



# Peripheral Neuropathy in the Orofacial Region after Third Molar Extraction as an Initial Manifestation of Anemia: Two Case Reports

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Third molar extraction, one of the important surgical treatments commonly practiced in dentistry, presents various symptoms after surgery ranging from temporary or mild symptoms to permanent or severe complications. However, oral burning pain, dysesthesia, paraesthesia, dry mouth, headache and pain in multiple teeth are not the common symptoms that patients often complain after dental extraction. Here, the authors report two cases who presented acute neuropathic symptoms mentioned above in the orofacial regions following third molar extraction. At the initial examination, the healing of the tooth sockets of two patients was normal. One patient was diagnosed as megaloblastic anemia associated with Vitamin B<sub>12</sub> deficiency and was referred to the Department of Hematology for assessing the underlying etiology of anemia. The laboratory test for the other patient revealed microcytic anemia related to iron deficiency. The patient with iron deficiency anemia was successfully treated with iron supplement. These two cases suggest that anemia, as an underlying systemic disease, may be a rare etiology explaining acute onset of peripheral neuropathy in the orofacial regions after third molar extraction and should be considered in the assessment of patients who report neuropathic symptoms after dental extraction.

**Key Words:** Anemia; Metabolic neuropathies; Peripheral neuropathy; Tooth extraction

## INTRODUCTION

Third molar extraction is one of the important surgical treatments commonly practiced in dentistry. After extraction, patients may present various symptoms ranging from temporary or mild symptoms to permanent or severe complications. Post-extraction complications include bleeding, swelling, pain, infection, dry socket, trismus, infection, osteonecrosis, sinus perforation and nerve injury etc. [1]. Oral burning pain, paraesthesia, dry mouth, pain in multiple teeth and headache are not the common symptoms that patients often complain after extraction.

In the field of dental surgery, anemia, a disorder that is attributable to imbalance the rate of red cell production and the rate of destruction leading to a decrease in the red blood cells (RBCs) or hemoglobin (Hb) level, has been considered

in terms of risk factors for bleeding and faulty wound healing, postoperatively and contraindication of general anesthesia when the Hb is less than 8 g/dL prior to operation [2].

Although acute anemia due to excessive bleeding after dental extraction in a patient treated with a vitamin K antagonist for heart problem was reported [3], to the best of the authors's knowledge, few data are available on the various neuropathic symptoms as an initial orofacial manifestation associated with previously undiagnosed anemia after third molar extraction.

Here, the authors first report two cases with acute trigeminal neuropathy including orofacial pain, dry mouth, headache, paraesthesia and pain in multiple teeth associated with undiagnosed underlying anemia after dental extraction and discuss the clinical implications of these cases.

## CASE REPORT

### 1. Case 1

A 70-year-old Korean man presented with a chief complaint of painful tongue and gingiva on spicy foods for approximately one month. Whenever the patient eats spicy foods, he felt an intense burning pain on the entire tongue and particularly suffered from severe pricking sensation in the entire gingiva. Apart from pain, the patient reported parageusia. He could discriminate the taste of the food but it was not the taste he had previously felt. In particular, water taste was changed into metallic taste. The patient claimed that his oral dysesthesia was caused by the dental surgery and demanded financial compensation on the hospital.

The patient had undergone extraction of mandibular 3rd molar in the right side due to the pain and swelling 2 months ago. After extraction, slight numbness of right mentum occurred and disappeared in a month. However, burning pain of mouth with parageusia replaced it. He said that he had no medical history but occasionally took the medicine with indigestion. Then, he was referred to the Department of Oral Medicine from the Department of Oral and Maxillofacial Surgery.

On physical examination, extraoral findings were not remarkable. However, the pale tongue with marginal depapillation (Fig. 1A) and the pale intraoral mucosa (Fig. 1B) were seen in the intraoral examination. The vermillion and overall gingiva were also pale. Except for the pallor of the intraoral mucosa, there was no ulcer, hemorrhage, swelling or deformity. Extraction site had completely healed. On radiologic examination, mandibular 3rd molar in the right side was impacted with pericoronal cystic change and was closely contact with the inferior alveolar nerve

in the preoperative panoramic radiograph (Fig. 2). Apical rarefaction with furcation involvement and caries of the mandibular first molar in the right side and the root rests of the maxillary first molar in the left side were also seen. Clinical sensory tests were performed on both mentum, lower lip, gingiva and tongue for evaluation of possible posttraumatic trigeminal neuropathy. There were no side differences on the proprioceptive, mechanical and thermal stimuli. Based on history taking, physical examination and radiologic examination, iatrogenic damage to the inferior alveolar nerve was ruled out. For the next step for screening the etiology of sudden oral dysesthesia, salivary flow rate test, fungal test and hematologic analysis including complete blood count (CBC) and blood chemistry were performed. Questionnaires for evaluation of psychological condition, such as depression and anxiety were also performed and revealed no abnormality. Unstimulated and stimulated saliva were 0.3 mL/min and 1.4 mL/min, respectively. Test for fungal infection was negative. CBC result of the patient revealed macrocytic anemia with increased mean corpuscular volume (MCV) (Table 1) [4]. Additional laboratory data revealed decreased level of Vitamin B<sub>12</sub> (Table 1). Megaloblastic anemia was diagnosed and the patient was referred to a hematologist for further evaluation.



