Clinical Characteristics of Localized Aggressive Periodontitis in Primary Dentition

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Objectives: *Due to the low prevalence of localized aggressive periodontitis (LAP), clinical characteristics of LAP in primary dentition are derived from a few case reports/series in the literature. The goal of this study was to determine common clinical characteristics such as bone and root resorption patterns, in a series of cases with LAP in primary dentition. We hypothesize these cases present aggressive periodontal bone destruction starting mostly around first primary molars and atypical root resorption patterns.* ***Study Design:*** *We have evaluated 33 LAP cases in primary dentition for pattern of bone destruction, root resorption and early exfoliation.* ***Results:*** *Cases evaluated were aged 5-12 (mean=8.7 years). Thirty cases presented more severe bone loss on first than second molars, with relatively fast progression to second molars, altered pattern of root resorption, mostly external (n=16) and early exfoliation of primary teeth due to periodontal bone loss, rather than physiologic root resorption (n=11).* ***Conclusions****: This study showed common clinical characteristics found in LAP in primary molars, including possible initiation on first primary molars and abnormal root resorption patterns. These characteristics are important to be early identified and treated in order to prevent possible progression into the permanent dentition.*

Key words*: localized aggressive periodontitis, atypical resorption, primary molars*

INTRODUCTION

Children and adolescents can develop any of the several forms of periodontitis, the most common being plaque-induced gingivitis. Nevertheless, aggressive forms of periodontitis although affecting less than 3% of north-Americans,[1] are more commonly diagnosed in the younger population, while chronic periodontitis is more commonly diagnosed in adults.[2]

Localized Aggressive periodontitis (LAP) is a less common form of periodontal disease, characterized by rapid progression, early age of onset, affecting systemically healthy individuals, mostly African descent, usually presenting no severe signs of clinical periodontal inflammation or much calculus around affected teeth, and a familial involvement.[1] When affecting permanent teeth, it also presents a unique clinical characteristic of rapid bone destruction around first molars and incisors, with vertical or "U" shaped bone defects upon radiographic observation. Secondary features that have been reported include phagocyte abnormalities and a hyper-responsive macrophage phenotype, although no diagnosed systemic diseases accompany these cases. [2,3]

This disease can also affect primary dentition, which was previously known as pre-pubertal periodontitits, less frequently reported in the literature, and often overlooked. Due to less frequent diagnosis of this disease at an early phase, the actual age of onset is actually unknown, although some authors have reported aggressive disease in young children as early as before the eruption of the 6-year

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molars. Suzuki (1988) reported cases presenting bone loss around primary molars (earlier called prepubertal periodontitis) between 5 and 8 years of age, [4] while Page (1983) first described this disease at an age of onset of 4 years of age or older. [5] Although initial review of reports of this disease stated premature exfoliation of primary teeth with aggressive periodontitis could not be observed, [6] later reports described early exfoliation of affected teeth, due to its rapid periodontal bone destruction, thus requiring early diagnosis and an effective periodontal treatment, [5,7,8] as some of these cases have been reported to progress to permanent dentition[9-13]. However, diagnosis of this disease in the primary dentition poses particular challenges, as other physiologic processes are usually going on at the same time. [1,6]

Previous studies and our preliminary results with our LAP population in Florida led us to believe that the disease in the permanent dentition can be early detected during primary dentition. A retrospective analysis of permanent dentition cases of our studied population showed that out of 23 cases of LAP in permanent dentition that previous radiographs could be obtained from their primary dentition ages, onset of bone loss at primary dentition was observed in 20 of them (87%), affecting them as early as 5 years of age. [14] Thus, treatment of this disease at early stages could prevent the progression of disease into permanent teeth, as suggested previously. [13,15,16]

Driven by our radiographic analyzes and literature reports, we also observed that patients with LAP in primary dentition may also present with different root resorption patterns. Earlier reports also mentioned pulp chamber anomalies in children with pre-pubertal periodontitis. [17,18]

Despite the low prevalence of periodontal disease in children, we have gathered a large population of African-American children with aggressive periodontal disease affecting permanent and primary dentition (clinicaltrials.gov # NCT01330719). Thus, the aim of this study was to evaluate some of the radiographic characteristics of different patterns of root resorption (internal and external), pulp chamber size and premature exfoliation of primary dentition, on teeth diagnosed with LAP in primary dentition, to confirm findings of previous few cases reported in the literature.

