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ORIGINAL ARTICLE

Dental findings and oral health status in patients with mucopolysaccharidosis: a case series

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Abstract

Objective. To present a mucopolysaccharidosis (MPS) case series evaluating oral manifestations (clinical and radiographic), oral health status and discussing its implications. ***Patients and methods.*** All patients with MPS attending the Genetics clinic/Brazil were evaluated by means of anamnesis, clinical and radiographic examinations. ***Results.*** The final sample consisted of 12 subjects (nine males and three females), with ages ranging from 3–31 years old. Concerning oral health, it was observed high levels of caries and periodontal problems. About oral manifestations, this study clinically observed more cases of delayed tooth eruption, thickness of alveolar process and thick lips. Radiographically, it was observed alterations on condyle, mandibular ramus and joint fossa. ***Conclusion.*** The dental changes in MPS population are high and consequently it is important to know them for differential diagnoses, early treatment intervention, prevention and education of both patients and parents/caregivers about oral health.

Key Words: *mucopolysaccharidosis, oral health, oral manifestations, signs and symptoms*

Introduction

Mucopolysaccharidosis (MPS) is a heterogeneous group of diseases resulting from a gene order change in which accumulation of lysosomal glycosaminoglycans occurs because of a poor production of enzymes accounted for their degradation [1]. They are related to several types of MPS: I (Hurler), II (Hunter), III (Sanfilippo), IV (Morquio), VI (Maroteaux-Lamy), VII (Sly), VIII (Di Ferranti), IX (Natowicz) [2].

MPS is an autosomal recessive condition in the majority of the cases, except for Type-II MPS, in which the pattern is an X-linked recessive mode. It is estimated that the overall incidence for this group of diseases is 1:25000 live births [3]. Each type of MPS is associated with a wide clinical heterogeneity [4]. Among the various physical features involving this syndrome, dental manifestations are characteristically present [2,5], thus making it important to know the dental implications from clinical and radiographic findings. In addition, it is necessary to know the oral health condition of these patients in order to intervene effectively with their treatment.

The first reports of dental alterations in patients with MPS were made in the 1960s. Until now, we have observed that the majority of scientific publications describe dental findings by reporting clinical cases [6-23] or some type of dental intervention [24]. Other studies seek more specific findings analyzing structural and chemical evaluation of enamel and dentine [23], analyzing presence of cells in gingival [25], the level of pulp chamber obliteration [26], delineating the area of dentine–enamel junction in deciduous teeth [27] and detecting morphological alterations in dental and periodontal tissues [28]. With the advanced treatment of MPS diseases by means of bone marrow transplantation, case reports on oral findings in patients undergoing this treatment also have been published [29–31].

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Based on the previously presented; this work aimed to present the prevalence of oral health conditions and oral features (clinical and radiographic characteristics). In addition, to discuss the dental implications for a group of patients with MPS.

Patients and methods

The sample consisted of total patients attending a referral center for MPS carriers whose parents and/or caregivers allowed them to participate in the study by signing a free informed consent. As *inclusion criteria*, only those patients aged more than 2 years old and presenting complete deciduous dentition and confirmed diagnosis of MPS were selected; whereas poor behavior and debilitating health status impeding the proposed clinical evaluation were the *exclusion criteria*.

In fact, this is an observational cross-sectional study of a group of patients described as a case series and which was submitted to and approved by the local Research Ethics Committee and it is accordance with the Helsinki Declaration.

In order to meet the goals proposed by the study, data were obtained from anamnesis as well as from clinical and radiographic evaluations. Anamnesis was performed by only one interviewer (APN), who collected the following variables: type of MPS, age, gender and presence of cognitive deficit or deleterious habits. The criteria to list the oral findings, both clinical and radiographic, in the present study were based on a literature search [3–31], which included determining the characteristic of the patient's condition. Clinical evaluation was also performed by only one investigator (LAAA), who were previously trained, and calibrated by a very experienced dentist in such a procedure, with the help of an assistant (APN), to note the following variables:

- Evaluation of dentition, occlusal relationship (overjet, overbite, terminal molar relationships) according to Moyers [32];
- Dental caries experience was determined by the DMFT and DMFT indexes established by the World Health Organization [33];
- Gingival inflammation was determined by evaluation of the index of visible biofilm established by Ribeiro et al. [34] and the simplified oral hygiene index (OHI-S) [35];
- Dental treatment need such as dental restorative treatment, periodontal therapy, oral and maxillofacial surgery and treatment for maloclusion; and
- Identification of the most common clinical oral manifestations such as occlusal alterations (anterior open-bite, posterior cross-bite, mandibular protrusion, giroversion, crowding and diastema); palatal shape (narrow and deep palate, wide and flat palate; presence of prominent palatal rugosity); dental eruption alterations (prolonged retention of deciduous teeth or delay in permanent tooth eruption); gingival alterations (hyperplasia, fibromatosis, thickness of alveolar process); soft tissue alterations (macroglossia, tongue protrusion, thick lips); enamel alterations (hypoplasia, colour alteration); limited mouth opening; and shape alterations (pointed cuspid teeth, occlusal wear, buccal or lingual/palatal concavity).

Panoramic radiographic evaluation was performed by using a magnifying glass and negatoscope by only one examiner (LAAA), who was previously trained and calibrated by a very experienced radiologist, and an assistant (APN) to record the following variables:

Developmental dental alteration

- Eruption prolonged retention of deciduous teeth or delay in permanent tooth eruption [36];
- Tooth germ formation: delayed tooth germ formation, delayed in root formation; and short root pattern [37];
- Dental shape alteration [32,38]: cervical constriction, taurodontism, pulp obliteration; ectopic teeth or dental transposition, impacted teeth and double formation or peg-shape; and
- Abnormal number of teeth [32,39]: tooth agenesis and supernumerary teeth.

Others alterations

- Alterations in bone support: wide mandibular base [29,40], irregular bone cortex [19];
- Shape alteration [11,14–16,19,20]: malformed glenoid cavity, condylar defect, flat mandibular notch, short mandibular ramus and wide coronoid process; and
- cystic lesions [41] or thickness of dental follicle [15,17].

After being collected, data were entered into a database for analysis of frequencies and then descriptively evaluated.

Results

From an initial sample of 19 patients with MPS who attended a referral center at the Genetics Clinics of Rio de Janeiro, Brazil, two declined to take part in the study because of the distance from their homes, two did not attend the evaluation appointments and three died. As a result, the final sample consisted of 12 subjects (two MPS-I, five MPS-II, one MPS-III, two MPS-IV-A and two MPS-VI), being nine males and three females with ages ranging from 3–31 years old, including three mentally handicapped ones (Table I).

Table I. Final MPS sample characterization.

Patient	MPS type	Eponym	Gender	Age (years)	Mental handicap
No.1	IV-A	Morquio typeA	F	9	No
No.2	II	Hunter	M	33	No
No.3	VI	Maroteaux-Lamy	F	18	No
No.4	VI	Maroteaux-Lamy	M	12	No
No.5	II	Hunter	M	9	Yes
No.6	IV-A	Morquio type A	F	16	No
No.7	III-C	Sanfilippo type C	M	15	Yes
No.8	II	Hunter	M	13	Yes
No.9	II	Hunter	M	13	Yes
No.10	II	Hunter	M	20	No
No.11	I	Hurler	M	3	No
No.12	I	Hurler	M	5	No

F, female; M, male.

Table II shows the dental characteristics of the patients. It was observed that a greater number of subjects had permanent dentition (n = 6). A few presented overjet (n = 2) and overbite (n = 1). With regard to terminal molars relationships, five subjects could not be evaluated due to the lack of eruption of the first permanent molar; of those analysed the majority presented class I relationships (n = 5). Seven subjects evaluated had already experienced dental caries, whereas periodontal diseases were involved in more cases (n = 9). In the analysis of deleterious oral habits, one could find that each patient exhibited more than one type, with the most frequent ones being snoring and mouth-breather (n = 10).

