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Lymphadenopathy of the Maxillofacial Area Caused by Periodontitis

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Abstract: The purpose of this study was to investigate the appearance of lymph nodes draining areas of periodontitis in the mandible using axial short T1 inversion recovery magnetic resonance imaging, to see if there is a characteristic pattern that may aid in diagnosis and treatment monitoring. The number and short-axis diameter of submental lymph nodes, submandibular nodes, superior internal jugular nodes, and spinal accessory nodes were measured on magnetic resonance images in 216 subjects (97 patients diagnosed with periodontitis, age 21–81 years and 119 patients undergoing magnetic resonance imaging of the brain without any diseases that would affect the mandible or lymph nodes, age 29-79 years). Between-group differences in the number and diameter of the nodes were analyzed. The size and number of submental nodes, submandibular nodes, and superior internal jugular nodes were significantly different between the periodontitis group and the non-periodontitis group (p < 0.01). The size and number of spinal accessory nodes were not significantly different between the two groups (p > 0.05). Our study found that a definite pattern of lymphadenopathy is associated with periodontitis. These findings indicate that lymphadenopathy should be considered as an inflammation condition commonly associated with periodontitis.

Key words: Bone marrow edema, Lymphadenopathy, Periodontitis, Magnetic resonance imaging

Introduction

Periodontitis is an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing depth formation, recession, or both1). At least two of these microorganisms, Porphyromonas gingivalis and Actinobacillus actinomycetemcomitans, are virulent organisms that invade the periodontal tissue. The clinical feature that distinguishes periodontitis from gingivitis is the presence of clinically detectable attachment loss1). The loss often is accompanied by periodontal pocket formation and changes in the density and height of subjacent alveolar bone. In recent years, questions have arisen about periodontal disease’s influence upon systemic diseases3-4). Many studies have reported periodontitis as a risk factor for chronic medical disorders, including cardiovascular disease, cerebrovascular accidents, and low-birth-weight infants. Diabetes mellitus, HIV infection, and cigarette smoking have been known as risk factors for periodontitis2-3).

Many lymph nodes are situated in the neck. In the overall schematic of the lymphatic system, the lymphatic vessels arise in the form of lymphatic capillaries in the soft tissues and merge to form larger vessels that pass into lymph nodes. The lymph then exits the node in a closed network of ducts, usually extending to other nodes and then eventually forming the thoracic duct, which enters the venous system at the confluence of the left subclavian and jugular veins. Thus all lymphatic flow filters through at least one node, and usually several nodes, before it reaches the thoracic duct or right lymphatic duct6). This is understood to be the nontraumatic portal of entry of most pathogens9). In the oral region, the submandibular nodes, submental nodes, internal jugular nodes, and spinal accessory nodes are especially significant. The submandibular (submaxillary) nodes are situated in the submandibular triangle of the neck, lateral to the anterior belly of the digastric muscle and near the submandibular gland. The submental nodes lie in the submental triangle of the neck, superficial to the mylohyoid muscle and between the anterior bellies of the digastric muscles. The internal jugular (deep cervical) chain lies close to the internal jugular vein. The spinal accessory (posterior triangle) chain of nodes follows the course of the spinal accessory nerve in the posterior triangle of the neck. These nodes drain the occipital and mastoid nodes, the parietal and occipital
regions of the scalp, the nape, lateral portions of the neck, and the shoulder. Enlargement of these nodes is known to occur not only with lymph node metastases of malignant tumors but also as part of the process of inflammatory conditions or other physiological defense reactions.

There has been little attention devoted to the relationship between lymphadenopathy and periodontitis. The purpose of this study was to characterize lymphadenopathy of the maxillofacial area associated with periodontitis.

### Materials and Methods

#### Study Design and Participants

We designed and implemented a retrospective cohort study, which was approved by our university ethics committee (EC12-009). This study included 108 patients (27 men, 81 women; 21-81 years of age, mean age 54.5 years) who underwent magnetic resonance imaging (MRI) of the brain at the Nihon University School of Dentistry Hospital, Matsudo, Chiba, Japan, from April 2012 to March 2015. Exclusion criteria were a history of radiotherapy, and disease (e.g., hematological disorders and diabetes mellitus, tumor or cyst of the mandible, inflammatory diseases, lymphomas, metastatic tumors) affecting the mandibular bone marrow and lymph nodes.

