原文題目(出處)：	Numb chin syndrome as first symptom of diffuse large B-cell lymphoma. Case Rep Dent 2014, Article ID 413162
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內文：

1. Introduction:

- **Numb chin syndrome** (NCS) or mental nerve neuropathy is a rare sensory neuropathy characterized by numbness, hypoesthesia, paraesthesia, and very rarely pain in the distribution of the mental nerve.
- **Etiologic factors**: dental causes, especially iatrogenic ones (oral surgery)
- Among malignant distant neoplasms that metastasize to the mandible, the most frequent is breast cancer followed by primary carcinoma of lung, thyroid, kidney, prostate, and nasopharynx.
- Other associated neoplasms include hematological malignancies like acute lymphocytic leukemia, Hodgkin and non-Hodgkin lymphoma (NHL), andmyeloma. Tumor and Trauma.
- If not related to a dental cause, this innocuous complaint is considered a "red flag" symptom of a malignant neoplasm.

NHL:

- NHL is a particular type of **lymphoma** in which **malignant neoplastic proliferation** of lymphocytes at different stages of mutation occurs.
- Nearly 40% of NHL arises in extranodal sites and the head and neck region is the second most frequent anatomic site of extranodal NHLs.
- Half of the extranodal NHLs of the head and neck are located in the Waldeyer ring.
- The histologic types of NHLs commonly found in the head and neck are B-cell neoplasms. Within these types **the diffuse large B-cell lymphoma (DLBCL)** and extranodal marginal zone lymphoma of themucosa associated lymphoid tissue (MALT) are the most frequent.
- **DLBCL (diffuse large B-cell lymphoma)** often involves the Waldeyer ring but can be also found in the soft tissue and bone of the jaws.
- Extranodal lymphomas: less than 5% of all oral malignant neoplasms, represent the third most common neoplasm involving oral cavity following squamous cell carcinoma and salivary glands neoplasm.
- arising in 1970, NHL is still the sixth most common cause for cancer-related deaths in the USA

2. Case report

P.I: A 71-year-old Caucasian woman was referred to our department in September 2013 because of the **development of anaesthesia of the lower right lip and chin.**

Past medical history:

Hypertension, chronic obstructive pulmonary disease, rheumatoid arthritis (RA), and an IgM monoclonal gammopathy of undetermined significance (IgM-MGUS) **first**

Clinical evaluation :

She was taking methotrexate (MTX) (10mg once a week), folic acid (5mg/daily), prednisone (7.5mg/daily), ibuprofen (80mg/daily), and calcium

Intraoral clinical examination:

Unremarkable, an ulcer of 1 cm wide could be seen in the lower lip
Pain (+) palpation in the lower right vestibular fornix in the premolar area and in homolatera submandibular space
Lymphadenopathies (+) in the right later cervical, supraclavicular, and subaxillary groups and in the left axillary group

Past dental history:

Chronic periodontitis, prosthetic therapy with dental implants and partial removable dentures
No direct dental or other local causes

X-ray (pano), CT, U/S examination

X-ray

Radiopaque area diffused from 4.5 to 4.8 with some microlacunae on the alveolar ridge and lower mandibular cortex.

CT

Confirmed the microlacunar reabsorptions due to bony structural rearrangement of all the mandibular cortices peripheral to the radiopaque lesion diffused from 4.5 to 4.8 centre of the lesion was characterized by hypodensity of the spongiosa mandibular canal was detectable only in the distal sections.

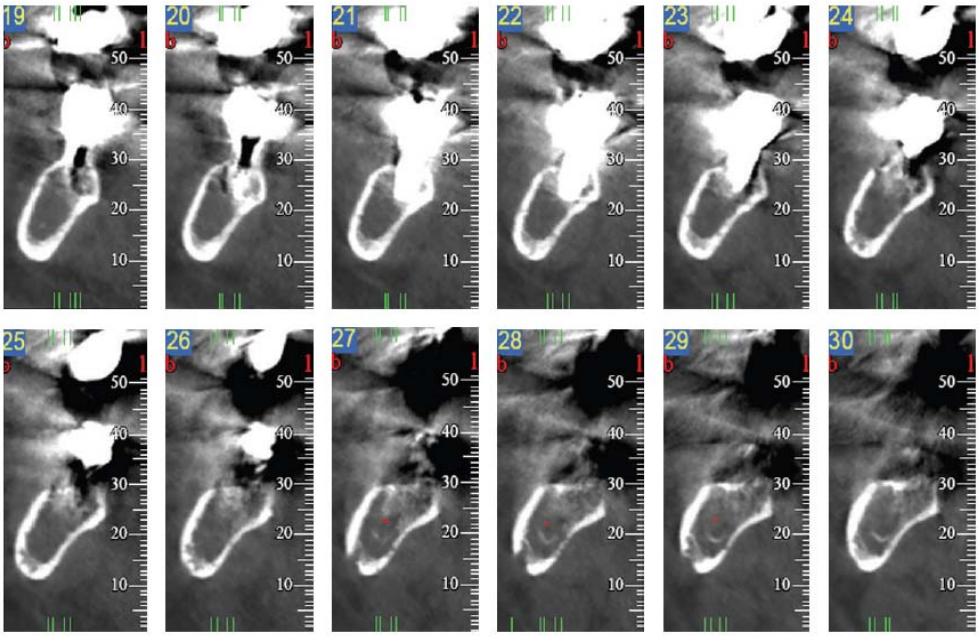

FIGURE 1: CT-scan examination. Note microlacunar reabsorptions of the mandibular cortices and hypodensity of the spongiosa, diffused from 4.5 to 4.8.

