Case report

Squamous cell carcinoma of the base of the tongue mimicking bulbar-onset amyotrophic lateral sclerosis

Hsin-Pin Lin, Leora Lieberman, Mitesh Patel, Miguel Chuquilin*

*Department of Neurology, College of Medicine, University of Florida, Gainesville, FL, USA

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ABSTRACT

One-third of patients with amyotrophic lateral sclerosis (ALS) present with bulbar symptoms, exhibiting progressive dysphagia and dysarthria. In comparison, squamous cell carcinoma (SCC) of the tongue can cause tongue paralysis secondary to hypoglossal nerve infiltration. In rare cases, SCC can mimic motor neuron disease. Here, we describe a patient with SCC of the base of the tongue related to human papillomavirus infection who was initially misdiagnosed with bulbar-onset ALS.

Introduction

Bulbar-onset amyotrophic lateral sclerosis (ALS) encompasses about 30% of all ALS cases [1]. It presents with speech and swallowing difficulties, with limb features developing later in the disease course. The tongue is often disproportionally affected. Thus, when patients present with tongue weakness and progressive dysphagia, ALS should be considered. Clinically definitive ALS diagnosis requires the presence of progressive, upper and lower motor neuron (UMN and LMN) signs in at least three body regions (cranial, cervical, thoracic, or lumbosacral) with evidence of active denervation on electro-myography (EMG) [2, 3]. Lack of progression after three years of symptom onset is very atypical for ALS. Alternative diagnoses should be entertained.

Case presentation

A 67-year-old female presented with three-year history of worsening dysarthria and dysphagia, choking episodes provoked when lying supine, a one-year history of constant pain at right occipital and cervical paraspinal areas and a 20-pound weight loss. She reported a distant one-year history of smoking with no alcohol or illicit drug use. She was evaluated by an otolaryngologist. Modified barium swallow, flexible laryngoscopy and thyroid ultrasound studies did not show any abnormalities. X-ray showed moderate degenerative changes at C5-6 and C6-7 levels. Laboratory testing for acetylcholine receptor antibodies, TSH, B12, ANA, ESR, and CK were normal. A subsequent neurology consult reported tongue deviation to the right, as well as EMG showing denervation. She was then referred to our clinic with a diagnosis of ALS.

On examination, there was right tongue deviation, atrophy of the right side of her tongue, limited tongue movements and difficulty with tongue protrusion, but no tongue fasciculation. She had lingual and palatal dysarthria, and slow, but symmetric palate elevation. The rest of her neurological exam, including muscle and facial strength and reflexes, was unremarkable. Repeat EMG showed active denervation changes in the left lower lumbar paraspinals and medial gastrocnemius muscle, and minimal active denervation in the left first dorsal interosseous and pronator teres. Subsequent MRI of the nasopharynx showed an infiltrative process at the base and root of the tongue, invading the most inferior aspects of the mouth floor, including the lingual neurovascular bundles (Figures 1A, B). Maxillofacial CT showed an enhancing, infiltrative, and partially necrotic mass of the floor of her mouth, centered on the left side and involving the midline, measuring 17 × 35 × 21 mm (Figures 1C, D). There was infiltration of the intrinsic tongue muscles with tongue atrophy. Further studies with flexible laryngoscopy showed base of the tongue fullness with prominent lymphatic tissue. Biopsy of the tongue showed active infiltration and necrosis with dysplasia and high-grade squamous cell carcinoma. The patient underwent a surgical debulking of her tumor.

* Corresponding author.

E-mail address: Miguel.Chuquilin@neurology.ufl.edu (M. Chuquilin).

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showed focal, non-keratinizing invasive squamous cell carcinoma (SCC), related to human papillomavirus (HPV) infection. P16–INK and Cyto5/6 immunohistochemistry were positive.

Discussion

Although our patient had progressive dysphagia and dysarthria, symptoms that could be caused by bulbar UMN or LMN dysfunction, she had no cardinal features of UMN signs on exam, with the caveat that UMN signs at the bulbar region may be subjective and difficult to elicit [4]. There were some active denervation changes in the cervical and lumbar regions seen on our patient’s EMG, but these changes were restricted to only a few muscles. They were caused by radiculopathy, not motor neuron diseases. As radiculopathy is very common, caution is particularly needed when interpreting EMG results for evidence of LMN loss. Lack of progression to other body parts is also unusual for ALS.

In this case, diseases that may affect the hypoglossal nerves and the neuromuscular junctions should be considered. Myasthenia gravis may present with bulbar symptoms and tongue atrophy [5]. Hypoglossal nerve palsy can be caused by postoperative, idiopathic, primary neoplastic, metastatic malignancy, inflammatory, radiation, and trauma.

Due to the high suspicion for a local compression or infiltrative process, MRI of the nasopharynx was repeated despite prior negative studies. It was only after the repeated MRI was reviewed by a head and neck radiologist that a tumor was discovered. This highlights the difficulty in distinguishing tumor infiltration, the ease at which misinterpretation can ensue, and the necessity for expert radiology readings.

There have been two other cases of SCC of the tongue mimicking bulbar-onset ALS reported in the literature [6, 7]. The patients presented with progressive weakness of the tongue with dysarthria, dysphonia, dysphagia and sialorrhea. In both cases, there were no fasciculations in the tongue, and denervation changes on EMG were minor and restricted to a few muscles. Like our case, both cases were diagnosed at advanced stages, which is not uncommon for SCC of the base of the tongue, considering its indolent nature, minimal pain, and radiological subtlety.

In the United States and many other developed nations, the overall incidence of oropharyngeal cancers has been rising in the recent years due to increase in HPV-mediated cases [8]. In fact, oropharyngeal SCC, arising in the base of the tongue or the tonsillar region, was the most common HPV-associated cancer in the United States in 2015 [9]. This presents further challenges for early diagnosis as HPV-mediated oropharyngeal cancers typically present in younger patients and patients without a history of excessive exposure to traditional risk factors, such as alcohol and tobacco, and have higher socioeconomic status [8]. The primary tumors of HPV-mediated oropharyngeal cancers tend to be smaller, but patients are more likely to have regional lymph node metastases at presentation [10].

The publication of this case report has been approved by the University of Florida’s Health Center IRB. Informed consent is not required for this case report based on the UF IRB and Privacy rules and the Elsevier Policy on the use of images or personal Information of patients or other Individuals.

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