

Burkitt non-Hodgkin lymphoma presenting with mental neuropathy ("numb chin" syndrome) in an HIV-positive patient

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Summary

Mental nerve neuropathy is usually due to local trauma or dental causes, but may be a manifestation of malignancy. A patient with virologically-controlled HIV infection presented with a “numb chin” on the background of long-standing night sweats, malaise and weight loss, worsening respiratory symptoms, and lymphadenopathy. Burkitt non-Hodgkin lymphoma was diagnosed from histology of a lymph node. Imaging (MRI and ¹⁸FDG-PET-CT) showed abnormal intracranial enhancement of the right mandibular nerve and extensive ¹⁸FDG-avid lymphadenopathy above and below the diaphragm, focal lesions in the spleen and within the right mandible. The patient received chemotherapy and remains in clinical and radiological remission seven years later. This case highlights the need for clinicians to maintain a high index of suspicion for underlying malignancy when an HIV-infected patient presents with new onset of a “numb chin”. Additionally, it demonstrates the importance of functional (¹⁸FDG-PET-CT) and neuroimaging in order to identify site(s) of pathology.

Key words: [Burkitt](#), lymphoma, mental neuropathy, numb chin syndrome, HIV, ¹⁸FDG-PET-CT.

INTRODUCTION

Mental nerve neuropathy, also known as “numb chin syndrome”, is characterized by hypoesthesia or anaesthesia in the mental branch of the trigeminal nerve. The majority of cases that are not due to local trauma or dental causes are associated with a primary malignancy such as Hodgkin or non-Hodgkin lymphoma, leukaemia, melanoma, rhabdomyosarcoma, as well as mandibular infiltration or base of skull metastases or carcinomatous meningitis due to carcinoma of breast, prostate, kidney, and lung. Other causes include amyloidosis, sarcoidosis, sickle cell disease, syphilis, vasculitis, aneurysms, multiple sclerosis, and diabetes mellitus [1][2]. We describe an HIV positive man with “numb chin” syndrome associated with Burkitt non-Hodgkin lymphoma, in who imaging showed both mandibular tumour and intracranial infiltration of the mandibular nerve.

CASE REPORT

A 34-year-old man with a 10-year history of HIV infection, and a previous AIDS-defining diagnosis of *Pneumocystis* pneumonia, presented with a three months history of night sweats and malaise, a five weeks history of weight loss, progressively worsening non-productive cough and dyspnoea, pleuritic chest pain and generalised abdominal discomfort and back pain, and a one day history of right sided peri-oral numbness. He was taking Truvada and ritonavir ‘boosted’ darunavir and had an undetectable viral load; the CD4 count was 580 cells/ μ L.

Examination revealed bilateral inguinal and axillary lymphadenopathy, bilateral pleural effusions and ascites. Peripheral neurological examination was unremarkable as was cranial nerve examination apart from sensory loss to light touch and pin-prick confined to the mental branch of the right trigeminal nerve. The jaw jerk was not accentuated, nor absent, and there was no masseter, temporalis or pterygoid weakness. Magnetic resonance imaging (MRI) showed lymphomatous involvement of the right mandibular nerve, with loss of normal bone marrow signal within the right anterior aspect of the mandible (fig 1a). Intracranially, there was thickening and enhancement of the right trigeminal nerve (fig 1b). A ¹⁸Fluorodeoxyglucose (¹⁸FDG) positron emission tomography-computerised tomography (PET-CT) scan showed ¹⁸FDG-avid extensive

mediastinal, axillary, retro-crural, retroperitoneal and mesenteric lymphadenopathy with associated bilateral pleural effusions and ascites. In [addition](#), there were ¹⁸FDG-avid focal lesions in the spleen and in the right mandible (fig 2). Histology of an ultrasound-guided biopsy of an axillary node showed Burkitt non-Hodgkin lymphoma. Pleural fluid aspirate included degenerate relatively monomorphic cells with cytoplasmic vacuoles, which stained with CD20, confirming their B cell lineage and the diagnosis of Burkitt lymphoma, as did histology from a bone marrow trephine, where a collection of CD20 positive cells showing the morphology of Burkitt Lymphoma was noted.

After two cycles of chemotherapy with R-CODOX-M/R-IVAC (rituximab, cyclophosphamide, vincristine, doxorubicin, and methotrexate/rituximab, etoposide, ifosfamide), together with intrathecal cytarabine, the patient achieved complete clinical and ¹⁸FDG-PET-CT remission. The neurological symptoms resolved completely and seven years later the patient remains in remission and continues to have undetectable viral load on antiretroviral therapy.

