

Tooth Loss Related to Systemic Diseases

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Abstract

Introduction: Multiple local and systemic factors can result in loss of teeth. The objectives of this review, is determining common systemic diseases can lead to tooth mobility or early tooth loss.

Methods: This study was a narrative review which reviewed the studies published between 1978 and 2014 by using electronic, academic and scientific resources. With this key words: Tooth Mobility, Systematic Disease, and Tooth Loss. At the end, the collected data were simply content analyzed.

Results: In this study, 17 common systemic disease were identified, as follows: 1.Diabetes Mellitus, 2.Female Sexual Hormones Condition, 3.Hyperpituitarism, 4. Hyperthyroidism, 5.Primary, Hyperparathyroidism, 6.Osteoporosis, 7.Hypophosphatasia, 8.Hypophosphatemia, 9.Acatalasia, 10.Erythromelalgia, 11.Gorham's Disease, 12.Sarcoidosis, 13.Wegener's Granulomatosis, 14.Burkitt, Lymphoma, 15.Non Hodgkin Lymphoma, 16.Multiple Myeloma, 17.Langerhans Cell Histiocytosis.

Conclusion: The recognition of these common systemic diseases and links between doctors and dentists can limit or reduce the speed and extension of oral complication with fast and accurate oral health measures.

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Submission Date: 20/9/2015

Accepted Date: 02/11/2015

Key words: Tooth Mobility, Systematic Disease, Tooth Loss

Introduction

Teeth play a crucial role in the oral cavity. They contribute in the process of mastication, speech, and maintaining the facial aesthetic. Edentulous can result in disturbance in daily-living activities such as chewing adequately as well as causing emotional problems (1,2). Loss of self-confidence and concerning about appearance and self-image are the emotional impacts of tooth loss (3). Early tooth loss or premature exfoliation of teeth is defined as loss of tooth in the oral cavity prior to the normal expected period of time. Since there are no references to address the exact natural expected age for loss of permanent dentition, early tooth loss is a relative term. There are both local and systemic factors that could result in such phenomenon. Poor oral hygiene could cause caries and periodontal disease leading to the loss of teeth (4,5). Additionally, there are a number of systemic diseases such as diabetes, hypophosphatasia, leukemia, hyperthyroidism, etc whose effects on the oral cavity could make the teeth susceptible to exfoliation. They could increase the risk of caries as a result of interrupting the normal function of salivary glands, or affect the periodontal tissues, which support the teeth (6). In this review, we aim to focus on the systemic diseases can lead to tooth mobility or early tooth loss.

Methods

Study Design

The present study was a descriptive or narrative review design that about tooth loss related to systemic disease.

Search Strategy

The data were collected by searching in electronic, academic and scientific resources and data bases. this study was searching in data bases include: Web of science, Science direct, Ovid, Cochrane, Scopus, Pub med and

Scientific Information Database (SID) with searching key words including " Tooth Mobility" , "Systematic Disease" , "Tooth Loss" and dentistry texts related to field assess health status and diseases, that published between 1978 and 2014 years, Afterwards the collected data relating to the study title and objectives, were identified, classified, and simply content analysed and finally selected and approved by some experts' point of view.

Inclusion and Exclusion Criteria

We included all reviews and descriptive studies reported about early tooth loss, tooth mobility and systematic disease , published in review journals and dentistry text. Studies not related to early tooth loss, tooth mobility and systematic disease were excluded too. Only articles and text books in English language were included in this study.

Article Categorization

We select common systemic diseases associated with early tooth loss and tooth mobility among articles and texts that was related to our object.

Results

This study had seventeen findings. In these common systemic diseases , evidence about early tooth loss and tooth mobility was noted in literatures.

1. Diabetes Mellitus (7,8)
2. Female Sexual Hormones Condition (9-13)
3. Hyperpituitarism (14)
4. Hyperthyroidism (6,15)
5. Primary Hyperparathyroidism (16)
6. Osteoporosis (17,18)
7. Hypophosphatasia (19,20)
8. Hypophosphatemia (6)
9. Acatalasia (21)
10. Erythromelalgia (22)



11. Gorham's Disease (23-25)
12. Sarcoidosis (26,27)
13. Wegener's Granulomatosis (23,28,29)
14. Burkitt Lymphoma (30-33)
15. Non Hodgkin Lymphoma (34)
16. Multiple Myeloma (35-39)
17. Langerhans Cell Histiocytosis (39-45)

Each of the above results will be explained in the discussion section.