#### Data Collection

MR imaging was performed with a 1.5-T superconductive MR unit (Intera Achieva® 1.5 T Nova; Philips Medical Systems, Best, Netherlands) and head coil. Short tau inversion recovery (STIR) images were obtained using a spin echo sequence with the following parameters: repetition time, echo time, and inversion time were set at 2500, 60, and 180 milliseconds, respectively. Other study conditions were set as follows: section thickness, 6 mm; matrix, 320 × 256; field of view, 230 × 195.5 mm; and 1 acquisition.

Analyzing the STIR axial images, the number and short-axis

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Figure 1. The mandibular image was divided into two regions: left mandibular and right mandibular.

Figure 2. 39-year-old women with periodontitis. A: Slight alveolar bone resorption is seen on panoramic radiograph of the mandible (Arrow head). B: Axial STIR MR image shows bone marrow edema (Arrowheads). Prominent superior internal jugular nodes are seen (Arrow). C: Axial STIR MR image shows prominent submandibular nodes (Arrowhead).
diameter of lymph nodes in the head and neck region were classified into four categories, with the location of lymph nodes following the description by Rouviere and the level system of Som et al.\textsuperscript{12-14}.

1) Submental lymph nodes: Nodes lying between the medial margins of the anterior bellies of the digastric muscles.
2) Submandibular nodes: Nodes lying above the hyoid bone, below the mylohyoid muscle and anterior to the back of the submandibular gland.
3) Superior internal jugular nodes: Nodes extending from the skull base to the inferior border of the body of the hyoid bone. Nodes located posterior to the back of the submandibular gland and anterior to the back of the sternocleidomastoid muscle. They may lie anterior, medial, lateral or posterior to the internal jugular vein.
4) Spinal accessory nodes: Nodes extending along the spinal accessory nerve in the posterior cervical space. Nodes are located to interior to the sternocleidomastoid muscle, and posterior to the internal jugular vein (in this study, those superior to the hyoid bone were studied).

Images including the mandible were divided into two regions: left mandible and right mandible (Fig. 1). We excluded sites with missing teeth from evaluation. A total of 216 sites were evaluated. All MR images were evaluated by two radiologists. The baseline structures adopted to evaluate STIR MR signal intensity were cerebrospinal fluid (high signal intensity), muscle (intermediate signal intensity), and fat (low signal intensity). We classified signal intensity into five categories that included intermediate-to-high signal intensity and low-to-intermediate signal intensity.

Normal bone marrow was considered to have low signal intensity. When bone marrow signal intensity was higher than that of fat, it was considered edematous. In consideration of Muramatsu et al.\textsuperscript{1} report, we defined bone marrow edema as periodontitis in this study\textsuperscript{15}.

Data Analysis
Each of the two groups were then compared using the Mann-Whitney \textit{U}-test. Spearman’s correlation coefficients were calculated using bone marrow signal intensity as the criterion variable and the number and short-axis diameter of lymph nodes as explanatory variables. These analyses were performed with a statistical package (SPSS version 21.0®, IBM Japan Inc., Tokyo, Japan). \textit{p} < 0.05 was considered to indicate significance.

Results
Table 1 shows the lymph node size and number in the presence of periodontitis. The number and size of submandibular nodes and superior internal jugular lymph nodes were significantly different between the periodontitis group and non-periodontitis group. The mean values of the size of submental nodes were 3.4 ±
0.9 mm and 3.0 ± 1.0 mm, corresponding to the periodontitis group and non-periodontitis group, respectively (p < 0.01). The mean values of the number of submandibular nodes were 2.4 ± 0.8 and 1.8 ± 0.6, corresponding to the periodontitis group and non-periodontitis group, respectively (p < 0.01). Mean values of the size of submandibular nodes were 5.2 ± 1.5 mm and 4.2 ± 1.0 mm, corresponding to the periodontitis groups and non-periodontitis group, respectively (p < 0.01).
non-periodontitis group, respectively \((p < 0.01)\). The mean values of the size of the superior internal jugular lymph nodes were 5.7 ± 1.5 mm and 4.9 ± 1.3 mm, corresponding to the periodontitis group, and non-periodontitis group, respectively \((p < 0.01)\). The periodontitis group showed significantly more lymph nodes, other than submental nodes and spinal accessory nodes, compared with the non-periodontitis group. (Figs. 2, 3 A, B, C). Table 2 shows the correlation between bone marrow signal intensity (periodontitis classification) and the number and short-axis diameter of each lymph node. There was significant correlation between bone marrow signal intensity and the number and short-axis diameter of each node other than spinal accessory nodes \((p < 0.01)\). Increased bone marrow signal intensity was associated with an increase in the number of lymph nodes.

