JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Otolaryngology

Case Report

Numb Chin Syndrome and Metastatic Lung Adenocarcinoma: A Prolonged Outcome and Propensity for Younger Age

Eric M Sugihara[1*], James P Dworkin-Valenti[1], Jamie G Taweel[2], Prasad J Thottom[1]

[1]*Department of Otolaryngology - Head and Neck Surgery, Detroit Medical Center,Huron Valley-Sinai Hospital,Michigan State University, Detroit, MI, USA*

[2]*Department of Internal Medicine,Detroit Medical Center,Huron Valley-Sinai Hospital,Michigan State University, Detroit, MI, USA*

**Corresponding author: Dr. Eric M Sugihara, Department of Otolaryngology – Head and Neck Surgery, 24002 Wedgewood Circle, Warren, MI 48091, Detroit Medical Center, Michigan State University, United States, Tel: (503) 407-0176, Email: ericsugihara@gmail.com*

Received: 03-31-2015

Accepted: 04-30-2015

Published: 05-07-2015

Abstract

Numb chin syndrome (NCS) is a rare neurological condition characterized by hypoesthesia distributed by the mental nerve in the absence of local or dental pathology and may represent a manifestation of systemic malignancy with metastasis to the mandibular subsystem. A 48-year-old patient presented with unilateral chin numbness. Initial imaging with panoramic jaw radiography, head and neck MRI/MRA, and maxillofacial CT were negative for local pathology. Further workup revealed bony metastasis involving the axial skeleton, which led to the underlying diagnosis of lung adenocarcinoma. Institution of palliative chemoradiotherapy resulted in patient survival of 25 months following the diagnosis of NCS. Although local imaging is frequently negative in NCS, attention needs to focus on pertinent family history, risk factors, and review of systems cues for a timely diagnosis. We attribute the described favorable course to prompt detection and the palliative regimen utilized. The distribution of hematopoietic bones in the axial skeleton and the decline in red bone marrow with age help to explain the typical clinical presentation of NCS in younger patients.

Keywords: Numb Chin Syndrome; Mental Neuropathy; Metastatic Cancer; Lung Cancer

Abbreviations
NCS: Numb Chin Syndrome;
EBRT**:** External-Beam Radiation Therapy;
NSCLC: Non-Small Cell Lung Cancer

Introduction

Numb chin syndrome (NCS) is a rare neurological condition that is sometimes referred to as mental sensory neuropathy. It is characterized by hypoesthesia, paresthesia, and less commonly chin pain in the region distributed by the mental nerve and its branches [1,2]. Regional involvement may encompass the lower lip and is usually unilateral. In up to 10% of cases symptoms may be bilateral [3].In the absence of an antecedent local injury, illness, or disease, NCS may represent a manifestation of systemic malignancy with metastasis to the mandible [2]. In nearly 50% of cases presenting with NCS, a metastatic malignant lesion proves to be responsible [4,5].

Historically, the clinical symptoms of NCS was first described by Charles Bell in his 1830 monograph The Nervous System of the Human Body, in which he described a lady with breast cancer who complained of unilateral lip paresthesia [4-6]. The

cause in this case was metastasis to the inferior alveolar nerve. As a result, NCS typically results from an invasive disturbance of the mandibular division of the trigeminal nerve (V_3), anywhere along the course from the leptomeninges or skull base to its distal branches [7].

The trigeminal or fifth cranial nerve has three branches, which provide sensory innervation from the face (V_1, V_2, and V_3), oral cavity (V_2 and V_3), and motor innervation to the muscles of mastication (V_3). These three branches converge to the trigeminal ganglion (semilunar/gasserian ganglion) located in Meckel's cave and harbor the cell bodies of the respective afferent sensory nerves. Proximally, a single sensory fiber carries all branches and enters the brainstem at the level of the pons. The pons contains the main sensory nucleus, which receives widespread touch and two-point discrimination feedback from both facial and oral surfaces. Sensations of dental and gingival pressure are distinguished by the supratrigeminalis subnucleus [8]. Distally, V_3 exits the skull through the foramen ovale and divides into the 1) anterior motor division that supplies the muscles of mastication, and 2) posterior sensory division that divides into the auriculotemporal, lingual, and inferior alveolar nerves. The inferior alveolar nerve is the pathway of focus as it enters the mandible through the mandibular foramen. The inferior alveolar nerve is accompanied by the inferior alveolar artery, a branch of the first segment of the internal maxillary artery that stems from the external carotid artery. The inferior alveolar nerve and artery exit the mandible through the mental foramen and become the mental nerve and artery. Together, they provide afferent sensory innervation and blood supply to the lower lip, chin, and mandibular buccal gingiva and teeth [9].