When oral manifestations were evaluated, one can find a higher frequency of clinical cases (Table III) of delayed eruption, thickness of alveolar process and thick lips (the three cases, n = 8). Radiographically (Table IV), condylar defect was the most frequent condition (n = 9), followed by short mandibular ramus (n = 8) and alteration in fossa shape (malformed glenoid cavity) (n = 7).

Clinical dental manifestations were more prevalent in the cases of MPS types II (Figure 1), IV-A (Figure 2), and VI (Figure 3). Patients with type-I MPS were the least clinically (Figure 4) and radiographically (Figure 5A) affected, even showing no syndromic facies (Figure 4). On the other hand, radiographic findings were more present in MPS types II (Figure 5B) and VI (Figure 5C).

Discussion

In the present study, a great number of patients with MPS had caries experiences and mainly periodontal diseases, which required major dental treatment. Some reports have cited few patients presenting caries [6-9,17,19,22,29]. Other studies have also reported the presence of gingivitis [11,19,29,34]. However, there are few studies using socio-dental indicators for evaluation, such as OHI-S, plaque index or even DMFT/DMFT. Evaluation of oral conditions in patients with MPS, as performed in the present work, seems to be scanty in view of the fact that the literature contains basically dental case reports [6–31]. Nevertheless, epidemiological surveys regarding all types of MPS are still very seldom [42], mainly because of the low prevalence of such a disease. Further multi-center studies on groups of MPS would be interesting.

With regard to clinical findings, prominent palatal rugosity [11,14,29], shape alterations (small-sized crown) [7,12,14,16,17] and presence of tooth abrasion (occlusal wear) [7,12,19] were not addressed in the present study. On the other hand, other clinical manifestations (anterior open-bite [9,11,16,19,21–23,30], posterior cross-bite [14,19], mandibular protrusion [14], giroversion [29], crowding [29,30], diastemas [7,9,11,13,19,21], narrow and deep palate [11,14,22], flat and wide palate [9], delayed eruption [11,17,21-23,30], thickness of alveolar process [22,29,30], hyperplasia/fibromatosis [11,14,16,17,23], macroglossia [11,14,19,21,30], tongue protrusion [11,16,21,30], thick lips [16,21], enamel hypoplasia [7–9,12,23,30], color changes [7,8,13,19], limited mouth opening [23,29,30], pointed cuspids [7–9,12,13,19,30] and buccal/occlusal concavity [12,13,19] were observed in both present case series and elsewhere.

With regard to radiographic oral manifestations, changes in the shape of the temporo-mandibular joint [8,11,14–16,19,29,40], articular fossa (glenoid cavity) [19,40] and coronoid process [11,40] were observed, besides the presence of wide mandibular

Table II. MPS patient's pattern of occlusion, oral health status, dental treatment needs and oral habits.

			Occlusion			Oral health status					Oral habits						
						Caries		Gingiva									
Patient	Type	Dentition**	Overjet	Overbite	Terminal molars relationships***	DMFT	dmft	Biofilm	OHI-S	Dental treatment needs****	Pacifier sucking habits	Digit sucking habits	Object biting habits	Onychophagy	Snore	Mouth-breathers	Bruxism
No.1	IV-A	M	+	–	Cl I	0	0	0	0	M	–	+	+	+	+	+	+
No.2	II	P	–	–	Cl I	1	*	0	0	M/S	–	–	–	–	+	+	–
No.3	VI	P	–	–	*	0	*	3	1	P	+	–	–	–	+	+	–
No.4	VI	P	–	–	*	0	*	3	9	P	–	–	–	+	+	+	–
No.5	II	M	–	–	*	1	5	3	2	R	+	+	–	–	+	+	+
No.6	IV-A	P	+	–	Cl II	4	*	0	0	S	–	–	–	+	+	+	–
No.7	III-C	P	–	–	Cl I	1	*	5	6	P	+	–	–	–	+	+	–
No.8	II	M	–	–	Cl I	0	1	3	1	P/S	–	–	–	+	+	+	–
No.9	II	P	–	–	Cl I	2	2	5	3	R/S/P	–	+	–	–	+	+	+
No.10	II	M	–	–	Cl III	0	0	3	2	P	+	–	–	–	–	–	+
No.11	I	D	–	+	*	*	0	1	1	P	–	–	+	+	+	+	+
No.12	I	D	–	–	*	*	1	1	1	P/R	+	–	+	+	–	–	+

+, yes; –, no.
* Subjects not evaluated; ** Dentition (d, deciduous; m, mixed; p, permanent); *** Terminal molar relationships (cl, class); **** Treatment needs (M, malocclusion treatment; S, surgical; P, periodontal treatment; R, restorative).

