"Failure in implant rehabilitation in a patient with Severe Congenital Neutropenia"

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ABSTRACT

Introduction .- Kostmann syndrome is an autosomal recessive disorder that precipitates severe congenital neutropenia (SCN). One of the most characteristic oral manifestations of this syndrome is severe periodontal disease with extensive bone loss in the primary dentition. This bone loss often extends into the permanent dentition leading to premature partial or total edentulism.

Objective.- This paper will review, discuss, and document the indications of implant placement as well as the dental and medical management of peri-implant infective complications in a patient with Kostmann syndrome.

Case report.- The dental management of patients with SCN has been poorly described in the literature thus far. In this paper we report a case of dental implant failure in a 24 years old patient diagnosed with Kostmann syndrome. This patient underwent implant supported rehabilitation with 8 upper maxilla and 4 mandible dental implants and returned to the Hospital 5 months post-operatively with an implant related submandibular abscess ultimately requiring removal of the mandibular implants despite extended IV antibiotics therapy.

Discussion.- There is currently no available data to guide the use of dental implants in patients affected from Kostmann disease. We believe the most likely cause of infective oral complications in this patient population occurs during the surgical stages of implant placement as this genetic immunodeficiency likely allows for increased ability of opportunistic oral microflora to colonize the implant surface as well as the oral soft and hard tissues.

Key words: *Kostmann Syndrome, Severe congenital neutropenia, Implant failure, Systemic disease*

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INTRODUCTION

It is well known that various drug treatments and systemic diseases may compromise the integrity of the oral tissues. Likewise these conditions may also affect the viability of dental implants and their surrounding tissue [1].

While recommendations exist for the avoidance of dental implants with certain systemic diseases [2], the scientific evidence to support such guidance is lacking. Moreover, estimating the risk of implant failure in these patient populations is challenging as often these patients rarely receive endo-osseous implants [3].

Severe congenital neutropenia is one such disease that may affect the survival rate of dental implants [4]. SCN, also known as Kostmann syndrome, is inherited in either an autosomal recessive (HAX-1 mutation) or autosomal dominant (ELA-2 mutation) manner [6]. The estimated incidence of SCN is 1-2 cases per million with equal distribution among genders [5]. The condition is usually diagnosed in the peripartum period and presents with impaired bone marrow myelopoiesis and a chronic absolute neutrophil count (ANC) less than 500/μL. Bone marrow examination often reveals promyelocyte / myelocyte arrest with little evidence of mature granulocyte formation.

Most patients with SCN, including those with Kostmann syndrome, are successfully treated with granulocyte colony stimulating factor (G-CSF). Treatment can lead to a 10-12 fold increase in neutrophil count and results in a higher life expectancy of patients with congenital neutropenia [7]. Unfortunately, around 10% of patients do not respond to this therapy. Treatment with G-CSF has improved the control of life-threatening bacterial infections previously common in these individuals.

The most common infections affecting these patients are median otitis, cutaneous cellulitis, perirectal abscesses, furunculitis, pneumonia, stomatitis, severe persistent gingival inflammation and various upper respiratoty infections, [9]. Patients with SCN may also present with periodontitis [5]. Periodontal manifestations range from marginal gingivitis to rapidly progressive periodontal disease with advancing alveolar bone loss affecting both primary and permanent dentition.

Full mouth rehabilitation using implants in periodontally healthy patients has been well documented [10]. However, implant therapy in periodontitis-susceptible individuals has been questioned. Periodontal pathogens may compromise the success rate of implant therapy in partially edentulous patients. Periodontal pathogens were traditonally believed to have been eliminated with the extraction of all natural teeth. Therefore an edentulous patient with a history of periodontitis was considered an appropriate candidate for dental implant placement. Contrary to this belief, recent research on bacterial flora in patients who have been edentulous for at least one year showed the presence of

multiple periodontal pathogens such as *Actinomyces sp* and *Porphyromonas gingivalis* [11].

Dental management, including the application of dental implant therapy, in patients with SCN has been poorly documented in the literature thus far. We report the first case of fixed full mouth rehabilitation in a 24-year-old patient with Kostmann syndrome diagnosed at 18 months of age.

CASE STUDY

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The patient was diagnosed with omphalitis at the age of four months and was subsequently affected at short intervals by a series of infectious diseases such as recurrent severe otitis, oral ulcers, campilobacter gastroenteritis, cutaneous mucormycosis and upper and lower respiratory tract infections leading to pneumonia. Peripheral blood hemogram and bone marrow aspirate showing maturation arrest and mutation of HAX-1 gene led to a final diagnosis of Kostmann syndrome at age 18 months . The patient's diagnosis and treatment was carried on at the University Hospital Virgen del Rocío in Seville.

At the age of 7, the patient had complete extraction of the primary dentition due to the presence of chronic gingivitis, generalized gingival recession and grade III mobility. During the patient's late adolescence, the patient had chronic untreated periodontal disease leading to the progressive loss of the permanent dentition and was completely edentulous at the age of 22 years. The final treatment plan consisted of a full-mouth implant rehabilitation after a favorable clinical and radiological assessment.

The implant treatment planning consisted of a total of eight maxillary implants to support a fixed prosthetic rehabilitation, and 4 mandibular implants for stabilization of an overdenture (Figure 1).