In consideration of the relevant neuro-anatomy, the pathophysiology of NCS can be explained in most cases by any extrinsic or systemic mechanism of action that disrupts functioning of the inferior alveolar nerve sheath or mental nerve [1]. In a small subset of cases, NCS may result from abnormal compression of the intracranial trigeminal nerve root secondary to leptomeningeal disease [7-10].

Several prior case reports and studies have established that NCS may be the first presentation of an underlying distant or local malignancy. This clinical condition has been clearly defined in prior reports, with strong emphasis on considering malignancy as the etiology in most cases. In all cases of NCS, early identification and appropriate intervention are of paramount importance. It has been accepted that the prognosis of NCS patients with malignant underpinnings is very poor, with median survival less than one year [11]. Due to the rarity of this disorder and the gravity of its course, we have elected to report our experiences with a patient who presented to us with NCS who lived over two years after his initial diagnosis.

Case Presentation

A 48-year-old man presented to his primary care physician with new onset left lower chin, lip, mouth, and gum numbness for one week. Other complaints included palpitations and right-sided back pain. His past medical history included osteoarthritis, hypertension, dyslipidemia, gastroesophageal reflux disease, and benign prostatic hyperplasia managed by ibuprofen, metoprolol, and omeprazole. He also had a history of right rotator cuff repair and benign rib tumor removal as a child. He was a non-smoker and rarely consumed alcohol.

On exam there was no sign of dental or local pathology. Further workup with electrocardiogram, stress echocardiography, troponin, thyroid function tests, and carotid duplex were all within normal. One week after presentation, he was seen by oral and facial surgery. On exam he had excellent dentition with no gross decay or periodontal problems. However, there was minimal sensitivity of tooth #17 (left mandibular third molar) to percussion compared to adjacent teeth. Panoramic jaw radiography revealed no pathologic condition, lytic lesion, or gross dental pathology.

Five weeks after initial presentation, he was seen by neurology. Brain MRI and MRA were negative. His symptoms progressed to include daily stabbing pain in the left masseter, supraorbital, and temporal regions. On exam he exhibited hyperesthesia of the left lower lip and chin region, but overall intact sensation. The initial diagnostic impression was trigeminal neuralgia. Ibuprofen was discontinued and he was started on oxcarbazepine and a tapered low dose steroid over one week. Neurology follow-up after one month of the aforementioned plan showed no change in symptoms. Oxcarbazepine was discontinued and gabapentin started. Neck MRA was obtained and revealed a prominent left vertebral artery, but otherwise unremarkable results.

Persistent symptoms of NCS at approximately four months from initial presentation led to further workup with a maxillofacial CT, which demonstrated nonspecific cutaneous inflammatory mandibular changes. Due to additional enduring symptoms of right-sided back pain, an MRI of the lumbar spine was performed, which revealed multiple lesions from the thoracic spine to the sacrum and right femur. Screening chest x-ray was performed and showed nodular lesions. CT chest confirmed several subcentimeter nodules and identified a spiculated right hilar mass. During this workup, the patient disclosed no pulmonary symptoms and, as a result, no prior chest imaging was available for comparison. A subsequent bone scan revealed metastases involving multiple sites involving the ribs, thoracic spine, sacrum, pelvis, and right femur.

The patient was immediately evaluated by pulmonology. Transbronchial biopsies were taken and confirmed the

presence of adenocarcinoma. Approximately four and a half months after initial presentation, diagnosis of primary lung tumor was made with clinical skeletal metastatic disease of his mandible, ribs, thoracic/lumbar spine, sacrum, hips, and right femur. A CT neck was performed shortly after lung biopsy due to persistent NCS symptoms and ultimately revealed a 2.2 x 2.4cm enhancing mass with osseous lytic changes of the left mandibular ramus. **Figures 1 and 2** illustrate these pathologic findings.

