

Expert Opinion

Numb Chin Syndrome

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The first author of the article coining the term “syndrome of the numb chin” was a young assistant professor in his first year at the University of Texas Medical Branch at Galveston. When the late Dr. John R. Calverley stepped down in 2002, he was the longest serving neurology chairman in the United States for 32 years.

CLINICAL HISTORY

This 67-year-old man was seen in neurological consultation with a 10-day history of numbness and tingling of the right chin which was intermittent for the first 3 days and then constant for one week. The chin could also be intermittently painful with an intensity ranging from 7 to 9/10 especially with chewing. He had no headache, speech disturbance, dysphagia, visual disturbance, or other neurological symptoms.

After seeing his primary care physician, he then saw both an ENT physician and oral surgeon without a cause being found. Mandible x-rays were negative.

There was a past medical history of prostate carcinoma initially diagnosed on biopsy 4 years previously when he was started on leuprolide injections.

He developed bony metastases requiring palliative radiotherapy to the hips and lower extremities

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completed about 6 weeks previously. His medications were ketoconazole and hydrocortisone.

Neurological examination was normal except for decreased sensation over the right chin and right lower lip. A magnetic resonance imaging (MRI) of the brain and skull base with and without contrast was normal. The Westergren erythrocyte sedimentation rate was 47 mm/hour.

Questions.—What is the diagnosis? What are the possible etiologies? What testing is indicated when presented with similar symptoms?

EXPERT OPINION

This patient presents with altered sensation and intermittent pain in the distribution of the right mental nerve. This is a classic presentation of numb chin syndrome (NCS) or mental neuropathy.

The mandibular branch of the trigeminal nerve divides into anterior and posterior trunks. The anterior trunk supplies the muscles of mastication and sensation to the buccal mucosa. The posterior trunk divides into the auriculotemporal nerve, lingual nerve, and the inferior alveolar nerve. The inferior alveolar nerve enters the body of the mandible through the mandibular foramen and travels in a plexiform network in the mandibular canal. It exits via the mental foramen as the mental nerve at the level of the canine teeth. It supplies sensation to the teeth, lateral gingiva, lower lip, and chin.¹

The first case of NCS was reported by Charles Bell in 1830 in his monograph *The Nervous System of*

the Human Body.² He described a patient with numbness of the left lower lip caused by a mandibular metastasis compressing the inferior alveolar nerve. Then, in 1937, Roger and Pallais described isolated mental neuropathy as a warning of metastatic cancer.³ Isolated cases were reported in both the neurological and dental literature until 1963 when Calverley and Mohnac reported 5 cases of mental neuropathy caused by metastases from systemic cancer and coined the name "syndrome of the numb chin."⁴

Numb chin syndrome has been reported in association with trauma, dental procedures or infections, tumors and cysts of the jaw, various malignancies, vasculitis, multiple sclerosis, connective tissue diseases, vertebro-basilar insufficiency, systemic infections, and toxic exposures.⁵

Trauma to the inferior alveolar nerve is a well-recognized complication of dental procedures such as root canal therapy, removal of teeth especially third molars, and injection of dental anesthetics.⁶⁻⁸ In these cases, the precipitating event is obvious and there is rarely any diagnostic uncertainty.

A 70-year-old woman, who presented with chin numbness associated with jaw claudication and new headache, was found to have temporal arteritis. The chin numbness resolved with her other symptoms with high dose prednisolone.⁹

Sickle cell crisis may cause a painful mental neuropathy due to vaso-occlusive disease or osteomyelitis of the mandible. The mandible is the most vulnerable area of the face because of relatively low blood flow.¹⁰

Many conditions may cause sensory loss or pain in the trigeminal nerve distribution that may be restricted to one division but isolated mental nerve distribution symptoms would be unusual. Fifteen of 92 patients with Sjogren's syndrome in a recent series had pure painless trigeminal sensory neuropathy, and an additional 24 patients had trigeminal involvement associated with other neuropathies.¹¹

Trigeminal neuralgia is a well-recognized complication of multiple sclerosis but trigeminal distribution sensory change without pain may also be caused by trigeminal nerve root entry zone plaques.¹²

Brain stem infarcts such as lateral medullary infarcts result in facial numbness and central pain when

lesions of the lower spinal trigeminal tract cause deafferentation of spinal trigeminal sensory neurons.¹³ Other neurological signs are also present.

