

Benign reactive lymphadenopathy associated with submandibular gland enlargement during orthodontic treatment

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Abstract

Lymphadenopathy may be caused due to various reasons, most common being infections, neoplasms and immunologic disorders. Considering the frequent use of biomaterials in dentistry, it is not uncommon to find allergic reactions in the oral mucosa. Delayed-type hypersensitivity is one mechanism of allergy, which may manifest as either contact stomatitis or rarely present as only lymphadenopathy. An unusual case of unilateral submandibular gland swelling with associated lymphadenopathy during orthodontic treatment is reported. The processes followed in the differential diagnosis of the condition have been elucidated. Delayed hypersensitivity as a possible causative factor has been discussed. The article highlights the possibility of such conditions manifesting at any time during orthodontic therapy.

Keywords: Delayed hypersensitivity, lymphadenopathy, orthodontic therapy, salivary gland enlargement

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INTRODUCTION

Lymphadenopathy is the term used to describe the clinical sign of swelling of the lymph nodes. Lymphadenitis is the pathologic term for inflammation of the lymph nodes. When enlarged lymph nodes are detected, a cause has to be determined by careful medical history, thorough physical examination, judicious selection of laboratory tests and if necessary, a lymph node biopsy.^[1] In general, there are two mechanisms of lymphadenopathy - hyperplasia and infiltration. The former occurs in response to immunologic or infectious stimuli, and the later is the result of infiltration by various cell types including cancer cells, lipid cells or

glycoprotein-laden macrophages. When this occurs, lymph nodes may be detected clinically.^[2]

Lymphadenopathy is a common clinical presentation. The cervical lymph nodes show a frequent tendency for enlargement considering their drainage from the oral cavity which houses the teeth communicating with the external environment. Cervical lymphadenopathy is often reactive and usually due to bacterial, viral infections, dental infections and surgical procedures in the head and neck region. Causes of cervical lymphadenopathy in a patient with other signs of systemic infection, trauma to oral structures or dental infections are easy to diagnose.^[3]

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Difficulty arises when lymphadenopathy is the only clinical finding in an otherwise healthy patient. A spectrum of serious illness then come to act as differential diagnosis such as lymphomas, AIDS and malignancy in any other part of the body. Cervical lymphadenopathy is also seen in many oral surgical procedures; however, it is seen very rarely following orthodontic treatment.

Orthodontic materials such as monomer containing acrylic resins and nickel-containing stainless steels have been known to cause allergies in individuals. Autopolymerized methacrylate resins have shown greater leaching effects as compared to heat-cured resin. Among the metals used in orthodontics, nickel is one of the most common causes of contact dermatitis and produces more allergic reactions than all other metals combined. Nickel is also a primary component of orthodontic wires used for aligning of teeth.^[4-6]

Unpolymerized resins have shown to cause varying effects when exposed to the oral environment, ranging from irritant contact dermatitis to neuropathy. Some studies have also shown methacrylate components to cause genetic and cellular damage. These leached monomers act as low-molecular weight molecules and penetrate the oral mucosa and lead to delayed type of hypersensitivity reactions. The antigens formed migrate to the regional lymph nodes through carrier system and present to the T-lymphocytes which undergo clonal expansion. This results in a localized inflammatory reaction on secondary exposure to the antigen, which can be in the form of a lymph node enlargement.^[7]

Submandibular gland enlargement may be due to nonneoplastic causes such as mumps, sialadenitis, Sjogren's syndrome, cysts, infections and neoplasms of the salivary glands, lymphomas or any metastatic masses. Obstructive sialadenitis due to stones may account for approximately half of benign salivary gland disorders. On the other hand, salivary glands tumors are relatively rare and constitute 6% of all head and neck tumors. Various diagnostic methods such as fine-needle aspiration cytology, incisional biopsy, ultrasonography, computed tomography and magnetic resonance imaging are employed in the diagnosis of their etiology. Fine-needle aspiration cytology (FNAC) is a commonly used method for preoperative diagnosis of salivary gland swellings/mass before opting for the surgical route.^[8]

The case report presented herewith is of a benign cervical lymphadenopathy and submandibular gland enlargement occurring in concurrence with orthodontic therapy.



