

Review Article

Olmsted syndrome: clinical manifestations, genetic insights and therapeutic approaches in a rare keratoderma condition

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ABSTRACT

Olmsted syndrome (OS) is a rare congenital disorder characterized by progressive, mutilating palmoplantar keratoderma, periorificial keratotic plaques, and severe pruritus. First described in 1927, OS presents with a myriad of clinical manifestations, making diagnosis challenging and often delayed. Recent advancements in genetic analysis have identified mutations in the TRPV3 gene as a primary etiological factor, offering new insights into the pathophysiology of the disease. This review aims to provide a comprehensive overview of OS, including its epidemiology, clinical features, genetic basis, and current therapeutic strategies. We also discuss the implications of recent genetic discoveries on future research and potential targeted therapies, underscoring the need for a multidisciplinary approach to manage this debilitating condition.

Keywords: Olmsted, Syndrome, Skin, Keratotic

INTRODUCTION

Olmsted syndrome (OS) is an exceptionally rare genodermatosis with fewer than 100 cases reported globally. The disorder, first detailed by Olmsted in 1927, is primarily recognized for its distinctive presentation of bilateral mutilating palmoplantar keratoderma (PPK) and periorificial hyperkeratosis. Patients often experience severe, intractable pruritus and pain, leading to significant morbidity. The clinical spectrum of OS is broad, with additional features such as alopecia, flexion deformities, and keratotic plaques extending beyond palmoplantar and periorificial regions.^{1,2}

The pathogenesis of OS remained enigmatic until recent genetic investigations unveiled pathogenic mutations in the TRPV3 gene, encoding a calcium-permeable ion channel implicated in skin barrier function and keratinocyte differentiation. These findings have not only elucidated the molecular mechanisms underlying OS but

have also opened avenues for targeted therapeutic interventions.^{1,2}

Despite these advancements, the management of OS remains predominantly symptomatic, with limited efficacy in available treatments. Standard approaches include topical keratolytics, systemic retinoids, and immunomodulatory agents, although patient responses are variable. The chronic and progressive nature of OS, coupled with the severe impact on quality of life, necessitates ongoing research to develop more effective and personalized treatment modalities.^{1,2}

In this article, we aim to provide an in-depth review of OS, emphasizing its clinical heterogeneity, genetic underpinnings, and therapeutic challenges. By synthesizing current knowledge and highlighting recent breakthroughs, we hope to contribute to a better understanding of OS and foster advancements in the care of affected individuals.

Epidemiology

OS is an exceedingly rare and enigmatic disorder with a limited number of reported cases worldwide. Since its initial description by Olmsted in 1927, fewer than 100 cases have been documented in the medical literature. The scarcity of cases presents significant challenges in accurately determining the true prevalence and incidence of OS. The condition appears to have no predilection for any specific geographic region, ethnicity, or gender, although there are slightly more reports of male patients than female.³

The rarity of OS contributes to its underdiagnosis or misdiagnosis, often being mistaken for other forms of palmoplantar keratoderma or similar dermatological conditions. This diagnostic ambiguity can delay appropriate treatment and exacerbate patient morbidity. The exact cause of OS remains elusive; however, the identification of mutations in the TRPV3 gene, a gene encoding a calcium-permeable ion channel, has provided significant insights. These mutations are inherited in an autosomal dominant pattern with high penetrance, although sporadic cases without a clear family history have also been reported. The variability in genetic presentation suggests that other genetic or environmental factors may influence the phenotypic expression of OS.^{4,5}

In terms of demographics, OS predominantly manifests in early childhood, often within the first year of life. However, there are instances where symptoms do not appear until later in childhood or even adolescence. The hallmark features of the syndrome, including mutilating palmoplantar keratoderma and periorificial keratotic plaques, typically present early and progress with age. Other associated features such as severe pruritus, flexion deformities, and alopecia contribute to the clinical variability observed among patients.⁶

Given the rarity of OS, epidemiological data are derived primarily from case reports and small case series. These sources, while valuable, have limitations in terms of comprehensive data collection and standardization. Efforts to establish patient registries and collaborative networks among dermatologists, geneticists, and researchers are crucial for enhancing our understanding of OS. Such initiatives can facilitate the accumulation of epidemiological data, identification of new cases, and enable long-term follow-up studies to better characterize the natural history of the disease.⁶

