Oral manifestations of congenital neutropenia or Kostmann syndrome

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Infantile congenital agranulocytosis or Kostmann syndrome is a rare hereditary kind of severe neutropenia. The typical symptoms, which appear since the first days of life, are abscesses located on various parts of the body: ear, cutis, lung and oral cavity. These abscesses are due to an almost total disimmunity typical of the neutropenia.

The aim of this article is to describe the most typical signs of this pathology in the oral cavity, reporting a case observed in our department in Florence, Italy. On the basis of the personally observed case and of the review of the literature, it is possible to consider, as a characteristic finding in Kostmann syndrome, a typical very serious periodontal pathology, which is similar to the prepubertal periodontitis in deciduous dentition. At the age of 19 years the patient showed a dramatic compromise of the masticatory function.

It is obvious that the lack of response of the host can obstruct the interaction between the host and the microbic flora, because the lack of neutrophils increases the susceptibility of the patient to every kind of infection, even to periodontitis. A periodontal prophylaxis, since the very first observations, followed by a rigorous maintenance with frequent and regular professional hygienic treatments could be effective in controlling the effects of periodontal disease and could reduce the tragic evolution. We need to recognise that it could be hard to monitor the oral situation correctly in these patients, as they have a continuously poor systemic condition. Finally in these cases the rehabilitative therapy is very problematical.
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INTRODUCTION

The infantile congenital agranulocytosis or Kostmann syndrome (1956) is a rare hereditary kind of severe neutropenia with a neutrophil count as low as 200 cells per mm^3, often associated with monocytosis and eosinophilia, with arrested granulocyte maturation in terminal phases (promyelocyte-myelocyte stage).

With the term "neutropenia" we generally indicate a blood pathology in which the number of neutrophils in the peripheral blood is lower than $1500/mm^3$.

The symptoms are characterized by various different clinical signs with varying etiological possibilities: drug-induced, infection-related, autoimmune and congenital.

Most authors agree to classify in Kostmann syndrome every severe hereditary agranulocitosys, probably having an autosomal recessive trait.

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CASE REPORT

V.G., female, 19 years old, was referred from the oncohematology department of the pediatric hospital "A. Meyer" of the same University.

She was first born, without complications, with a dystocic delivery (forceps). The weight at the birth was 3650gm and psychomotor development was normal.

When she was 40 days old, she was hospitalized for an abscess in the left leg in the pediatric hospital in her town, and routine examinations showed an almost total absence of neutrophils in the peripheral blood.

Until she was 2 years old, she had frequent abscess pathologies in different structures: ear, parotid glands, tongue, nape. The laboratory examinations always con-

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firmed a very low percentage of neutrophils, lymphomonocytosis and high VES.

After the resolution of these problems, she had a normal and regular statural and ponderal growth, and only when she was 10 years old did she have new abscesses with bronchopneumonia, first on the left, and then on the right side.

During these hospitalizations, the finding of a serious neutropenia, positivity to the antigranulocyte antibody test and presence, in the suctioned bone marrow, of a small global hypoplasia with a slow myeloid maturation curve was always confirmed. The phagocytosis reduction, as reported by the hematological study, was probably from the high percentage of eosinophils and basophils; the neutrophils, instead, showed a normal phagocytic activity, but being too few in number to allow for a quantitative evaluation.

ORAL MANIFESTATIONS

When she was 8 years old, during a hospitalization in the Pediatric Department of the University of Florence, she had her first specialized visit to our Department (Figures 1 to 4). She had a panoramic radiograph, made when she was 6 years old (Figure 5) to investigate the causes of the clinically detectable mobility of the lateral-posterior deciduous teeth. This radiograph, even if it was of bad quality, showed a serious reduction of the alveolar bone, particularly on the first deciduous molars, which had no caries.

At the time of our visit the clinical analysis and a new radiograph (Figure 6) revealed a dramatic situation of progress early loss of deciduous molars and cuspids, a situation that when compared with the previous radiograph can be defined as "quickly progressive".

Instructions for scrupulous oral hygiene were given and a rigorous program of periodontal maintenance, which had to be done in patient's town, very far from Florence, was suggested.

