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# Radiological and clinical difficulties in the management of chronic maxillary sinusitis in β Thalassemic paediatric patients

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ABSTRACT

*Introduction:* Beta thalassemia is a blood dyscrasia that caused a marked expansion of active marrow spaces and extramedullary haematopoiesis results. In these patients various alterations and abnormalities affects different body areas, including increased risk of sinusitis. The marrow expansion in the facial bones results in delay in pneumatisation of the sinuses, overgrowth of the maxillae, and forward displacement of the upper incisors with skeletal deformities.

In current literature, maxillary sinuses are not deeply evaluated by CT scan studies in these kind of patients.

The aim of our study was to investigate the presence of maxillary sinuses abnormalities by the use of CT in patients with beta-thalassemia major and to compare these findings with a control group free from this disease.

*Materials and methods:* A retrospective analysis of 22 paediatric patients with beta-thalassemia major and 22 control subjects without sinonasal diseases was performed. CT was done using a 64-multidetector-row CT scanner without contrast injection, obtained in axial plane using thin-slice technique. Evaluated parameters were: bone thickness of the lateral and anterior wall, density and volume of the maxillary sinuses.

*Results:* Significant difference was found between the study group and control group in the evaluation of all the parameters examined. The maxillary sinus of β thalassemic patients was smaller respect of controls, the bone was more dense and thick in the side and anterior wall. Beta-thalassemic patients have a relative risk of 2.87 to develop a maxillary sinusitis.

*Discussion:* In these patients there is an increased incidence of sinonasal infections due to the abnormal development of cranio facial skeleton. These bone alterations might confuse the physicians and lead to an increased rate of sinusitis diagnoses.



## 1. Introduction

β-Thalassemia is a blood dyscrasia caused by defective synthesis of the beta chain of haemoglobin. This disease is responsible of a severe anaemia due to ineffective erythropoiesis and peripheral haemolysis of the defective red cells [1]. Marked expansion of active marrow spaces and extramedullary haematopoiesis results [2]. Homozygous beta-thalassemia major or Cooley's anaemia requires continuous treatment and regular type of transfusion and iron chelation to ensure survival and good quality of life of affected patients [3–5].

β-Thalassemia major mutation mostly affects survival of patients [6]. Patients develop signs and symptoms in childhood of severe anaemia and growth retardation [7,8]. In these patients huge alterations and abnormalities are present in different body areas, from diarrhoea to fever and recurrent infections, including increased risk of sinusitis, epistaxis, bleeding and wide alterations of the skeleton with pathological fractures and osteoporosis, endocrine abnormalities, splenomegaly, loss of the normal stages of sexual maturation, and growth retardation [9]. Transfusion

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therapy can decrease and prevent irreversible bone abnormalities progress in paediatric patients. There are still some countries where the disease is endemic and the population is unable to access medical care with characteristic and pathognomonic clinical presentation. Skeletal deformities are the result of bone marrow hyperplasia, which expands the bone cavities and cause a thinning of the cortical structures [10,11]. The typical facial changes are due to active marrow hyperplasia. The marrow expansion in the facial bones results in overgrowth of the maxillae, and forward displacement of the upper incisors. Malocclusion as well as cosmetic deformity occur.

This involves radiographic features of the skull (up to "skull brush"), the face ("facies rodents"), the stomatognathic apparatus, the costae ("spatula" or "club"), vertebrae ("palisade"), pelvis and long bones (loss concave diaphyseal). In the skull, in particular, the overall thickness is increased, the diploic space expanded and the outer cortex reabsorbed. In severe cases the typical "skull brush" may be observed, due to the presence of bone spicules directed perpendicularly towards the outside [12].

A further characteristic feature of the disease is barely addressed: the occurrence of typical craniofacial alterations, represented by the characteristic facial expression "facies rodent": increased head circumference, prominent cheekbones, hypertelorism, depressed nasal root.

Disproportionate growth of the maxilla compared with the mandible is present: it appears most retruded, probably due to several factors such as increased muscle weakness at this level or reduced condylar growth. This can be explained by the fact that the branch of the mandible is more susceptible compared to other districts to the various causes of stunting, related to severe anaemia, endocrine dysfunction and insensitivity to growth hormone.

