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Case Report

CASE REPORT

Two cases of numb chin syndrome diagnosed as malignant disease

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Abstract

Numb chin syndrome (NCS) is defined as reduced or absent sensation in an area of the chin and lower lip within the distribution of the mental or inferior alveolar nerves. The causes of NCS may be neoplastic, traumatic, dental, toxic, drug-induced, inflammatory, autoimmune or infectious. NCS may be the preliminary symptom of malignancy or recurrence/metastasis in patients with cancer. Therefore, the occurrence of NCS warrants careful examination and monitoring of such patients. This article presents two cases of NCS reported in a patient with prostate cancer and in a patient with Burkitt lymphoma/leukaemia.

INTRODUCTION

Numb chin syndrome (NCS) is defined as reduced or absent sensation in an area of the chin and lower lip within the distribution of the mental or inferior alveolar nerves. The causes of NCS may be neoplastic, traumatic, dental, toxic, drug-induced, inflammatory, autoimmune or infectious (Table 1). The pathophysiologic mechanism of NCS involves the compression or infiltration of the mental or inferior alveolar nerves. In patients with cancer, NCS may be the preliminary symptom of malignancy or recurrence/metastasis [1]. NCS is associated with a poor prognosis in patients with metastatic disease. Thus, the occurrence of NCS warrants careful examination and monitoring of such patients [2].

This article presents two cases of NCS reported in a patient with prostate cancer and in a patient with Burkitt lymphoma/leukaemia.

CASE REPORT

Case 1

A 73-year-old male experienced episodes of lumbar back pain. The patient became conscious of numbness in the left lower lip and chin three months later. The lumbar back pain worsened, and the levels of alkaline phosphatase in the blood were 2 369 U/L (reference range: 100–325 U/L). Blood examination did not reveal other abnormalities, and he was referred to the Kumamoto University Hospital, Japan. The patient reported weight loss (~4 kg/month) and loss of appetite. Blood examination showed a blood alkaline phosphatase fraction 3 of 85%. Moreover, abdominal ultrasonographic findings of the liver and gallbladder were unremarkable. Radiography revealed the presence of a cystic radiolucent shadow in the thoracolumbar vertebrae (Fig. 1). Thus, the treating physicians suspected bone metastasis associated with a malignant tumour and complicated

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by NCS. Bone scintigraphy showed abnormal, increased uptake in the bones of the skull, left mandible, trunk and limbs (Fig. 2). Furthermore, the observed levels of prostate-specific antigen were high (662.4 ng/mL; reference range: <4.0 ng/mL). Based on these findings, the treating physicians suspected the presence of prostate adenocarcinoma. Magnetic resonance imaging (MRI) and a prostate biopsy were performed (Fig. 3). The patient was diagnosed with prostate adenocarcinoma with mandibular and bone metastasis complicated by NCS. Maximum androgen blockade hormonal therapy was initiated at a different hospital. Twenty months after the diagnosis, the patient continued to receive chemotherapy on a regular basis. However, the symptoms of NCS persisted.

Table 1: Differential diagnosis of numb chin syndrome (NCS)

Neoplasm	Breast cancer, lymphoma, prostate cancer, leukaemia, etc. Metastatic lesions of the oral and maxillofacial regions are rare. They comprise ~1–3% of oral and maxillofacial malignancies [3–6]. The major primary tumour sites are breast (40%), followed by lymphoma (21%), prostate (7%) and leukaemia (5%) [7].
Dental and traumatic injury	Iatrogenic injury, removal of impacted teeth or cysts, local anaesthetic block, bone grafting, endodontic therapy, orthognathic surgery, dental implant placement, etc. The most common cause of NCS
Toxin or drug-induced	Bisphosphonate, mefloquine, allopurinol, interferon-alpha, trichloroethylene, etc.
Infection	Syphilis, Lyme disease, herpes simplex virus, human immunodeficiency virus, etc.
Inflammatory/ Autoimmune	Multiple sclerosis, sensorimotor mononeuritis multiplex, giant cell arteritis, post-hepatitis B vaccination, systemic lupus erythematosus, Sjögren syndrome, scleroderma, rheumatoid arthritis, mixed connective tissue disease, dermatomyositis, etc. Rare causes of NCS

Case 2

An 18-year-old male reported fever, fatigue and joint pain in both elbows, hips and knees. The patient received treatment for acute pharyngitis in an internal medicine clinic. However, 2 weeks after the initiation of treatment, the symptoms persisted and he was referred to the Kumamoto University Hospital, Japan. Despite suffering night sweats, the patient did not experience gastrointestinal or respiratory symptoms or weight loss. Physical examination did not reveal abnormal physical findings. The complete blood count was within the normal range, the erythrocyte sedimentation rate was 65 mm/h, and the levels of C-reactive protein were 64.4 mg/L. No abnormality was observed in the levels of electrolytes, liver or renal function, complement titre, thyroid function, levels of