Moreover, there is a need for heightened awareness and education among healthcare professionals to recognize the distinct clinical features of OS. Early and accurate diagnosis is critical for managing the condition effectively and mitigating its debilitating effects. Genetic counseling is also essential, particularly for families with a history of OS, to understand the inheritance patterns and potential risks for future offspring.⁷

The epidemiology of OS underscores its rarity and the consequent challenges in studying this disorder. The identification of TRPV3 mutations has marked a significant advancement in understanding the genetic basis of OS. Continued efforts in research, case documentation, and collaboration are imperative to elucidate the epidemiological landscape of OS, improve diagnostic accuracy, and develop targeted therapies to enhance patient outcomes.⁷

CLINICAL MANIFESTATIONS

OS is characterized by a distinct and progressive constellation of dermatological and systemic manifestations, which often present in early childhood and lead to significant morbidity. The hallmark features of OS include mutilating palmoplantar keratoderma (PPK) and periorificial keratotic plaques, but the clinical spectrum is broad, and the severity of symptoms can vary widely among affected individuals.⁷

Mutilating palmoplantar keratoderma

The most prominent feature of OS is the development of severe, transgradient, and often mutilating keratoderma affecting the palms and soles. The keratoderma typically begins in infancy or early childhood and progressively worsens, leading to thickened, hyperkeratotic plaques that can extend to the dorsal aspects of the hands and feet. This hyperkeratosis is associated with painful fissures, ulcers, and secondary infections, which can significantly impair mobility and quality of life. The severity of palmoplantar keratoderma (PPK) in OS often results in digital constrictions, flexion contractures, and autoamputation of digits, contributing to the mutilating aspect of the disease.^{8,9}

Periorificial keratotic plaques

In addition to PPK, patients with OS exhibit hyperkeratotic plaques around orifices, including the eyes, mouth, and nostrils. These periorificial lesions are typically erythematous and scaly, causing considerable discomfort and aesthetic concerns. The keratotic plaques can also involve the genital and anal regions, leading to further complications and discomfort.¹⁰

Severe pruritus

Intense, intractable pruritus is a common and debilitating symptom of OS. The severe itching often exacerbates the hyperkeratosis due to repetitive scratching, which can lead to excoriations, lichenification, and an increased risk of secondary infections. Pruritus significantly affects the quality of life, causing sleep disturbances and psychological distress.¹¹

Alopecia

Alopecia, particularly affecting the scalp, eyebrows, and eyelashes, is frequently observed in OS. The hair loss is typically non-scarring and may vary in extent. Some patients may experience diffuse thinning, while others might present with complete baldness in affected areas.¹¹

Flexion deformities and digital constriction

The progressive nature of PPK can lead to flexion deformities of the fingers and toes. Digital constriction bands, also known as pseudoainhum, may form, resulting in painful constriction and potential autoamputation of digits. These deformities further contribute to functional impairments and disability in patients with OS.¹¹

Additional dermatological features

Other dermatological manifestations include generalized ichthyosis-like scaling, follicular hyperkeratosis, and nail dystrophy. Some patients may present with diffuse, fine scaling of the skin resembling ichthyosis, while others have keratotic papules and plaques on the extremities and trunk. Nail abnormalities, such as thickening, ridging, and onychodystrophy, are also common.¹¹

Non-dermatological manifestations

While the primary manifestations of OS are dermatological, systemic involvement can occur. Some patients may experience growth retardation, failure to thrive, and delayed developmental milestones. Sensory abnormalities, including reduced sensitivity to pain and temperature, have been reported, potentially linked to the underlying TRPV3 gene mutation, which affects ion channel function in sensory neurons. Other rare systemic manifestations may include dental anomalies, ophthalmologic issues, and gastrointestinal disturbances.¹¹

Genetic basis and variability

The identification of mutations in the TRPV3 gene has provided significant insights into the pathophysiology of OS. TRPV3 encodes a calcium-permeable ion channel involved in skin barrier function and keratinocyte differentiation. Mutations in this gene lead to altered ion channel function, contributing to the hyperkeratotic and pruritic phenotype of OS. The clinical presentation can vary depending on the specific mutation and its effect on TRPV3 function, highlighting the genetic heterogeneity of the disorder.¹¹