MATERIALS AND METHOD

Utilizing the clinical database of LAP cases already enrolled in our clinical trial (clinicaltrials.gov # NCT01330719), we looked at all 176 patients enrolled in our study with confirmed diagnosis of LAP in permanent and/or primary teeth. All images were retrospectively analyzed from patients previously enrolled in our study. The inclusion criteria for this study were: systemically healthy individuals, African Americans, aged 5 to 25 years, diagnosed with LAP as defined by the American Academy of Periodontology classification. [2,19] We retrospectively reviewed all these patients radiographs for the presence and patterns of bone loss in the primary dentition. Fifty-three patients presented radiographs in their primary dentitions. At least bite-wings needed to be present for the first analysis. Periapical evaluation was also conducted when these were present for the investigation of exfoliation patterns. Thus, only 49 were suitable to be analyzed due to radiograph suitability/quality and finally 33 cases presented clear signs of bone loss in primary dentition and confirmed LAP diagnosis to be evaluated here, which was a presence of radiographic bone loss (bone resorption) of >2 mm apical to the CEJ, localized on primary molars and or incisors, associated with pocket depth >4mm and attachment loss ≥2mm. A schematic table was created with a few characteristics to look for in these cases: bone loss pattern and teeth involved, root resorption patterns (internal, atypical external, and physiologic), pulp chamber size, possible contributing factors (such as caries, stainless steel crowns or prior endodontic treatment of involved teeth) and timing of exfoliation. Only the cases that presented clear signs of bone loss, with confirmed clinical diagnosis of LAP, and clear/good quality radiographs to be evaluated were included.

All evaluations were performed by two calibrated individuals (KS and LMS). Calibration was performed by the blinded evaluation and diagnosis of a random 30 sets of radiographs of LAP and periodontally healthy controls prior to this study. Individuals were considered calibrated once at least 90% of diagnosis achieved a perfect match, including the severity of bone loss.

Chi-square analysis was performed to compare the presence of radiographic characteristics observed (prevalence of different patterns of root resorption (internal and/or external), pulp chamber size and premature exfoliation of primary dentition, on teeth previously diagnosed with LAP). Prism software was utilized to perform this analysis (GraphPad Prism, version 6, La Jolla, CA)

RESULTS

As part of a NIH funded study (clinical trial registration: Clinicaltrials.gov registration *#NCT01330719),* 176 LAP cases were diagnosed in north Florida. That study started in 2006, more specifically at the Leon County Health Department, Tallahassee, where first cases of LAP were observed. The study then expanded to include Duval County Health Department, Jacksonville (2010) and then recently to Jackson County, Marianna, and to south Florida, in Collier County, Naples.

A final count of 33 cases of LAP affecting the primary dentition with suitable radiographs and clear presence of bone loss and confirmed diagnosis were observed and evaluated for specific clinical characteristics of different patterns of root resorption (internal and external), pulp chamber size and premature exfoliation of primary dentition, on teeth diagnosed with LAP (age range 5-12 years, mean age 8.7 years).

When looking at resorption patterns of the roots, 16 cases with abnormal root resorption patterns were found, all of them with signs of external root resorption (see *figure 1* for an example), and 7 of those with both external and internal independent of other contributing factors (see *figure 2* for example, p=0.037). Eleven cases were found with confirmed early tooth loss due to periodontal bone loss (see *figure 3*) and 7 cases could not be determined due to lack of follow up radiographs. Six cases were found to have enlarged pulp chambers on teeth associated with LAP affected teeth, although some appeared to be confounded with other contributing factors, such as caries or internal/external root resorptions (see *figure 4*). Five cases presented local factors, such as caries (2) or stainless steel crowns (3) that could be associated with one of the teeth presenting root resorption (see table 1 for all these characteristics).

Most teeth affected were first and second primary molars (30 cases, p<0.0001) with one of those cases affecting both primary molars and a canine (*figure 2B*), 2 cases affecting only first primary molars (*figure 5*) and one case affecting only second molar (*figure 6*). We noticed from previous radiographs and bone loss patterns in all cases that the first molar is usually the first one affected by bone loss and the disease migrates to the second primary molar in less than one year (*figure 7*).

Figure 1: Illustration of a case of bone loss in primary dentition of an LAP case diagnosed in permanent dentition. Note in 1A, 9 year-old and bone loss present around primary molars, including furcation on most teeth and external root resorption on A distal (red arrow). 1B: patient now at 11 years with no apparent signs of bone loss on permanent dentition. Note initial bone resorption on 19 distal, often hard to diagnose at this stage. 1C: progression of bone loss on 19D and 30D one year later. Patient went through orthodontic treatment at this time. 1D: Patient now at age 15, referred to a periodontist for treatment. Vertical bone loss now severe on 19 and 30.