Discussion

In the results of this study, 17 common systemic diseases that could result in tooth loss and tooth mobility was determined. These diseases are noted in literatures and have been accepted and approved by many experts.

1) *Diabetes Mellitus*

Diabetes Mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism. Type 1 DM is most common in children and adolescents, whereas type 2 DM (T2DM) affects adults. T2DM constitutes about 90–95% of all patients having the disease. Patients with T2DM usually have insulin resistance which alters the utilization of endogenously produced insulin at the target cells. During the early stage of the disease, insulin production is increased resulting in hyperinsulinemia. However, as the condition progresses, the production of insulin decreases leading to insulin deficiency. Whereas both type 1 DM and T2DM have a genetic predisposition, the etiology of T2DM is also related to life style factors such as high fat and sugar intake, physical inactivity and obesity. Worldwide, 346 million people suffer from DM and this disease is ranked as the ninth most common disorder amassing a 68% increase from 1990 to 2010. Between the years 2010 and 2030, the number of adults with DM in developing countries is expected to increase by 70% (7).

The role that diabetes plays in the initiation and progression of periodontal disease involves multiple factors. Particularly, poor metabolic control as well as extended duration of diabetes is a risk factor for periodontitis when extensive local irritants are present on teeth. The prevalence of periodontal disease in diabetic patients has been reported 86.8% (gingivitis 27.3% and periodontitis 59.5%). There is a statistically significant correlation between glycemic status and tooth mobility, and it was found in 43.7% of patients with diabetes mellitus (8). Tooth mobility was reported more prevalent among T2DM patients compared to their non-diabetic matched controls (7). This is maybe because all the aspects of bone growth and mineralization are diminished in the absence of insulin i.e. hyperglycemia, and vascular changes also increase with an increase in the blood glucose levels (8).

2) *Female Sexual Hormones Condition*

Changes in woman's hormonal milieu have surprisingly strong influence on oral cavity and are reflected in her periodontal tissues as well (9). Androgen, estrogen, and progesterone receptors are also localized in periodontal tissues. In women, estrogen and progesterone contribute to physiological changes at specific life phases. For example, estrogens can influence the cyto differentiation of stratified

squamous epithelium, as well as the synthesis and maintenance of fibrous collagen. Progesterone exerts direct effects on the periodontium and may play an important role in the coupling of bone reabsorption and bone formation. Taken together, hormones influence a variety of tissues and may influence an individual's health. Puberty, menstrual cycle, pregnancy, and menopause are all phases that specifically influence oral and periodontal health in women (10). Pregnancy gingivitis ranges from asymptomatic erythema to severe cases with pain and bleeding of the gingival tissue, affecting 30%-100% of pregnant women in industrialized countries (11).

Tooth mobility is increased in pregnancy and is sometimes associated with the menstrual cycle or the use of hormonal contraceptives (12). In contrast, there are reports that show no significant changes in tooth mobility at the menstrual cycle (9,13).

3) *Hyperpituitarism*

Acromegaly is a chronic disease due to growth hormone (GH) hypersecretion, mostly caused by a benign adenoma of the pituitary gland. This adenoma usually measures over 10 mm. It is a rare condition, with an estimated annual incidence of three to four cases per million and a prevalence of 40–60 cases per million worldwide. The GH hypersecretion increases insulin-like growth factor (IGF-I) which affects bone metabolism. The change in appearance, characterized by enlargement of the feet, hands, and mandible, is remarkable, but cardiovascular, metabolic, and respiratory complications as well as neoplasias are also present in patients with this disorder.

Acromegaly exhibits various oral characteristics, most commonly prognathism, macroglossy, everted and edematous lips, tooth mobility, interdental spaces (diastemas) and tooth loss and more rarely, gingival overgrowth.

