Scholastic Case Reports

Case Report

Volume 1 Issue 3 December 2025

Dental management particularities of Werner syndrome: a report of two cases

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Received: October 18, 2025**; Published:** November 02, 2025

Abstract

Werner syndrome (WS) is a rare genetic disorder inherited in an autosomal recessive pattern, characterized by accelerated aging. While extensive research has been conducted on its systemic manifestations, the specific dental implications of WS remain poorly understood. The medical history and the oral health status of two patients diagnosed with WS were detailed. Our findings revealed a high prevalence of dental problems in both patients, including periodontitis, xerostomia, and temporomandibular joint disorders. This article aims to investigate the dental challenges faced by individuals with WS as well as the prosthetic options envisaged through two clinical cases contributing to a deeper understanding of the dental implications of WS and to choose the appropriate prosthetic solution in this population. Future research should focus on larger scale studies and clinical trials to validate these proposed strategies.

Keywords: Adult progeria, clinical symptoms, oral manifestations, dental care, prosthetic management

Introduction

Werner syndrome (WS) is a rare autosomal recessive genetic disorder discovered in 1904 by the german scientist Otto Werner [1] characterized by pronounced premature aging known as progeria manifested in adolescence or early adulthood [2]. The prevalence of Werner syndrome fluctuates with the level of consanguinity in populations [3]. The Japanese population has the highest frequency ranging from 1/20,000 to 1/40,000 [4]. In Tunisia, the rate of consanguineous marriages is roughly 30%, increasing the prevalence of Werner syndrome [5].

Mutations in the WRN gene, discovered in 1996 lead to impaired DNA repair mechanisms in WS, promoting cellular senescence and premature aging [3]. This manifests in a diverse range of clinical features, including cataracts, osteoporosis, diabetes, early-onset cancers [6] and, the oral cavity is not exempt from these age-related deteriorations, ranging from xerostomia and periodontal disease to tooth loss and jawbone resorption [7]. Literature research shows a lack of information about the oral manifestations and dental care of these patients underscoring the need for further investigation.

This article explores the little-studied area of dental care for WS by presenting two clinical cases diagnosed and treated in the department of removable partial dentures, emphasizing physical and oral examination, focusing on the clinical and anatomopathological aspects of this syndrome, as well as the precautions and different therapeutic approaches.

Cases Presentation

First clinical case:

Patient A.J., a 38-year-old male, presented to the removable partial denture department at the dental clinic of Monastir in Tunisia, for functional and aesthetic reasons. His medical history revealed a complex chronic disease with accelerated biological decline. A diagnosis of Werner syndrome was made, complicated by type 2 diabetes mellitus diagnosed at the age of 30, long-term corticosteroid therapy for adrenal insufficiency discovered at the age of 34, osteoporosis, hypothyroidism following thyroidectomy and bilateral cataract.

The patient's physical examination revealed a striking discrepancy between his chronological age and his aged body appearance (fig.1). A prematurely aged face etched with deep wrinkles, grey hair and moderate baldness belied his younger years. A bird-like facial profile and flat feet, atrophied skin, lacking the radiance of youth, and a hoarse voice, struggling to find its full resonance, completed the clinical presentation of accelerated ageing.

Figure 1:
A: Normal physical appearance at the age of 8
B: discrepancy between his age and his body appearance at the age of 28

The consequence of infertility, coupled with the dissolution of his marriage, underlined the profound personal impact of his condition.

Extra-oral examination revealed atrophied skin and a limited mouth opening.

Intra-oral examination revealed bilateral maxillary edentulism and subtotal mandibular edentulism with poor oral hygiene associated with foul odour, gingival inflammation, extensive plaque, particularly on the maxillary incisors, xerostomia and caries (fig.2).

Figure 2 : Intra oral photos

Panoramic radiographs were taken prior to extraction of teeth 24, 25, 26, 14, 11, 17 and 42. The results were: Insufficient filling of the root canal of tooth 37, agenesis of the upper lateral incisors and obvious bone loss in the mandible. Teeth 13, 23 and 37 have a radiological crown to radiological root ratio < 1, while teeth 11 and 21 have a radiological crown to radiological root ratio > 1 and teeth 46 and 43 have a radiological crown to radiological root ratio = 1(fig.3).

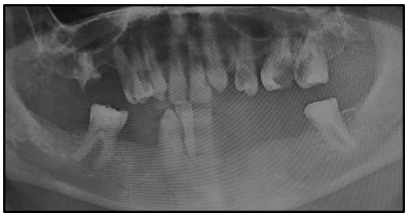

Figure 3: Panoramic Radiograph.

The examination of study casts separated and mounted on articulator showed a preserved occlusal vertical dimension (OVD), extrusion of the (46) limiting the prosthetic space, lingoversion of upper incisors and rotation of the 43 (fig.4).