In the U/S

A **2 cm wide hypoechogenic mass** was clearly visible.
This mass was very **close to the right corpus of the mandible** with **well-defined** margins. The cortical bone peripheral to this finding revealed signs of cortical erosion. Three swollen lymph nodes were detectable close to the mass in the submandibular space. These glands showed a metastatic pattern. Other reactive lymph nodes were detectable **bilaterally** in the later cervical groups.

Biopsy

Fragment from: mandibular periosteum, medullary and cortical mandibular bone, and inferior alveolar nerve

Histopathological examination:

A diffuse proliferation of large lymphoid cells with quite abundant basophil

cytoplasm and pale perinuclear ring, oval nuclei with dispersed chromatin, and one or more nucleoli (hematoxylin-eosin 400x).

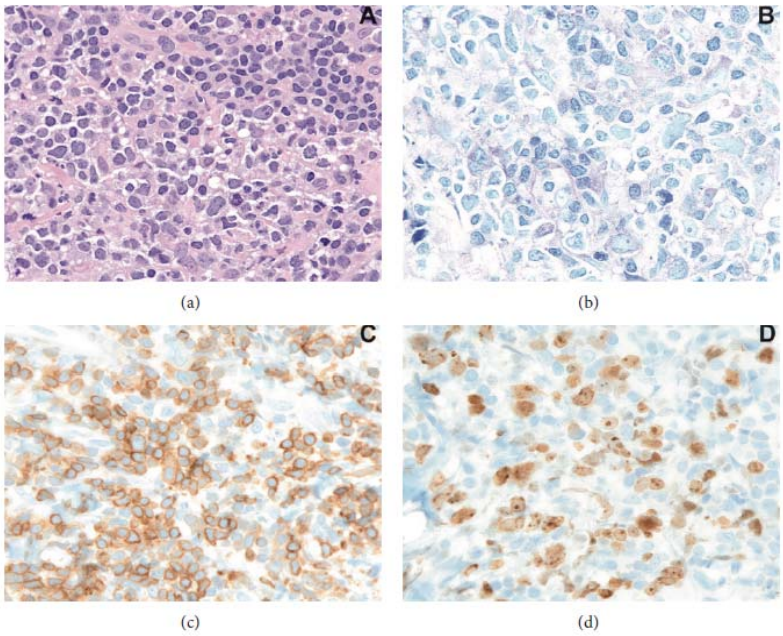

FIGURE 2: (a)-(b) Histopathological examination (hematoxylin-eosin and Giemsa stains); (c) immunohistochemical reactions for BCL2+; and (d) proliferation index (Ki67, MIB1). Magnification: 400x.

Immunohistochemical reactions

The neoplastic cells were diffusely positive for CD20 and BCL2 and weakly positive for BCL6.

Proliferation index: evaluated with Ki67, MIB1 clone, was high: about 70%

Diagnosis:

The PET examination: increased uptake in right mandible and in lymph nodes of the supradiaphragmatic, mediastina, aortic, and subcarinal groups.

The CT examination:

Lymphadenopathies were detected bilaterally in the submandibular, digastric groups and in the right subclavicular group.

The final diagnosis:

A **DLBCL IVA** with bonemarrow involvement (BM+) and a monoclonal IgM component (CM IgM-MGUS) in association with RA.

Classification of DLBCL

Stage	Area of Involvement
I	Single lymph node group
II	Multiple lymph node groups on same side of diaphragm
II	Multiple lymph node groups on both sides of diaphragm
IV	Multiple extranodal sites or lymph nodes and extranodal disease
X	Bulk > 10 cm
E	Extranodal extension or single isolated site of extranodal disease
A/B	B symptoms: weight loss > 10%, fever, drenching night sweats

Including the World Health Organization (WHO)/Revised European American Classification of Lymphoid Neoplasms (REAL) system and the Cotswolds modification of the Ann Arbor system

http://emedicine.medscape.com/article/2007789-overview

3. Discussion

- In this case, NCS represented the first specific symptom of a hematologic

malignant neoplasm.

- NCS could be the inaugural manifestation of a malignancy in 30% of cases and the first sign of relapse or progression of cancer in patients with malignancy history in 40% of cases.
- The most common neoplastic cause of NCS is metastatic breast cancer (40% cases) followed by NHL (20%) and prostate cancer (6%).
- The onset of DLBCL in association with RA, IgM-MGUS, and the previous therapy with methotrexate for RA.
- Several studies have linked certain autoimmune and chronic inflammatory conditions, including rheumatoid arthritis (RA), Sjogren's syndrome, systemic lupus erythematosus (SLE), celiac disease, and chronic thyroiditis, to an increased risk of lymphoma.
- Another particular feature of our case was the presence of an IgM monoclonal gammopathy
- **The exact pathophysiology of NCS in patients with cancer is still unknown.**
- Direct perineural and neural invasion may be an important pathway in primary tumours of the inferior alveolar nerve, squamous cell carcinoma, and lymphoma.
- malignancies in their initial stage are accompanied by a significant inflammatory response
- The possible confinement of the inflammatory process within the bony canal may lead to ischemia and nerve damage

題號	題目
1	Non-Hodgkin's lymphomas (NHLs) are a relatively common group of neoplasms (more than 50,000 cases per year) that often occur **(A)** lymph nodes (nodal) **(B)** extranodal sites **(C)** salivary tissues **(D)** head and neck sites
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題號	題目
2	About "Hodgkin's lymphoma", which statement is wrong? **(A)** Lymphomas are malignant neoplasms of component cells of lymphoid tissues **(B)** Hodgkin's lymphoma is very rare in the oral cavity **(C)** lymphoid stroma composed of large numbers of neoplastic cells **(D)** presence of large binucleated cells called Reed-Sternberg cells
答案(C)	出 處 ： **ORAL PATHOLOGY:** CLINICAL PATHOLOGIC CORRELATIONS 6th, P229