Tooth mobility is a common dental finding in acromegalics. All 16 patients studied in Lima et al study exhibited class-I mobility, found mainly in the lower incisor region, and nearly all presented it with diastemas. Macroglossia, that commonly found in acromegalic patients, may also promote the onset of interdental spaces and dental mobility through the pressure of the tongue on the teeth (14).

4) *Hyperthyroidism*

An increase of circulating thyroid hormone, results in elevation of the basal metabolic rate. This usually occurs in middle-aged adults, although about 5% of all patients are younger than 15 years of age. In childhood, symptoms occur gradually. Emotional disturbances are accompanied by motor hyperactivity (6). Symptoms of overt hyperthyroidism include heat intolerance, palpitations, anxiety, fatigue, weight loss, muscle weakness, and, in women, irregular menses. Clinical findings may include tremor, tachycardia, lid lag, and warm moist skin. Symptoms and signs of subclinical hyperthyroidism, if present, are usually vague and non-specific (15). In advanced cases, there are atrophy of the alveolus, premature loss of primary teeth and accelerated eruption of permanent teeth (6).

5) *Primary Hyperparathyroidism*

Parathyroid Hormone (PTH) is the principal calciotropic hormone, and its secretion from the parathyroid glands is tightly controlled by ambient concentrations of extracellular ionized calcium. PTH secretion is increased by hypocalcemia, and decreased by hypercalcemia, through the interaction of ionized calcium with calcium-sensing receptors (CaSR) that are located on the plasma membrane of parathyroid cells. The hallmark of primary hyperparathyroidism (PHPT) is hypercalcemia, which results from the excessive secretion of PTH by one or more of the four parathyroid glands. PHPT occurs as a result of a specific defect in a parathyroid gland. Thus, PHPT is fundamentally distinct from secondary hyperparathyroidism, in which increased secretion of PTH is an adaptive response to low serum levels of calcium or vitamin D. Although serum levels of calcium and PTH are both elevated in patients with tertiary hyperparathyroidism, this condition reflects a maladaptive response to antecedent hypocalcemia or vitamin D deficiency. Primary hyperparathyroidism affects 0.3% of the general population. The mandible is the predominantly affected site in the maxillofacial area. Maxillary involvement is rare and it can also be mentioned that tooth mobility has been observed among patients with primary hyperparathyroidism (16).

6) Osteoporosis

Osteoporosis is one of the most common chronic diseases and is a disease in which the bone becomes porous and more susceptible to fracture. It is estimated that one in three postmenopausal women and one in five men over the age of 50 years are affected.

Osteoporosis is a disease that has provoked considerable interest amongst dentists in the context of its possible impact upon periodontal disease, residual alveolar ridge resorption and implant success rates (17). Accumulating evidence suggests that osteoporosis independently influences alveolar bone loss, which can ultimately lead to tooth loss (17,18).

7) Hypophosphatasia

Hypophosphatasia is characterized by defective mineralization of bone and/or teeth in the presence of low activity of serum and bone alkaline phosphatase. Clinical features range from stillbirth without mineralized bone at the severe end to pathologic fractures of the lower extremities in later adulthood at the mild end. At least six clinical forms are currently recognized based on age at diagnosis and severity of features which include: perinatal (lethal) hypophosphatasia characterized by respiratory insufficiency and hypercalcemia, perinatal (benign) hypophosphatasia with prenatal skeletal manifestations that slowly resolve into the milder childhood or adult form, infantile hypophosphatasia with onset between birth and age six months of rickets without elevated serum alkaline phosphatase activity, childhood hypophosphatasia that ranges from low bone mineral density for age with unexplained fractures to rickets, adult hypophosphatasia characterized by early loss of adult dentition and stress fractures and pseudo fractures of the lower extremities in middle age (19).

Odontohypophosphatasia as an isolated finding or as part of the above forms of hypophosphatasia can lead to severe

dental caries, mobility and premature exfoliation of primary teeth (19,20).

8) Hypophosphatemia

Hypophosphatemia (X-linked) is the most common inherited abnormality of renal tubular transport. Features include short stature and bowing of the lower extremities in affected boys. Symptoms and signs arise in the second year of life. Unlike vitamin D-deficient rickets, there is a lack of myotonia, tetany and convulsions.