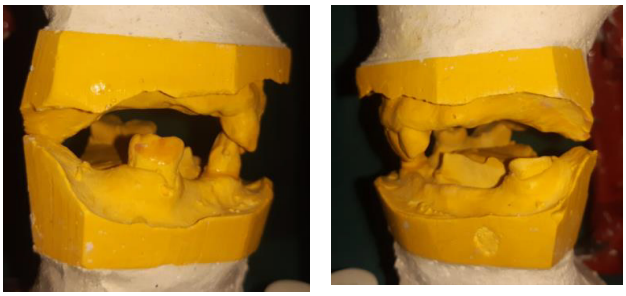

Figure 4: Study casts mounted on non-adaptable articulator.

Various treatment options have been discussed. The use of implants would offer optimal stability, function and aesthetics, but Werner's syndrome, adrenal insufficiency and the use of corticosteroids raise fears of osteoporosis, which contraindicates implant placement. Microstomia and scleroderma further limit the feasibility of implants. The decisions taken were: in the maxilla, a complex composite prosthesis combined with milling and extra-coronal attachments (4 metal-ceramic crowns on 13, 11, 21 and 23 with an articulated extra-coronal attachment on 13 and 23); in the mandible, a complex composite prosthesis combined with milling and axial attachment (2 metal-ceramic crowns on 46 and 37 with an axial attachment on 13).

A prospective model was made to visualise the feasibility of the proposed prosthetic project (Fig.5) and the pre-prosthetic endodontic treatment of teeth 11, 21, 37, 43 and 46 as well as provisional crowns and removable dentures have been achieved (Fig.6).

Unfortunately, the prosthetic process was delayed due to the patient's hospitalisation for severe cavum cancer...

Figure 5: The prospective model

Figure 6: Provisional denture.

Second Clinical Case:

Patient S.J, 37 years old (brother of 1st patient A.J), suffering from Werner syndrome, who consulted the removable partial denture department for prosthetic rehabilitation. His medical history revealed unbalanced diabetes mellitus, hypothyroidism, hypercholesterolemia, who had previously been treated with chemotherapy for head cancer in 2011, at the age of 28. He was asthmatic and suffered from allergic rhinitis. Despite his young age, the patient had an aged appearance with hair loss, skin atrophy, wrinkles and moderate microstomia. (fig.7)

Figure 7: Physical appearance at the age of 37.

Extra-oral examination showed atrophied skin and a limited mouth opening. Intra-oral examination revealed poor hygiene with a foul odour and xerostomia. The maxilla showed extensive terminal unilateral edentulism and dental caries affecting almost all the teeth, with root-form teeth due for extraction. In the lower arch, 47 was missing, 36 and 37 are at root-form destined for extraction, 45 has a distal carie and 46 has a prominent mesial amalgam filling (fig.8).

Figure 8: intra oral photos.

Panoramic radiography confirmed distal caries on the 45 and the overhanging amalgam on 46, the radiological crown/ radiological root ratio (CR/RR) was 1 for all teeth, the osteoporotic aspect was visualised at the mandibular angles, showing the potential impact of changes in bone density on oral health (fig.9).

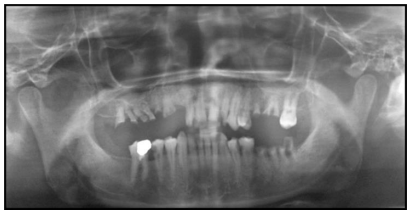

Figure 9: Panoramic radiograph.

Examination of the occlusion showed a preserved occlusal vertical dimension (OVD) but a disturbed occlusal plane by the egression of 27, 43, 44, 45 and 46, limiting the available prosthetic space.

A removable partial resin prosthesis in the maxilla was indicated in this case for the following reasons: insufficient hygiene, high cost of treatment, the implant solution was ruled out due to the high risk of osteochimionecrosis, infection and osteoporosis and bone resorption would be accelerated by diabetes.

The restoration of the oral cavity began with extraction of the maxillary root tips and endodontic treatment of 12, 21, 22, 33, 34, 45 and 46.

Working impressions would be taken using an individual tray and polysulfide, given the xerostomia, followed by occlusion registration and the fabrication of resin prostheses. Unfortunately, the patient died of a myocardial infarction.

Discussion

The aetiology of WS is attributed to mutations in the WRN gene, which takes place on the short arm of chromosome 8 at position 12 [3], impacting the function of the Werner protein crucial for maintaining DNA integrity.