Impact on quality of life

The chronic and progressive nature of OS, coupled with severe pruritus, pain, and functional impairments, has a profound impact on the quality of life of affected individuals. The visible skin lesions and associated

deformities can lead to social stigmatization, psychological distress, and reduced self-esteem. Comprehensive management strategies focusing on symptomatic relief, psychological support, and rehabilitation are crucial for improving patient outcomes and quality of life.¹²

OS presents with a complex and severe array of clinical manifestations primarily affecting the skin and appendages. Early recognition and diagnosis are essential for implementing appropriate management strategies and mitigating the disease's impact on the patient's quality of life. Ongoing research into the genetic and molecular mechanisms underlying OS holds promise for the development of targeted therapies that may offer more effective and personalized treatment options for this debilitating condition.¹³

DIAGNOSTIC METHODS

The diagnosis of OS involves a multifaceted approach that includes clinical evaluation, histopathological analysis, and genetic testing. Given the rarity of the condition and the overlap of its symptoms with other dermatological disorders, a thorough and systematic diagnostic process is essential for accurate identification and management. Herein, we delineate the current diagnostic methods employed in the identification of OS.^{13,14}

Clinical evaluation

Patient history and physical examination

The initial step in diagnosing OS involves a comprehensive patient history and physical examination. Clinicians should inquire about the onset and progression of symptoms, focusing on the characteristic features of OS, such as mutilating palmoplantar keratoderma, periorificial hyperkeratosis, severe pruritus, and any familial history of similar dermatological conditions. A detailed physical examination is crucial to identify the extent and severity of hyperkeratosis, the presence of periorificial plaques, and any associated findings such as alopecia, nail dystrophy, and flexion deformities.¹⁵

Differential diagnosis

Given the clinical overlap with other keratinization disorders, a differential diagnosis must be considered. Conditions such as Vohwinkel syndrome, Mal de Meleda, and other forms of hereditary palmoplantar keratodermas (PPKs) should be ruled out. The presence of severe pruritus and periorificial involvement can help differentiate OS from these conditions. Additionally, secondary infections, digital autoamputation, and the specific pattern of keratoderma observed in OS provide valuable diagnostic clues.¹⁵

Histopathological analysis

Skin biopsy

Histopathological examination of a skin biopsy can aid in confirming the diagnosis of OS. Typical findings include hyperkeratosis, acanthosis, and a thickened granular layer. The presence of spongiosis and a perivascular lymphocytic infiltrate may also be noted. These histological features, while not pathognomonic, support the clinical diagnosis when correlated with the patient's presentation.¹⁶

Genetic testing

TRPV3 gene sequencing

The definitive diagnosis of OS is established through genetic testing, specifically sequencing the TRPV3 gene. Mutations in the TRPV3 gene, which encodes a calcium-permeable ion channel involved in skin barrier function and keratinocyte differentiation, are responsible for the pathogenesis of OS. Next-generation sequencing (NGS) or whole-exome sequencing (WES) can identify pathogenic variants in TRPV3, confirming the diagnosis. In some cases, targeted Sanger sequencing may be employed if a specific mutation is suspected based on the clinical and familial context.^{16,17}

Genetic counseling

Given the autosomal dominant inheritance pattern of OS with high penetrance, genetic counseling is an integral part of the diagnostic process. Counseling provides patients and their families with information about the genetic nature of the disorder, the risk of transmission to offspring, and the implications for family planning. In cases of sporadic mutations, counseling can also address the potential for de novo mutations and their impact.^{17,18}

Adjunctive diagnostic methods

Imaging studies

While not routinely necessary for diagnosing OS, imaging studies such as X-rays or MRI may be utilized to assess the extent of digital constrictions, flexion deformities, and bone involvement. Imaging can help evaluate the degree of functional impairment and guide surgical planning if needed.^{17,18}

Laboratory tests

Routine laboratory tests, including complete blood count (CBC), inflammatory markers (such as ESR and CRP), and metabolic panels, are typically performed to rule out secondary infections and systemic involvement. These tests, however, are generally nonspecific and serve to support the overall clinical evaluation.^{17,18}

Multidisciplinary approach

Collaboration with specialists

The complexity and rarity of OS necessitate a multidisciplinary approach involving dermatologists, geneticists, pediatricians, and other relevant specialists. Collaborative care ensures comprehensive evaluation, accurate diagnosis, and the formulation of an effective management plan tailored to the patient's needs.^{18,19}

