ib and II. His disease was clinically staged as T3N2a. Patient had trismus and his mouth opening was 15 mm. Histopathology examination of the punch biopsy showed moderately differentiated squamous cell carcinoma (MDSCC). Patient was treated with primary concomitant chemoradiation using methotrexate 50 mg/m^2 with BDX external radiation to the dose of 52.5 Gy/15 F. Four weeks after the radiation there was a residual lesion in the primary, a salvage surgery was advised for the residual tumor which was refused by the patient and he was lost to follow-up.

Patient reported back with a fungating lesion and oro-cutaneous fistula six months later, a surgical salvage with full thickness excision and a double flap reconstruction was planned. While the patient was being worked up for surgical excision, a chest X-ray showed evidence of pulmonary tuberculosis, that was confirmed by sputum AFB. Patient was started on anti tubercular treatment and surgery was deferred due to presence of open tuberculosis. Meanwhile, patient was started on chemotherapy with single agent oral methotrexate. A month later he presented with progressive difficulty in breathing and back pain radiating to both lower limbs. A CT scan was taken that showed multiple vertebral metastases involving dorsal and lumbar vertebrae and flared tuberculous status probably due to concomitant use of methotrexate (Figure 1, 2). He died of respiratory failure 15 days after the diagnosis of vertebral metastases.

Table 1: Case reports on osseous involvement in squamous cell carcinoma.

Case reports	Primary site	Site of osseous involvement
Kerin R (1983) [27]	3 cases of oral malignancies	metacarpals
Mathew BS *et al.*, (1997) [26]	1 case of SCC buccal mucosa	Vertebrae & ribs
Carlson ER & Ord RA (2002) [34]	4 cases of OSCC	vertebrae
Mendes RL *et al.*, (2004) [35]	2 cases (Oral tongue & vocal cord)	vertebrae
Lee KH et.al., (2007) [36]	2 cases (tongue)	Lumbar vertebrae
Vahtsevanos K *et al.*, (2007) [37]	4 cases (lip)	Scapula, vertebrae, clavicle & ribs
Shrivastava R *et al.*, (2009) [38]	1 case of alveolar SCC	Phalanges
Pichi B *et al.*, (2009) [23]	Tongue & floor of mouth	Talus

Discussion

Head and neck squamous cell carcinoma (HNSCC) is a tumor with high propensity for loco-regional spread. With newer management regimens and improved understanding of squamous cell carcinoma, loco-regional control of cancer above the clavicles has increased [7]. However, the overall disease free survival rate has not improved accordingly [23]. Distant metastases and second primary tumors are being recognized as a cause for an increasing proportion of failures in patients with head and neck malignancy [21].

The reported incidence of distant metastases on autopsy is high as many distant metastases are asymptomatic and go undiagnosed [4-18]. The incidence of distant metastases varies with locations of the primary tumor in head and neck region [7, 9, 17, 24 - 25]. Hsu & Chen (2005) [24] in their report of distant metastasis in 147 patients with HNSCC found out that the lungs were the most-common site of distant metastasis for patients with hypopharyngeal cancer and oro- pharyngeal cancer. For oral cavity cancers, the probability of metastasis to bones and lungs was equal. NPCs were more likely to metastasize to bone, followed by the liver and lungs.The most common primary sites metastasizing to distant sites are floor of mouth and tongue [25 - 26] and usually there are involvements at multiple distant sites [8, 12, 24, 27 - 28]. Metastasis from the buccal mucosa is extremely rare and only one case report on bone metastasis from buccal mucosa had been found in our literature search [26].

Various clinical analyses have reported the correlation of occurrence of metastases with the stage of the primary tumor, the nodal involvement at diagnosis, and the development of recurrence on the primary site [24,29 - 30]. Betka (2001) [31] reported a 10% risk for stage IV disease and patients with locoregional relapse versus 3% for earlier stage disease for the development of distant metastasis. Patients with clinically palpable neck disease (N1-N3), histological evidence of nodal disease, extracapsular spread, and 3 or more positive lymph nodes are at greater risk of developing failure at distant sites [13]. De Bree *et al.*, (2000) [32] reported the following risk factors for distant metastasis : three or more lymph-node metastases (almost 50% risk), bilateral lymph-node metastases, lymph nodes of 6cm or larger, low jugular lymph-node metastases, locoregional tumour recurrence, and second primary tumour. The incidence of distant metastasis has been found to be higher in patients with locoregional failure than in those with loco-regional control and 21.4% in

Table 2 : Case series on incidence of distant metastases and bone involvement.