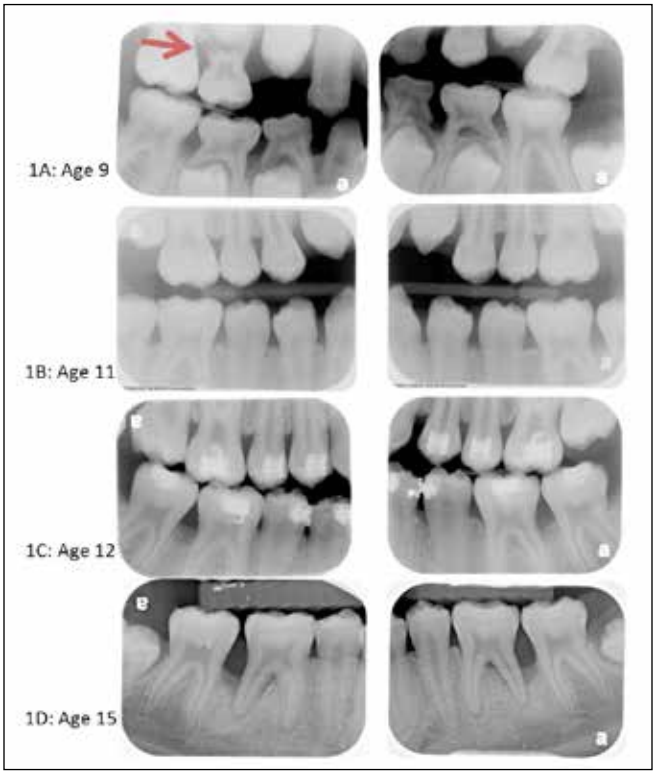


Figure 2A: Patient age 8 diagnosed with severe LAP on primary molars. Note greater bone loss on first primary molars and initiation of loss on mesial of second primary molars, indicative of disease initiating on first molars. Internal and external root resorption can be observed on L distal root, and absence of apical root resorption on teeth L and S, which are being lost primarily due to periodontal bone loss. Figure 2B: Patient age 8 diagnosed with severe LAP on primary molars and upper canines. Note internal and apical external root resorption on L (red arrow) and greater bone loss on first primary molars with bone loss starting on the mesial of second primary molars, indicative of disease initiating on primary molars.

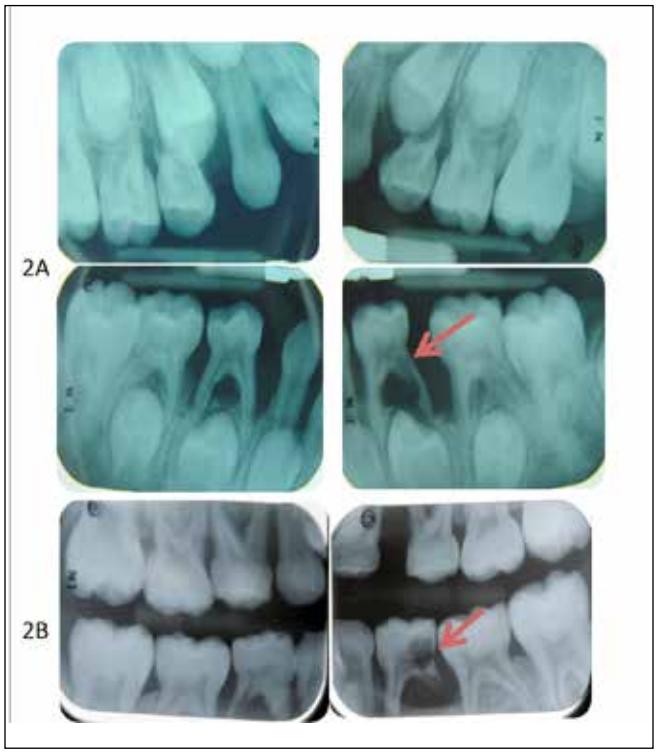


Table 1: Clinical characteristics of LAP in primary dentition

Patient totals	Mean age at first sign of Bone loss	Early tooth loss*	Atypical root resorption pattern	External root resorption	Internal root resorption	Pulp chamber enlargement	Presence of contributing factors**	Systemic/ Environmental factors
33	7.87±5.6 (5-12)	11 7?	16	16	7	6	5	none

Affected teeth	Both first and second molars	Only 1st molar	Only 2nd molar	Other teeth
Number of cases	30	2	1	1 (both molars +canine)

All clinical characteristics of primary teeth with localized aggressive periodontitis (LAP). *11 cases showed definitive early loss according to previous and future radiographs, age of patient as well as eruption patterns of other teeth and upcoming permanent teeth. 7 cases were deemed undetermined (?) as all these conditions could not be properly accessed. ** contributing factors included caries (2) or stainless steel crowns (3) around at least one tooth presenting bone loss.

Figure 3: LAP in primary dentition at 9 years. 3A: severe bone loss around all primary molars, greater severity on the first molars, indicative of initiation pattern of disease on the first primary molars. Initial external resorption can be observed on B (red arrow). Note also lower primary molars being lost due to periodontal bone loss in the absence of physiologic root resorption. 3B: Four months later. Note progression of bone loss, and atypical pattern of external root resorption on B, with no apical/physiologic root resorption (red arrow). On lowers, note early loss of L and progression on periodontal bone loss around S without apical root resorption.

