

## Tumor-related denervation pseudohypertrophy of the tongue: A clinical entity in disguise!

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### ABSTRACT

Isolated hypoglossal nerve palsy in the base of tongue carcinomas is seldom noticed. The clinical signs are subtle in early stage and can often be overlooked. There may be slight tongue deviation to the affected side, and the tongue feels soft and edematous on careful palpation. There may be associated enlargement of the affected side of the tongue known as “pseudo hypertrophy” due to denervation of its motor supply. Contrast-enhanced magnetic resonance imaging is the gold standard of diagnosis which shows diffuse fatty changes in the affected half of tongue with the preservation of architecture. Clinicians need to be aware of this clinical entity to distinguish it from actual tumor invasion.

**Key words:** Denervation injury, Isolated hypoglossal nerve palsy, Oropharyngeal tumor, Pseudohypertrophy

The base of tongue squamous cell carcinomas has witnessed a rising trend in the recent years which is related to an increased incidence of human papillomavirus (HPV)-related oropharyngeal cancers [1]. It is estimated that about 3200 new cases of HPV-associated oropharyngeal cancers are diagnosed in women and about 13,200 are diagnosed in men each year in the United States [2]. Unfortunately, prospective data to quantify HPV burden in India are not yet available. Isolated denervation hypertrophy of the tongue due to tumor invasion of hypoglossal nerve has been infrequently described in the literature. There may not be any symptoms of this clinical entity and signs are often subtle in early stages of its development. Magnetic resonance imaging (MRI) with contrast enhancement is the diagnostic modality of choice. Mature fat deposition in between sparsely distributed atrophic muscle fibers is the pathophysiological hallmark of denervation pseudohypertrophy. Clinicians need to be aware of this entity to distinguish it from actual tumor invasion.

### CASE REPORT

A 60-year-old man presented to our clinic in November 2017 with the complaints of difficulty in speech and swallowing for 1.5 months. He was referred to us by his family physician after his difficulties aggravated despite symptomatic management (oral gargles, antibiotics and painkillers). He suffered dysphagia to solids alone and it had increased rapidly in this duration. There was no history of odynophagia, shortness of breath, hemoptysis, and weight loss. He had been a chronic smoker for the past 25 years

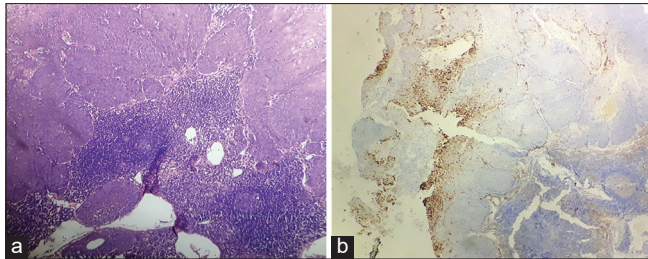
smoking two packets (20) cigarette per day on an average. There was no history of alcohol or other forms of tobacco abuse.

On clinical examination, he had a performance status of the Eastern Cooperative Oncology Group 2 [3]. General examination was essentially normal and local examination showed hard fixed lymph nodes on bilateral level- IIA, both about 3 cm in size. The primary lesion was a hard nodular growth in the base of tongue measuring around 5 cm and just invading anterior tongue. The classical “hot potato voice” was also noted which corroborated with the base of tongue involvement [4].

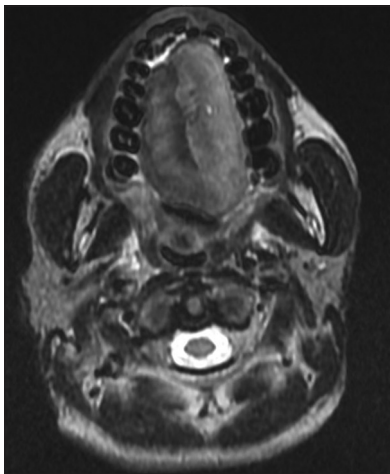
Direct laryngoscopy showed a proliferative growth involving the base of tongue, left vallecula, left tonsillar fossa, lingual epiglottis, and the pharyngeal surface of epiglottis. Biopsy of a tumor was taken, and a diagnosis of keratinizing (moderately differentiated) squamous cell carcinoma was given (Fig. 1a). Immunohistochemical staining with p16 showed it to be HPV-negative tumor (Fig. 1b). There were no symptoms or signs suggestive of distant metastases anywhere in the body. Hence, clinical staging was cT3N2cM0 as per the AJCC 7<sup>th</sup> edition staging [5]. Contrast-enhanced computed tomography scan and MRI of head–neck region were taken for the purpose of radiotherapy planning. MRI showed ill-defined T2 intermediate signal lesion of size 42.1 mm×22 mm involving pre-epiglottic space with extension to the floor of the mouth. Laterally, the lesion was infiltrating the hyoid bone. Enlarged lymph node of size 32 mm×18 mm was noted in the left parapharyngeal space abutting the carotid sheath. Enlarged necrotic bilateral level II and right level III lymph nodes were also noted, largest at the right level III measuring 20 mm×18.5 mm. The left half of the tongue

was swollen with an increased signal intensity, and the medial end was demarcated by the lingual septum. The right half of the tongue showed normal signal intensity. No mass lesion or muscle atrophy was noted (Fig. 2).