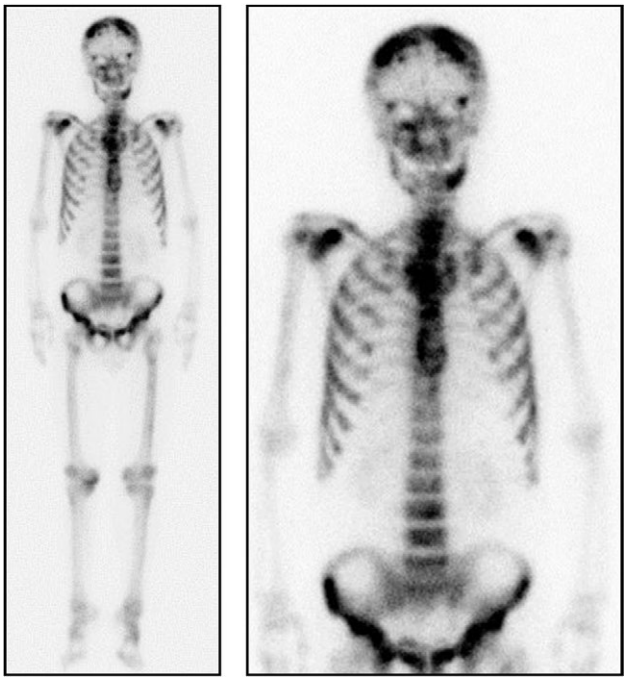

Figure 2: Skeletal scintigraphy indicated a metabolic active lesion in the bones of the skull, left mandible, trunk and limbs.

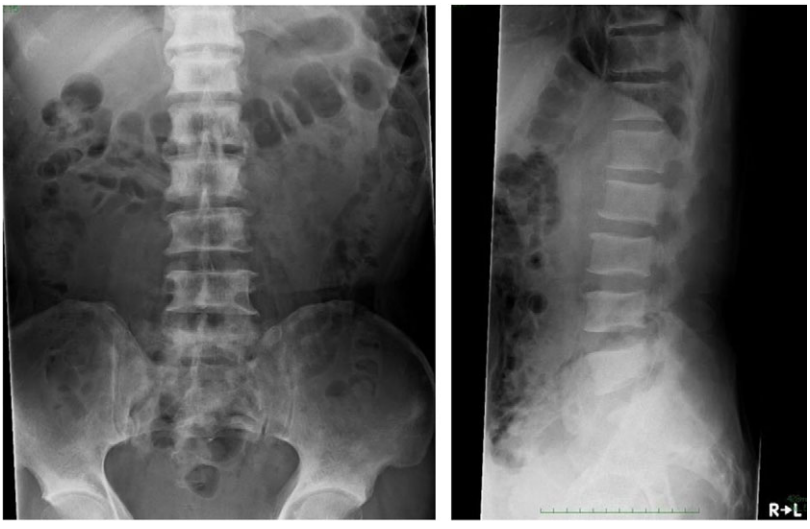

Figure 1: Radiography showed a cystic radiolucent shadow in the thoracolumbar vertebrae.

autoantibody, levels of cytomegalovirus antibody or the levels of Epstein—Barr virus antibody. The treating physicians suspected a viral infection or drug-induced fever. One week after the examination, the patient reported hypaesthesia from the left lower lip to the lower jaw. A dental examination did not show any abnormality. Although whole-body non-contrast computed tomography (CT), brain MRI and abdominal ultrasonography were performed, the results did not identify a primary lesion. Three weeks after the initial presentation to the hospital, a blood examination revealed a decreased platelet count from 358 000 to 95 000/μL. Additionally, the levels of lactate dehydrogenase and uric acid increased from 513 to 8617 IU/L and from 7.2 to 18.1 mg/dL, respectively. The proportion of abnormal lymphocytes in the peripheral blood was 6%. The treating physicians suspected metastasis associated with a

