Numb Chin Syndrome: An Uncommon Presentation of Metastatic Non-Small Cell Lung Cancer Diagnosed by ^{18}F-FDG PET/CT Scan

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ABSTRACT

Objective: To present an uncommon presentation of metastatic non-small cell lung cancer at mandible causing numb chin syndrome (NCS), diagnosed by PET/CT scan.

Case presentation: A 72-year-old man presented with decreased sensation of left lower lip without motor deficit or taste alteration, so called NCS. Work up was initially focused on benign etiology as patient had no known malignancy. However, malignancy was suspected after excluding all possible benign causes. Further investigation showed high level of adenocarcinoma markers and a lytic lesion at sacrum leading to provisional diagnosis of bone metastasis with unknown primary cancer. The subsequent fluorine-18 fluorodeoxyglucose positron emission tomography/computerized tomography (^{18}F-FDG PET/CT scan) showed a pulmonary mass, representing primary lung cancer with multiple metastatic sites, including the destructive lesion at left mandible which was a cause of NCS.

Conclusion: NCS could be an atypical presentation of malignancy. Among several investigations for NCS, PET/CT scan may rarely be used. However, PET/CT scan may provide substantial benefits, particularly for metastatic disease with unknown primary cancer.

Keywords: Numb chin syndrome; mandibular metastasis; F-18 FDG PET/CT scan; non-small cell lung cancer (Siriraj Med J 2018;70: 77-80)

INTRODUCTION

NCS also known as mental nerve neuropathy is a sensory neuropathy characterized by altered sensation and numbness along the distribution of the mandibular branch of trigeminal nerve (CN V_3). Common etiologies are odontogenic problems or procedures and malignancy involving distribution of CN V_3 or mandible.

In this case report, we present a case of NCS due to metastatic non-small cell lung cancer (NSCLC). Our patient presented with numbness of left lower lip, abnormal tumor markers and sacral metastasis without previous history of malignancy. The PET/CT scan was performed to identify primary tumor and the cause of NCS was proved as bone metastasis.

CASE PRESENTATION

A 72-year-old man, presented with numbness of left lower lip for few months. He had history of right Bell's palsy diagnosed 20 years ago, well-controlled psoriasis and smoking for 50 pack-years. Remarkable findings from physical examination were decreased sensation along the distribution of CN V_3 and decreased skin fold below left chin. He denied history of malignancy and odontogenic problems. Magnetic resonance imaging (MRI) of brain performed to evaluate pathology of trigeminal nerve was unremarkable. His pertinent laboratory testing were hemoglobin 10.9 g/dl (normal 12-18), hematocrit 34.6 % (normal 37-52), red blood cell 3.76x10^6/µl (normal 4.2-5.4), erythrocyte sedimentation rate (ESR) 96 mm/hr

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(normal 0-15), C-reactive protein (CRP) 8.76 mg/L (normal <3.02), serum iron 4.8 µmol/L (normal 9-29), total iron binding capacity (TIBC) 36.9 µmol/L (normal 45-70), transferrin saturation 13% (normal 30-50), ferritin 829.4 ng/ml (normal 30-400), prostate-specific antigen (PSA) 3.21 ng/ml (normal 0-4), alpha-fetoprotein (AFP) 1.87 IU/ml (normal 0-5.8), CEA 137.3 ng/ml (normal 0-3.4) and CA 19-9 267.1 U/ml (normal 0-39). Abnormal tumor markers along with history of bowel habit change led to esophagogastroduodenoscopy (EGD), colonoscopy and contrast-enhanced CT scan of whole abdomen. Both EGD and colonoscopy failed to identify malignancy. However, CT scan of whole abdomen revealed bony destruction with soft tissue formation at sacrum (Fig 1).

The PET/CT scan was subsequently performed to identify primary malignancy. The study revealed a 3.1 x 3.4 cm. hypermetabolic spiculated mass at anterior segment of left upper lung, a 2.4 x 2.1 cm. hypermetabolic left hilar lymph node (Fig 2), multiple hypermetabolic pulmonary nodules, multiple hypermetabolic foci at several vertebrae, bilateral 7th ribs, right proximal humerus, pelvic bones and both femori and bony destruction with soft tissue forming at left ramus of mandible (Fig 3), left scapula (Fig 4), left manubrium and sacrum. These findings most likely represented primary lung cancer with mediastinal lymph node, intrapulmonary and bone metastases.