The dental manifestations can be the first indications of the disorder and include loose, abscessed teeth with fistulous tracts, leading to early loss of teeth. Delayed eruption of the teeth and enlarged pulp chambers may be additional signs of the disease. Vitamin D-deficient rickets does not show the dental defects found in hypophosphatemic rickets (6).

9) Acatalsia

Acatalsia (acatalasemia), an autosomal-recessive disorder resulting from a lack of the enzyme catalase, is marked by progressive oral gangrene. The majority of homozygous individuals reported have been from Japan, but other cases have been reported in Switzerland, Israel, Peru, and Austria. Homozygous individuals are most severely affected, showing almost no blood catalase activity. Heterozygotes have blood catalase activities ranging from normal to almost nonexistent. In the most severe form, the destructive gangrenous process leads to loosening and exfoliation of the teeth (6), as two brothers have been reported from Peru presenting gingival necrosis and severe alveolar bone destruction with (21).

10) Erythromelalgia

Erythromelalgia (EM) is a rare episodic disorder first described in the mid-1800s, characterized by intermittent or continuous flushing, redness, warmth, and burning sensations of the distal extremities. This syndrome is seen rarely as an isolated entity, and there is only one reported incident among 2.5 to 3.3 per million in the Norwegian population. Symptoms are often symmetrical involving most commonly the lower extremities, although the upper extremities may become involved in some cases. These signs, however, may not always be present during a physical examination, as the patient may be symptom-free between the painful episodes. Importantly, elevated skin temperature, erythema, and burning fluctuating pain must all occur together as a prerequisite for this condition. The attacks can last from several minutes to a few hours and can intensify during the summer months. A temperature range of 32° to 36°C has been described as a "trigger zone" for most patients and is considered pathognomonic for this condition. Symptoms can be precipitated by exercise, wearing shoes and gloves, or even placing extremities close to heating appliances. Immersing the affected parts in buckets of ice water or applying wet towels help relieve the burning sensation.

The age at first presentation of this disease varies from 2 months to 6 years old. Alveolar necrosis and premature tooth loss are the only reported dental findings. Although this condition may be similar to acrodynia, the absence of generalized stomatitis in EM helps differentiate between the 2 disorders. Additionally, EM occurs most commonly in the maxilla, while acrodynia has a predilection for the

mandible. Prabhu N et al. have reported a child patient with premature loss of primary teeth that during investigations and procedures to determine a diagnosis many of her primary teeth exfoliated pathologically. Some of the reasons for this rapid progression could be the fact that the underlying systemic risk factors can influence the periodontium through their effect on the immune and inflammatory defenses and fasten the process of tooth exfoliation. Additionally, the periodontal ligament in children is far more vascular and less fibrous than the adult dentition, leading to a rapid rate of periodontal destruction (22).

11) Gorham's Disease

Gorham Disease (GD), or disappearing bone disease, is a rare bone disorder with only 200 reported cases. GD is characterized by massive and spontaneous osteolysis, which results in the proliferation of thin blood or lymphatic vessels. Synonyms often used for GD include "vanishing bone," "disappearing bone," "phantom bone," and "massive osteolysis. The clinical presentation usually consists of pain or pathologic fracture in people between birth and 75 years of age. A peak incidence in the second and third decades is noted, and males are more commonly affected. There is no racial predilection or family history of GD in affected people (23).

This disease can affect different skeletal regions: pelvic and shoulder girdles, spine, ribs, and facial skeleton. Jaw lesions are most often described when there is involvement of the head. Soft tissues can also be affected by extension (18) and tooth mobility has been reported in some cases (24,25).