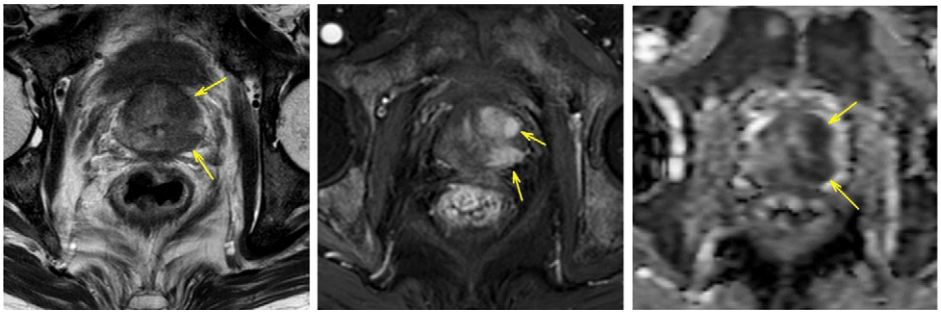

Figure 3: Magnetic resonance imaging showed an irregularly shaped T2-weighted low signal area that could be recognized from the bilateral external glands to the left side of some internal glands. The same area presented with a high signal in diffusion-weighted images (DWI) and a low signal in the apparent diffusion coefficient (ADC) map. The area exhibited stronger staining than that observed in the early phase of the dynamic study.

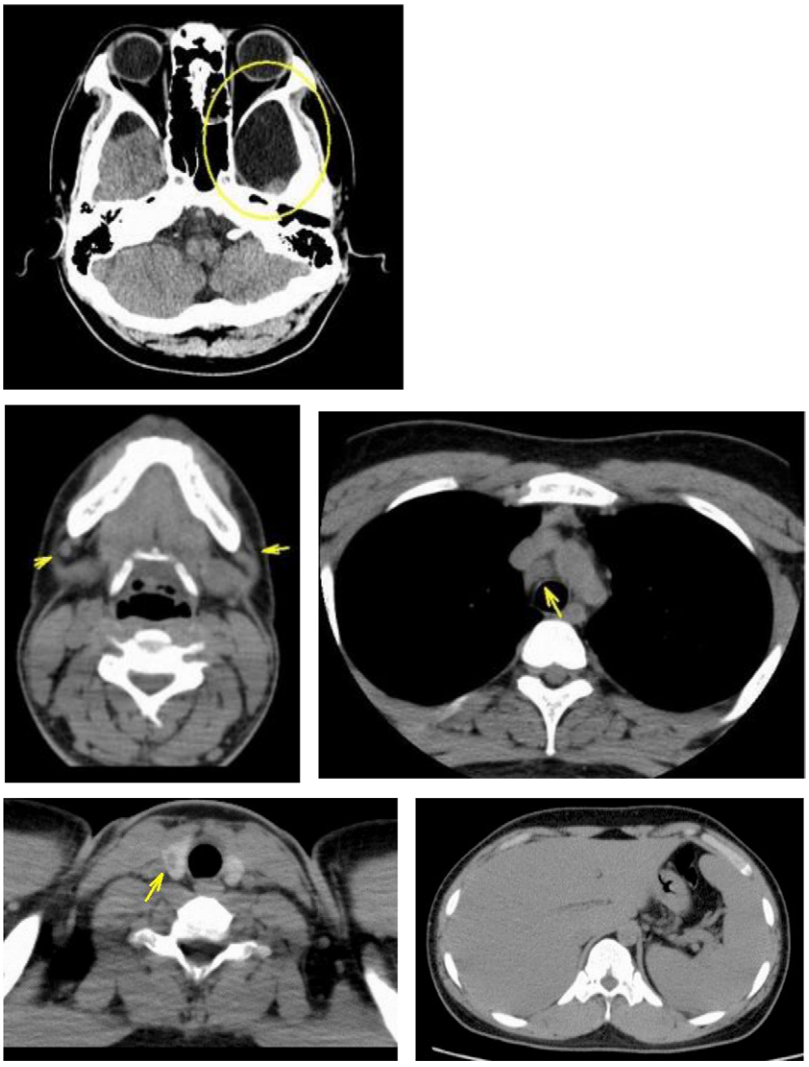

Figure 4: Computed tomography revealed the presence of an arachnoid cyst, enlargement of the cervical/mediastinal lymph node and splenomegaly.