Table III. Clinical findings in patients with MPS.

Patient	Type	Anterior open-bite	Posterior cross-bite	Mandibular protrusion	Giroversion	Crowding	Diastema	Narrow and deep palate	Wide and flat palate	Retention delayed teeth	Thickness of alveolar process alveolar	Hyperplasia, fibromatosis gengival	Macroglossia	Tongue protrusion	Thick lips	Enamel hypoplasia	Colour alteration	Limited mouth opening	Pointed cuspid teeth	Buccal or lingual/ palatal concavity
No.1	IV-A	–	+	–	–	–	+	–	+	–	+	–	+	+	+	–	–	–	+	+
No.2	II	+	–	–	–	–	+	–	+	–	+	–	+	+	+	–	–	+	+	–
No.3	VI	+	+	–	–	–	+	+	–	+	+	+	+	+	+	–	–	+	–	–
No.4	VI	–	+	–	+	–	+	–	+	+	+	–	–	–	–	+	–	–	–	–
No.5	II	–	–	–	–	–	–	+	–	+	+	–	–	–	–	–	–	+	–	–
No.6	IV-A	–	–	–	–	–	+	–	–	–	–	–	–	–	+	+	+	–	+	+
No.7	III-C	–	–	–	–	–	–	+	–	+	–	–	–	–	–	+	–	–	–	–
No.8	II	+	+	–	–	–	+	+	–	+	+	+	+	+	+	–	–	+	–	–
No.9	II	–	–	–	–	–	–	–	+	+	+	–	–	–	+	–	–	+	–	–
No.10	II	+	+	+	–	–	+	–	+	+	+	–	–	–	+	–	–	–	–	–
No.11	I	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No.12	I	–	–	–	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Absolute frequency		4	5	1	1	1	7	4	5	8	8	2	4	4	8	2	1	5	3	2

+, Yes; –, no.

Table IV. Radiographic findings in patients with MPS.

Patient	Type	Delay/ Retention eruption	Delay in tooth germ formation	Delay in root formation	Dilaceration	Taurodontism	Short mandibular ramus	Wide mandibular base	Irregular bone cortex	Malformed glenoid cavity	Condilar defect	Flat mandibular notch	Wide coronoid process	Thickness of dental follicle	Ectopic teeth	Impacted teeth	Supranumerary
No.1	IV-A	–	–	–	–	–	+	+	+	+	+	+	+	–	–	–	–
No.2	II	+	–	–	–	–	+	+	+	+	+	+	+	–	+	+	-
No.3	VI	+	–	+	–	–	+	+		+	+	–	–	–	+	+	+
No.4	VI	+	–	–	+	+	+		+	+	+	+	+	+	+	+	–
No.5*	II	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
No.6	IV-A	–	–	–	–	–	–	–	–	+	+	+	+	–	–	+	–
No.7*	III-C	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
No.8	II	+	–	+	+	–	+	+	–	+	+	–	+	+	+	+	+
No.9*	II	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
No.10	II	+	–	–	–	–	+	+	–	+	+	–	–	–	+	+	–
No.11	I	–	+	–	–	–	+	–	–	–	+	+	–	–	–	–	–
No.12	I	–	–	–	–	–	+	–	–	–	+	+	–	–	–	–	–
Absolute frequency		5	1	2	2	1	8	5	3	7	9	6	5	3	5	6	2

+, Yes; –, no.
* Patients not evaluated due to negative behavior that causes the impossibility to obtain the radiography.