Case registries and databases

Participation in case registries and databases dedicated to rare genetic disorders, including OS, can enhance diagnostic accuracy and facilitate research. These registries compile clinical, histopathological, and genetic data from multiple cases, providing valuable insights into the disease's natural history, phenotypic variability, and genotype-phenotype correlations.^{18,19}

The diagnosis of OS relies on a combination of meticulous clinical evaluation, supportive histopathological findings, and confirmatory genetic testing. A thorough differential diagnosis is essential to distinguish OS from other keratinization disorders. Advances in genetic testing, particularly the identification of TRPV3 mutations, have revolutionized the diagnostic process, allowing for more precise and early diagnosis. Multidisciplinary collaboration and participation in case registries further contribute to improving diagnostic accuracy and understanding of this rare and debilitating condition.¹⁸

CURRENT THERAPEUTIC APPROACHES

The treatment of OS poses a significant challenge due to the rarity of the condition, its progressive nature, and the severe impact on the patient's quality of life. Current therapeutic strategies are primarily symptomatic, aimed at alleviating the debilitating symptoms such as pruritus, hyperkeratosis, and pain, and improving the patient's overall functional status. Herein, we explore the various therapeutic modalities currently employed in the management of OS.^{19,20}

Topical therapies

Keratolytics

Topical keratolytic agents, such as salicylic acid, urea, and lactic acid, are commonly used to manage hyperkeratosis in OS. These agents help to soften and reduce the thickened keratin layers, facilitating the shedding of scales and improving skin texture. Regular application of these agents can alleviate some of the physical discomfort associated with hyperkeratosis, although their efficacy is variable and often limited in severe cases.²⁰

Emollients and moisturizers

The use of emollients and moisturizers is essential in the management of OS to maintain skin hydration, reduce transepidermal water loss, and provide a barrier against external irritants. Emollient-rich formulations, often containing ingredients like ceramides, glycerin, and lanolin, help to soothe dry and irritated skin, thereby reducing pruritus and discomfort.²⁰

Topical corticosteroids and calcineurin inhibitors

Topical corticosteroids and calcineurin inhibitors, such as tacrolimus and pimecrolimus, are employed to manage inflammation and pruritus in OS. These agents can provide symptomatic relief from severe itching and reduce inflammatory skin lesions. However, long-term use of topical corticosteroids is limited by potential side effects, including skin atrophy and tachyphylaxis.^{20,21}

Systemic therapies

Retinoids

Systemic retinoids, such as acitretin and isotretinoin, are frequently used in the management of OS due to their keratolytic and anti-inflammatory properties. Retinoids help to normalize keratinocyte differentiation and reduce hyperkeratosis. Despite their efficacy, systemic retinoids are associated with significant side effects, including mucocutaneous dryness, teratogenicity, and potential hepatotoxicity, necessitating careful monitoring and patient education regarding their use.²¹

Immunosuppressive agents

Immunosuppressive agents, including methotrexate and cyclosporine, have been utilized in refractory cases of OS. These agents can modulate the immune response, reduce inflammation, and improve severe keratoderma and pruritus. However, their use is limited by potential side effects such as immunosuppression, nephrotoxicity, and hepatotoxicity, requiring close monitoring by healthcare providers.²¹

Biologic therapies

Biologic agents targeting specific inflammatory pathways, such as tumor necrosis factor-alpha (TNF- α) inhibitors (e.g., etanercept, infliximab) and interleukin inhibitors, represent emerging therapeutic options for OS. These agents have shown promise in reducing inflammation and pruritus in other inflammatory dermatoses, and their role in OS is currently being explored through case reports and small clinical studies. Their use is generally considered in severe, refractory cases where conventional therapies have failed.²¹

Symptomatic management

Pain management

Pain management is a critical component of the therapeutic approach in OS, given the severe discomfort and pain associated with hyperkeratosis, fissures, and digital constrictions. Analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, are commonly used. In cases of severe pain, opioids or adjuvant analgesics such as gabapentinoids may be necessary, though their use requires careful consideration due to potential side effects and the risk of dependency.²¹