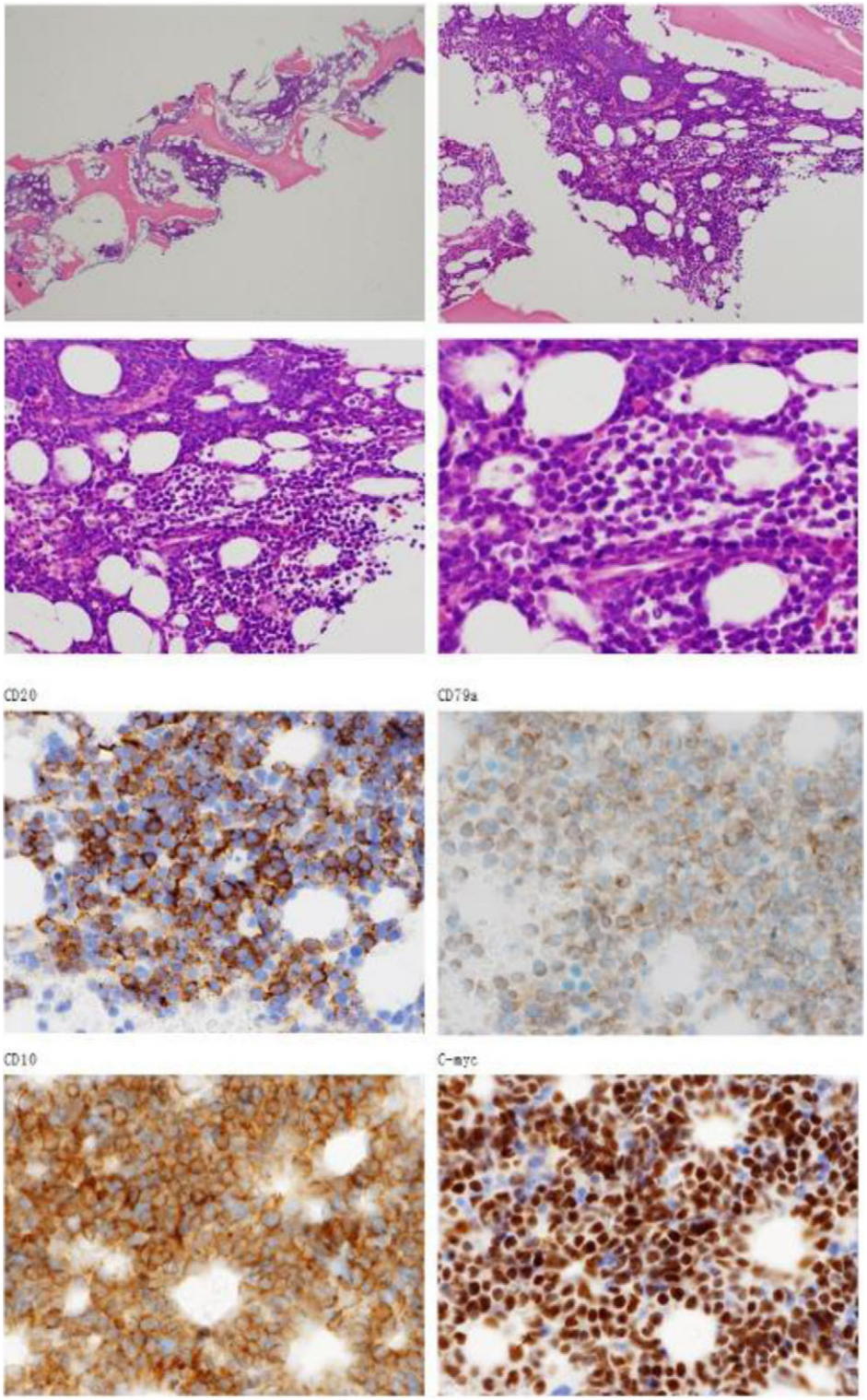

Figure 5: Bone marrow aspiration biopsy showed 84% blast cells and large immature mononuclear cells with high nuclear morphological irregularity (cytoplasmic ratio, basophilic cytoplasm and cytoplasmic vacuolation). Analysis of the bone marrow aspirate using flow cytometry showed positivity for CD4 (weak), CD10, CD19, CD20, CD79a and c-myc.

blood disease such as leukaemia complicated by NCS. Repeated whole-body non-contrast CT and examination of the bone marrow were conducted (Figs 4 and 5). Cytogenetic analysis revealed the t (8: 14) chromosomal translocation and the patient was diagnosed with Burkitt lymphoma/leukaemia. Chemotherapy was initiated one month after the presentation to the hospital. However, 10 days after the initiation of treatment, the patient developed facial nerve palsy. The results of a brain MRI and an examination of the cerebrospinal fluid (Figs 6 and 7) presented a finding of dissemination of lymphatic leukaemia. The patient was diagnosed with