Eight years later (!), the patient returned to our clinic, and the control visit showed a very serious periodontal compromise: the permanent teeth were still in the mouth but, as seen on the panoramic radiograph (Figure 7), they will be lost shortly.

In fact, they appeared as suspended through the vascular-neural tract, to a thick bone of support, and it can explain the grade 3 clinical mobility according to Lindhe.[9]

The bone atrophy on every tooth of both jaws proceeded in very quick progression, and led to a resorption similar to the very elderly edentulous people.

At the next observation, in December 2000, after 3 years, the panoramic radiograph (Figure 8) shows the presence of few teeth with a dramatic compromise of the masticatory function.

DISCUSSION

On the basis of the personally observed case and of the review of a few cases in the literature, it is possible to

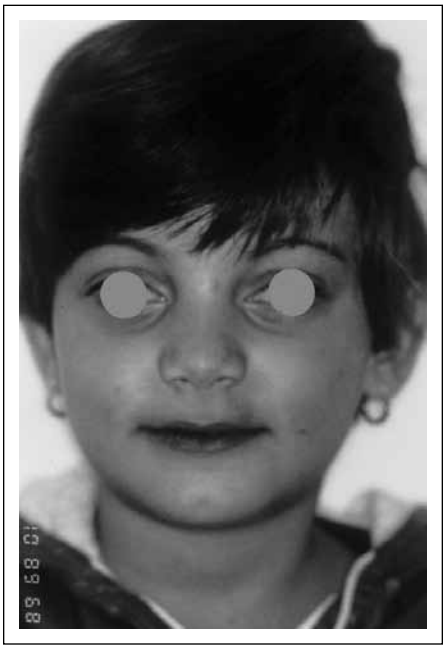
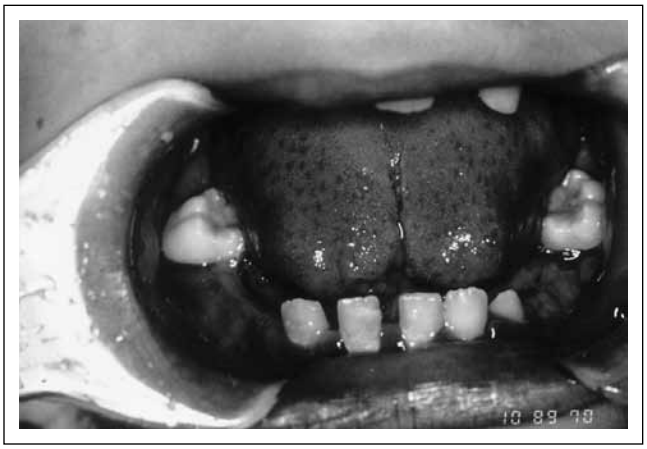
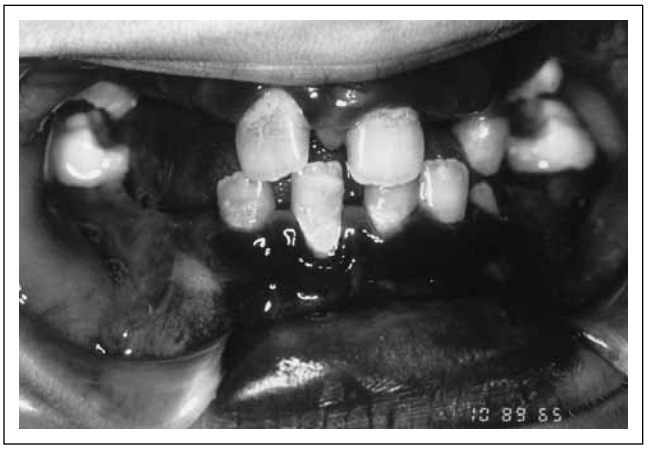


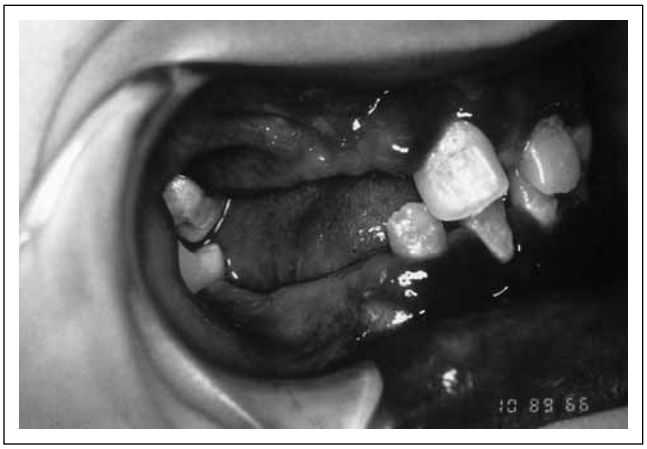
Figure 1. Frontal view of the patient at the time of the first visit.