Figure 1: (a) Pretreatment photographs, (b) frontal photograph with left-side swelling

CASE REPORT

A 13-year-old girl reported to the Department of Orthodontics and Dentofacial Orthopaedics, Army College of Dental Sciences, Secunderabad, with the chief complaint of forwardly placed upper front teeth and spacing [Figures 1a, 2a and 3a].

A full set of records needed for treatment planning were obtained which included:

- Study models
- Lateral cephalogram
- Orthopantomogram (OPG)
- Intraoral periapical (IOPA) X-rays of all the anterior teeth
- Extraoral and intraoral photographs.

Analysis of the records showed the patient to be a skeletal Class II malocclusion with a deficient mandible which necessitated functional orthopedic therapy with the “Twin-Block appliance”^[9-11] to aid in mandibular advancement enabling correction of the sagittal skeletal discrepancy initially. The case would be reassessed for further dental treatment after completion of the functional phase. The functional appliance was a two-piece type with separate upper and lower components fabricated in heat-cured acrylic resin. Retention was obtained with stainless steel ball end clasps [Figure 4].

The patient reported with a diffuse swelling measuring approximately 40 mm in height and 53 mm in length on the left side of the face in the submandibular region after a period of 40 days [Figures 1b and 2b]. Case history revealed that the swelling developed over a period of 3 days with no signs of any respiratory tract infection or fever. On extraoral examination, a single, diffuse nonmovable swelling was observed in the left submandibular region

which was nontender on palpation and firm in consistency. Intraoral examination showed no lesions, ulcerations or any tooth-related anomaly [Figure 3b]. Moreover, the oral hygiene status of the patient was also good. Bimanual palpation of the submandibular gland showed a normal gland texture. Salivary gland duct evaluation showed no abnormality with no history of “meal time syndrome.” Salivary flow tests were done, and results were within normal limits. Lymph node examination of the body in general was carried out to rule out generalized lymphadenopathy. The only positive clinical finding was a slight reduction in mouth opening owing to the swelling present in the region. A provisional diagnosis of reactive lymphadenopathy was made.

The functional therapy was immediately discontinued. Diagnostic IOPAs of the developing second molar regions as well as an OPG were recorded [Figure 5]. The patient was advised investigations including a complete blood picture, ultrasonographic (USG) evaluation of the left

submandibular gland region [Figure 6] and a FNAC. The blood reports were nonspecific with the only significant finding being a mildly elevated erythrocyte sedimentation rate. USG scan revealed that the left submandibular gland was slightly enlarged as compared to the right with altered echotexture and increased vascularity on color Doppler. Enlarged cervical lymph nodes were noted at Levels I mainly and few in Level II and III during USG examination, with the largest one measuring 2.3 cm × 1.0 cm. Acid-fast bacillus smear and Mantoux test were done to rule out tuberculosis, and the test results were negative. Microscopic evaluation of the FNAC from left submandibular gland revealed few cells. It contained mostly blood and occasional salivary gland acini which were inadequate for diagnosis.

A final diagnosis of reactive lymphadenopathy with submandibular gland sialadenitis was given. After discussion with an oral surgeon, a period of observation without



Figure 2: (a) Pretreatment oblique lateral photograph, (b) oblique photograph with left side swelling



