



Lateral Rectus Palsy: A Rare Sequel of Perineural Invasion by Oral Squamous Cell Carcinoma

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Abstract

Oral squamous cell cancers usually metastasize by lymphatic route, to the neck lymph nodes and in few cases by hematogenous route to other organs. The perineural invasion is a less prevalent phenomenon. It occurs when the growth penetrates nerve sheath of nerve present in vicinity and grows alongside nerve bundle. It is associated with poor prognosis and high mortality as it is often missed preoperatively resulting in incomplete removal of the disease.

Here we present a case of buccal carcinoma where the perineural spread along mandibular nerve led to malignancy spread to the skull base, causing inflammation of cavernous sinus and leading to lateral rectus palsy due to abducens nerve involvement.

Keywords: Oral Squamous Cell Carcinoma; Perineural Invasion; Base of the Skull Metastasis; Prognosis; Lateral Rectus Palsy; Cranial Nerve Infiltration

Introduction

Oral squamous cell carcinoma (OSCC) corresponds to 95% of head and neck cancers and it is the 6th most frequent cancer world-wide [1]. In India due to prevalence of tobacco chewing habit, it is a major health problem. It often carries high morbidity and mortality. Its prognosis is affected by many factors like usual lymphatic and blood invasion. Perineural invasion (PNI) is considered as a rare and very different mode of tumor metastasis [1]. The incidence of perineural tumor spread ranges from 2.5% - 5% occurring with wide variety of head neck malignancies [2].

Trigeminal (maxillary and mandibular division), facial and hypoglossal nerves may get involved by OSCC via perineural invasion, due to their long course and rich network of branching, in head-neck region, but remain asymptomatic in early cases, thus often missed. Even in advanced cases it may have sensory and motor

function abnormalities, but often missed due to masking of symptoms by main disease, poor pathological and radiological reporting.

Case Report

A 45-year-old male presented to our ENT department with chief complaints of a non-healing ulcer on the left buccal mucosa with difficulty chewing food and earache. General physical examination was unremarkable, the patient was non hypertensive and non-diabetic.

Intraoral examination revealed a ulcero-proliferative growth of size 4 cm X 2 cm involving left buccal mucosa, lower gingiva-buccal sulcus, extending from lower 2nd molar to retromolar trigone area. The growth was erythematous with slough covered ulcer in between. It was friable, tender and was indurated on palpation. There were no palpable cervical lymph nodes. Punch biopsy from the lesion confirmed moderately differentiated squamous cell carcinoma.

ma. Contrast enhanced computed tomogram (CECT) neck showed no cortical erosions. Patient underwent supra omohyoid neck dissection and primary excision with marginal mandibulectomy and posteriorly based lateral tongue flap repair. The surgery and post-operative period were uneventful. The histopathological report revealed moderately differentiated squamous cell carcinoma, with negative nodes and no bone involvement, but with perineural invasion (Figure 1).

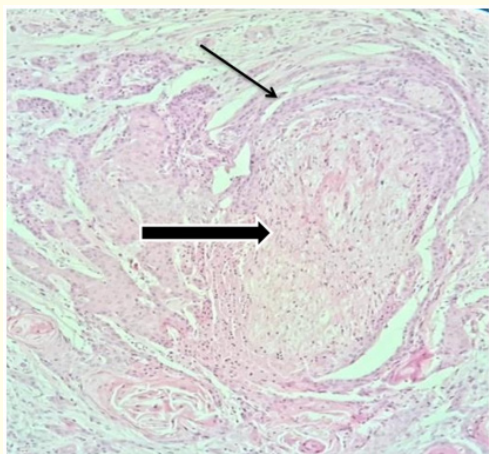


Figure 1: Histopathological picture of nerve section, showing thick arrow mark over nerve and thin arrow over perineural invasion by the tumor. (H&E stain, 40X).

After one-month patient presented with severe left side headache, retro-orbital pain and diplopia on left lateral gaze (Figure 2).



Figure 2: Postoperative clinical picture showing inability of left eye to have lateral gaze, suggesting left eye lateral rectus palsy.