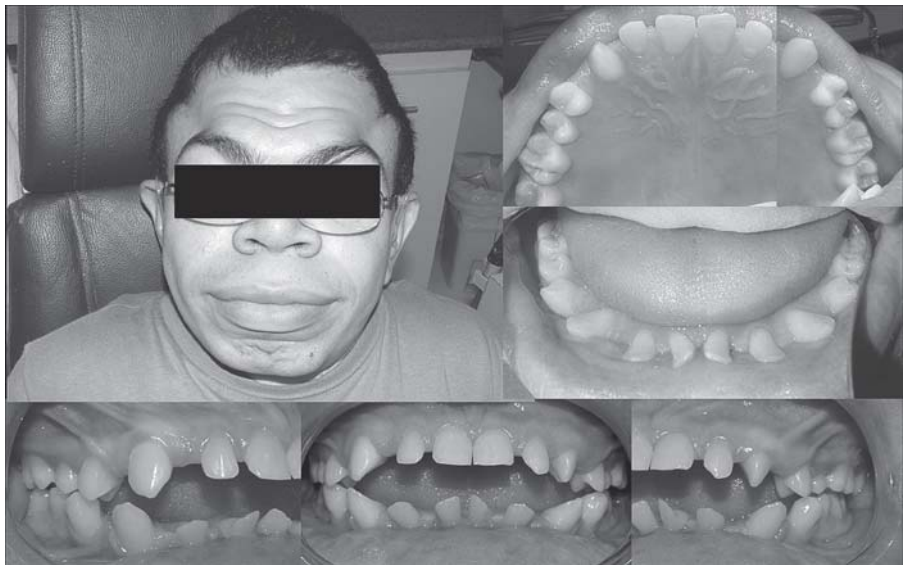

Figure 1. Facies syndromic and oral clinical characteristics MPS II (patient no.2): anterior open-bite, diastema, wide and flat palate, thickening of the alveolar process, macroglossia, tongue protrusion, lip thick, limited mouth opening, pointed cusp (element 22).

base [29,40] and short mandibular ramus [29,40]. No agenesis was observed [20], only cases of supernumerary teeth, characteristic of patients with MPS type II (case 8) and IV (cases 3 and 4). In all these cases, one could also find delayed dental eruption, dental impaction and thickness of dental follicle as described in the literature [15,17], but no cyst formation or radiolucency was found at all [11,14–16,22,23,29].

Other radiographic manifestations described in the literature were not found in this sample, such as pulp obliteration [23,26], secondary dentin layer [23] and cervical constriction. Root shortening [29] was not reported in the present study for posterior teeth, although this radiographic manifestation was not taken into account for anterior teeth because buccal inclination due to macroglossia or tongue protrusion was clinically observed. However, there were findings reported only in the present study, such as root dilacerations (cases 4 and 8) and delay in germ formation (case 12).

The clinical manifestations common to MPS lead us to believe that there exists a correlation with systemic manifestations, in view of the symptoms exhibited by patients having this syndrome. The type-I MPS may manifest more severely, characterized by mental retardation, severe somatic involvement and death before the age of 10 years (also known as Hurler's syndrome) or may manifest as a milder form characterized by preserved cognition and less somatic involvement (known as Scheie's syndrome) [44]. In the present study, there were two younger patients with the less severe form of type-I MPS (cases 11 and 12) in which very few oral findings were observed, including concomitant absence of syndromic facies.

The knowledge oral health condition, prevalence of oral manifestations (clinical and radiographic) and their implications for patients with MPS is necessary and timely, since the care these patients need should