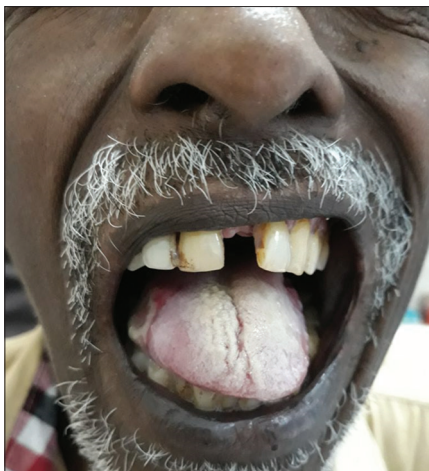
The feature was probably suggestive of denervation injury of left hypoglossal nerve. We reexamined the patient and noted slight deviation of a tip of the tongue which was missed in initial examination (Fig. 3). The left half of anterior tongue was soft



**Figure 1:** (a) Photomicrograph showing H and E section of keratinizing squamous cell carcinoma (moderately differentiated) with lymphoid stroma ( $\times 100$ ). (b) Photomicrograph showing p16 immunohistochemical staining (only focal cytoplasmic positivity seen) final diagnosis: Keratinizing squamous cell carcinoma - human papilloma virus negative



**Figure 2:** Magnetic resonance imaging showing disease extent and "pseudohypertrophy" of the left side of tongue



**Figure 3:** Picture showing deviation of tip of the tongue due to hypoglossal nerve injury

and mushy in palpation compared to the other half. However, no signs of muscle wasting were clinically observed. On inquiry, the patient reported no symptoms such as the pooling of food or saliva on the left side of the mouth. Rest of the cranial nerves were examined to be normal.

His performance status deteriorated further and was suitable only for palliative radiotherapy. Therefore, he was treated by conventional radiotherapy technique to a dose of 30 Gy in 10 fractions over 2 weeks to the primary and bilateral neck. 2 weeks post-radiotherapy completion, his symptoms had decreased significantly and oral intake had improved. Now, he has been kept on 2 monthly follow-up after an adequate explanation on poor prognosis of his disease. Palliative care with or without oral metronomic chemotherapy is the only option left for him in event of disease progression.

## DISCUSSION

The base of tongue cancers mostly presents in advanced stages due to late symptoms and hence diagnosis. The index case also had a brief history of only 1.5 months for a Stage IV B (AJCC 7<sup>th</sup> edition) at presentation [5]. The recent increase in HPV-positive oropharyngeal tumors is observed commonly in younger (<40 years age) patients than the elderly. HPV negativity in our case corroborates with this observation.

Multiple cranial nerve palsies due to tumor infiltration or compression have often been cited in case reports [6]. The tumors reported in these reports are quite varied such as gliomas, glomus jugulare tumors, lymphoma, and clivus tumors. Among squamous cell carcinomas of the head-neck region, nasopharyngeal carcinomas are mostly implicated in cranial neuropathies [7,8]. Hypoglossal nerve palsy is mostly associated with other cranial nerve palsies, and different etiologies such as trauma during surgery, medullary infarctions, multiple sclerosis, Guillain-Barre neuropathy, tumors, and infections have been recorded [9]. In contrast, isolated hypoglossal nerve palsy is rarely encountered [10]. Similar to most other causes of neurogenic denervation, hypoglossal nerve palsy generally leads to an atrophy of the tongue [11]. However, rarely, cases of motor denervation may induce a paradoxical enlargement of muscle which is known as denervation pseudohypertrophy. This features extensive fatty replacement in contrast to true hypertrophy, where there is an increase in number or size of muscle fibers. The pathophysiology has been described as a reduction in muscle fiber size, resulting in the reduction of muscular tension and relative inactivity. The pluripotent mesodermal cells are stimulated to form lipocytes, leading to fatty infiltration [12]. Mostly, such cases of pseudohypertrophy present as a painless, palpable mass. Imaging modalities show generalized enlargement of the affected muscle, with a diffuse distribution of fat and preservation of normal architecture. Muscle edema can be demonstrated by intermediate-to-hyperintense signal changes on T2-weighted sequences [12]. Other than tongue, denervation hypertrophy has also been

reported in calf muscles due to diabetic nephropathy or radiculopathy [12,13].

Radiographically, our case also presented with similar features. The left half of anterior tongue was soft as compared to the right half which suggested muscle edema and fatty replacement. Ideally, a biopsy would have confirmed the diagnosis; however, the patient was unwilling to undergo a repeat biopsy for purely academic interest when he was explained that the procedure would not have any treatment or prognostic implications. Additional studies such as electromyography and nerve conduction testing were not feasible due to unavailability at our center.

## CONCLUSION

Denervation hypertrophy of tongue may be missed in clinical examination owing to the lack of conspicuous findings. The case reported here stands significant because such pseudohypertrophy often mimics tumor invasion which can mislead to upstaging of the tumor. Contrast-enhanced MRI can clinch the diagnosis, and the oncologist needs to discuss with a radiologist in such confusing cases. Although not extremely rare, it is quite infrequent and oncologists should remain aware about such an entity in routine practice. Last but not the least, it is always advisable to go back and reexamine meticulously as subtle clinical signs may be discovered anew.

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