Fig. 2. Panoramic view of the patient (1).



Fig. 1. (A) A pale tongue and upper lip. (B) A pale mucosa of the lower lip, vestibule and gingiva.

**Table 1.** Laboratory findings

Test	WBC (10 <sup>3</sup> /μL)	RBC (10 <sup>6</sup> /μL)	Hb (g/L)	Hct (%)	MCV (fL)	MCHC (g/dL)	PLT count (10 <sup>3</sup> /μL)	ESR (mm/h)	Vitamin B <sub>12</sub> (pg/mL)	Folate (ng/mL)	Ferritin (ng/mL)	Serum iron (mcg/dL)	TIBC (mcg/dL)	UIBC (mcg/dL)
Case 1 (M)	7.9	2.8	11.6	34.8	124.2	33.4	87	13	25	11.6	22.2	52	281	229
Case 2 (F)	6.4	4.3	9.8	30.3	70.5	32.4	301	33	277	21.2	3.5	22	459	437
Reference values [4]														
M	4.4-11.3	4.5-5.9	14.0-17.5	42-50	80-96	33.4-35.5	130-400	1-15	160-970	1.5-16.9	10-20	50-150	250-410	110-370
F	4.4-11.3	4.1-5.1	12.3-15.3	36-45	80-96	33.4-35.5	130-400	1-20	160-970	1.5-16.9	10-20	50-150	228-428	110-370

WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; ESR, erythrocyte sedimentation rate; TIBC, total iron binding capacity; UIBC, unsaturated iron binding capacity; M, male; F, female.

## 2. Case 2

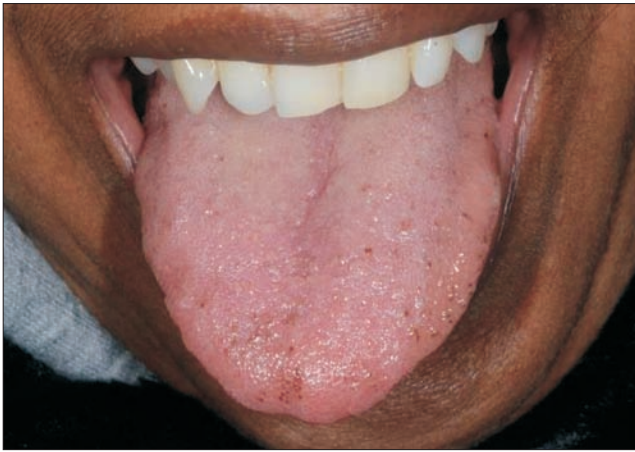
A 47-year-old, South African woman, presented dry mouth, headache and toothache after extraction of the mandibular third molar on the left side 1 month ago (Fig. 3).

The patient initially complained that the surgical site was dry and tight. Dryness and tight sensation of the extraction site spread throughout the entire mouth over time. Especially at night, oral dryness became worse. However, she had no discomfort on swallowing or speaking with dry mouth. Headache and toothache were also prominent in the left side. Headache became worse at night like dry mouth. The toothache in the left jaws occurred mainly spontaneously, but occasionally showed sensitivity to thermal stimuli, but there was no difficulty in chewing food with toothache.

The results of neurologic examination on the mandibular sensory branch was not remarkable. Temporomandibular and cervical muscle examination also revealed unremarkable findings except crepitus sounds of both temporomandibular joints. On the intraoral examination, the extraction site was not remarkable, but pallor with telangiectasia of the tongue was seen (Fig. 4). Laboratory test was done. The CBC result of the patient showed the decreased level of Hb, hematocrit (Hct), MCV. Further laboratory test revealed the low level of serum ferritin and serum iron and increased level of total iron binding capacity (TIBC) and unsaturated iron binding capacity (UIBC). The serum level of Vitamin B<sub>12</sub> and folate were within normal range. History taking revealed that she was a vegan. She denied any previous episodes of intraoral numbness and burning pain. She was diagnosed as iron-deficiency anemia associated with malnutrition. Although she was diagnosed as microcytic,