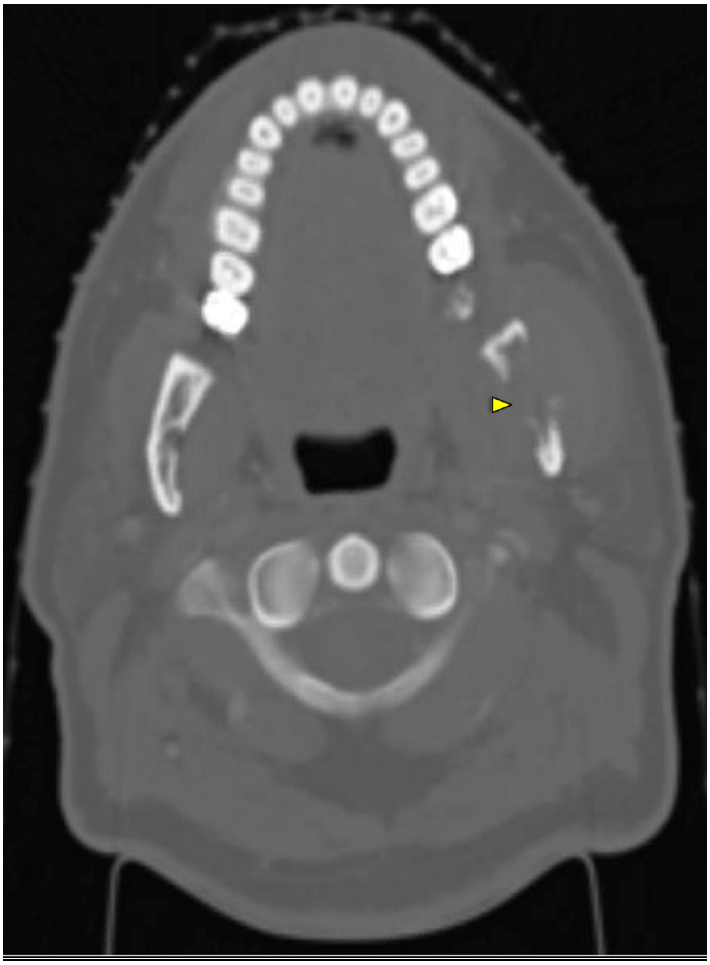

Figure 1. Axial CT with contrast in bone window display. Arrow signifies the left mandibular ramus lytic lesion with surrounding soft tissue edema.

He was referred to oncology for further management and palliative treatment was initiated, five months after initial presentation. This consisted of external-beam radiation therapy (EBRT) to the mandible, thoracic spine, sacroiliac joint, and right hip with first-line combination chemotherapy (Carboplatin, Paclitaxel) and Bevacizumab for 21 cycles over the next eleven months. He exhibited responsive and stable disease, yielding maintenance therapy with Bevacizumab and daily Erlotinib for 14 cycles. During his treatment course, surveillance PET/CT studies were performed every three months. For 15-months post-treatment, the patient showed no evidence of disease. Shortly thereafter, he exhibited new foci of disease and transitioned to Cisplatin and Pemetrexed for three cycles. Repeat PET/CT revealed disease progression notwithstanding such treatment. The patient continued with palliative chemotherapy until he passed away 30 months after his NCS symptoms began.

