Review

ORAL MANIFESTATIONS IN PAGET'S DISEASE: A NARRATIVE REVIEW

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ABSTRACT

Paget's disease (PD) is a bone disorder that can affect both single and multiple bones, leading to bone hypertrophy, cortical expansion, and a pathological bone structure that may predispose individuals to fractures. Paget's disease is a complex disorder. Current evidence suggests that genetic factors are crucial in susceptibility, but it is not the only cause. Numerous studies have found a possible association between paramyxovirus exposure and the disease. Today, the role that the paramyxoviruses may play in this disease is still unclear, and the chance that earlier exposure to a viral infection early in life might play a part in PD cannot be totally excluded. This literature review highlights the most common aspects among patients with Paget's disease, including jaw and dental alveoli deformation with possible loss of dental elements, pulp calcification, and the rare occurrence of mandible fractures.

KEYWORDS: *Paget, bone, disease fracture*

INTRODUCTION

Paget's disease (PD) is a bone disorder that can affect both single and multiple bones, leading to bone hypertrophy, cortical expansion, and a pathological bone structure that may predispose individuals to fractures. These consequences result from accelerated skeletal remodeling (1). This disease exhibits a unique epidemiology characterized by its geographical distribution. Specifically, PD is expected in the United Kingdom, North America, Australia, New Zealand, France, and Germany (2). In the last decades, the prevalence has decreased in Europe, as well as the severity of the disease has declined in New Zealand (3,4). PD is more common in males, in certain ethnic groups and in people after the age of 50 years (2).

The development of PD typically occurs in three stages: osteoclastic (lytic) activity is the initial stage, followed by a phase of osteoblastic and osteoclastic (mixed) activity, and finally, a sclerotic/blastic (late inactive) phase, resulting in bone weakness, disorganization, and more pronounced clinical manifestations. These clinical symptoms include joint and bone pain, bending or arching of bones, cranial deformities, fractures, and neurological complications such as deafness, cranial nerve palsy, or spinal compression (5). In the early stages of PD, increased bone deposition follows an excessive bone resorption. The most familiar expression of the disease is skeletal disfigurements, usually present in the skull and lower extremities. Specifically, the jaws are affected in less than 15% of cases, with a maxilla-to-mandible ratio of 2:1 (5). Pathological fractures happen frequently, especially in the femur. Pain is typical in subjects with PD from

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muscle, skeletal, or neurological origin (6). The primary lesion is a localized area of raised bone resorption and hypertrophy of an immature new bone. The result is bone expansion with structural weakness. This disease exhibits a unique epidemiology characterized by its geographical distribution (7). While its etiology remains unknown, there are two prevailing hypotheses: one based on viral involvement and the other on genetic factors (8,9). Chronic infection with paramyxoviruses is the most relevant etiology for PD (10, 11). Gene mutations have also been associated with the development of PD, especially genes mediating cytokine signaling (7).

Juvenile Paget's disease (JPD) has a robust genetic predisposition. JPD affects all the bones and causes progressive deformities, growth retardation, short stature, and facial deformities like maxillary expansion and progressive macrocephaly. Due to the bone expansion, structures like the auditory and optic nerves are affected. The morbidity and mortality of JPD is high. In case of no treatment, a significant number of patients can be led to wheelchairs before the age of 15. The first-choice treatment for JPD is oral bisphosphonates. Early therapy reduces bone turnover and controls the development of deformities (7).

MATERIALS AND METHODS

This study utilized PubMed research conducted on May 2, 2023, using the MeSH term "Paget's disease and Oral Manifestations." All original papers reporting randomized controlled clinical trials and observational studies (including cohort and case-control studies, cross-sectional investigations, case series, and single case reports) describing the correlation between Paget's syndrome and manifestations in the maxillofacial region were included. Proceedings, letters, editorials, theses, abstracts, and studies written in languages other than English were excluded. PubMed was searched without limitations on the year of publication, from the earliest available date up to May 2023. Titles and abstracts of research papers were examined, and papers that did not meet the inclusion criteria were excluded. If the abstract did not provide sufficient information for evaluation, the full text of the paper was considered. Subsequently, the full texts of the remaining articles were reviewed to assess their relevance and suitability for qualitative synthesis.

RESULTS

A total of 32 articles were identified, and only 7 met the inclusion criteria (12-18). The initial search yielded 32 results. The titles and abstracts derived from the survey were independently screened by two authors (RAA, FL). Removing duplicates and after screening the titles, seven abstracts were then analyzed; full-text articles were obtained for all agreed titles, and discrepancies were resolved by discussion. Finally, seven studies were included in the present review. We summarized and schematized the seven studies in Table I.

Table I. *Main data extracted from the seven included papers.*

Type of Study	Authors (ref.)	Year	Number of Patients	Description of the Study	Findings
Case report	Seehra et al. (13)	2009	1 patient	A 20-year follow-up is reported of a patient who was diagnosed with Paget's disease following the investigation of her initial oral complaint. Following surgical extraction of two teeth in her maxilla, the sockets have failed to heal, despite numerous attempted interventions.	Highlights both the cranio-maxillofacial and oral manifestations of Paget's disease of bone, its effects on surgical exodontia and the possible effects of bisphosphonate therapy. Prevention and conservation of the patient's remaining teeth are paramount as the extraction complications are significant.
Case report	Campolongo et al. (18)	2018	1 patient	The study highlights how it possible by a general dentist recognised Paget's disease, observing, rapid bone resorption trought dental malposition and blatant prognatism	Clinicians should consider PDB in differential diagnosis for an elderly patient undergoing unexplained alteration in face