Figures 2. Intraoral photographs at the age of 8 years.



Figures 3. Intraoral photographs at the age of 8 years.



Figures 4. Intraoral photographs at the age of 8 years.

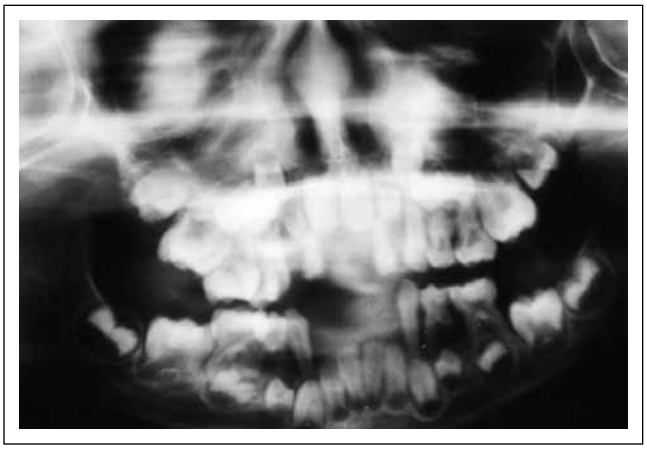


Figure 5. Orthopantomogram taken at the age of 6 years.

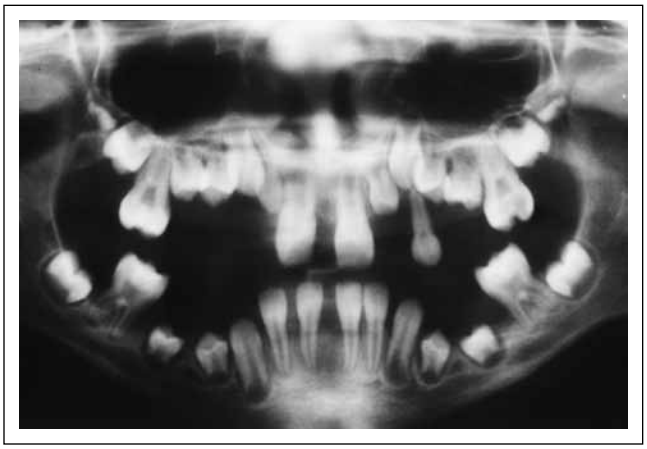


Figure 6. Orthopantomogram taken at the age of 8 years.

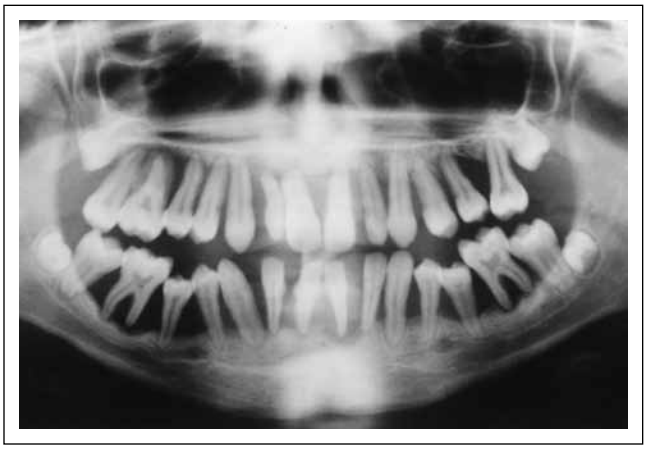


Figure 7. Orthopantomogram taken at the age of 16 years.