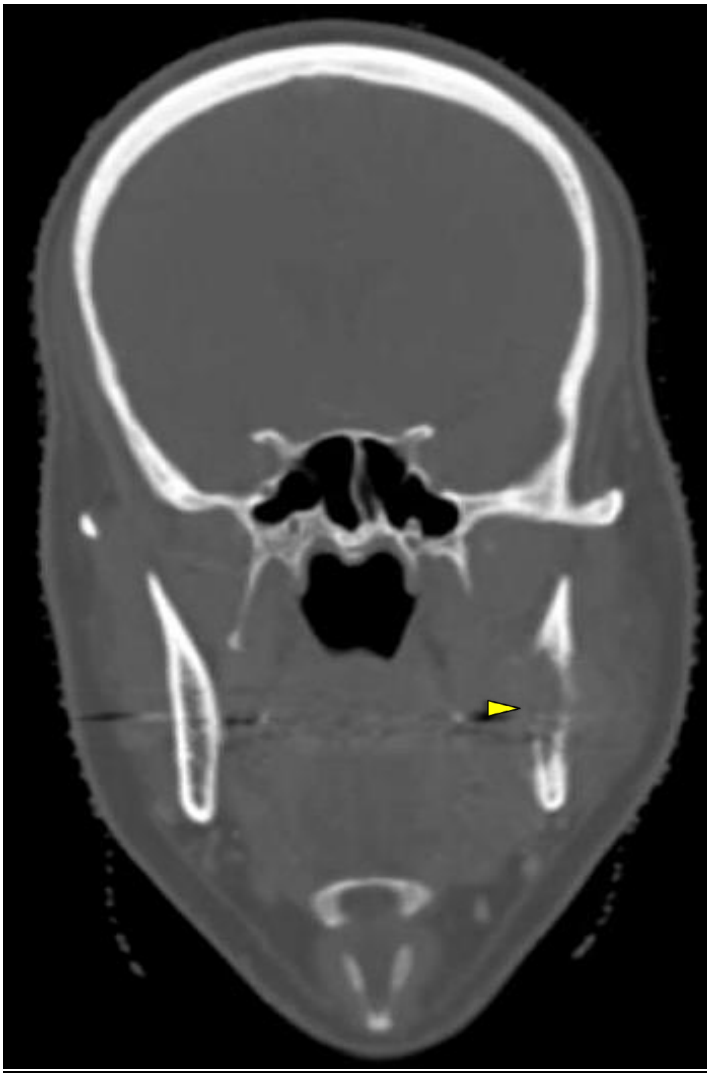

Figure 2. Coronal CT with contrast in bone window display. Arrow signifies the left mandibular ramus lytic lesion with surrounding soft tissue edema.

Discussion

The initial diagnosis of NCS is largely empirical and dependent upon the presenting symptoms and history of the patient. Explanation of the complaint relies on the examiner's understanding of the neuro-anatomy and pathophysiology of the lips, chin, and mandibular musculature and mucocutaneous distribution. Comprehensive workup is essential to discover the underlying etiology of the problem, especially for cases where there may be a high index of suspicion for metastatic

disease. Since a large percentage of individuals with NCS suffer from an associated distant malignancy, astute clinicians should focus their diagnostic attention on ruling out carcinoma as the cause. This concern is most important in cases without histories of local trauma, illness, or disease.

To facilitate the diagnosis radiographically, panoramic mandibular images are typically obtained. Initial findings may include osteoblastic or osteolytic involvement of the mandible and its nerve supply. If such testing proves inconclusive, CT, MRI, and nuclear bone scintigraphy may be employed in cases of NCS for clarification [3-7]. However, imaging studies may produce paradoxical and misleading results. The literature is replete with reports of patients with NCS whose initial panoramic jaw radiography and CT imaging were erroneously negative [1,2,10,11]. Whereas MRI with gadolinium contrast may be more sensitive in cases with NCS [10], the evidence for this conclusion is sparse. In fact, in our patient, the panoramic jaw radiography, brain and neck MRI/MRA, and initial maxillofacial CT imaging were negative and could not elucidate the underlying cause of his chief complaints. At first we concluded that his symptoms were likely due to some underlying benign condition. As his symptoms progressed and worsened, our diagnostic acumen strengthened; we focused away from local-regional explanations and towards distant systemic sites for possible neoplastic origin. Imaging of the spine and chest, along with full body bone scan proved indispensible to the ultimate diagnosis of metastatic disease, with evident pathologic involvement of the mandibular subsystem. It is not clear, however, that our delayed diagnosis negatively influenced our patient's eventual treatment outcome. Perhaps earlier detection may have enabled the institution of palliative therapies sooner. From a quality of life perspective, this difference cannot be considered insignificant. Our current workup algorithm with similar cases has sharpened as a result of this case experience. As NCS often presents without radiographic evidence of local metastatic lesions, focus needs to shift away from NCS local symptoms toward pertinent family history, risk factors, and review of systems cues for prompt identification of a possible underlying malignancy elsewhere.