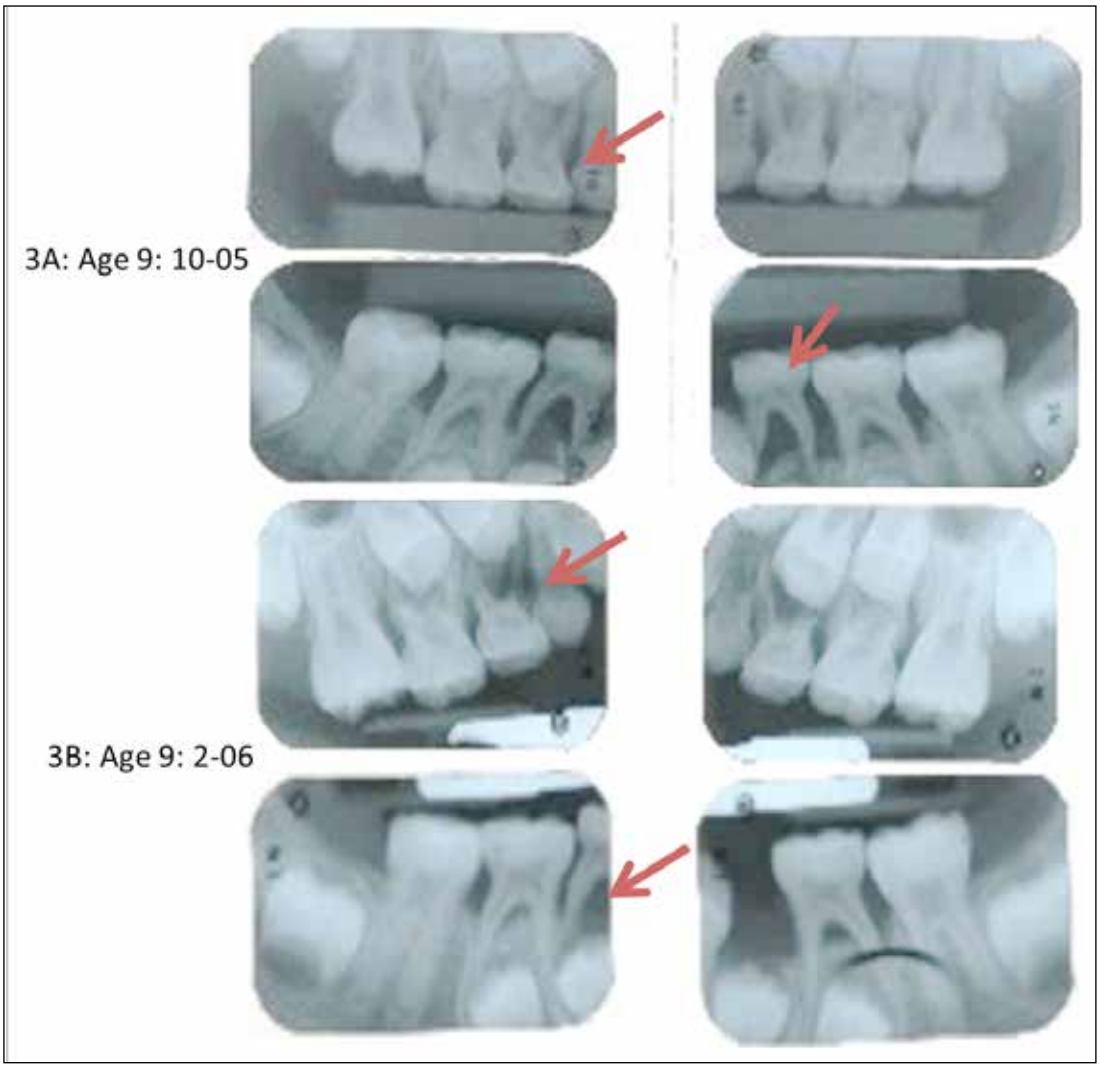


Figure 4: 8 year-old patient with LAP in primary dentition. Note bone loss around mostly first primary molars and some on the second primary molar mesial. Note what appears to be an enlarged pulp chamber on teeth S and L. Tooth S appears to be also associated with internal/external root resorption.