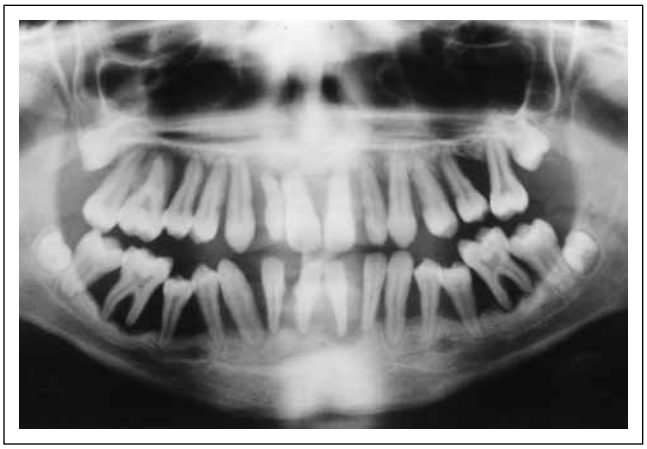


Figure 8. Orthopantomogram taken at the age of 19 years

consider, as a characteristic finding in Kostmann syndrome, a typical very serious periodontal pathology. This disease is similar to the prepubertal periodontitis in deciduous dentition, described by Lindhe.[9]

It is obvious that the lack of response of the host in individuals with systemic disorders like the congenital neutropenia can obstruct the interaction between the host and the microbic flora, because the lack of neutrophils increases the susceptibility of the patient to every kind of infection, even to periodontitis.

Besides the importance of polymorphonuclear leucocytes in the periodontal homeostasis was already showed for some time by various authors through histological studies.[6,11] The literature describes many cases of serious gingival phlogosis and loss of bone support in subjects with benign qualitative and quantitative reductions of polymorphonuclear leucocytes in sulcus.[8,10] Most of the authors state that the elective therapy is the interceptive one, with the aim to prevent the inevitable serious periodontitis that the surgery seems to be unable to resolve.[97,13]

The muco-gingival surgery is not effective because in these subjects the gingival tissue is clinically fragile and then difficult to manage for the surgeon, even during the suturing. In addition a surgical intervention, not even much extended, in a subject with a chronic immunodepression, could result in great risks even in the postoperative phase and will be probably be unsuccessful.[7]

Consequently the most effective way to prevent the serious oral side effects seems to be a rigorous oral hygiene program with periodic assessments and regular professional hygiene, together with a constant motivation for domiciliary oral hygiene. We have also to observe that with these children, the attention of the pediatrician is focused primarily on critical infections of most functionally critical *quoad vitam* organs, especially of the respiratory system, even if there is an almost total loss of the masticatory function.

Pernu *et al*.[12] correctly state that the necessity of a periodontal prophylaxis, since the very first observations, through scaling and root planing, followed by a rigorous maintenance with frequent and regular professional hygienic treatments. We agree with these authors about the fact that this clinical approach could be effective in controlling the effects of periodontal disease and could reduce the tragic devolution. We need to recognize that it could be difficult to monitor the oral situation correctly in these patients as it is a continuously a poor systemic condition. Finally, in these cases, the rehabilitative therapy is problematical.

Sparse scientific literature about syndrome did not help planning a right therapeutic protocol.

Another important limit is survival expectation.[2] Unfortunately as a systemic disease affecting the oral cavity, it creates tissue fragility that is not compatible with traditional prosthetic methods. Implants are difficult to imagine because of almost total absence of bone support tissue and also because, intending to do a pre – prosthetic surgical maneuvre, involving autolog bone drawing, the insurmountable limit should be represented by patients affected by Kostmann syndrome showing generalized notes of bone resorption and osteoporosis, even with a bone metabolism in the normal range.[15]

A final consideration is that every surgical act made under general anesthesia could cause a serious lowering of the levels of neutrophils, which are already low.[5]

Actually attention is concentrated on therapeutic advantages offered by the administration of granulocyte maturation stimulating factors as recombinant-methyonil-human granulocyte colony-stimulating factor (r-metHuG-CSF). Dong *et al*.[4] for first demonstrated a punctiform somatic mutation in the GCSF receptor, which will be unable to produce an adequate maturation signal. According to these new findings, the genetic therapy could be the future horizon in the treatment of the subjects affected by Kostmann syndrome or by other similar pathologies.

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