Management of pruritus

Severe pruritus in OS is often refractory to conventional treatments and significantly affects the patient's quality of life. Antihistamines, both sedating and non-sedating, can provide some relief. More potent agents, such as gabapentin and pregabalin, have been used to address neuropathic pruritus. Recent advances have introduced the use of JAK inhibitors (e.g., tofacitinib) for their antipruritic effects, although their application in OS requires further study.²¹

Surgical interventions

Surgical debridement and excision

In cases of severe and refractory hyperkeratosis, surgical debridement may be necessary to remove thickened keratotic plaques and relieve pressure on underlying tissues. Surgical excision can also address digital constrictions and prevent autoamputation of digits. These procedures, while effective, are typically reserved for severe cases due to the risk of complications and the need for postoperative care.²¹

Laser therapy

Laser therapy, including carbon dioxide (CO₂) lasers and erbium-doped yttrium aluminum garnet (Er: YAG) lasers, has been explored for the treatment of hyperkeratotic lesions in OS. Laser therapy can ablate hyperkeratotic tissue with precision, promoting skin regeneration and reducing the thickness of keratotic plaques. This approach offers a less invasive alternative to surgical excision but requires specialized equipment and expertise.²²

Genetic and emerging therapies

Gene therapy and molecular approaches

Advances in understanding the genetic basis of OS, particularly mutations in the TRPV3 gene, have opened avenues for potential gene therapy. Experimental approaches, such as CRISPR-Cas9 mediated gene editing, aim to correct pathogenic mutations at the genomic level. While these therapies are in the experimental stage, they

hold promise for future treatment modalities that address the underlying genetic defects in OS.²²

Personalized medicine

The application of personalized medicine, guided by genetic and molecular profiling, represents a frontier in the management of OS. Tailoring treatments based on individual genetic mutations and molecular pathways can enhance therapeutic efficacy and minimize adverse effects. Personalized approaches may include the use of specific inhibitors, modulators, or gene-editing technologies designed to target the aberrant TRPV3 gene function.²²

Multidisciplinary care and support

Multidisciplinary approach

Effective management of OS requires a multidisciplinary approach involving dermatologists, geneticists, pediatricians, pain specialists, and other healthcare providers. Collaborative care ensures comprehensive management of the diverse symptoms and complications associated with OS, optimizing patient outcomes.²²

Psychological support

Given the significant psychological burden of OS, including social stigmatization, depression, and anxiety, psychological support and counseling are integral to the therapeutic approach. Support groups, cognitive-behavioral therapy, and psychiatric interventions can help patients and their families cope with the emotional and psychological challenges of living with OS.²²

In conclusion, the management of OS necessitates a multifaceted and individualized approach, combining topical, systemic, and emerging therapies to alleviate symptoms and improve quality of life. Advances in genetic and molecular research offer hope for the development of targeted and personalized treatments that address the underlying pathophysiology of this debilitating condition. Ongoing research, clinical trials, and collaborative care are essential to enhance our understanding and management of OS, ultimately leading to more effective and innovative therapeutic strategies.²²

PROGNOSIS

The prognosis for patients with OS is influenced by the severity and progression of the disease, the presence of complications, and the response to therapeutic interventions. OS is a chronic, progressive condition with significant morbidity, primarily due to its severe dermatological manifestations and associated symptoms.

Herein, we provide a detailed overview of the factors affecting the prognosis of OS patients, including clinical

outcomes, potential complications, and the impact of emerging therapies.^{22,23}

Clinical course and disease progression

OS typically manifests in early childhood, often within the first year of life, with progressive palmoplantar keratoderma and periorificial hyperkeratosis. The disease course is marked by gradual worsening of hyperkeratosis, leading to painful fissures, ulcerations, and digital constrictions.

These manifestations result in significant functional impairment and disability. The mutilating nature of the keratoderma, especially in the hands and feet, often leads to autoamputation of digits, further complicating the patient's physical abilities.²³

Quality of life

The chronic and severe symptoms of OS, including intense pruritus, pain, and disfigurement, have a profound impact on the quality of life of affected individuals. Pruritus, in particular, can be debilitating and refractory to treatment, causing sleep disturbances, psychological distress, and a reduced ability to perform daily activities.

The visible skin lesions and associated deformities contribute to social stigmatization and emotional challenges, such as anxiety and depression. Comprehensive management, including psychological support and counseling, is essential to address these quality of life issues.²³

Complications

Patients with OS are at risk for several complications due to the chronic nature of the disease and its severe cutaneous manifestations.