On careful examination there was left side 6th nerve palsy while rest of the cranial nerves were normal. Operated site was normal with good uptake of graft and no residual or recurrent pathology. Gadolinium enhanced Magnetic resonance imaging (MRI) showed bulky mandibular division of trigeminal nerve in the region of foramen ovale with heterogenous enhancement of left cavernous sinus (Figure 3). Radiotherapy of the patient was started, and symptoms of retro-orbital pain and headache subsided, but diplopia persisted. Patient had a follow-up of 1 year postoperative surgery.

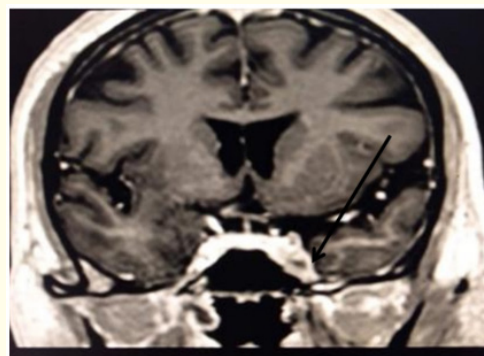


Figure 3: Coronal section of gadolinium enhanced MRI showing arrow mark over left side bulky, enhanced mandibular nerve (V3).

Discussion

Term PNI is used when at least 33% of the nerve circumference is involved by the tumor [1]. The mechanism by which cancer spreads remains unclear but few hypotheses suggest that it arise by altered signal interactions and the capacity of the tumor cells to promote it. The tumor cells are known to have affinity for neural tissues “Neurotropism” [3]. The stroma of perineural sheath promotes tumor growth and the perineural space acts as a passage for tumor to grow. It is known that nerves closer to resection margin and with large diameter have more propensity for PNI [4]. Koivisto, *et al.* advocated that the synapses (neural junctions) give a possible route for interneural spread of carcinoma from one nerve to another [5]. PNI is also related to axogenesis stimulation which in turn leads to tumor progression.

Evidence of PNI, signifies poor prognosis due to increased risk of local recurrence and high probability of metastasis, thus highlighting the need for early detection and recognition [6]. PNI should be suspected when patient complains of disabling, persistent pain along the nerve distribution and is confirmed on histopathology and widening of foramen on radiology [7].

A study compared 5-year disease specific survival for patients with and without PNI and concluded that it was statistically significant ($p < 0.001$). 5-year survival for patients with PNI was 56.6% and for those without PNI, it was 94.6% [4]. PNI necessitates aggressive excision along with lymph node dissection and adjuvant chemo-radiation therapy.

Almost all the patients with high risk features like positive tumor margin, nodal spread and extracapsular invasion of OSCC undergo radiation treatment and it is important to know about any PNI being present on histopathology to start radiotherapy, after the surgery [8].

PNI was usually associated with adenocystic carcinoma of salivary glands, but these days it can be seen in OSCC. Cancer of the salivary gland has a nerve invasion rate of up to 60% [3]. There is increased risk of PNI in OSCC in male population and the risk increases with increase in tumor size and poor differentiation. The risk is also more in tumors of midface location and in recurrent disease [9].

Contrast enhanced T1-fat suppressed MRI is considered gold standard imaging tool for early diagnosis [10]. In early stage, the break in blood-nerve barrier caused by the tumor, the enhancement of the nerve precedes the nerve enlargement. This nerve enhancement may be continuous or present with a skip lesion at a distant site in nerve probably travelling via perineural lymphatics. With tumor growth there occurs replacement of perineural fat and widening/erosion of foramen in skull base. Muscle denervation seen as hyperintense T2 signals in the muscle secondary to edema can supplement the MRI diagnosis of PNI [11]. PET/CT accuracy in detection of PNI is lower than MRI, but it may compliment. Asymmetric increased linear/curvilinear FDG uptake in the region of nerve course may suggest PNI.

The presence of headache, retro orbital pain and diplopia, in our case, indicated 5th and 6th cranial nerve involvement via perineural spread along the V3 (mandibular nerve). The tumor ascended along the nerve, up to the root of trigeminal nerve and later caused inflammation of cavernous sinus, which involved abducens, causing lateral rectus palsy.

Conclusion

Perineural invasion often carries poor prognosis in OSCC patients. While reporting biopsy a pathologist should comment on PNI as it drastically alters the outcome.

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