BMJ Case Reports

Unusual presentation of more common disease/injury

Non-Hodgkin lymphoma presenting with numb chin syndrome

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Summary

Numb chin syndrome (NCS) is a rare yet potentially ominous sensory neuropathy characterised by unilateral hypoesthesia or paraesthesia over the lower lip, chin and occasionally gingival mucosa. Recognising NCS clinically is important as this may be a subtle sign of occult malignancy progression or relapses. Current expert opinion is that patients with NCS without apparent cause should be assumed to have a malignant aetiology until proven otherwise. By far the most common non-haematologic neoplastic cause of NCS is breast cancer, while the most common haematologic neoplastic cause is non-Hodgkin lymphoma (NHL). The pathophysiology of NCS has been shown to be either direct compression of the mental nerve by tumour mass, leptomeningeal invasion or a bony lesion at mental foramen. Here we report a case of NHL presenting with NCS with no evidence of metastasis in brain parenchyma, cerebrospinal fluid or mandibular bone. Instead, diffuse dural thickening and focal lesion in clivus were identified. We propose that these may represent novel mechanisms of NCS.

BACKGROUND

Numb chin syndrome (NCS) is a rare yet potentially ominous sensory neuropathy characterised by unilateral hypoesthesia or paraesthesia over the lower lip, chin and occasionally gingival mucosa.[1] It is also called mental neuropathy, reflecting the anatomical substrate of this syndrome. Specifically, the mandibular branch (V3) of the trigeminal nerve exits the skull through the foramen ovale and divides into an anterior motor trunk innervating the muscle of mastication and a posterior sensory trunk that travels through the mandible as the inferior alveolar nerve. The inferior alveolar nerve exits the mental foramen as the mental nerve, which supplies sensation to the mucosa of the lower lip, skin of the chin and the mandibular gingival around the incisors.[2] Recognising NCS clinically is important as this may be a subtle sign of occult malignancy progression or relapses.[3 4] Current expert opinion is that patients with NCS without apparent cause should be assumed to have a malignant aetiology until proven otherwise.[5] By far the most common non-haematologic neoplastic cause of NCS is breast cancer, while the most common haematologic neoplastic cause is Hodgkin lymphoma (NHL).[6] The pathophysiology of NCS has been shown to be either direct compression of the mental nerve by tumour mass, leptomeningeal invasion or a bony lesion at the mental foramen.[1] Here we report a case of NHL presenting with NCS with no evidence of metastasis in brain parenchyma, cerebrospinal fluid (CSF) or mandibular bone. Instead, diffuse dural thickening and focal lesion in clivus were identified. These findings suggest that mechanisms other than neoplastic infiltration of the mandible and leptomeningeal spread may exist. We propose that these may represent novel mechanisms of NCS.

CASE PRESENTATION

The patient is a 51-year-old right-handed Caucasian female with non-contributory medical history and family history. She was in her usual state of health until she developed sudden onset dull lower back pain radiating to right leg without any apparent history of trauma or sports injury. The patient received physical therapy and chiropractic manipulation for presumed sciatica. However, her symptoms progressed over the next few days such that she developed non-specific deep pain in both legs, especially in the knees. The patient was then given oral prednisone and muscle relaxant at a local emergency department (ED) for presumed arthritis. She stopped prednisone after 1 day due to improvement in symptoms. Approximately 10 days after the onset of lower back pain, the patient noticed a numb sensation in her right lower lip and right chin region, described as 'feeling like local anaesthesia at the dentist's