Despite all the improvements, thalassemia remains a complicated disease and the search for a definitive cure continues. Nowadays, the only available curative option for β-thalassemia major is hematopoietic stem cell transplantation (HSCT) or bone marrow transplant (BMT) [13]. The first successful bone marrow transplant for a patient with β-thalassemia was carried out by Thomas et al. in 1981 [14]. After more than 30 years, HSCT from an HLA-identical subject is now a widely applied alternative to traditional transfusion and chelation therapy. Results are very encouraging for both children and adults. On the other hand transplantation leads to profound immunodeficiency that is obviously the main triggering factor of such infections like rhinosinusitis, since the airway is the location most exposed to the environment and its microorganisms. Post BMT patients have about a 37% risk for developing rhinosinusitis after transplantations, compared to a 15% rate in patients with normal immune status [15,16].

The typical anatomical modifications of skull, maxillary and mandibular structures are well described in the literature by means of standard XRay evaluation. Multislice computed tomography (msCT) adds a third dimension to paranasal sinuses and face abnormalities imaging. Using transverse and coronal reformats, accurate assessment of the paranasal anatomy can be achieved. Evaluation of bony characteristic and involvement of soft tissue structures of the face can be elicited. Furthermore, CT accurately defines lesions extension into the pterygopalatine fossa, orbit, and cranial cavity, pivotal informations in therapy planning [17].

In our knowledge maxillary sinuses are not actually routinely imaged by msCT scan in these particular category of patients [18].msCT is fast in providing superior anatomic and osseous detail. It is the gold standard for inflammatory sinonasal disease because of its high spatial resolution and superior osseous depiction in order to provide a surgery road map before endoscopic sinus surgery [19].

The aim of this study was to investigate the presence of maxillary sinuses abnormalities by the use of msCT in patients with beta-thalassemia major and to compare these findings with a normal age matched control group.

## 2. Materials and methods

A retrospective analysis of 22 patients with β-thalassemia major (19 males and 3 females; age range 3–20 years, mean age 11 years) and 22 control subjects was performed.

Selection criteria were age of 3–20 years and previous diagnosis of β-thalassemia major.

We enrolled patients without any signs and symptoms of sinonasal infection before BMT.

The cases patients developed clinical signs suspected for high respiratory infections (sinusitis or pneumonia) in the late phase post-transplant and underwent CT scan of the lung and the paranasal sinuses, in order to exclude any respiratory disease after bone marrow transplantation.

Exclusion criteria for both groups were pre-existing medical conditions known to be associated with anamnesis of craniofacial surgery or previous orthodontic treatment, with concomitant disease or previous facial trauma.

In selecting controls, we considered sex and age matched series. The control group had a normal craniofacial morphology, without nose sinus disease or anatomical abnormalities. They were randomly chosen from children presented to our Radiology Department for neurological problems.

Imaging Study: msCT was performed using a 64-multidetector-row CT scanner (LightSpeed VCT, GE Medical Systems), without contrast injection.

Scan parameters were 80–100 kV, 100 mAs, 0.5 rotation time, 0.094 pitch.

CT of the paranasal sinuses was obtained using thin-slice technique, taken in parallel to the hard palate or orbitomeatal unit. Coronal and sagittal reformats were then reconstructed to better evaluate the sinonasal anatomy. Raw data were processed with both bone and soft-tissue algorithms. A team of two head and neck radiologists and an otolaryngologist evaluated the images reformatted on axial and coronal planes. For image analysis, CT data were exported and analysed on a workstation (Advantage Workstation, version 4.4 GE Medical Systems, Waukesha, WI). Density values were measured in Hounsfield Units (HU) with a 5 $mm^2$ area small ROI (region of interest) that was manually designed and positioned in correspondence of the first premolar. The maxillary sinus volume ($cm^3$) was evaluated too.

Study parameters were:

(1) Bone thickness of the lateral sidewall of the maxillary sinus.
(2) Thickness of the anterior wall of the maxillary sinus.
(3) Density of the maxillary sinus.
(4) Volume of the maxillary sinus.

Patients involved had clinical criteria of chronic rhinosinusitis (CRS). The diagnosis of maxillary sinusitis was established according to the symptoms and signs on physical examination, in addition to nasal endoscopy results, according to the Guidelines on Rhinosinusitis of ABORL-CCF and EPOS.10 [20]. A diagnosis of CRS was made if 12 weeks or longer of two or more of the following signs and symptoms were present: mucopurulent drainage (anterior, posterior, or both), facial pain-pressure-fullness, nasal obstruction/congestion, or cough. Inflammation was documented by one or more of the following findings: purulent mucus or oedema in the middle meatus or anterior ethmoid region, polyps in nasal cavity or the middle meatus, and/or CT imaging showing inflammation of the paranasal sinuses.