A survey of the literature regarding malignancy as the underlying etiology in NCS revealed several large case series. Lossos and Siegal described 42 cases of NCS for whom the most common causes were breast cancer or lymphoproliferative malignant metastasis to the mandible with invasion or compression of the inferior alveolar or mental nerve. Gil et al examined 16 different studies with a total of 136 cases of NCS. This review revealed that malignancies most commonly associated with NCS include breast cancer (40%), prostate cancer (6%), lymphoproliferative processes (6%), multiple myeloma (6%), and leukemia (5%) [12]. Hirshberg et al conducted the largest cumulative review to date, wherein 390 cases of NCS of metastatic origin were examined. In women, the most common underlying malignancies were of breast, adrenal, colorectal, gynecological, and thyroid origin, respectively. In men, the most common sites of origin were the lungs, prostate, kidney, bone, and adrenals, respectively [4-13]. Moreover, it was discerned that the most common site of mandibular metastasis was to the molar and premolar regions. Non-malignant conditions known to result in NCS include odontogenic infection, trauma, diabetes mellitus, amyloidosis, syphilis, sarcoidosis, sickle cell disease, AIDS, radiotherapy, chemical toxicity, or systemic vasculitis [7,14,15,16].

Our patient's survival of 30 months following symptom onset represents the longest clinical course of metastatic NCS in the literature to date. Most patients with this condition succumb to the disease within seven months [12,13]. This result may be a testament of the testing algorithm and treatment regimen we employed.

Another factor contributing to the more favorable outcome in our case versus other reported cases of NCS may be the clinical utility of EBRT with the aforementioned chemotherapy regimen in the setting of stage IV non-small cell lung cancer (NSCLC). Sugiura et al's 2008 study showed that NSCLC with bony metastatic disease stratified primary lesions to adenocarcinoma in 70% of cases (n=118). Although they found adenocarcinoma and combination chemotherapy independently yielded a favorable prognosis, they reported a mean survival of 9.7 months [17]. In comparison, our patient experienced a 15-month period of radiographic disease free survival, and a total survival period of approximately 25 months following diagnosis of NSCLC and three regionally separate sites of bony metastasis. The application of the presented course of palliative therapy to similar cases may be favorable. Perhaps it is reasonable to postulate that EBRT and combination chemotherapy may increase patient survival in stage IV NSCLC, even in cases of extensive bony metastasis, as shown in our patient.

Although the manifestation of systemic malignancy with bony lesions is not uncommon, metastasis of cancer to the mandible is rare. However, this can be explained by the physiology and dynamic bony anatomy with age. Bone marrow comprises of several elements and is classified into two types, red and yellow. Red bone marrow is a myeloid tissue that has active hematopoietic cells, whereas yellow bone marrow consists mainly of fat and is not hematopoietically active. The presence of hematopoietic red bone marrow is characteristic of higher bone turnover, increased skeletal blood flow, and the close approximation of venous sinuses [18]. In children, these hematopoietic centers reside in the long bones. In adults, sites of hematopoiesis shift to the axial skeleton, with active bone marrow present in the pelvic bones (34%), vertebrae (28%), cranium and mandible (13%), sternum and ribs (10%), and proximal humerus and femur (4-8%) [19]. The distribution of active bone marrow in adults is congruent with the sites of bony met-

astatic disease seen in our patient, with lesions of the pelvic girdle, thoracic and lumbar spine, mandible, ribs, and right femur. However, the amount of red bone marrow decreases with age, due to a gradual conversion to yellow bone marrow – an approximate 10% decrease in bone marrow cellularity occurs with each decade of life altogether [18-20]. This clarifies the more common occurrence of oral metastatic lesions reported in younger patients, aged 40 to 70 years [13]. This is consistent with NCS literature, wherein Gil et al's systemic review of 136 cases reported a mean patient age of 47.8 years [12]. In succession with the hematogenous dissemination of many malignancies, the presentation of this disease process in our 48-year-old patient becomes better understood.