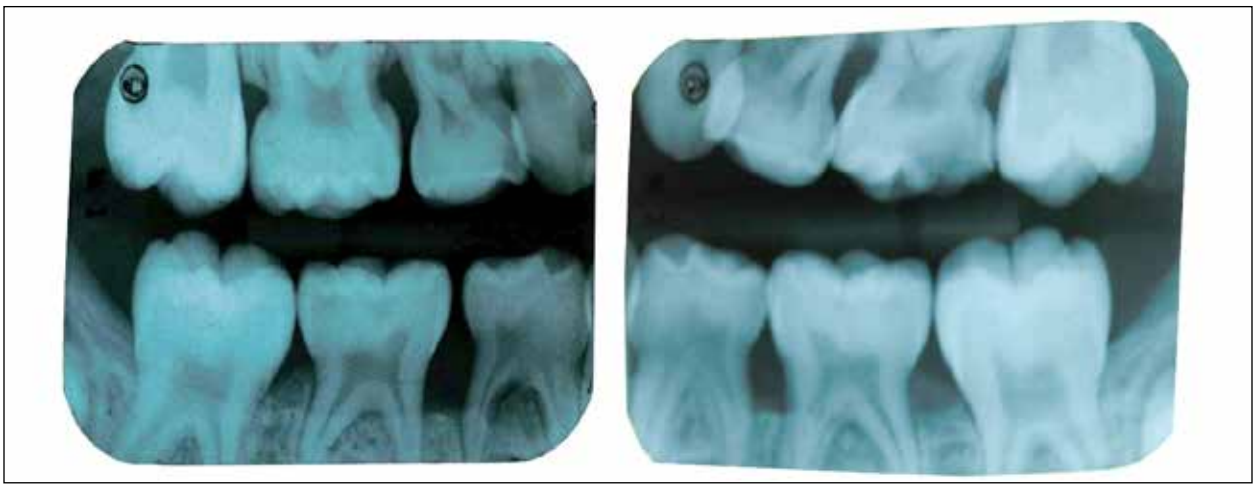


Figure 5: 7 year-old patient with LAP in primary dentition. Note bone loss around first primary molars only (teeth I and L) and no involvement of second primary molar yet (although some calculus can be observed on enamel of tooth T mesial with no bone loss).

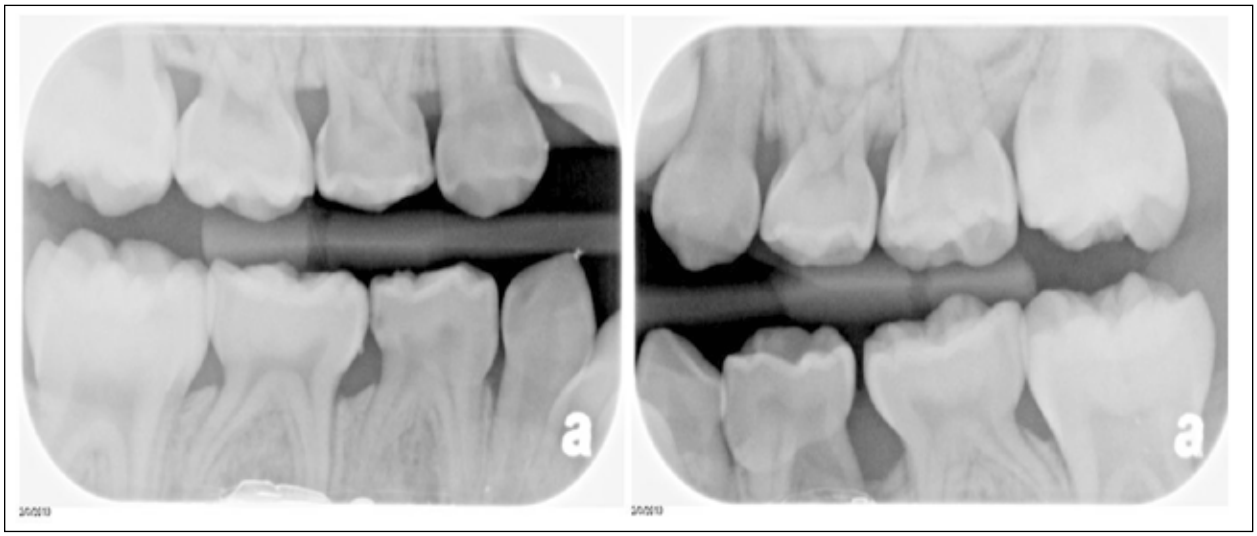


Figure 6: 7 year-old patient with LAP in primary dentition. Note bone loss around only second primary molars (teeth J and K distal surfaces–arrow) and no involvement of first primary molars (7A). 7B: Periapical of tooth K 9 months later clearly showing vertical defect still at tooth K distal.