An isolated NCS might be an interesting anatomical finding but of little clinical significance except for its association with malignancy as first described by Bell. NCS may be caused by mandibular metastases, base of skull metastases, and leptomeningeal spread of cancer.

Metastases to the mandible are the most common cause of neoplastic NCS.¹⁴ The mandible is a relatively infrequent site of metastatic disease with only 9 cases identified in 763 patients presenting with non-specific jaw pain to a maxillo-facial surgery department.¹⁵ In 1994, Hirshberg et al reviewed 390 cases of metastatic lesions to the jawbones reported in the literature and found that 81% were in the mandible, 13.6% in the maxilla, and 5.4% in both. In the mandible, the molar and premolar areas were the most common sites. Breast cancer was the most common primary site in women, followed by adrenal, colorectal, gynecological, and thyroid cancers. In men, lung cancer was the most common primary followed by prostate, kidney, bone, and adrenal cancers. Patients presented with swelling (57%), pain (39%), or paresthesia (23%). In 29%, the patients did not have a previous diagnosis of cancer and in 53% of patients with known malignancy, the jaw metastasis was the first known metastatic lesion. Prognosis of all patients was dismal, with a mean survival of only 7.3 months from diagnosis of the jaw metastasis.¹⁶

Fourteen percent of the patients with NCS in the series of Lossos and Siegal had base of skull metastases compromising the mandibular nerve. Direct infiltration of the trigeminal nerve or gasserian ganglion has also been reported.¹⁷

Leptomeningeal spread of cancer is postulated to have caused NCS in some patients with no evidence of mandibular or base of skull metastases on imaging and positive cerebrospinal fluid (CSF) for malignant cells.^{5,14} Lossos and Siegal reported that 22% of their 36 fully evaluated patients had malignant cells in the CSF and negative investigations otherwise.

But caution should be used in attributing NCS to leptomeningeal spread of cancer particularly if there are no other symptoms of leptomeningeal spread. In a

study of 50 patients with leptomeningeal cancer, only 6 had trigeminal symptoms and of these, only one had isolated decreased sensation in the mandibular division.¹⁸ Small metastases to the jaw may not be apparent on imaging.^{19,20} In Nobler's series of 8 patients with NCS, 3 patients with multiple cranial nerve involvement did not have improvement of their NCS with brain irradiation although their other cranial nerve symptoms did improve. After the patients were treated with radiation to the symptomatic mandible, the NCS improved in all.²¹ It is difficult to know if modern imaging techniques might have shown the responsible lesion in some of the earlier case series.

The classic symptom of NCS is isolated numbness in the lower lip and chin. The teeth may also have loss of sensation if other branches of the inferior alveolar nerve are involved. Patients may bite their lip inadvertently causing painless ulcers. Symptoms are usually unilateral but up to a third may have bilateral symptoms.⁵ Pain is less frequent, reported in only 5 of 19 patients in one series. It was described as aching and continuous and not tic like.²² Other cranial nerve symptoms may be associated with NCS. In patients with base of skull lesions, cranial nerves VI or VII may be involved with lesions near the gasserian ganglion. With leptomeningeal spread of cancer, other cranial neuropathies or spinal radiculopathies may be present or develop rapidly after presentation.