He underwent ultrasound-guided biopsy at posterior aspect of left scapula. Histopathologic findings were adenocarcinoma, moderately differentiated with positive mucin, positive CK7, negative CK20 and negative TTF-1. He received palliative external beam radiotherapy at left scapula, left mandible, right femur and sacrum followed by palliative chemotherapy and tyrosine kinase inhibitor. His disease rapidly progressed and he developed several complications during hospital admission including deep vein thrombosis at left brachial and left axillary vein, upper gastrointestinal (GI) bleeding due to stress ulcer and coagulopathy, malignant pleural effusion, obstructive pneumonitis and delirium. He died of sepsis 5 months after his first presentation of NCS.

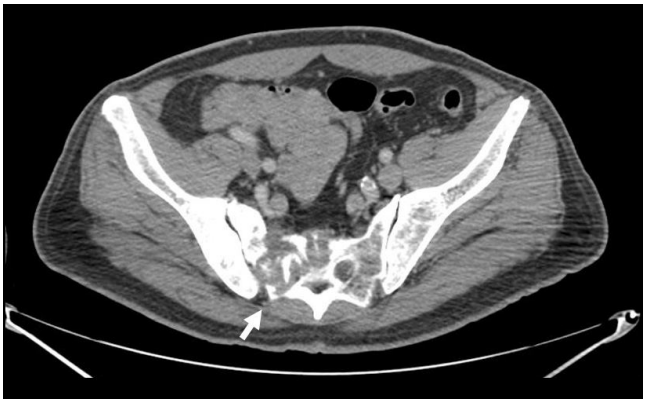

Fig 1. Whole abdominal CT scan showed osteolytic lesion with soft tissue formation at sacrum.

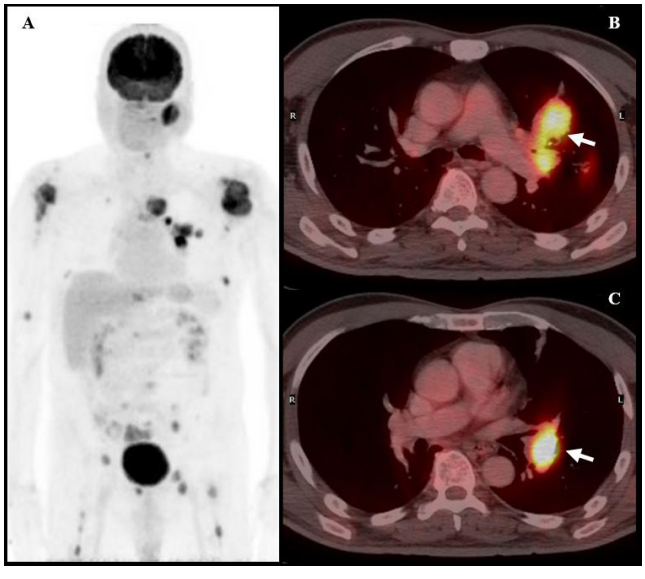

Fig 2. PET/CT scan (A) Maximum intensity projection image showed multiple hypermetabolic lesions throughout the body, (B) axial view of fused image showed a 3.4 cm. hypermetabolic lung mass at left upper lobe and (C) axial view of fused image showed a 2.4 cm. hypermetabolic left hilar lymph node.