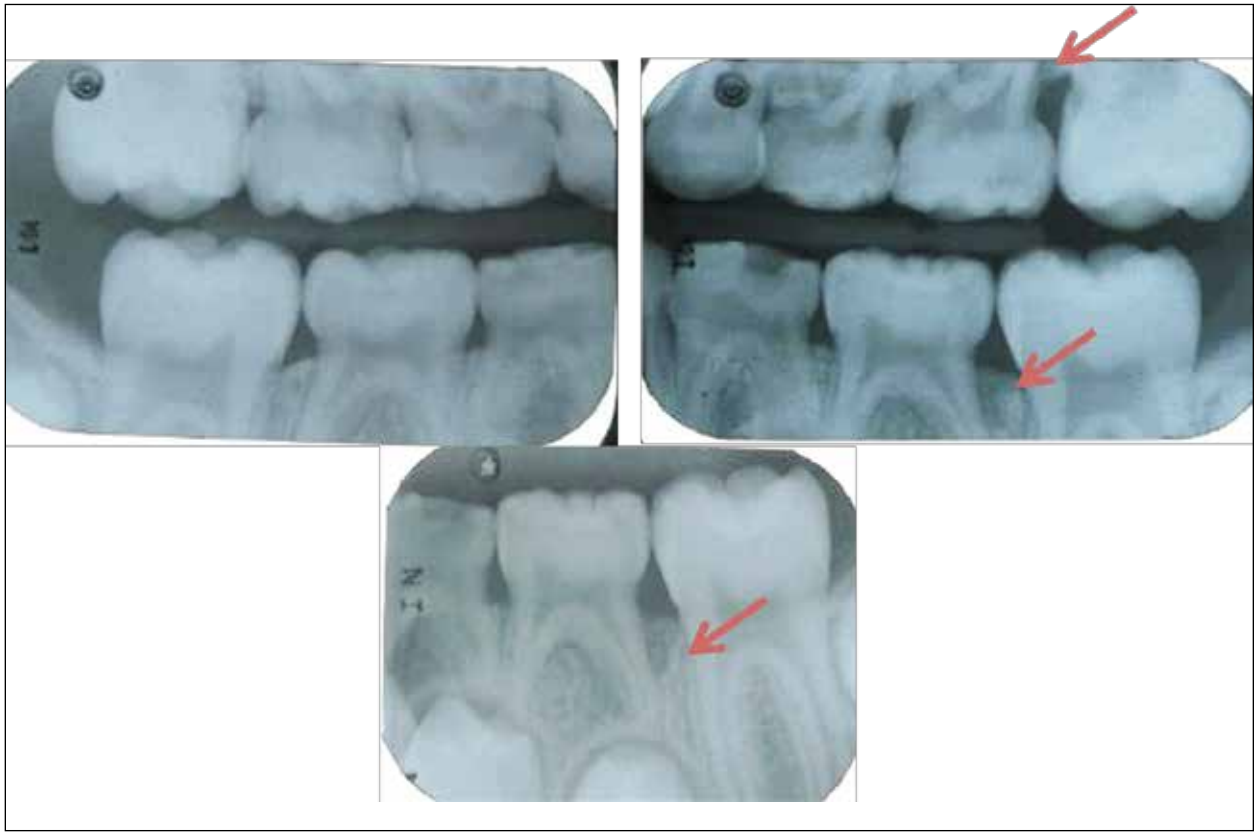
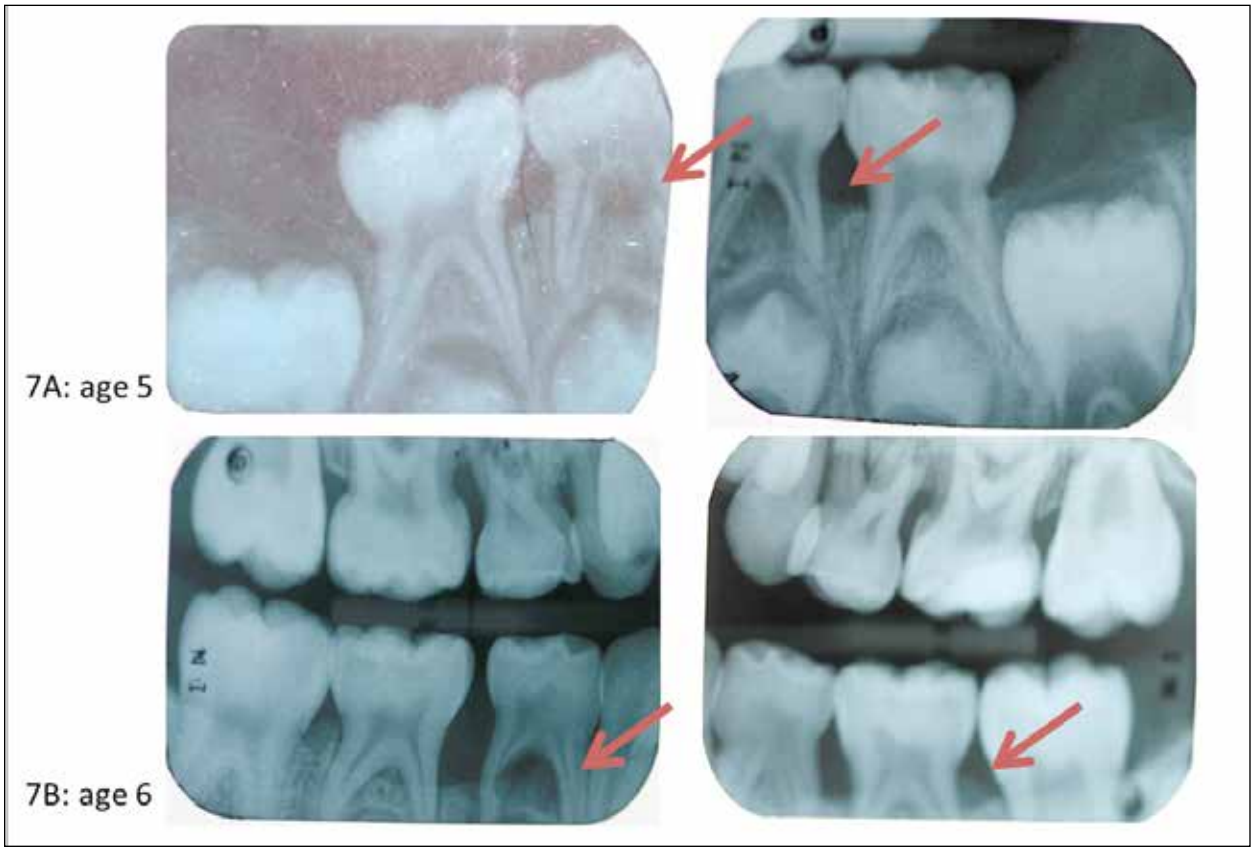