**Fig. 3.** Panoramic view of the patient (1).



**Fig. 4.** A pale tongue with telangiectasia.

iron-deficiency anemia associated with complete vegetarianism, considering the relevance of iron deficiency anemia to gastrointestinal cancer [5], she was recommended further assessment in the hematologic department, but she refused. The patient was placed on oral iron supplements with orange juice for 3 months. Her oral dysesthesia including toothache and dry mouth and headache had mostly resolved. Her laboratory index was also improved. RBC, Hb, Hct, and MCV were  $4.52 \times 10^6/\mu\text{L}$ , 12.8 g/dL, 37.2%, and 82.1 fL, respectively. The serum concentration of ferritin, iron, TIBC and UIBC were recovered to normal range of 18.0 ng/mL, 62  $\mu\text{g/dL}$ , 359  $\mu\text{g/dL}$ , and 297  $\mu\text{g/dL}$ , respectively.

## DISCUSSION

Anemia is defined by the World Health Organization as a Hb level of <13 g/dL in men and <12 g/dL in women [6]. Anemia, although it is considered “old disease” and common affecting 32.9% of general population [7,8], may not be easy to diagnose due to the highly variable signs and symptoms, including pallor, atrophic glossitis, angular stomatitis, sore and burning mouth, dysphagia, magenta tongue, paresthesia, petechiae and post-extraction bleeding [9]. The above clinical manifestations are non-specific in the differential diagnosis of anemia. There is a lot of etiology of anemia depending on inflammation, nutritional deficiency, chronic disease, autoimmune condition, medication and chemotherapy [10]. In these two cases, decreased Hb level was identified in CBC. A male patient was diagnosed megaloblastic anemia from increased MCV and decreased

Vitamin B<sub>12</sub>. Vitamin B<sub>12</sub> is an essential component for synthesis of DNA and cell division and thus deficiency in Vitamin B<sub>12</sub> can be associated with hematological disorder via impaired erythropoiesis or neuropathy via nervous system demyelination [7,11]. Although the exact etiology of B12 deficiency in this case was not identified, the burning mouth and parageusia are considered to be neurologic manifestations caused by lack of Vitamin B12. In the second case, the laboratory test of a female patient confirmed the decreased MCV and the lowered serum ferritin level, more accurate and sensitive biomarker of iron-deficiency anemia than red cell indices, below the normal range [12]. Iron plays a crucial role in various metabolic and enzymatic activities and thus iron deficiency are associated with metabolic dysfunctions including mitochondrial electron transport, synthesis and degradation of neurotransmitters, and synthesis of proteins that have an influence on central and systemic organs and decreased enzymatic process of monoamine oxidase that plays a crucial role in neurochemical reactions in the central nervous system [13]. These essential roles of iron in physiologic regulations can be an explanation for various clinical manifestations of the patient in this case.

Clinical features of iron deficiency anemia depend on the severity of the anemia, age, comorbidities, and speed of onset and range from asymptomatic to pallor, fatigue, vertigo, headache, dyspnea, tachycardia, dry skin, dry mouth, aberrant taste and koilonychias [12,14]. Iron deficiency particularly affects rapidly changing epithelium, leads to mucosal atrophy and dryness [15]. Interestingly, the patient in this case complained of constant toothache in the left upper and lower quadrants in addition to intraoral paresthesia, dry mouth and headache. Considering the teeth sensitivity to thermal stimuli rather than biting, it can be suggested that anemia might affect the pulpal nerves. This case suggests that toothache might be included in the oral manifestations of patients with anemia.

The exact pathophysiological mechanism explaining acute orofacial manifestation of sensory neuropathy associated with undiagnosed underlying anemia after dental extraction is currently unclear. In these two cases, it seems that anemia, which was pre-existing, but asymptomatic, has symptoms after dental extraction. As a first consideration,

asymptomatic anemia may have been symptomatic due to operative blood loss during surgical extraction although excessive bleeding and hemostasis problems were not reported during surgery. Reduced oxygenated Hb in patients with anemia may result in delayed tissue healing process and related oral symptoms due to increased oxygen requirement after operative blood loss. As a second consideration, inflammatory cytokines (IL-1, interferon- $\gamma$ , and TNF- $\alpha$ ) after surgery can cause decreased iron absorption, erythropoietin function and production [16,17].

These two cases suggest that anemia, as an underlying systemic disease, may be a rare etiology explaining acute onset of peripheral neuropathy in the orofacial regions after third molar extraction and should be considered in the assessment of patients who report neuropathic symptoms after dental extraction. These cases also emphasize the essential role of basic laboratory test of CBC for further screening of hematologic disorders in the diagnosis of acute onset of neuropathy after dental extraction in the clinical settings.

### CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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