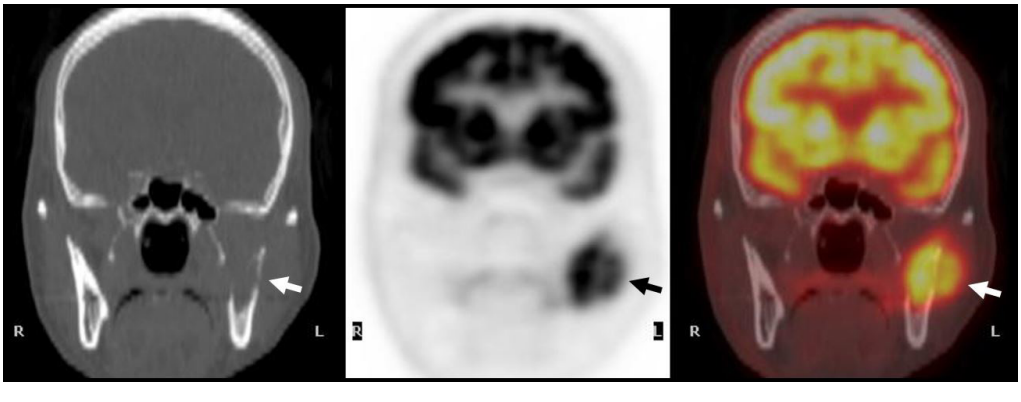

Fig 3. Coronal view of CT image, PET image and fused image showed hypermetabolic bone destruction at left ramus of mandible (arrow) that caused NCS in this patient.

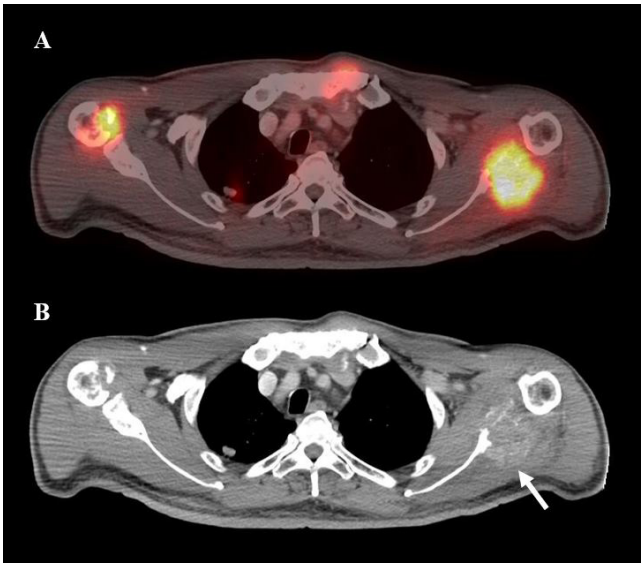

Fig 4. PET/CT scan (A) Axial view of fused image showed hypermetabolic bone lesions at sternum, right humeral head and left scapula and a hypermetabolic pulmonary nodule at right upper lobe. (B) CT image show bone destruction at right humeral head and destructive lesion with soft tissue formation at left scapula where the ultrasound-guided biopsy was performed (arrow).

DISCUSSION

NCS is a pure sensory neuropathy only affecting the sensation along the distribution of mandibular branch of trigeminal nerve (CN V) without motor involvement and alteration of taste. The trigeminal nerve is an intracranial structure, which divides into 3 branches - ophthalmic branch (CN V_1), maxillary branch (CN V_2) and mandibular branch (CN V_3). Mandibular branch exits the skull through foramen ovale and divides into several branches. One of them is an inferior alveolar nerve that continues through the mental foramen of mandible and becomes mental nerve supplying sensation of chin and lower lip area. Regarding the pathway of mandibular branch, causes of NCS could be considered as intracranial and extracranial level. Intracranial cause or selective involvement – e.g. from leptomeningeal metastasis at the level of trigeminal root, is rare.[1-4] In contrast, extracranial causes or literally direct involvement of mandibular region are more common. Odontogenic causes are always the first to be considered. Other concerned causes are primary bone tumor at mandible, head and neck cancer with mandibular involvement, bone metastasis to mandible and systemic diseases – e.g. sarcoidosis, multiple sclerosis and amyloidosis.[5]

Diagnosis of NCS is mainly based on clinical and physical examination, but the cause of NCS may require further investigations. A very useful screening test is a panoramic radiograph of mandible which helps excluding odontogenic conditions and may reveal osteoblastic or osteolytic lesions in approximately 40% of NCS patients with malignancy.[6-7] CT scan of brain including base of skull and mandible may be considered for evaluation of intracranial causes, base of skull destruction and extracranial causes missed by panoramic radiograph of mandible.[6,8] MRI may also assist in identifying involvement of leptomeninges or inferior alveolar nerve.[6] In extremely rare case, when all non-invasive tests have failed to identify cause, surgical exploration may be required.[9]