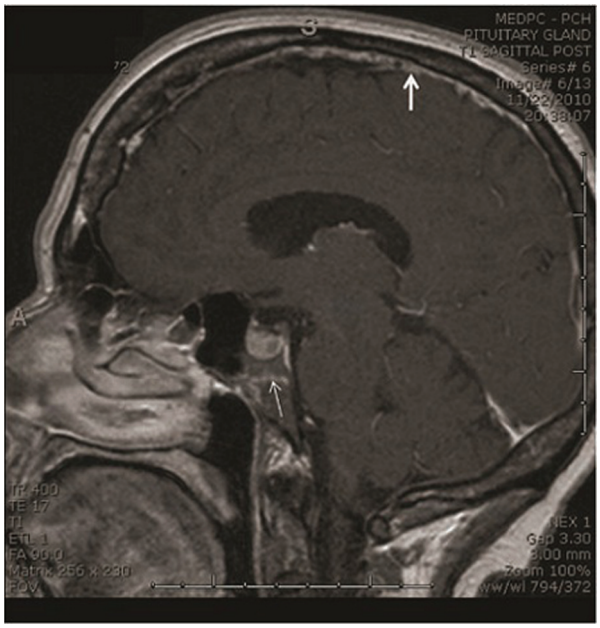

Figure 1 Sagittal section postcontrast T1-weighted brain MRI image showing the dural thickening with gadolinium-contrast enhancement (thick arrow) and the bone marrow signal enhancement in the clivus (thin arrow).

office'. The chin numbness was non-painful. There was no motor deficit, dysphagia or dysarthria. Concomitantly, the patient developed generalised fatigue, malaise and vague diffuse aching all over the body. Her original leg pain worsened to the point that she was unable to walk. There were no other constitutional symptoms reported such as fever, weight loss, night sweat or headache. The patient then presented to ED to rule out 'stroke', and was hospitalised for further workup.

INVESTIGATIONS

At the hospital, no dental pathology was found. Brain MRI revealed contrast-enhancing dural thickening and bone marrow lesion in the clivus (figure 1). On routine blood test, the patient was noticed to be anaemic (Hb: 11.3 g/dl) and thrombocytopenic (platelet: 69 K/μL). Serum lactic dehydrogenase level was 4000 U/l (normal range: 116–245 U/l). Alkaline phosphatase was 190 U/l. Liver enzymes were elevated with aspartate transaminase of 223 U/l and alanine transaminase of 80 U/l. However, γ glutamyl transpeptidase was within normal limits (42 U/l). Bone marrow biopsy revealed evidence suspicious for B-cell lymphoproliferative disorder. The patient was then transferred to the haematology/oncology service at our tertiary care medical centre. Brain MRI was repeated, which confirmed the early findings at outside hospital (figure 2). CSF studies were unremarkable with glucose of 83 mg/dl, protein of 15 mg/dl and normal cell counts (white cell count: 1/ μl, red blood corpuscles: 2/μl). CSF cytology was negative for any malignant cell. Flow cytometry study of the peripheral blood smear showed ~3% malignant lymphoid cells. Bone marrow biopsy slides from outside hospital were revisited and a pathological diagnosis of NHL (indeterminate high-grade B-cell lymphoma with features between diffuse large B-cell lymphoma and Burkitt's lymphoma) was confirmed

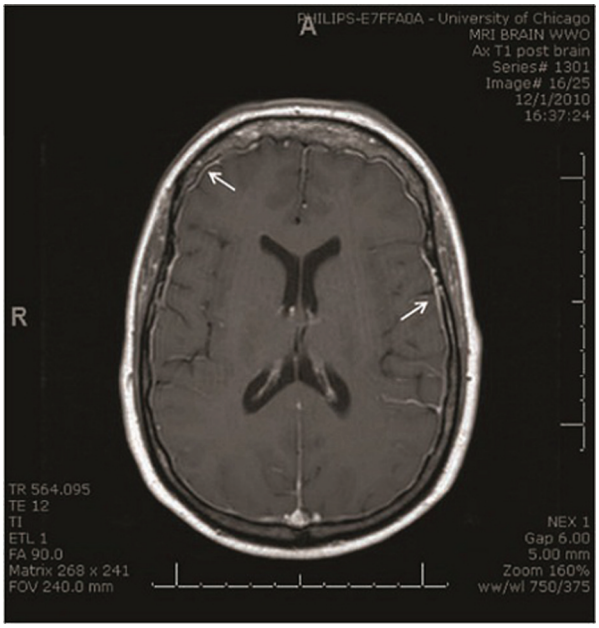

Figure 2 Axial section of postcontrast T1-weighted brain MRI image showing the dural thickening with gadolinium-contrast enhancement (arrow).