Figure 4: “Twin-Block” functional appliance used in the patient

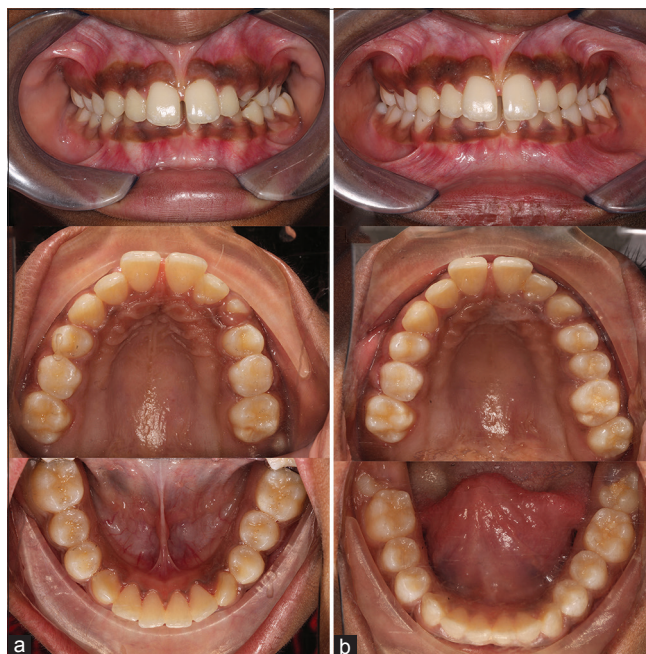


Figure 3: (a) Pretreatment intraoral photographs, (b) normal intraoral appearance during the onset phase



Figure 5: No relevant findings evident on orthopantomogram examination

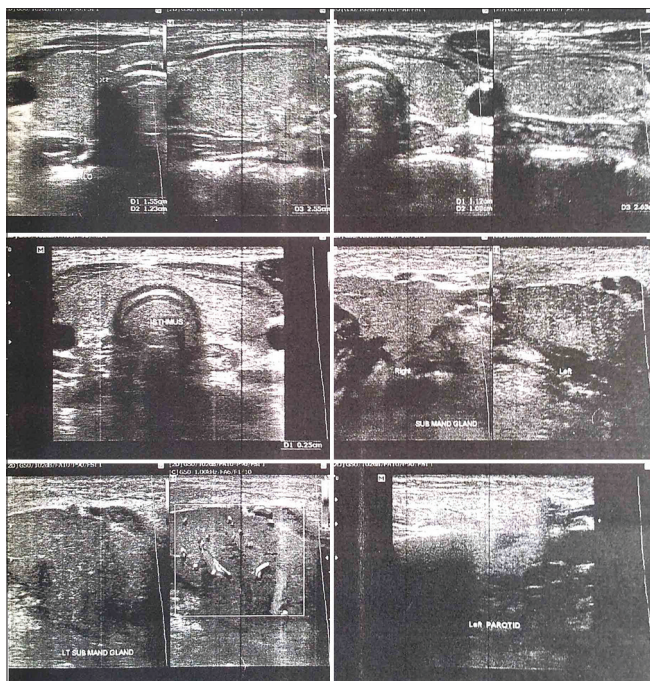


Figure 6: Ultrasound of left submandibular gland

using any medication and temporary discontinuation of the appliance was decided on. The patient reported to the clinic 3 days later without any swelling which was surprising considering its size on initial presentation. As a matter of precaution, orthodontic appliance therapy was temporarily halted for another 3 weeks. The patient started wearing the removable functional appliance after completion of the period of observation. Treatment progressed smoothly with no further recurrence in symptoms.

DISCUSSION

Lymphadenopathy is a term that describes an abnormality in either size, consistency or number of lymph nodes. It can be broadly classified as either generalized or localized. Generalized lymphadenopathy requires the involvement of at least two or more noncontiguous areas while localized involves only one area.^[3]

There are various causes for lymphadenopathy ranging from infections, immunologic disorders, malignancies, drug reactions, etc.,^[2] [Table 1]. The most common cause for submandibular lymphadenopathy is infections of the head, neck, sinuses, ears, eyes, scalp and pharynx. Less common causes for submandibular lymphadenopathy include malignancies or immunologic disorders such as Sjogren's syndrome. Drug hypersensitivity uncommonly is also a cause for submandibular lymphadenopathy. Similarly, hypersensitivity to dental biomaterials can also cause allergic manifestations.^[12]

