Case report

Dental considerations in a 4-year-old girl with Lennox-Gastaut Syndrome. Case report and literature review.

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Abstract

We present the developmental, oral, clinical, radiographic findings and oral treatment of a 4-year-old girl presenting with Lennox-Gastaut syndrome (LGS), which is a severe disabling childhood epilepsy diseases that is treated with one or multiple anti-epileptic drugs (AEDs). The

child was wheel-chair bound, developmentally delayed, gastrostomy tube (G-tube) fed, and suffered from multiple seizures and infantile spasms.~~,~~ The child's medical history included an under-developed pituitary gland, gastro esophageal reflux disease, vision and hearing impairment, history of chronic aspiration pneumonia, and allergies. The oral findings included no carious lesions, heavy calculus accumulation, spontaneous bleeding from the gingiva, generalized gingival hyperplasia (GH) and abnormal increased mobility in several ~~primary~~deciduous teeth. The comprehensive radiographic and clinical examination and the treatment under general anesthesia are described. ~~The etiologies of the calculus accumulation and GH are reviewed.~~

Key words: calculus, gingival overgrowth, anti-seizure medication, Lennox-Gastaut Syndrome

Introduction

Lennox-Gastaut syndrome (LGS) is a severe and disabling childhood epilepsy that is characterized by a triad of symptoms: 1) ~~generalized treat~~ seizures resistant to multiple therapies~~;~~ 2) slowness of intellectual growth and cognitive impairment; 3) a specific electroencephalogram (EEG) disturbance called a slow spike-and-wave pattern that is present when the child is awake.[1-5] LGS patients may have multiple daily seizures that may cause sudden and unpredictable stiffening followed by a drop to the ground; this being a key diagnostic feature.[5-7] The pharmacologic treatment may include one or multiple antiepileptic drugs (AEDs),[4] some of which have the potential to induce gingival hyperplasia (GH).

A review of the literature identified only one report of the oral findings in a LGS patient, ~~of~~ a 26-year-old female who had macroglossia, supragingival as well as subgingival calculus, red,

swollen and friable gingiva with generalized bleeding and localized suppuration, and gingival recession.[4] The present manuscript includes an additional , comprehensive case report of a 4-year-old girl with LGS, and presents a review of the literature on LGS and related anti-seizure medication that may have ~~-~~induced gingival overgrowth.

Case presentation

A 4.5-year-old Caucasian female with LGS was referred to a University Clinic for dental treatment. The medical history indicated that *she* was born at 32 weeks of gestation, along with her healthy twin. The patient had infantile seizures and spasms 15-16 times per day and was diagnosed with LGS. As a result of her condition, she experienced ~~Her medical history was significant for~~ developmental delay, wheelchair-bound, had a gastrotomy tube (G-tube), under-developed pituitary gland, gastro esophageal reflux disease, vision and hearing impairments, history of chronic aspiration pneumonia, allergies to Depakote and Amoxicillin and leukodystrophy (degeneration of the white matter in the brain[8]). Her medications included; Vigabatrin, Clobazam, Topiramate, Fycompa, Diazepam and Rufinamide reducing the daily seizures to 3-6, and Albuterol/atropine via nebulizer. At the time of this study, she had recently been hospitalized dye to seizures,~~Recent hospitalizations resulting from seizures,~~ chronic pneumonia, and adrenocorticotropic hormone therapy. Her~~The~~ surgical history included adenoid and tonsils removal, Nissen fundoplication with hernia repair, and G-tube placement. The chief complaint as expressed by her mother was risk of aspirating exfoliating primary teeth: the previous night the patient had a seizure, after which she was “choking and was missing a lower tooth that was swallowed or aspirated”.

On examination, she had no apparent respiratory difficulties,but was non-verbal, had a small "hypoplastic" face, inability to cooperate, extensive drooling, short stature and slight overweight.[9] A limited oral examination revealed sialorrhea, deciduous ~~primary~~ dentition with missing mandibular deciduous~~primary~~ central incisors, heavy calculus on the majority of teeth surfaces, abnormal mobility (2-3 mm) in both mandibular ~~primary~~deciduous lateral incisors (teeth #N and #Q), as well as generalized moderate GH. Tongue size appeared normal. A chest radiograph did not reveal tooth aspiration.