12) Sarcoidosis

Sarcoidosis is a multisystem granulomatous disease of unknown cause which may affect any organ system. It manifests most frequently with bilateral hilar lymphadenopathy, pulmonary infiltration, and skin or eye lesions. The diagnosis is established when clinical-radiographic findings are supported by histologic evidence of widespread non caseating epithelioid-cell granulomas in more than one organ or a positive Kveim-Siltzbach skin test. The onset of sarcoidosis is most commonly seen between 20 and 40 years of age. There is no gender predilection, although in a few studies a slight tendency for women has been observed. In the United States, the majority of patients are black with a black to white patient incidence of 10-20 to 1. Approximately 20% to 40% of patients are symptom free and their disease is discovered by routine chest radiography. In 30% to 50% of most studies, respiratory symptoms such as cough, dyspnea, chest pain, and nasal complaints may announce the clinical onset. Specific symptoms are related to the extent of organ involvement (26).

Oral presentations of sarcoidosis, unrelated to lymph node or salivary gland disease, have been reported infrequently. Reported sites of oral involvement have included the lips, tongue, buccal mucosa, gingiva, hard and soft palate, and floor of the mouth. Oral lesions have typically been described as non-tender, well-circumscribed nodules or papules, occasionally with superficial ulceration, which are brownish red or violaceous in color. Cases involving the maxillofacial skeleton have been reported even less

frequently (26). Also, tooth mobility has been observed in some patients (27).

13) Wegener's Granulomatosis

Wegener's Granulomatosis (WG) is an autoimmune multisystem disease of unknown etiology, characterized by necrotizing granulomatous vasculitis that primarily affects the upper and lower respiratory tract and kidneys, but can affect any area of the body, including the oral cavity. The diagnosis is made by clinical symptoms and signs, the presence of c-ANCA and a positive biopsy. The anatomic pathology is characterized by vasculitis, granulomatous inflammation with multinuclear giant cells and necrosis. Various theories have been proposed regarding the etiology of the GW, where autoimmunity, hypersensitivity or infection are a precipitating factor for the disease. The bacterial infection has been associated with the occurrence and onset of the disease (28).

Oral lesions may be seen in 10 to 62 percent of patients and may be the initial sign in the 5-6 percent of patients (23). The most common oral lesion is hyperplastic gingiva, which is red to purple, with many petechiae. Tooth mobility, loss of teeth, poor healing after extraction, alterations of the parotid gland, unusual oral ulcers and rapidly progressive periodontitis in pediatric patient are other oral manifestations of the disease (28,29).

14) Burkitt Lymphoma

Burkitt's Lymphoma (BL) is a rare, extra nodal malignant tumor of undifferentiated (small, non-cleaved) lymphocytes occurring predominantly in children; it is worldwide in distribution. The tumor, which originally was described by Dr. Denis Burkitt in 1958 as a jaw sarcoma, involved children in endemic areas of equatorial East Africa. BL is classified into either the endemic (African) form or the non-endemic (American) form. Non-endemic American BL frequently presents an abdominal tumor at an early stage, and less often exhibits jaw involvement, facial swelling, and jaw or head and neck tumors. BL comprises approximately 20% of AIDS-related non-Hodgkin lymphomas. Sites frequently affected by the disease include the central nervous system, bone marrow, gastrointestinal tract and mucocutaneous tissue (30).

Diffuse neoplastic osteolysis in areas of the alveolar process caused by the B-cell tumor mass resulted in the loss of supporting alveolar cortical bone and its associated bundle bone. The hypereruption of posterior teeth is related to the expansile nature of the B-cell tumor mass. The same physiologic pressure causing the lateral expansion of the jaws also may cause the teeth to hypererupt. This phenomenon of disarticulated or "floating teeth" can be explained by the replacement of supporting bone by tumor with an intact epithelial attachment at the dentogingival junction (30). Therefore, there are many patients who are exhibited with tooth mobility (30-33).

15) Non Hodgkin Lymphoma

Malignant lymphomas are a diverse group of neoplasms affecting the lymphoreticular system. Hodgkin's disease is a condition histologically characterized by the presence of large multi-nucleated Reed-Sternberg cells. All other neoplasms of the lymphoid system are referred to as Non-Hodgkin's Lymphoma (NHL), and are derived

predominantly from the cells of the B lymphocyte series. Hodgkin's disease and NHL are commonly presented as non-tender, enlarged lymph nodes, accompanied by diffuse symptoms of fatigue and low grade intermittent fever. The cervical, axillary and inguinal lymph node groups are typically affected. In contrast to Hodgkin's disease, NHL may develop extra-nodally outside the lymphoid system and can occur in the stomach, skin, lung, salivary glands and rarely in the mouth. Oral lesions of NHL may develop in the soft tissues or centrally within the jaws, frequently as one of many lesions throughout the body or rarely as a primary entity prior to spread to the regional lymph nodes (34).