Conclusion

The frequent negative head and neck imaging among NCS patients with underlying malignancy emphasizes this condition as a clinical diagnosis until proven otherwise. As primary lesions of NCS commonly root in breast cancer, lung cancer, and lymphoma, judicious attention needs to be drawn toward pertinent family history, risk factors, and review of systems to yield a timely diagnosis and a probable etiology.

Although survival is usually less than one year, in cases of metastatic NCS, our patient survived 30 months following initial presentation. We attribute his favorable course to prompt detection and the treatment regimen we utilized. The application of the above palliative chemoradiotherapy algorithm may also be advantageous to other cases of stage IV NSCLC. Although metastasis to the mandibular subsystem is uncommon, the distribution of hematopoietic bones in the axial skeleton and the decreased composition of red bone marrow with age help to explain the characteristic clinical and pathologic findings typically associated with NCS lesions in younger patients.

References

1. Baskaran RK, Krishnamoorthy, Smith M. Numb chin syndrome- a reflection of systemic malignancy. World Journal of Surgical Oncology. 2006, 4(52).
2. Zaheer F, Hussain K, Rao J. Unusual presentation of 'numb chin syndrome' as the manifestation of metastatic adenocarcinoma of the lung. International Journal of Surgery Case Reports. 2013, 4(12): 1097-1099.
3. Lossos A, Siegal T. Numb chin syndrome in cancer patients: etiology, response to treatment, and prognostic significance. Neurology. 1992, 42(6): 1181-1184.
4. Evans RW, Kirby S, Purdy RA. Numb chin syndrome. Headache: The Journal of Head and Face Pain. 2008, 48(10): 1520-1524.
5. Massey EW, Moore J, Schold SC. Mental neuropathy from systemic cancer. Neurology. 1981, 31(10):1277-1281.
6. Furukawa T. Charles Bell's Description of numb chin syndrome. Neurology. 1988, 38(2): 331.
7. Marinella MA. Numb chin syndrome: a subtle clue to possible serious illness. Hospital Physician. 2000, 36(1): 54-56.
8. Dworkin JP. Bite-block therapy for oromandibular dystonia. Journal of Medical Speech-Language Pathology. 1996, 4(1): 47-56.
9. Drake RL, Vogl W, Mitchell AWM. Gray's Anatomy for Students. Edinburgh: Churchill Livingstone, 2009.
10. Biasotto M. Numb chin syndrome as the presenting symptom of carcinomatous meningitis. Annals of Oncology. 2007, 19(3): 599-601.
11. Friedrich RE. Mental neuropathy (numb chin syndrome) leading to diagnosis of metastatic mediastinal cancer. Anticancer Research. 2010, 30(5): 1819-1822.
12. Gil SG, Diago MP. Malignant mental nerve neuropathy: systemic review. Med Oral Patol Oral Cir Bucal. 2008, 13(10): 616-621.
13. Hirshberg A, Leibovich P, Buchner A. Metastatic tumors to the jawbones: analysis of 390 cases. Journal of Oral Pathology and Medicine. 1994, 23(8): 337-341.
14. Burt RK, Sharfman WH, Karp BI, Wilson WH. Mental neuropathy (numb chin syndrome): a harbinger of tumor progression or relapse. Cancer. 1992, 70(4): 877-881.
15. Marinella MA. Ophthalmoplegia: an unusual manifestation of hypocalcemia. The American Journal of Emergency Medicine. 1999, 17(1): 105-106.
16. Horton J, Means ED, Cunningham TJ, Olson KB. Then numb chin in breast cancer. Journal of Neurology, Neurosurgery & Psychiatry. 1973, 36(2): 211-216.
17. Sugiura H, Yamada K, Sugiura T, Hida T, Mitsudomi T. Predictors of survival in patients with bone metastasis of lung cancer. Clin Orthop Relat Res. 2008, 466(3): 729-736.
18. Compston JE. Bone marrow and bone: a functional unit. Journal of Endocrinology. 2002, 173(3): 387-394.
19. Elgazzar AH. Anatomy and physiology of bone marrow. Orthopedic Nuclear Medicine. Springer, Berlin Heidelberg 2004.
20. Zacchariades N. Neoplasms metastatic to mouth, jaws and surrounding tissues. J Cranio Maxillofac Surg. 1989, 17(6): 283-290.