Table 1: Causes of lymphadenopathy

Infectious diseases
Viral - infectious mononucleosis (EBV, CMV), Infectious hepatitis, herpes simplex, HHV-6, VZV, rubella, measles, adenovirus, HIV
Bacterial - <i>Streptococcus</i> , <i>Staphylococcus</i> , cat-scratch disease, brucellosis, tularaemia, chancroid, tuberculosis, atypical mycobacterial infection, primary and secondary syphilis, diphtheria, leprosy
Fungal - histoplasmosis, coccidioidomycosis, paracoccidioidomycosis
Chlamydial - lymphogranuloma venereum, trachoma
Parasitic - toxoplasmosis, leishmaniasis, trypanosomiasis, filariasis
Rickettsial - scrub typhus, rickettsialpox
Immunologic diseases
Rheumatoid arthritis
Mixed connective tissue disease
Systemic lupus erythematosus
Dermatomyositis
Sjogren's syndrome
Serum sickness
Drug hypersensitivity
Primary biliary cirrhosis
Graft-versus-host disease
Silicone-associated
Malignant disease
Hematologic (Hodgkin's, non-Hodgkin's, ALL, CLL, hairy cell leukemia, malignant histiocytosis, T-cell lymphoma, multiple myeloma with amyloidosis)
Metastatic - from primary sites
Lipid storage disease - Gaucher's, Niemann-Pick, Tangier
Endocrine disease - hyperthyroid, adrenal insufficiency, thyroiditis
Other disorders
Castleman's disease (giant lymph node hyperplasia)
Sarcoidosis
Dermatophytic lymphadenitis
Lymphomatoid granulomatosis
Kikuchi's disease (histiocytic necrotizing lymphadenitis)
Kawasaki's disease (mucocutaneous lymph node syndrome)
Histiocytosis X
Severe hypertriglyceridemia

CMV: Cytomegalovirus, CLL: Chronic lymphocytic leukemia, ALL: Acute lymphocytic leukemia, EBV: Epstein-Barr virus, VZV: Varicella zoster virus, HHV: Human herpesvirus

All dental biomaterials release substances into the oral cavity to a varying degree. The biological reactions between dental biomaterials and the oral mucosa can take place at a local level or far from the site of contact. Most components of these materials are of low-molecular weight. By acting as haptens and combining with body proteins, they may form complete antigens capable of inducing sensitization of immunologically competent cells. Methyl methacrylate (MMA) is a widely used monomer in dentistry and has been reported to cause various abnormalities such as irritation to skin, eyes and mucous membranes, allergic dermatitis, stomatitis, asthma, neuropathy, disturbances of central nervous system, liver toxicity and fertility problems. Thus, the monomer from the MMA acts as a hapten sensitizing the T-lymphocytes which in turn undergo clonal expansion leading to lymphadenopathy.^[7]

Delayed hypersensitivity reactions (Type IV) hypersensitivity is involved in the pathogenesis of many autoimmune and

infectious disorders. It may also be caused by foreign antigens such as chemicals and heavy metals. Contact dermatitis and stomatitis are an important form of delayed-type hypersensitivity. The reaction time take in delayed hypersensitivity reactions can vary from 48 to 72 h up to 21–28 days.^[13]

The vascularity and semi-permeability of the oral mucosa allow the easy penetration of the monomer that is leached out of the orthodontic appliance into the underlying tissues and blood vessels which in turn can lead to a possible delayed hypersensitivity reaction that may manifest either as contact stomatitis or as lymphadenopathy. The present case did not show any infective, immunologic or neoplastic cause for the lymphadenopathy which was ruled out by doing a series of investigations based on a diagnostic algorithm for the lymphadenopathy.

There are various causes for submandibular gland enlargement as listed in Table 2. Allergic reactions are an established cause for gland enlargement as listed by the WHO.^[14] A study conducted by Kamogashira *et al.*^[15] involving the use orthodontic appliances in rats showed submandibular and sublingual gland swelling. However, no human studies are available to corroborate the same till date.

We can deduce from this that the leaching of monomer from the appliance might have caused a delayed-type hypersensitivity reaction which caused the enlargement of the submandibular gland.

This paper presents a unique first of its kind situation involving orthodontic therapy causing this unexpected condition. Dentists need to be aware of the possibility of lymphadenopathies and salivary gland enlargement occurring in conjunction with orthodontic procedures and undertake preventive methods to avoid such circumstances.