Regarding the presented case, signs and symptoms were quite typical for NCS but identifying cause was challenging. We initially focused on intracranial cause and MRI of brain was chosen. Nevertheless, MRI of brain showed no explainable cause of NCS. Differential diagnosis then focused on extracranial causes. Patient denied odontogenic problem which is the most common cause of NCS. Thus, further investigations emphasized on malignancy. Local mandibular invasion from primary head and neck cancer was excluded because the only abnormal finding from physical examination was decreased sensation along CN V_3. Primary bone tumor was also less concerned due to its high incidence in young patients. Therefore, the most likely cause of NCS at that time was mandibular metastasis from cancer of unknown primary (CUP).

Evaluation of CUP in this patient began with tumor markers. In the studies of tumor markers - CEA, AFP, PSA, squamous-cell carcinoma antigen, CA 19-9, CA 15-3 and CA 125 in CUP with bone metastasis, these tumor markers match with histological diagnosis in 70% of cases.[10] This patient had high serum CA 19-9 and CEA and bowel habit change. As a result, investigation focused on GI malignancy. However, the only remarkable finding from GI work up was an osteolytic lesion with soft tissue formation at sacrum on CT scan and his bowel symptoms also resolved spontaneously.

With evidence of elevated adenocarcinoma markers, an osteolytic lesion and history of smoking for 50 pack-years, provisional diagnosis was metastatic NSCLC and cause of NCS was suspected to be mandibular metastasis. To prove our assumption, PET/CT scan was an imaging of choice. Firstly, PET/CT scan has a role in detection of primary tumor in CUP. According to a study by Kwee et al., primary tumor detection rate of PET/CT scan ranged from 22-73% with an average of 37% and common sites of primary tumor were lung (33%) followed by oropharynx (16%), pancreas (4.9%), breast (4.3%) and colon (3.7%).[11] In this patient, PET/CT scan successfully revealed a hypermetabolic lung mass supporting a diagnosis of primary NSCLC.

Secondly, PET/CT scan provides a complete staging in a single study. Instead of performing CT scan of chest including upper abdomen for evaluation of intrathoracic lesion, liver and adrenal metastasis and ^{99m}Technetium methyl diphosphonate (^{99m}Tc-MDP) bone scintigraphy for evaluation of bone metastasis, performing PET/CT scan solely may save time and expense for investigation. Regarding PET/CT scan of this patient, evidence of a lung mass, mediastinal lymph nodes involvement and multiple metastatic lesions were sufficient to diagnose stage IV disease without requirement of additional imaging.

Thirdly, PET/CT scan is a whole body imaging. Mandibular metastasis is rare accounting for only 1% of all metastatic sites.[12] Therefore, presence of other bone lesions could support bone metastasis and led to diagnose of mandibular metastasis more confidently. Bone scintigraphy can evaluate bone lesions throughout the body the same as PET/CT scan. However, abnormal lesions on bone scintigraphy may require additional single photon emission computed tomography with computed tomography (SPECT/CT imaging) to confirm their exact locations or to characterize their natures. Therefore, PET/CT scan which simultaneously provides both functional and anatomical imaging in a single study seems to be more appropriate than bone scintigraphy in this specific circumstance. Regarding the presented case, PET/CT scan revealed multiple hypermetabolic bone lesions, including at left mandible raising the suspicion of bone metastasis. CT image of PET/CT scan clearly demonstrated a destructive bone lesion with soft tissue formation at left ramus of mandible, supporting mandibular metastasis as an etiology of NCS.

Lastly, PET/CT scan may aid in biopsy site selection.[13-15] PET/CT scan guided biopsy of hypermetabolic bone metastasis in lung cancer provided a diagnostic success rate of 96.1% at first attempt and 100% for overall.[15] Regarding the presented case, PET/CT revealed several hypermetabolic lesions, including a lung mass, pulmonary nodules, mediastinal lymphadenopathies and bony lesions. Nevertheless, PET/CT guided biopsy was the most appropriate for a biopsy site at left scapula and histopathological findings confirmed the provisional diagnosis of NSCLC.