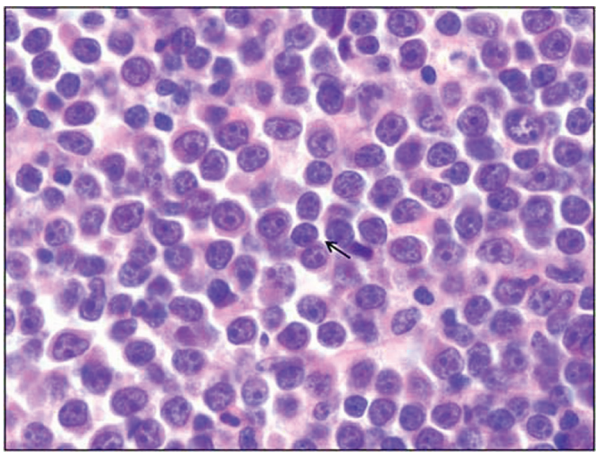

Figure 3 Representative bone marrow biopsy section stained with haematoxylin & eosin showing abundant malignant lymphocytes (arrow) (magnification: 500×).

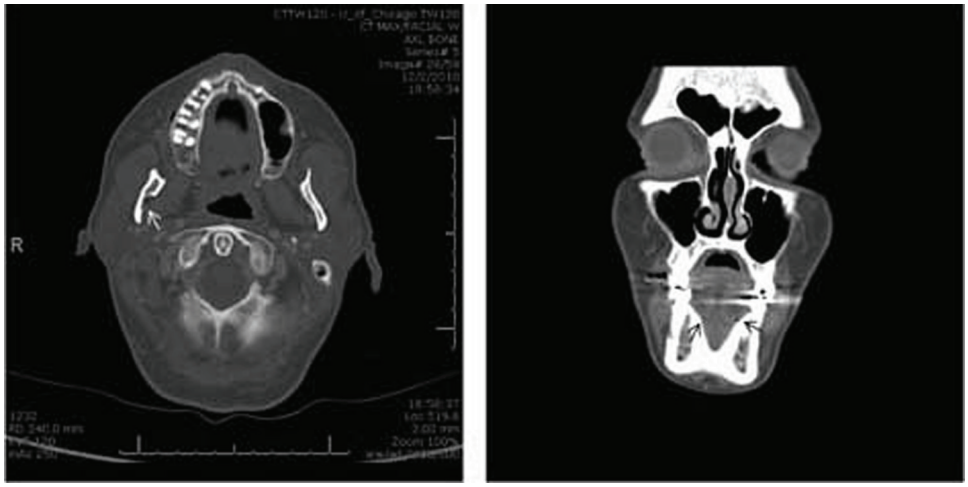

Figure 4 Axial section (left panel) and coronal section (right panel) of maxillary/facial CT scan with contrast showing no evidence of bony metastasis in the mandible. Note the relatively larger right-side mandibular foramen (white arrow), which could be normal anatomical variation or lesion. Also note the intact bilateral mental foramen (black arrows).