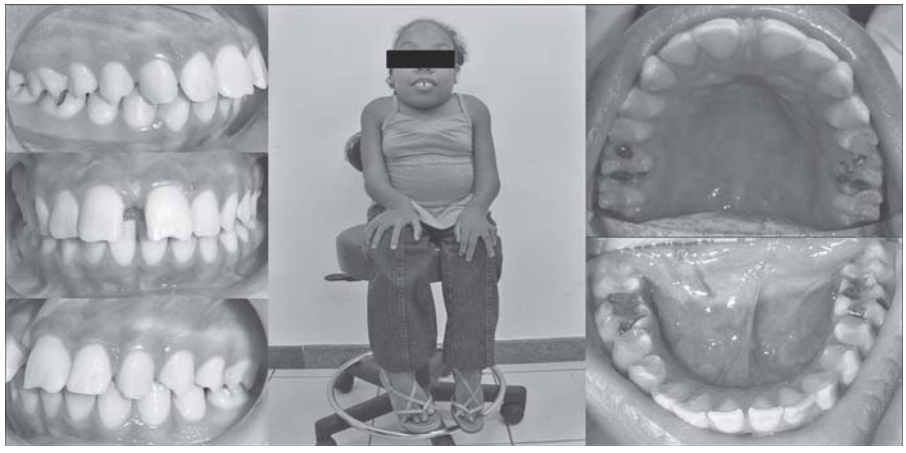

Figure 2. Featured dental clinics in MPS IV-A (patient no.6): central diastema, enamel hypoplasia and wrinkled, color change, change in teeth's shape (anterior teeth with bevel shape; canines, premolars and molars with sharp cusps; molars with buccal, lingual/palatal concavity).

Figure 3. Oral clinical feature of MPS VI patient (no.4): posterior crossbite (elements 14 with 44), giroversion, diastema, wide and flat palate, delayed eruption (absences of permanent molars), thickening of the process alveolar and enamel hypoplasia (elements 11, 32, 41, 42 and 43).

be multidisciplinary, which includes dental care. Within this context, emphasis is given to differential diagnosis, prevention, education of patients and parents/caretakers and early intervention in oral conditions.

Differential diagnosis between MPS and other conditions can be helped by means of oral findings. Radiographic images of multiple rosettes in the cavity of dental follicles is a condition suggesting differential diagnosis of MPS [15] in relation to Gorlin's syndrome [41,45], which also presents several cystic lesions in upper and lower maxillas as well as permanent and supranumerary teeth inserted into alveolar bones [41]. With regard to MPS diseases, dental findings are important for type-IV, since these contribute to confirmation of the diagnosis of type A and disregard other types (B and C) in which dental alterations do not occur [19].

There is little emphasis on treatments for dental manifestations in patients with MPS [15,43]. In the literature, one can find a preventive care protocol according to the patient's needs, which includes pit and fissure sealing, fluoride supplementation, careful tooth brushing and flossing under supervision by parents, diet counselling and frequent visits to the dentist [30]. For the treatment of oral findings, Smith et al. [17] mention surgical exposure of the intruded teeth, orthodontic traction and extraction with enucleation of follicles. However, the dental procedure may only require follow-up of the surgical

Figure 4. Patients MPS I (patient no. 11, 12) with absence of clinical syndromic face and without a clinical aspect of some alteration (patient no.11).