Infections

Secondary bacterial and fungal infections are common in OS due to the compromised skin barrier and presence of open fissures and ulcers. Recurrent infections can exacerbate the severity of keratoderma and contribute to systemic morbidity.²³

Digital constrictions and autoamputation

The progressive keratoderma can lead to the formation of constriction bands around the digits, resulting in pseudoainhum and eventual autoamputation. This complication not only causes pain but also significantly impairs hand and foot function.²³

Flexion contractures

Chronic hyperkeratosis and digital constrictions often result in flexion contractures, limiting joint mobility and

contributing to functional disability. These contractures may require surgical intervention to restore some degree of functionality.²³

Psychosocial impact

The psychosocial impact of OS is considerable, with many patients experiencing social isolation, low self-esteem, and psychological disorders. The visible nature of the skin lesions can lead to stigmatization and discrimination, affecting social interactions and mental health.²³

Therapeutic response and advances

Current treatments

The therapeutic response in OS is highly variable, with many patients experiencing only partial relief from current treatments. Topical therapies, systemic retinoids, immunosuppressive agents, and biologics offer symptomatic relief but often fall short of completely controlling the disease. Pain management and antipruritic therapies are essential components of treatment but may not fully alleviate symptoms.²⁴

Emerging therapies

Advances in genetic and molecular research have opened new avenues for the treatment of OS. The identification of TRPV3 mutations has paved the way for potential targeted therapies aimed at correcting the underlying genetic defect. Experimental approaches such as gene therapy and CRISPR-Cas9 mediated gene editing hold promise for future treatment options that could alter the disease course. Additionally, the development of biologic agents targeting specific inflammatory pathways offers hope for more effective symptom management.²⁴

Long-term outcomes

The long-term outcomes for patients with OS remain challenging due to the chronic and progressive nature of the disease. While early and aggressive management can mitigate some symptoms and complications, the overall prognosis is guarded. Regular follow-up with a multidisciplinary team is crucial to monitor disease progression, manage complications, and adjust therapeutic strategies as needed.²⁴

Monitoring and support

Ongoing monitoring for disease progression and complications is essential. Regular dermatological assessments, along with supportive care from pain specialists, physical therapists, and mental health professionals, can help manage the complex needs of OS patients. Genetic counseling is also important for affected families to understand the inheritance patterns and implications for future offspring.²⁴

Research and clinical trials

Participation in clinical trials and research studies is encouraged for OS patients to access emerging therapies and contribute to the growing body of knowledge about the disease. Collaborative efforts among researchers, clinicians, and patient advocacy groups are vital to advancing the understanding and treatment of OS.²⁴

The prognosis for patients with OS is influenced by the severity of symptoms, the effectiveness of therapeutic interventions, and the presence of complications. While current treatments provide symptomatic relief, the progressive nature of the disease poses ongoing challenges. Advances in genetic research and emerging therapies offer hope for improved outcomes in the future. Comprehensive, multidisciplinary care and continued research are essential to enhance the quality of life and long-term prognosis for individuals with OS.²⁴

CONCLUSION

OS represents a formidable challenge in the realm of dermatological and genetic disorders, characterized by its severe, mutilating keratoderma and systemic manifestations. Despite its rarity, the profound impact on the quality of life of affected individuals necessitates a thorough understanding of its clinical presentation, diagnostic approaches, and therapeutic strategies. As we delve into the complexities of OS, several key points emerge that underscore the importance of continued research and comprehensive care. The impact of OS on the quality of life is profound, affecting physical, emotional, and social well-being. While current treatments can provide some relief, the chronic and mutilating nature of the disease poses ongoing challenges for patients and their families. Enhancing the quality of life for OS patients requires a holistic approach that addresses both the physical symptoms and the psychosocial aspects of the disease. Long-term follow-up and supportive care are essential to manage the complex needs of OS patients and improve their overall prognosis. In conclusion, OS remains a challenging and debilitating condition with significant implications for affected individuals. Advances in genetic research and emerging therapies offer hope for more effective and personalized treatments, but ongoing research and multidisciplinary care are essential to optimize patient outcomes. As our understanding of OS continues to evolve, a comprehensive and patient-centered approach will be key to improving the quality of life and long-term prognosis for those living with this rare and severe disorder.

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