Adults over the age of 60 years are most commonly affected by NHL, although children may be affected by more aggressive intermediate- and high-grade lesions. Almost all subtypes of NHL, including those with oral lesions, show a slight to moderate male preponderance (34).

Oral lesions appear as non-tender swellings commonly affecting the vestibule, gingiva or posterior hard palate and develop slowly, mimicking a dental abscess of endodontic or periodontal origin that may lead to the loosening of the teeth. In contrast, a lesion arising in bone may present with a vague pain or discomfort which might be mistaken for toothache (34).

16) Multiple Myeloma

Multiple myeloma is one of the most common hematologic malignancies, with an annual incidence of 60–70 cases per million. Most cases occur between the fifth and seventh decade of life, but disease manifestation at younger ages has been reported infiltration of the maxillofacial region. Multiple myeloma typically appears as punched out osteolytic lesions of the jaws (35). Less commonly, the disease may be manifested orally with jaw or tooth pain, paresthesias, swelling, soft tissue masses, mobility of teeth, migration of teeth, hemorrhage, and pathologic fracture due to cortical destruction of bone (35,36). The prevalence of oral manifestations as the first sign of the disease is about 12% to 15% of the patients(35,37,38).

Multiple myeloma usually involves a number of bones in the same individual. It most frequently occurs as small, circular, multiple but separate, well defined (punched out) radiolucencies in radiographic view. In advanced cases, it may appear as a generalized rarefaction of the skeleton or as numerous radiolucencies with ill defined, ragged borders (39).

17) Langerhans Cell Histiocytosis

Langerhans Cell Histiocytosis (LCH) is a complex disease entity comprised of three distinct clinical syndromes that demonstrate indistinguishable histology. These syndromes are: eosinophilic granuloma, which is predominantly osseous or pulmonary in radiographic view often the radiolucent lesions have faint, ragged border in juveniles, but adult cases commonly show definitive radiolucencies with some sclerosing borders. Hand-Schüller-Christian's disease, which involves multiple organ systems and, most typically, the skull base. The bony lesions may appear ragged and patchy and may tend to coalesce, giving a geographic appearance on radiographs of the skull. The multiple punched out lesions also appear fairly frequently on radiographs of the jaw. Letterer-Siwe's disease: when

there are extensive bony lesions, a severe pancytopenia is produced because of the masses of proliferating langerhans cells that displace the hematopoietic marrow. When the skeleton is involved, lesions are usually presented in several bones and may appear as multiple small, rounded radiolucencies with well-defined borders (39,40).

Studies in the early 1960s showed the probability that a child under the age of 3 would develop Letterer-Siwe disease was 3.6 per million. Studies from the Danish Health Registry from 1975 to 1989 demonstrated a prevalence of histiocytosis X of 1 per 50,000 (41).

Oral soft tissue lesions without bone involvement are rare. Oral involvement is characterized by increased gingival volume and bleeding, deep pockets, alveolar bone loss, and tooth mobility, resembling periodontitis (42,43). According to S Annibali et al.'s study, 16.7% of 31 patients with LCH exhibited tooth mobility (44). In another study, among the 22 patients with eosinophilic granuloma, 12 cases showed tooth mobility (45). In Letterer-Siwe's disease if teeth are present in the affected region, they are frequently mobile (39).

Conclusion

Through the recognition of the systemic disease that causes tooth mobility and early tooth loss, more links can be created between doctors and dentists. That it would carry out preventive and curative measures in the field of oral health. Fast and accurate oral health measures can limit or reduce the speed and extension of oral complication.

Since the early loss of teeth has nutritional complications and psychological effects, it could affect the quality of life. So, identifying systemic diseases associated with this condition, leading to preventive measures and effective treatment to keep the teeth and delaying the loss of teeth.

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