**Discussion**

Significant differences were observed in the number and short axis diameter of lymph nodes between the periodontitis group and the non-periodontitis control group in this study. Significant correlations between bone marrow signal intensity (periodontitis classification) and the number and short-axis diameter of submandibular and superior internal jugular nodes were noted. Of the approximately 800 lymph nodes in the body, 300 lymph nodes are situated in the head and neck. Thus, approximately 40% of the lymph nodes in the body are located in approximately 20% of the body’s volume. This is, in part, understandable, as they drain the nontraumatic portal of entry of most pathogens\(^{12-14}\). The cervical lymph nodes are often divided into five groups, all of which are contiguous with each other. The classification system is based on the work of Rouviere\(^{12}\). According to Harnsberger lymphatic drainage in the head and neck region from the mandible, lips, cheeks, and oral cavity occurs via the submental lymph nodes, submandibular nodes, and then the deep cervical lymph nodes\(^{16}\). The deep cervical lymph nodes also receive drainage from the parotid gland and the retropharyngeal area. The spinal accessory nodes receive lymphatic drainage from the occipital, mastoid, parietal scalp, lateral neck and shoulder areas. Submandibular nodes and superior internal jugular nodes of comparatively larger size than those in other regions are regarded as normal because they receive lymphatic drainage from the oral region, and the oral cavity is a region frequently affected by various diseases such as tooth decay and periodontal diseases, which are regarded as bacterial infections caused by the flora resident in the oral cavity\(^{141}\).

On the other hand, periodontitis is a highly prevalent chronic inflammatory disease caused by primarily by anaerobic gram-negative oral infection that leads to gingival inflammation, destruction of periodontal tissues, loss of alveolar bone, and loss of teeth. This disease is also associated with an increased risk of heart attack, stroke, and other serious health problems. The clinical parameters of alveolar bone loss, gingival bleeding, and probing depth have been used routinely to determine periodontal disease status. The most common cause of bone destruction in periodontal disease is the extension of inflammation from the marginal gingiva into the supporting periodontal tissues. The inflammatory invasion of the bone surface and the resulting bone loss marks the transition from gingivitis to periodontitis\(^{139}\).

The mandible is a tubular structure of dense cortical bone filled with trabecular bone and bone marrow\(^{10}\). The bone marrow in the body of a normal adult is known to consist of red marrow and yellow marrow. Kaneda et al reported marrow conversion from the immature red to the mature yellow stage was first seen in the anterior region of the mandibular body on MR images\(^{17}\). With aging, marrow conversion was observed in the premolar/molar region, angle, ramus, and condyle in that order. Muramatsu et al reported bone marrow abnormalities in a high percentage of MR images of mandibles of patients with periodontitis\(^{139}\). Bone marrow edema is a hallmark of periodontitis in the mandible. Evaluation of bone marrow is critical for the diagnosis, treatment, and prognosis of patients with lymphohematopoietic disorders including anemias, inflammatory diseases, leukemias, lymphomas, and metastatic tumors.

MRI has been used in lymph nodes to examine their size, signal intensity, and morphology. It has become an important noninvasive imaging technique for bone marrow disorders. Therefore, our study investigated relationship between lymphadenopathy and bone marrow edema (periodontitis). To investigate this relationship, we used STIR axial imaging and focused on the lymph nodes. STIR sequences are sensitive to changes in both T1 and T2; these relaxation time signals are additive and so increase the contrast between different soft tissues. We found a direct correlation between the presence of periodontitis and abnormalities of the lymph nodes draining the oral cavity regions.

In conclusion, our results suggest that lymphadenopathy is associated periodontitis. This information may be useful for the differential diagnosis of abnormal lymph nodes. This knowledge may contribute to the diagnosis of lymphadenopathy and avoid misinterpretation of lymph node disease as primary lymphadenopathy.

**Conflict of Interest**

The authors have declared that no COI exists.

**References**

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