DISCUSSION

Among the general population “numb chin” syndrome is most often due to dental disease or to trauma to the jaw, however primary (osteosarcoma) or metastatic tumour involving the mandible may directly damage the mental nerve by compression or infiltration. Intracranial pathology, including cerebral metastases, base of skull tumour and malignant leptomeningitis, may also involve the mandibular nerve. Additionally, vasculitis or endarteritis/infarction may cause damage to the mental nerve in non-malignant systemic disease such as sarcoidosis [3].

The facial nerve is the most commonly involved cranial nerve among HIV-infected patients with Burkitt lymphoma [4][5] and central nervous system involvement, classified as stage IV disease, is associated with a poorer prognosis. Involvement of other cranial nerves is less common, and a small number of reports from the pre-HAART era describe patients with HIV-associated lymphoma and involvement of the trigeminal nerve in the form of mental neuropathy [6][7]. The majority of patients in these case series died within a year of the onset of mental neuropathy

despite receipt of chemotherapy. [Tumour involvement of the jaw is characteristic of endemic \(“African variant”\) Burkitt lymphoma. In the sporadic and immunodeficiency-associated variants it occurs less commonly \[8\].](#)

Knowledge of the anatomy of the trigeminal nerve has been applied to propose a variety of mechanisms whereby lymphoma can involve the mandibular nerve. Where central involvement of the sensory root of the trigeminal nerve is suspected, there may be multiple cranial nerve involvement, while potential causes of peripheral involvement include local pressure on the mental nerve foramen of the mandible by enlarged lymph nodes or direct infiltration of the nerve [7]. The case presented here is unique, as imaging revealed lymphoma both in the mandible and intracranially involving the mandibular nerve, [although the presentation was likely due to the mandibular lesion, as no other levels of the trigeminal nerve were affected.](#) With chemotherapy lymphomatous disease at both sites was treated, and the “numb chin” resolved.

In conclusion, this case serves to remind clinicians first, that trigeminal nerve involvement in the form of “numb chin syndrome” is an important “foreboding” clinical sign and that a high index of suspicion for underlying malignancy should be maintained when an HIV-infected patient presents with new onset of a “numb chin”. Second, that early investigation and use of both functional (¹⁸FDG-PET-CT) and neuroimaging are important to identify the site(s) of pathology.

REFERENCES

1. Gálan-Gil S, Peñarrocha Diago M, Peñarrocha Diago M. Malignant mental nerve neuropathy: systematic review *Med Oral Patol Oral Cir Bucal* 2008; 13: E616-21.
2. Lee W. Lymphoma presenting as cranial nerve neuropathies in HIV-infected patients *AIDS Reader* 2008; 18:606-610, 621.
3. Colella G, Giudice A, Siniscalchi G, Falcone U, Guastafierro S. Chin Numbness: a symptom that should not be underestimated: a review of 12 cases. *Am J Med Sci* 2009; 337: 407-10.
4. Riancho J, Delgado-Alvarado M, Valero C, Echevarria S. Clinical spectrum of peripheral facial paralysis in HIV-infected patients according to HIV status. *Int J STD AIDS* 2013; 24: 39-41
5. Woodcock H, Nelson M. Burkitt's non-Hodgkins lymphoma presenting as facial nerve palsy in HIV-positive patients. *International Journal of STD & AIDS* 2011; 22:112-114
6. Chand V, Sweeney C, Agger WA. Mental neuropathy in patients with AIDS-associated malignant lymphoma. *Clin Infect Dis* 1997; 24: 521–22.
7. Milam SB, Rees TD, Leiman HI. An unusual cause of bilateral mental neuropathy in an AIDS patient. *J Clin Periodontol* 1986; 57:753-5.
8. [Harris NL, Jaffe ES, Diebold J, et al. The World Health Organization classification of neoplastic diseases of the hemopoietic and lymphoid tissues. Report of the clinical Advisory Committee Meeting, Airlie House, Virginia, November 1997. *Ann Oncol* 1999; 10: 1419-32.](#)

Figure Legends

Figure 1a) Coronal T1-weighted MRI showing loss of normal bone marrow signal within the right anterior aspect of the mandible (arrow); the bone cortical margins appear slightly irregular.

Figure 1b) Coronal T1-weighted, gadolinium-enhanced MRI. The 3rd division of the trigeminal nerve (arrows) is shown along its course within the right cavernous sinus and as it approaches the right foramen ovale.

Figure 2. Fused ¹⁸F-FDG-PET-CT image showing focal ¹⁸F-FDG avidity within the right mandible.