Author & year	Incidence of distant metastases	Incidence of bone metastases
Hoye RC *et al.*, (1962) [39]	55% (23/42)	39.1% (9/23)
Ju DMC (1964) [40]	52% (152 /293)	35.5% (54/152)
O'Brien PH *et al.*, (1971) [25]	46.7% (57/122)	23% (13 /57)
Probert *et al.*, (1974) [8]	12.3% (96/ 779)	25% (24/96)
Merino OR *et al.*, (1977) [6]	10.9% (546/5019)	20.3% (110/546)
Dennington ML *et al.*, (1980) [41]	40% (25/64)	24% (6/25)
Vikram B *et al.*, (1984) [7]	17.5% (20/114)	35% (7/20)
Papac RJ *et al.*, (1984) [9]	30.7% (52/ 169)	44.2% (23/52)
Zbaren & Lehmann (1987) [11]	40% (40 /101)	15% (6/40)
Kotwall C *et al.*, (1987) [12]	47% (387/ 832)	30% (118/387)
Leeemans CR *et al.*,(1993) [29]	9.3% (26/281)	30.7 % (8/26)
Calhoun FH *et al.*, (1994) [20]	11.4% (83/727)	31.1% (26 /83)
Wollenberg, B., *et al.*, (1994) [42]		37% (41/108)
Troell RJ,& Terris DJ (1995) [43]	14.4% (14/97)	35.7% (5/14)
Shingaki S *et al.*,(1996) [30]	20% (21/103)	23.8%(5/21)
Hsu LP & Chen PR (2005) [24]	12% (35/291)	51.4% (18/35)
Garavello *et al.*, (2006) [43]	9.2%(181/1972)	9.9% (18/ 181)
Basu *et al.*, (2007) [22]		1.9% (13/683)

patients with loco-regional recurrence [15, 24, 33].

In a limited literature review that was carried out, we came across several case reports on osseous metastatic involvement from OSCC and HNSCC (Table I) [26, 27, 34- 38] and retrospective analyses which reported on the incidence, sites of involvement and probable predictors of distant metastases from OSCC and HNSCC are detailed in Table 2. [6-9, 11, 12, 20, 22, 24, 25, 29, 39-44].

These studies have shown the bone to be the second common site of distant spread, yet the incidence is much lower when compared with pulmonary involvement. Because of the relatively low frequency of bone metastases, screening for distant metastases at sites other than the lungs is usually not carried out. For oral squamous cell carcinoma, bone metastases traditionally have only come to attention through pain and symptoms of pathologic fractures, or abnormal laboratory test results, all of which are insensitive for early lesions [22]. Vertebral involvement in our patient was suspected because of severe back pain radiating to lower limbs.

Bone scintigraphy has not yet become a routine screening tool, and is carried out only in cases where there is high suspicion of osseous involvement. There are mixed reports of the usefulness of scintigraphy. Belson (1980) [45] reported positive bone scintigraphy in 2% of patients while Ampil *et al*, (1995) [46] could not detect any case on screening bone scans of 93 patients with locally advanced head and neck cancer.

The reported frequencies of bony metastasis vary from 11 to 54%, but with loco-regional control of disease, the incidence decreases considerably [15, 18, 22, 24].The osseous distant metastases have been commonly reported in vertebrae, ribs, long bones, ilium, clavicles, and skull [7-8,19,26,34-37,40,47-49]. Usually multiple bones are involved [8, 25,

48].Rarely phalanges and talus have been involved [22, 27, 37, 47]. Major symptoms of osseous metastasis are related to pain and pathologic fractures that direct attention to metastatic foci. In cases of vertebral involvement, spinal cord compression has been reported [34-37]. Our patient suffered from spinal cord compression due to involvement of lumbar and dorsal spines.

Carlson & Ord (2002) [34] reported a 0.7% incidence of vertebral metastasis in 597 patients with OSCC. All patients reported with stage IV disease of gingival or retromolar area. Basu *et al*., (2007) [22] reported bone metastasis in 13 patients with HNSCC. All of the patients had advanced-stage disease at initial presentation, and most developed bone metastases early in the post therapeutic course. 4 cases (30.7%) were SCC of base of tongue and one was from oral tongue.

Most studies found that distant metastases are diagnosed within a year of presentation [9-10] so there is probably subclinical seeding of malignant cells before the eradication of the primary tumor. The average survival with distant metastasis ranges between 4.3 months and 7.3 months [9,11-12]. Our patient developed vertebral involvement after 7 months of primary treatment.

Conclusion

Squamous cell carcinoma of the head and neck region tends to spread by direct extension and lymphatic metastasis, with hematogenous dissemination occurring late in the natural history of the disease. The distant metastases can affect different organ systems and almost invariably herald a poor prognosis and treatment is usually palliative. Constant vigil is required to detect the metastases early and any unexplained bony pain or functional deficits should alert the clinicians to the probability of bone metastases, as these may be the only symptoms of bone involvement.

Authors' Contributions

LPR: Did the literature search and prepared the draft manuscript.
SS: Helped with literature search and preparation of manuscript.
MS: Helped with preparation of manuscript and revision
MP: Conceived and designed the study and edited the final manuscript
All authors read and approved the final manuscript for publication.

Conflict of Interests

The authors declare that there are no conflicts of interests.

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Ethical Considerations

Patients consent was obtained for publication of this case report.

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