The absence of a pubertal growth spurt in adolescence is a characteristic sign. Individuals with WS typically experience normal development until they reach adolescence, when accelerated aging phenotypes starts to be seen like visible wrinkles, fragility and shrinkage of the underlying skin, premature greying and hair loss, and a variety of age-related illnesses emerge. Symptoms begin to appear between 20 and 30 years old and the median age of death was 54 years old. Myocardial infarction and cancer were the most common causes of mortality in earlier research. The prevalence of cataracts was 100%. At the time of diagnosis, the prevalence of osteoporosis was 90.6%, hypogonadism was 79.5%, diabetes mellitus was 70.8%, atherosclerosis was 39.5%, and neoplasms was 43.6% [8]. The high-pitched voice, pinched face, thin limbs, truncal obesity and flat feet are all distinctive features that contribute to the physical appearance of WS patients [5]. wrinkles, fragility and shrinkage of the underlying skin, premature greying and hair loss, and a variety of age-related illnesses emerge. Symptoms begin to appear between 20 and 30 years old and the median age of death was 54 years old. Myocardial infarction and cancer were the most common causes of mortality in earlier research. The prevalence of cataracts was 100%. At the time of diagnosis, the prevalence of osteoporosis was 90.6%, hypogonadism was 79.5%, diabetes mellitus was 70.8%, atherosclerosis was 39.5%, and neoplasms was 43.6% [8]. The high-pitched voice, pinched face, thin limbs, truncal obesity and flat feet are all distinctive features that contribute to the physical appearance of WS patients [5].

Oral manifestations of Werner Syndrome:

When providing dental care to patients with WS, several co-morbities that affect the oral cavity should be taken into consideration. In fact, due to diabetes, there is an increased risk of carious lesions and periodontal disease so the patient is more vulnerable to mechanical damage, particularly in the area that supports the prosthesis. Teeth loss is probably caused by decreased salivary flow, which also would increase the risk of oral diseases like candidiasis [7]. In addition, xerostomia is associated with three conditions: drug use, scleroderma, and diabetes. It results in dry mouth (non-stimulated saliva flow of 0.2 ml/min), unlubricated oral mucosa, multiple tooth decay, difficult swallowing, phonation, mastication and also malnutrition.

Patients with WS may experience restricted mouth opening due to perioral soft tissue fibrosis. This microstomia may make more

difficult to perform dental treatments like anesthesia, exodontia, taking impressions, and installing prostheses, which also make it challenging to manage intraoral tissues and maintain good oral hygiene [7]. The temporomandibular joint (TMJ) is also affected by Werner syndrome due to masticatory muscle fibrosis. The muscles that control the movement of the jaw grow increasingly rigid and fibrous, causing discomfort, joint dysfunction, and limited mobility. [7] There is also a startling link between TMD and scleroderma. It results in stiffness, pain, and restricted movement of the jaw as it affects the ligaments and muscles surrounding the TMJ. Further aggravating the symptoms of TMD, patients may also develop a gradual degradation of the mandibular condyle.

Particularity of dental care for WS patients

In order to preserve oral health and general well-being, patients with Werner Syndrome (WS), require extra care in the dentist chair. So, starting with a serious motivation for oral hygiene consistently would provide a strong commitment to dental care by drawing attention to the connection between systemic disorders and dental health. Periodontal care must be optimised to reduce gingival inflammation aggravated by systemic diseases, particularly diabetes.

Biological tests prior to treatment, such as blood count (CBC), glycated haemoglobin and international normalised ratio (INR), may be requested in order to establish a personalised treatment plan. Particular care should be taken when using non-steroidal and steroidal anti-inflammatory drugs, bearing in mind the risk of renal failure and possible interactions with insulin, which could affect the drugs' ability to reduce glycaemia and treat hypertension.

Precautions during the surgical treatment:

For surgical treatments, in the case of patients receiving immunosuppressive therapy, it is preferable that all dental work would be completed prior to the start of immunosuppressive therapy. If dental care is required, neutrophil counts may help in the decision to use antibiotic prophylaxis. It has been recommended that antibiotics may be considered in patients with an absolute neutrophil count of between 1000 and 2000/mm3. If the neutrophil count is below 1000/mm3, dental treatment should be deferred, or it is recommended that antibiotic coverage be discussed with the medical team prior to treatment [9]. non-traumatic extractions should be preferred in order to reduce the postoperative complications. In addition, to prevent osteoporosis from worsening and accelerate the healing process, cutting-edge methods such as platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) should be used [10]. Caution should be exercised when using dental implants in patients with severe osteoporosis, given the increased risk of infection, instability and delayed bone healing in this population [11].

Precautions during the conservative treatment:

For conservative treatments, decay lesions, even if they do not have obvious cavities, must be treated very quickly because in an acidic environment, caused by xerostomia, these lesions can progress rapidly. The use of fluoride splints is recommended [12]. Prescription fluoride toothpastes and gels are a common preventive strategy for preventing cavities and maintaining good dental health [13].