Figure 7: Patient aged 5 years and 10 months (5-2006) presenting bone loss on L furcation and distal root (arrow) and at figure 7A. Note external root resorption associated with furcation involvement on S (7A). 7B patient is now 6 years and 8 months (3-2007). Note clear progression of bone loss to the second primary molars and continuation of external root resorption on distal root of tooth S and progression of bone loss, now including T and K. Note somewhat enlarged pulp chamber on affected teeth.



DISCUSSION

In the present study we reviewed several cases of LAP in primary dentition to confirm much of the controversy regarding its clinical characteristics, such as early exfoliation patterns and enlarged pulp chambers.[17-19] We found that the predominant characteristics of ~~this~~ LAP in this African-American children ~~diagnosed with LAP~~ to be: ~~disease~~ affecting mostly first primary molars maxillary, mandibular or both, possibly initiating at first primary molars, due to the pattern of more severe bone loss on these teeth, and rapidly progressing (mostly within a year) to the second primary molar. This progression does not often occur that rapidly in permanent dentition affected[1]. A possible reason for that initiation in the first primary molar could be the same reason hypothesized as to why LAP also start in the first permanent molar: the first primary molar is also the first of the molars to erupt in the oral cavity, and to accumulate dental plaque and to elicit a host inflammatory response. A specific microbiota as well as a unique host response to this microbiota then begins the process of break down in these teeth,[20] and somehow the host arrest this process at one point, only in a few cases continuing its progression to other teeth in the mouth. [1] However, this has been reported only in permanent dentition and little is known about the process of progression of this disease in primary dentition. We reported here, for the first time, a very common (30 out of 33 cases) more severe involvement of the first primary molar with involvement and progression of disease to the second primary molars, as early as one year, which has never been reported before, although cases involving both first permanent and primary molars have indeed been previously reported. [11] Moreover, the reason why there could be rapid progression of the disease to the second primary molar, which does not usually happen in the permanent dentition, is the fact that second primary molars usually erupt within a year or so after first primary molars. On the contrary, second permanent molars will erupt much later, approximately 6 years after first permanent molars have erupted. Thus, we hypothesize here that the host may be able to arrest the progression of this disease in the permanent dentition before second molars erupt, thus confining the disease only to first permanent molars. The relatively fast eruption of the second primary molars after the first primary molar may be the reason why progression happens in this dentition.

In all our cases of LAP in primary dentition so far diagnosed, we only found 1 case with concomitant canine involvement.