Around the third postoperatively period the patient developed local infectious symptoms consistent with peri-implantitis and the subsequent loss of one mandibular implant. Mild oral local signs of infection persisted for four months despite continuous oral antibiotic therapy.

At month 5 postoperatively the patient developed acute onset of dysphagia and distress upon swallowing requiring hospital admission. The diagnosis was consistent with implant-related submandibular abscess. The treatment included surgical incision, debridement and drainage via penrose tube through the suprahyoid region and daily intravenous infusion of antibiotics (tobramycin 200mg and clindamycin 600mg) for a total of 4 days. Specific antibiotic therapy was selected according to the results of an antibiogram after isolation of two possible causative bacterias (*Streptococcus intermedius* and Prevotella). (Table 1)

Two days after admission the remaining mandibular implants were removed. Full blood count (Table 2) showed a slightly low total white blood cell count (<

2.78 x 10^9L). Differential white blood cell count showed leukopenia mainly associated with total absence of neutrophils and partially hidden by eosinophilia and monocytosis specific of Kostmann syndrome.

Three months postoperatively, oral and radiographic exams were taken demonstrating an asymptomatic, fully healed disease-free mandibular arch.

DISCUSSION

Implantology is undergoing a continuous transformation regarding what are considered relative and absolute contraindications to implant therapy. Some controversy exists on the significance of systemic disorders as risk factors to dental implants outcome. While various systemic disorders and medical therapies have been reported to potentially compromise the stability of dental implants, there is little evidence to support such association since only few studies compare the occurrence of these disorders within a controlled environment [1, 3].

The use of dental implants involves breaking a defensive barrier such as the oral mucosa, within a habitat rich in bacterial flora. Since this type of patients often presents with unstable immune systems, even when they are receiving appropriate treatment, [15, 16,17] it would be advisable to weigh carefully the cost/benefit of implant surgery and the range of therapeutic options should be meticulously assessed in relation to the patient's condition.

In our case report, the patient presents with SCE, a rare haematologic immune disorder commonly associated with severe periodontitis. Various disorders such Papillon-Lefevre syndrome, Down syndrome, Ehlers-Danlos syndrome, Langerhans cell histiocytosis, Chediak-Higashi syndrome, hypophosphatemia, and Leukocyte adhesion deficiency have also been reported to present in association with generalized periodontitis [4, 12, 13]

Thus, periodontal disease could be considered as a significant trigger for early diagnosis of an underlying systemic disease due to its virulence in this type of patients.

The present case study is not resolved with the removal of lower jaw remnant implants, because as we can observe in the different panoramic X-rays, upper implants show bone loss of approximately more than half the size of the implant. These implants will be revised in successive follow-up visits in order to offer a more accurate assessment of the present case report.

Despite the lack of scientific evidence regarding the possibility of implant rehabilitation in patients with these disorders, it would be reasonable to think that susceptibility to periodontitis associated to systemic disorders might have a negative influence on the outcome of implant therapy. [14]

Although we are conscious of the bias posed by the publication of positive outcomes in clinical studies and small series, in those cases in which the

medical conditions are so serious that implant therapy has not been well-documented yet, it is extremely difficult to offer a higher level of evidence [1].

Occasionally, the indication for oral implants should be thoroughly evaluated in patients with local or systemic risk factors that may interfere with the implant treatment stability. [18]

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FIGURES

Figure 1. – Initial panoramic X-ray, five months after insertion of jaw implants.

TABLES

Sample type		*Cutaneous abscess / soft tissue*		
Gram tinction		*> 25 PMN, absence of epithelial cells*		
Aerobic culture		*Streptococcus intermedius is isolated*		
Anaerobic culture		*Prevotella sp is isolated*		
Antibiotics	*Streptococcus intermedius*		*Prevotella sp*	
Description	*Values*	*M.I.C*	*Values*	*M.I.C*
Clindamycin	S	-	R	-
Erythromycin	S	-	-	-
Penicillin	S	-	R	-
Vancomycin	S	-	-	-
Amoxicyllin / Clavulanic acid	-	-	S	-
Imipinem	-	-	S	-
Moxifloxacyn	-	-	S	-
Metronidazole	-	-	S	-

Table 1. Microbiologic analysis and antibiogram of patients at admission. (M. I. C Minimum inhibitory concentration – S Sensitive – R Resistant)

Cell type	***Values***	***Units***	***Range***
Leukocytes	* 2.78	x10e9/L	[3.8-11.5]
Neutrophils	* 0.0	x10e9/L	[2.5-7.5]
Neutrophils %	* 0.0	%	[25-65]
Lymphocytes	1.5	x10e9/L	[1.5-4]
Lymphocytes %	* 53.2	%	[20-53]
Monocytes	0.8	x10e9/L	[0.2-0.8]
Monocytes %	* 27.7	%	[2.5-11.5]
Eosinophils	0.47	x10e9/L	[0.05-0.5]
Eosinophils %	* 16.90	%	[0.3-5]
Basophils	0.06	x10e9/L	[0.01-0.15]
Basophils %	* 2.2	%	[0.6-1.8]

Table 2.- Hemogram at admission