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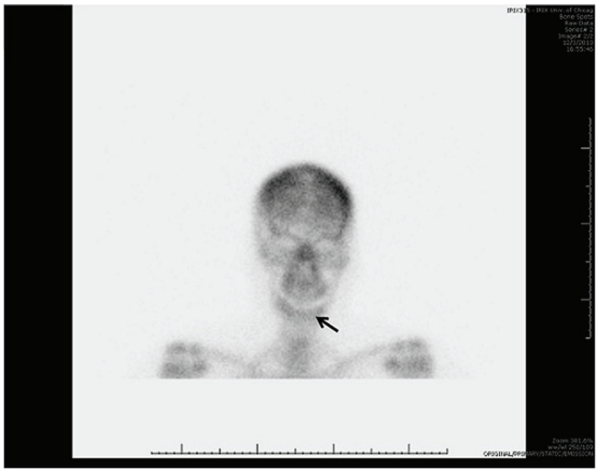

Figure 5 Coronal section of skull nuclear bone SPECT showing no abnormal uptake in the skull to suggest bone metastasis (arrow points to the mandible).

(figure 3). Due to the persistent chin numbness, neurology service was consulted. The patient was found to be neurologically intact without any focal deficit on physical examination other than the area of decreased sensation in right chin and right lower lip to tactile stimuli and pinprick. No tenderness could be elicited in the chin area. From the symptom onset, the chin numbness remained unchanged in terms of nature and distribution. Given the patient's underlying NHL, NCS was suspected. Maxillofacial CT was obtained, which showed no evidence of bony metastasis or any frank osseous abnormality (figure 4). However, the right-side mandibular foramen appears to be widened compared with the left side without contrast enhancement. This might represent normal anatomical variation versus bony lesion. We then proceeded to single photon emission CT (SPECT) of the skull, but no scintigraphic evidence of skull bone metastasis was identified (figure 5).

DIFFERENTIAL DIAGNOSIS

Some other non-systemic malignancy aetiologies of NCS include

- Dental or odontogenic processes: trauma, infection, locally invasive tumours and mandibular osteomyelitis.
- Sickle cell disease.
- Multiple sclerosis.
- Sarcoidosis.
- Lyme disease.
- Temporal arteritis.
- Diabetic neuropathy.

DISCUSSION

NCS has been well documented in the literature. Nevertheless, it is still largely under-recognised by many first-line physicians such as primary care physicians, ED physicians and dentists. The lack of awareness conceivably causes delay in diagnosis and treatment.

Our case supports the concept that malignant aetiologies should be considered in patients who present with NCS. One previous study reported that numb chin was the presenting symptom of malignancy in 47% of patients with NCS and systemic malignancy.[7] The prognosis appears to be affected by the mechanism of NCS.[1 8 9] Specifically, the average survival time after the diagnosis is approximately 5 months if the NCS is caused by mandibular metastases and 12 months if caused by leptomeningeal metastases. Interestingly, neither mandibular nor leptomeningeal lesions were found in our case. The lack of CSF findings of malignant cells also argues against carcinomatous meningitis. It is not clear how exactly the lesions in dural and clivus cause the numb chin. Theoretically, if a dural compression mechanism exists, one may expect to find other associated cranial nerve deficits.

Another possibility is microscopic seeding of the malignant cell in the nerve per se not visible on radiograph. In support of this possibility, one case report has shown that tumour infiltration of the inferior alveolar nerve was only identified through surgical exploration after a negative CT scan.[10] Some postmortem studies in patients exhibiting NCS with underlying neoplastic processes have found heavy infiltration of tumour cells in the trigeminal nerve and destruction of axons and myelin in the mandibular nerve.[11] It has been postulated that the particular vulnerability of inferior alveolar nerve/mental nerve to malignant metastasis is due to their tortuous course through the bony mandible.[12]

Learning points

- Recognising NCS clinically is important as this may be a subtle sign of occult malignancy progression or relapses.
- Patients with NCS without apparent cause should be assumed to have a malignant aetiology until proven otherwise.
- By far the most common non-haematologic neoplastic cause of NCS is breast cancer, while the most common haematologic neoplastic cause is NHL.
- The exact pathophysiology of NCS is still unclear. Currently known mechanisms include direct compression of the mental nerve by tumour mass, leptomeningeal invasion or a bony lesion at mental foramen. However, other mechanisms may exist, such as dural lesion.

Competing interests None.

Patient consent Obtained.

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