Another characteristic we found on this disease was an atypical pattern of root resorption (not a usual physiologic apical resorption often encountered at this age). What we observed quite often here was a pattern of either external (most cases) or internal root resorption, as well as a predominant periodontal bone loss compared to a somewhat "delayed" physiologic root resorption of the affected roots, leading to early exfoliation of primary dentition due to the

periodontal bone loss rather than the biological process of apical root resorption. This different pattern of root resorption has been reported before. [5]

Much controversy exists about the mechanism(s) of cellular resorption of bone versus teeth. Although it is believed that 'odontoclasts' possess properties common to 'osteoclasts', the regulatory mechanisms that mediate odontoclastic tooth resorption may differ from osteoclastic bone resorption. [21-26] Indeed, key differences in odontoclastic and osteoclastic activity have been reported in the literature: a) the cell size – odontoclasts are smaller and have fewer nuclei when compared to osteoclasts;[21,25] b) regulation by systemic factors – dentin resorption, as opposed to bone resorption, is not regulated by parathyroid hormone (PTH),[27] and c) response to drugs – indomethacin seems to enhance root resorption but doesn't interfere with bone resorption during orthodontic tooth movement.[28,29] Thus, the unusual pattern of tooth resorption in LAP patients here support previous research findings that osteoclasts and odontoclasts do not respond identically to inflammatory mediators. Our clinical and radiographic observations indicated that atypical patterns of external root resorption occurs and apical/physiological root resorption appears to occur more slowly while surrounding bone resorption occurs more aggressively around primary teeth in LAP patients. It has been reported an increase in odontoclastic activity in the pulp chamber of primary teeth even in the absence of trauma or cavities,[30] the most common etiologic factors of internal root resorption, which we have also shown in a few cases here. One plausible hypothesis is that the immunological and genetic traits associated with LAP have a disruptive role in the coordination of 'clastic' cell activity. The inflammatory process going on during LAP is known to accelerate osteoclastic activity and may indeed accelerate root resorption.[22,31] However, in a pathological situation as the one presented in this study, it may trigger an imbalance of clastic activity, dominated by osteoclastic activity, while odontoclastic activity is disrupted, causing either delay of the physiologic root resorption, or pathological external or internal root resorption, as shown in this report. Thus, the excessive osteoclastic activity induced by the inflammatory process of periodontal disease here may in fact accelerate root resorption, as previously reported,[22] but in this case, in a pathological way. The fact that an aggressive, almost acute inflammatory process is going on around these teeth this early in life, may serve as a trigger for this disruptive clastic activity around the primary roots. However, the mechanisms by which the differentiation of osteoclasts and odontoclasts and which dominant activity occur are not fully understood.[22] Earlier reports have indeed corroborated that LAP is associated with early exfoliation of primary teeth.[5,7,8] Most of those reports, however, showed the loss of the tooth being actually related to loss of bone around roots and not accelerated root resorption, which was also shown in some of our cases here.

Another controversial topic is the enlarged pulp chambers, as a characteristic of LAP affected primary molars. Page et al. reported abnormally large pulp chambers and different patterns of root resorption in patients with advanced bone loss in primary dentition. [5] It is known that there is an increase in odontoclastic activity in the pulp chamber of primary teeth even in the absence of trauma or cavities,[30] the most common etiologic factors of internal root resorption, and this could be the cause of this observed entity here. Thus, some of the cases of enlarged pulp chamber found here could be a result of internal process of root resorption in these teeth surrounded by an inflammatory process.

Lastly, although all children in the present study were deemed systemically healthy, some of them were ongoing pre-puberty or puberty stages. The influence of sexual hormones in the LAP inflammatory process is unknown at this point. However, we do know that sexual hormones can influence inflammation during puberty[32] and also during pregnancy.[33] Another systemic factor that could be considered here, especially in the cases associated with root resorption and LAP is the serum levels of phosphate. Although no children have been previously diagnosed with hypophosphatemia, lower levels of phosphate have been associated with some cases of LAP, [5] as well as root resorption. [34]

A possible limitation of this study is the clear determination of early tooth loss by radiographic analysis. The age range of tooth loss is not well defined and varies tremendously individually and are coordinated by many factors. [35] Hence, many of the cases in this study (n=7) were deemed undetermined for this characteristic. We only deemed early exfoliation where there was clear early loss of the primary tooth according to age and also formation and approximation of the permanent tooth bud underneath.

In conclusion, we reported clinical characteristics found in an African-American population diagnosed with LAP in the primary dentition, including first and second primary molars mostly affected, with a possible initiation in the first primary molar, and an unusual pattern of root resorption around LAP affected teeth, including mostly external root resorption and a few cases of internal root resorption, not associated with normal/biological pattern of root resorption due to exfoliation or contributing factors.

CONCLUSIONS

- LAP in primary dentition in the African-American population most commonly affects molars, most commonly starting with the first primary molar, relatively fast progressing to the second primary molars.
- This disease may also present altered root resorption patterns, including external and internal root resorptions associated with teeth affected by periodontal bone loss, independent of other contributing factors.
- Early exfoliation of LAP affected primary teeth may occur in some cases, depending on the aggressiveness of the disease and timing of rendered treatment, usually due to periodontal bone loss rather than physiologic apical root resorption.
- Knowledge of the clinical characteristics of LAP disease in primary dentition is essential for proper early diagnosis and successful treatment of this disease and possible prevention of future progression into the permanent dentition.

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