In a study done by Bural *et al.*^[16] it was established that the effects produced by leaching of the monomer can be minimized by immersion of the appliance for 1–2 h in boiling water before the final delivery. Hence, it is recommended to follow these simple, yet important steps before insertion of dental appliances to avoid the possibility of leaching monomer and subsequent hypersensitivity reactions.

CONCLUSION

Delayed-type hypersensitivity can manifest as contact stomatitis or lymphadenopathy or even rarely salivary gland enlargement. Materials used in orthodontic appliances may possibly leach over a period of time and can cause delayed

Table 2: Causes of submandibular gland enlargement

Inflammatory
Viral: Mumps, Coxsackie-A, CMV, influenza, parainfluenza virus
Bacterial
Allergic
Sarcoidosis
Obstructive
Noninflammatory
Autoimmune: Sjögren's syndrome, Mickulicz's disease
Alcoholic cirrhosis
Diabetes mellitus
Nutritional deficiency
HIV-associated

CMV: Cytomegalovirus

hypersensitivity reactions. Hence, it is important for dental professionals to be aware of this possibility and follow proper procedures to minimize the leaching of monomers after insertion of the appliance.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Peters TR, Edwards KM. Cervical lymphadenopathy and adenitis. *Pediatr Rev* 2000;21:399-405.
- Parisi E, Glick M. Cervical lymphadenopathy in the dental patient: A review of clinical approach. *Quintessence Int* 2005;36:423-36.
- Ferrer R. Lymphadenopathy: Differential diagnosis and evaluation. *Am Fam Physician* 1998;58:1313-20.
- Bass JK, Fine H, Cisneros GJ. Nickel hypersensitivity in the orthodontic patient. *Am J Orthod Dentofacial Orthop* 1993;103:280-5.
- Veien NK, Borchorst E, Hattel T, Laurberg G. Stomatitis or systemically-induced contact dermatitis from metal wire in orthodontic materials. *Contact Dermatitis* 1994;30:210-3.
- Schweikl H, Spagnuolo G, Schmalz G. Genetic and cellular toxicology of dental resin monomers. *J Dent Res* 2006;85:870-7.
- Gosavi SS, Gosavi SY, Alla RK. Local and systemic effects of unpolymerised monomers. *Dent Res J (Isfahan)* 2010;7:82-7.
- Wilson KF, Meier JD, Ward PD. Salivary gland disorders. *Am Fam Physician* 2014;89:882-8.
- Clark WJ. The twin block technique. A functional orthopedic appliance system. *Am J Orthod Dentofacial Orthop* 1988;93:1-18.
- Clark WJ. *Twin-Block Functional Therapy*. London: Mosby-Wolfe; 1995.
- Clark WJ. The Twin-block technique. In: Graber TM, Rakosi T, Petrovic AG, editors. *Dentofacial Orthopedics with Functional Appliances*. 2nd ed. St. Louis: Mosby-Yearbook, Inc.; 1997. p. 268-98.
- Syed M, Chopra R, Sachdev V. Allergic reactions to dental materials-a

- systematic review. J Clin Diagn Res 2015;9:ZE04-9.
13. Shafer WO, Hine MK, Levj BM. A Textbook of Oral Pathology. 4th ed. Philadelphia: Saunders; 1983. p. 582-8.
 14. Diseases of Salivary Glands. WHO Manual of Classification of Diseases. 2013. p. 867-8.
 15. Kamogashira K, Yanabu M, Ichikawa K, Itoh T, Matsumoto M, Ishibashi K, *et al.* The effects of upper incisor separation on the submandibular and sublingual glands of rats. J Dent Res 1988;67:602-10.
 16. Bural C, Aktas E, Deniz G, Ünlüçerçi Y, Bayraktar G. Effect of leaching residual methyl methacrylate concentrations on *in vitro* cytotoxicity of heat polymerized denture base acrylic resin processed with different polymerization cycles. J Appl Oral Sci 2011;19:306-12.