This case report presents the diagnostic process of NCS and NSCLC by PET/CT scan. However, one should be reminded that advanced imaging is not always required. Osteolytic lesion of mandible and lung mass might be seen even on the simplest test as plain radiograph. Therefore, routine imaging should not be overlooked, as it may be adequate for diagnosis and helps avoiding delay in treatment and expensive investigation.

In conclusion, presentation of NCS may be a red flag of malignancy. For an elderly patient with history of smoking, a rare condition – NSCLC with mandibular metastasis is a possible diagnosis. Investigation of NCS may begin with panoramic radiograph of mandible as a screening test and advanced imaging may be applied accordingly. PET/CT scan is rarely used for diagnosis of NCS. However, in specific circumstances, PET/CT scan can provide benefits in evaluation of unknown primary tumor, staging before treatment and provide guidance for biopsy.

REFERENCES

1. Kuroda Y, Fujiyama F, Ohyama T, Watanabe T, Endo C, Neshige R, et al. Numb chin syndrome secondary to Burkitt's cell acute leukemia. Neurology. 1991;41:453-4.
2. Biasotto M. Numb chin syndrome as the presenting symptom of carcinomatous meningitis. Ann Oncol. 2008;19:599-601.
3. Fenaux P, Lai JL, Miaux O, Zandecki M, Jouet JP, Bauters F. Burkitt cell acute leukaemia (L3 ALL) in adults: a report of 18 cases. Br J Haematol. 1989;71:371-6.
4. Divya KS, Moran NA, Atkin PA. Numb Chin Syndrome: a case series and discussion. Br Dent J. 2010;208:157-60.
5. Narendra H, Ray S. Numb chin syndrome as a manifestation of metastatic squamous cell carcinoma of esophagus. J Cancer Res Ther. 2009;5:49-51.
6. Marinella M A. Numb Chin Syndrome: A Subtle Clue to Possible Serious Illness. Hosp Physician. 2000; 36:54-6.
7. Massey EW, Moore J, Schold SC. Mental neuropathy from systemic cancer. Neurology. 1981;31:1277-81.
8. Lossos A, Siegal T. Numb chin syndrome in cancer patients: etiology, response to treatment, and prognostic significance. Neurology. 1992;42:1181-4.
9. Friedrich E. Mental neuropathy (numb chin syndrome) leading to diagnosis of metastatic mediastinal cancer. Anticancer Res. 2010;30:1819-21.
10. Destombe C, Botton E, Le Gal G, Roudaut A, Jousse-Joulin S, Devauchelle-Pensec V, et al. Investigations for bone metastasis from an unknown primary. Jt Bone Spine. 2007;74:85-9.
11. Kwee TC, Kwee RM. Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. Eur Radiol. 2009;19:731-44.
12. Irani S. Metastasis to the Jawbones: A review of 453 cases. J Int Soc Prevent Communit Dent. 2017;7:71-81.
13. Klaeser B, Wiskirchen J, Wartenberg J, Weitzel T, Schmid RA, Mueller MD, et al. PET/CT-guided biopsies of metabolically active bone lesions: applications and clinical impact. Eur J Nucl Med Mol Imaging. 2010;37:2027-36.
14. Cornelis F, Silk M, Schoder H, Takaki H, Durack JC, Erinjeri JP, et al. Performance of intra-procedural 18-fluorodeoxyglucose PET/CT-guided biopsies for lesions suspected of malignancy but poorly visualized with other modalities. Eur J Nucl Med Mol Imaging. 2014;41:2265-72.
15. Guo W, Hao B, Chen HJ, Zhao L, Luo ZM, Wu H, et al. PET/CT-guided percutaneous biopsy of FDG-avid metastatic bone lesions in patients with advanced lung cancer: a safe and effective technique. Eur J Nucl Med Mol Imaging. 2017;44:25-32