					profile and occlusion.
Case Report	Thomas et al.(16)	1994	1 patient	The study describes the case of a 59-year-old woman with already established paget's disease. It analyzes all oral manifestation.	Evidence just a case of prognathism.
Case Report	Gage et al. (15)	1965	1 patient	The study describes clinical situation of a 77 years old female.	Bilateral enlargement of the maxilla.
Case Report	M. Marks et al. (12)	1980	1 patient	Intra-oral clinical investigation of oral manifestation in 40 years old man.	Prognathism with III Class malocclusion. Diastemas between all anterior teeth. Pulpal calcification and generalized hypercementosis. Extra-oral radiographs show classic cotton wool aspect in parietal and frontal bones.
Case Report	Cook et al. (17)	1957	3 patients	Research of clinical and radiographic findings in 3 cases of conclamate Paget's desease.	Enlargement of alveolar process. With bone changes. The maxilla and Mandible may be affected.
Observational study	Sofaer et al. (14)	1984	360 patients	The results of a postal questionnaire completed by 360 patients with Paget's disease of the bone suggest that dentists are aware of the possible consequences of dental extractions in patients but yet patients still suffer more difficulties at extraction and more post-extraction complications than normal.	Paget's disease patients in general are indeed more likely than normal to suffer from difficulty at extraction and from post-extraction complications. The greater frequency of heavy or prolonged bleeding following extractions in the younger compared to the older age range for Paget's patients is consistent with initial vascularity and progressive sclerosis of the supporting bone

Marks et al. (12) recommended periodic examinations for edentulous patients. They emphasized the importance of paying attention to edentulous patients, as ridge widening can cause denture fracture and pressure on supporting tissues, leading to ulceration or necrosis. Marks proposed extraction strategies, as did the study by Seehra et al. (13), which examined patients with an established diagnosis of PD obtained from clinical (examination and biochemistry) and radiological evaluation. Clinical chemistry analysis reveals an elevated serum alkaline phosphatase level (normal range 40-129u/L) and urine hydroxyproline level (normal range 6-22 mg/day/m2), reflecting increased bone turnover. A distinctive histologic feature of pagetoid bone is the "mosaic" appearance. Examining the skeleton with radionuclide bone scintigraphy can lead to a definitive diagnosis. The study highlights the challenges of performing oral surgical procedures in patients with PD, as previously mentioned in the study by Sofaer JA et al. (14). The study also reported a connection between osteonecrosis of the jaws and bisphosphonate therapy, as described in the literature. The most commonly used bisphosphonates are pamidronate and zoledronate, administered intravenously, and alendronate, administered orally.

Most cases of osteonecrosis of the jaws are associated with intravenous therapy. Seehra et al. (13) emphasized that the origin of osteonecrosis in these patients is unknown and could be attributed to both the disease and the use of bisphosphonates. However, given the higher prevalence of pathology in the maxilla, it could be a discriminating factor. What is certain is that bisphosphonates worsen a condition already prone to post-surgical complications. Surgical extractions are recommended if a tooth requires extraction due to the risk of hypercementosis of the roots and ankylosis.

Dentists should also be mindful of the improved possibility of bleeding from the socket if a tooth is removed during the early stages of PD and should administer pre- and post-operative antibiotics to reduce the risk of localized osteitis and osteomyelitis development. The recommendations regarding bisphosphonate therapy are the same as for patients undergoing chemotherapy or radiotherapy. This includes a comprehensive dental assessment to identify and treat dental caries, periodontal disease, and teeth removal with a poor prognosis before commencing treatment. If a tooth requires removal, antibiotic coverage should be provided, and extraction should be performed at least one month before starting bisphosphonates. The patient's dentition should be closely monitored during therapy (15). As with all medically compromised patients, implementing excellent oral hygiene practices should minimize the need for surgical treatment.

Other studies examined one of the most common aspects of PD: involvement of the skull, which is a frequent occurrence. Growth of the outer table during the appositional phase results in an increasing size typically observed as a 'cotton wool' appearance on radiographs. Clinically, deformities can also affect the jaws, especially the maxilla. This deformation can lead to alveolar deformity and tooth loosening. Enlargement of the jaws may cause pain and altered sensation because of irritations of the periosteum or nerve compression (15-17). Campolongo et al. followed a case in which they observed gradual mandibular deformation. Other manifestations that may occur in these patients, as reported in the literature, include the involvement of salivary glands with calculi (18).

DISCUSSION

PD is a complex disorder. Current evidence suggests that genetic factors are crucial in susceptibility (10), but it is not the only cause. Numerous studies have found a possible association between paramyxovirus exposure and the disease. Indeed, Viral infections have been considered a potential environmental trigger in many multifactorial genetic disorders (19-21). Today, the role that the paramyxoviruses may play in this disease is still unclear, and the chance that earlier exposure to a viral infection early in life might play a part in PD cannot be totally excluded (10,11).

The literature study highlights the most common aspects among patients with PD, including jaw and dental alveoli deformation with possible loss of dental elements, pulp calcification, and the rare occurrence of mandible fractures.

Analyzing an older review by Smith et al. (22) reported the most common oral manifestations of the condition: teeth may become unusually solid during ankylosis or, during the osteolytic stages of the disease, teeth may migrate, and root resorption may lead to tooth mobility. The study also noted pulpal calcifications that may compromise endodontic treatments. Dental extractions pose a risk of osteonecrosis.

One of the most significant considerations relates to dental extractions, where complications may be exacerbated by using bisphosphonates, especially intravenous ones. Therefore, dentists should adhere to precise protocols and, whenever possible, evaluate the patient's general health status before initiating bisphosphonate therapy once the disease is identified.

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