For endodontic treatment, it is essential to complete the treatment in a single session, thus reducing the possibility of distant infectious foci and eliminating the need for repeated interventions, thus guaranteeing the best possible results for these patients [14]. If it is difficult to reach the canals due to the limited mouth opening, extraction is recommended, particularly for posterior teeth. The aim of this calculated procedure is to improve therapeutic efficacy while responding to the challenges posed by this fibrosis [15].

Precautions during the prosthetic treatment

Before receiving a prosthesis, the patient should be instructed to extend their facial muscles and apply moist heat therapy to release their TMJ pain and open their mouth. The most effective way to increase mouth opening is thought to be mouth exercise physiotherapy, either alone or in conjunction with other techniques.

Certain rehabilitation equipment, such as the Sauterelle or Benoist mobilizator, can be used to encourage buccal opening and muscle elasticity [16, 17].

- **Removable prostheses:**

Thermoplastic prostheses are an excellent way of compensating for loss of vertical dimension, improving aesthetics and restoring masticatory function. Because of its flexibility, it is a patient-friendly option that facilitates prosthesis administration for people with microstomia [7].

Removable dentures can be unstable and difficult to maintain for patients with xerostomia [18]. then complementary therapies such as saliva substitutes, xylitol-based tablets or stimulating gums can be used to improve denture stability.

Preventing problems such as osteoporosis and osteonecrosis is crucial when receiving prosthodontic treatment. To maintain long-term oral health, prostheses must be designed so as not to damage the supporting tissues.

The removable partial dentures must meet the following criteria:

- Reduce the number of fractures

- Be as flexible as possible in the face of limited mouth opening

- select an insertion/disinsertion axis that is comfortable for the patient

- Design dental prosthesis that are easy to clean and handle

- Preserve tooth roots.

- Exploit as many supporting surfaces as possible to increase prosthesis stability and retention.

- Choose clasps with the least over-contouring and with the retentive end at a distance from the gums

- **Dental implants:**

Patients with Werner syndrome have significant obstacles to overcome when considering receiving dental implants [11]. The viability and effectiveness of dental implant surgeries in this particular patient population are greatly impacted by complex issues as following:

- Severe osteoporosis: is a defining characteristic of Werner syndrome and a major barrier to dental implant installation. Concerns surrounding the support required for a successful implant integration and long-term durability are raised by the reduced bone density.

- Diabetes: is known to delay healing and increase the risk of infection, which can have an impact on the quality of osseointegration of implants

- Osteonecrosis: might affect the viability of bone tissues that are essential for implant durability and integration.

- **Fixed dentures:**

Before undertaking processes requiring a fixed dental prosthesis, patients with Werner syndrome may need to be carefully assessed, taking into account issues such as bone health and tissue integrity. Osteoporosis, osteonecrosis and diabetes in these individuals exacerbate the periodontal condition, making fixed prostheses difficult

to fit. The fixed prosthesis is appropriate in the absence of periodontal problems. When compared to constructs built using other alloys and conventional methods, zirconium-based restorations made using CAD/CAM technology offer superior outcomes in terms of marginal fit, inflammation reduction, maintenance, and the restoration of periodontal health and oral hygiene. Supragingival margins provide superior oral hygiene than subgingival margins, which is more maintainable and does not result in secondary caries or periodontal disease [19].

Conclusion:

Patients with Werner syndrome require specific dental care due to the pathophysiology of the disease on oral health. Managing the particular problems associated with premature ageing involves the oral and dental management of Werner syndrome. Dentists need to be aware of the particular difficulties that come with WS and adjust their approach accordingly. These patients often suffer from oral symptoms, periodontal problems and early tooth loss, so appropriate prosthetic treatment must be carried out. The primary objective of dental practitioners is to provide comprehensive care, which includes periodic dental examinations, preventive measures and individualised treatment plans. To maintain the best possible oral health, oral hygiene practices such as flossing and tooth brushing are recommended. A comprehensive approach to the well-being of these patients also requires cooperation between dentists and other health professionals. Personalised protocols and further research are needed to address the particular concerns of this particular population.

Data Availability

The data supporting this study's findings are available from the corresponding author (EA) upon reasonable request.

Consent

The patients have given their consent towards publishing their photographs and details.

Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this article.

Authors' Contributions

All authors contributed to the manuscript and read and approved the final version of the manuscript.

Emna Abid: Investigation, Validation, Visualization, Writing – original draft

Linda chebbi: Investigation, Resources, Writing – original draft Yosra Mabrouk: Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing

Amel Labidi: Writing – review & editing, Project administration, Supervision

Mansour Lamia: Writing – review & editing, Project administration, Supervision

Funding statement

There is no Funding.

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