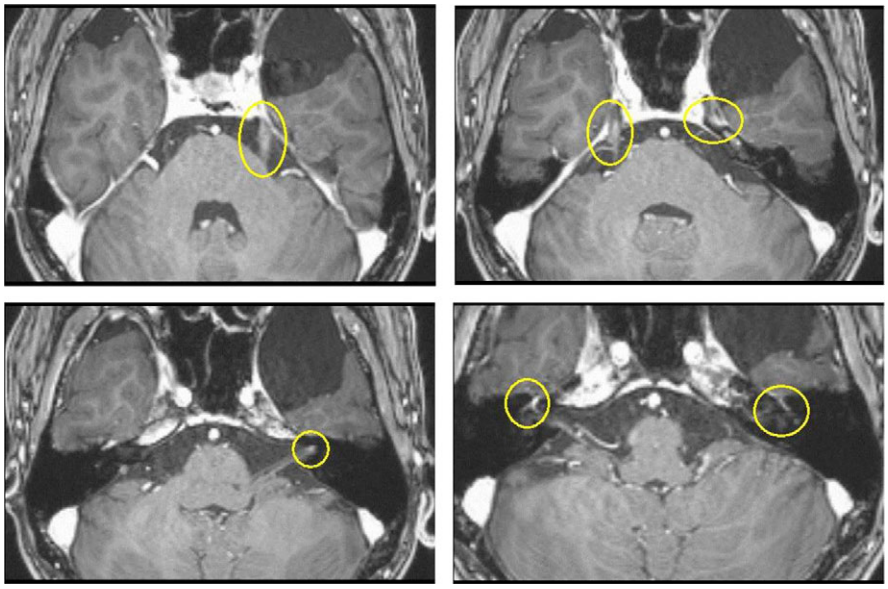

Figure 6: Brain magnetic resonance imaging indicated enhancement of the bilateral facial nerve on the distal internal auditory meatus, labyrinthine segment, geniculate ganglion, tympanic part and mastoid part. In addition, the bilateral trigeminal nerves were enhanced.

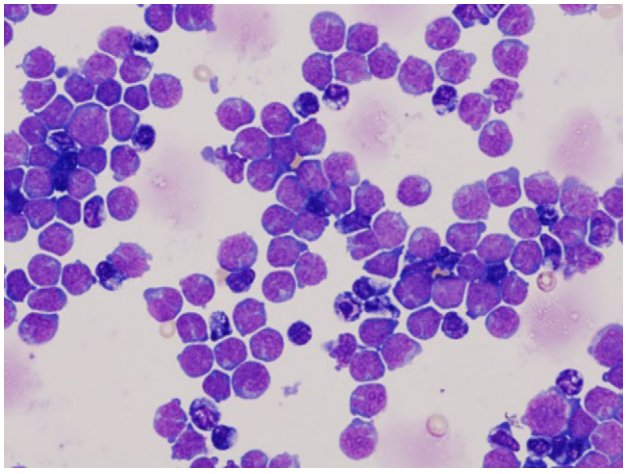

Figure 7: Examination of the cerebrospinal fluid showed the presence of numerous lymphoid atypical cells with marked irregularly shaped nuclei and large-size nucleoli.

Burkitt lymphoma/leukaemia of the central nervous system (CNS) associated with NCS. Chemotherapy was re-administered and the patient achieved remission. However, he relapsed. Subsequently, the patient received peripheral blood stem cell transplantation. Regrettably, the patient expired 12 days following transplantation. The cause of death was neutropenic fever and disseminated intravascular coagulation induced by *Pseudomonas aeruginosa* sepsis.

DISCUSSION

In the cases present herein, bone invasion in prostate cancer (Case 1) and CNS invasion in Burkitt lymphoma/leukaemia (Case 2) were responsible for the occurrence of NCS. The occurrence of NCS in patients with malignancy is indicative of metastasis, with a reported overall mortality of 79% and a weighted mean survival of ~7 months [7]. Although CT revealed the presence of an arachnoid cyst in Case 2, the origin of the lesion was congenital and was unrelated to the reported hypaesthesia from the left lower lip to the lower jaw. In Case 1, the occurrence of NCS was as a result of direct bone invasion. In Case 2, NCS was caused by CNS invasion as opposed to direct invasion. One hypothesis for how CNS invasion can cause NCS is the involvement of autoantibodies such as anti-Hu antibodies. These are specific autoantibodies recognizing neuronal cell-surface antigens, and are often associated with pulmonary small cell carcinoma and paraneoplastic neurologic syndrome. A previous study suggested that autoimmune mechanisms against an unknown antigen may be involved in the occurrence of NCS [8]. We did not, however, identify any antibodies. Further research is warranted to investigate this hypothesis.

In conclusion, NCS is indicative of the presence of malignancy. Therefore, the presence of NCS warrants careful examination and monitoring of patients.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

FUNDING

None.

ETHICAL APPROVAL

None required.

CONSENT

Informed consent was obtained from the patients.

GUARANTOR

Kosuke Maeda is the guarantor of this article.

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