Breast cancer is reported to be the most common cause of neoplastic NCS.^{14,23} As might be expected from the data on metastatic lesions to the mandible, many other cancers are also implicated including prostatic carcinoma as in this case.²⁴⁻²⁶ Lymphoproliferative neoplasms may also cause NCS and there are numerous case reports of patients with leukemias, lymphomas, or multiple myeloma presenting with NCS.⁵ Nobler reported a small series of 8 patients in 1969.²¹ Case series of NCS have reported that 14-47% of patients have lymphoproliferative neoplasms.^{14,22}

Numb chin syndrome may be the first presentation of malignancy in up to 47% of patients.²² It may also be the first symptom of metastatic disease. Lossos and Siegal reported that in 67% of their 42 patients, NCS was associated with disease progression and that in 31% of the 42, NCS was the first symptom of tumor relapse.¹⁴

The prognosis for cancer patients with NCS is poor regardless of whether the patient has previously diagnosed malignancy or not. Reported survivals in case series range from less than 3 months to 12 months.⁵

Numb chin syndrome is important to recognize because of the association with malignancy. The symptoms may be ignored by the patient or minimized by the physician, particularly in a patient without known malignancy, unless the syndrome is recognized. Unfortunately, lack of awareness of the sinister implications may result in delayed diagnosis of a new malignancy or metastatic disease. While systemic cancers usually are incurable when metastatic disease is present, some lymphoproliferative neoplasms still may be salvageable.

In a patient with known malignancy, NCS should be assumed to be due to metastatic disease. In this case, this patient had known bone metastases and NCS has been reported in patients with prostatic cancer. Plain x-rays of the mandible may show the responsible lesion as a lytic or osteosclerotic area in the bone. A bone scan should be performed if the plain x-rays are uninformative, looking for hot spots in the mandible or base of skull. An MRI with gadolinium enhancement may show change in the marrow signal of the mandible or evidence of intracranial disease. Other symptomatic areas may help direct investigations but even if there is known leptomeningeal spread or brain metastases, the mandible should be imaged. Other potential sites of metastatic disease and tumor markers (such as the prostatic specific antigen in this case) should be evaluated.

Patients with NCS and no history of malignancy should be assumed to have a malignant etiology until proven otherwise. Investigations should aim to answer 2 questions: first, what lesion is responsible for the NCS?, and second, is there an underlying malignancy? The first question is investigated as for a patient with known malignancy. The second question requires additional investigations. In a female, breast examination and mammogram is essential as breast cancer is the most common cause of NCS. A chest x-ray may show a lung primary or other metastatic disease. Lymphoproliferative neoplasms should also be ruled out given their relative frequency as a cause

of NCS. Other investigations should be directed by the patient's symptoms, history, and risk factors.

If a malignancy is confirmed, the site causing NCS is treated as any other disease site. Treatments may include systemic chemotherapy, local radiotherapy, hormonal manipulation, and other systemic therapies. If pain is present, medications such as gabapentin or pregabalin may improve neuropathic type pain and nonsteroidal anti-inflammatory drugs are often helpful for pain from bony metastases. Most studies do report improvement in symptoms with treatment although the symptoms may relapse with disease progression.¹

As indicated, pain is uncommon, and on its own deserves further assessment and other diagnostic considerations. Certainly, the lower jaw has C2 dermatomal representation and as a result any process involving the C2 or even C1 root, which does not have skin representation, can cause pain. This may include local disease, including malignancy as noted, neuralgic pain or mononeuropathy, as well as trauma and degenerative disease. Jaw claudication must also be considered. A common cause of jaw pain is referred cardiac pain and jaw pain can be part of cardiac cephalgia.

Follow-up.—The patient was placed on pregabalin 75 mg bid with some improvement in the pain. He was referred to an oncologist. A bone scan revealed extensive abnormal uptake of the right facial or mandible area changed from the prior study and greater activity of the long bones. A serum prostate-specific antigen was 237 ng/mL (normal 0-4). He was started on docetaxel every 3 weeks with improvement in the right mandible symptoms after the first 2 treatments.

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