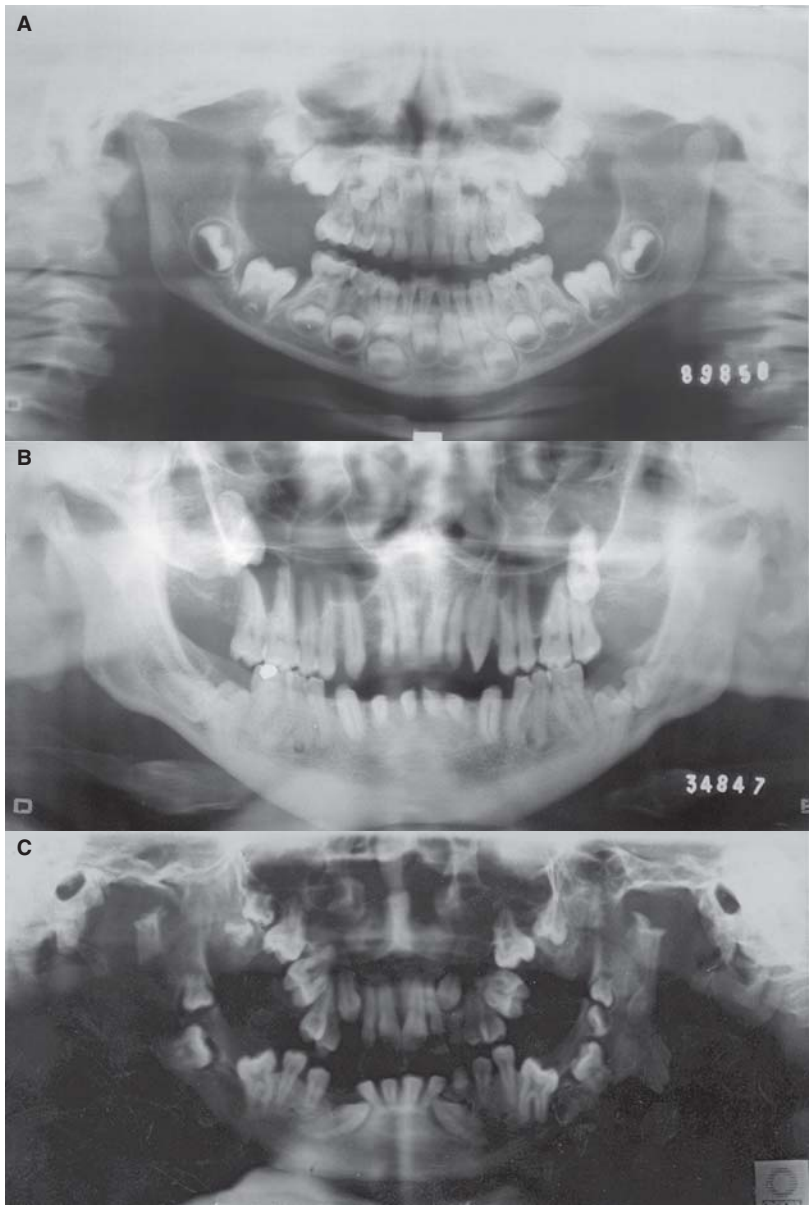

Figure 5. (A) Radiographic findings in patient MPS I (patient no.12). Note the condylar defect and flat mandibular notch. (B) Radiographic findings in patient MPS II (patient no.2): Delay/retention eruption, short mandibular ramus, wide mandibular base, irregular bone cortex, malformed glenoid cavity and condylar defect, flat mandibular notch, wide coronoid process, ectopic teeth and impacted teeth. (C) Radiographic findings in patient MPS VI (patient no.3): Delay/retention eruption, delay in root formation, short mandibular ramus, wide mandibular base, condylar defect, thickness of dental follicle, ectopic teeth, impacted teeth and supernumerary.

needs as these pose risk situations in surgical interventions under anesthesia, since such patients have a poor general health status (cardiovascular and respiratory systems).

Rooling et al. [19] and Hingston [29] have pointed out the importance of early and regular dental care in the cases of MPS. The use of preventive methods not only in the dental practice, but also in other health areas, is important, including information for patients and caregivers on the manifestations that may occur during craniofacial growth, thus attenuating the clinical outcomes in individuals affected by this disease. Early detection and intervention in oral manifestations are also reported by Smith et al. [17]. For instance, in the case of detecting an impacted tooth and knowing that the thickness of dental follicle in patients with MPS can result in a cyst, the author states that the delay in dental eruption should be treated as soon as possible by exposing surgically the impacted teeth before the follicles become thick, thus helping root formation and preventing cyst formation in the future.

The present case series has found: (i) poor oral health associated with high caries experience and mainly periodontal disease, in patients with MPS, which indicated great necessity of dental treatment; (ii) more prevalence of clinical oral manifestations: delayed eruption/retention of teeth, thickness of

alveolar process, thick lip; and (iii) more prevalence of radiographic oral manifestations: condylar defect, short mandibular ramus and irregular articular fossa. Generalizing our results, it could potentially help clinicians understand the magnitude of the benefits associated with the knowledge of the high dental alterations in a MPS population and consequently it could influence differential diagnosis, early treatment intervention, prevention and education of both patients and parents/caregivers about oral health.

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