The patient ~~MG~~ was admitted to the hospital the day before the dental treatment under general anesthesia (GA), maintained with intravenous fluid to avoid the conflict between being fed ~~*nil*~~ *per os* and her need for frequent gastrostomy tube (G-tube) feeding. The mother reported that the patient was apparently having pain while grinding her teeth. Under GA, ~~a~~ radiographic and clinical examinations revealed no caries, no evidence of dental pulp pathology (Figure 1), all maxillary ~~primary~~deciduous incisors (Teeth D, E, F, G), and both mandibular lateral ~~primary~~deciduous incisors (Teeth N and Q) had abnormal mobility (about 3 mm), nearly all teeth were covered with heavy calculus (Figure ~~2~~), generalized moderate GH, and a band of gingiva over the occlusal surface of the mandibular right first ~~primary~~deciduous molar (~~Tooth S, Figure 3A~~Figures 2,3, 4A), and gingiva over the occlusal surface of the maxillary right first deciduous ~~primary~~ molar (Tooth B, Figure 4a). The GH was non-hemorrhagic, soft, slightly fluctuant and pink (Figures 2, 3~~a&b, 4a&b~~). Calculus removal was accomplished with an ultrasonic and hand instrumentation, followed by an application of a fluoride varnish. The gingival tissue over teeth B and S were removed with a surgical blade (Figures ~~3b &~~ 4b). Teeth # D, E, F, G, N and Q were extracted. The post-operative recovery was uneventful .The patient's irritability associated with her oral pain has subsided significantly.~~.~~

Discussion and literature review

Dr. William Lennox, first described LGS in the 1930s, Lennox and Davis later reported its triad, which was further expanded by Gastaut.[11-12] The median onset age of LGS is about 4 years (range: 0.6-28.9 years) with a peak onset of 5 years.[13-14] LGS is uncommon (3-10% of childhood epilepsy) and has a mortality rate ranging from 3% to 7%.[2, 3, 12] The ~~tonic~~ seizures are characterized by an EEG diffuse high voltage slow wave followed by generalized low voltage fast activity, reflecting sustained fast neurological firing over a wide cortical area.[5, 15] 80% of LGS patients will continue to have seizures into adulthood.[2, 16]

Based on our literature review, this is the second case in which the oral characteristics of LGS are described, and the first one in a child. In this~~our~~ case the dental consideration included behavioral and management issues, gingival hyperplasia as a result of side effects caused by anti seizure medication, poor oral hygiene (OH) and a risk of aspiration from loose teeth and difficulties in swallowing. Comparison of both cases is restricted by the patients' ~~different~~ age ~~groups~~difference~~;~~. ~~t~~The previous report was in a 26-year-old female.[4] Both cases received AEDs and had GH and severe calculus accumulation, the previous case had periodontitis and macroglossia that encumber proper OH while in the present case the tongue size was normal and there was ~~increased~~ abnormal tooth mobility~~. with no radiographic evidence of alveolar bone loss~~. Oral pain was reported in the previous case associated with gingival swelling, gingival recession and periodontitis while in the present case, pain was assumed to be related to biting on the gingival tissue over the occlusal surfaces.

GH commonly starts with the eruption of the permanent dentition and may be influenced by genetic predisposition.[17] However, in the present case there was no history of GH in the family~~,,~~[17] indicating that the GH may have been caused by one or more AEDs most likely

vigabatrin. The aim of AEDs is to control or decrease seizures without producing unacceptable adverse effects that impair quality of life. ; hHowever, AEDs have been most frequently associated with drug side effectsadverse drug reactions.[17] The pharmacologic treatment of LGS includes AEDs such as Vvigabatrin, Vvalproates, Ffelmabate, and Bbenzodiazepines which may potentiate each other's side effects, as in cases in which GH is potentiated by the combination of phenytoin and calcium channel blockers, or cyclosporine and calcium channel blockers.[18-20]

Interestingly, multiple AEDs have an additive effect on GH, that might explain the additive effect of multiple anticonvulsant therapy to GH.[25]

GH might include an abundance of dense connective tissue or acellular collagen that can be an impediment to tooth eruption.[36, 37] Delayed eruption has also been associated with severe bruxism in children with cerebral palsy.[38, 39] In the present case, the primary dentition was normal.[40] However, the clinical crowns of the deciduous primary teeth appeared shorter than normal and there was gingival tissue at the occlusal surfaces of teeth B and S, suggesting a combination of GH and delayed eruption that could be related to the GH and bruxism (Figures ,3a, 3b).

Despite the positive correlation between plaque scores, gingival inflammation, and severity of GH in children, the role of OH as an etiologic factor for GH has not yet been fully clarified since most of the studies have been cross-sectional.[19, 25] However, the relevance of OH is emphasized in the previously reported LGS case in which non-surgical periodontal therapy was effective in controlling periodontal disease, and prevention of oral diseases is preferable for a high-risk patients.[4] In the present case however, OH performance is complicated by the child's inability to perform the most simple measures and to cooperate with her parents.

A full mouth gingivectomy in the primary dentition was reported by Breen et al. (2009) in a case of a 28 month old with hereditary gingival fibromatosis in which only 4 mandibular teeth were partially erupted.[17] In the present case, we included the removal of the gingival tissue from the occlusal surfaces of the primary molars that most likely were the origin of oral pain (Figures 3~~b~~ & 4b); in retrospective, a gingivectomy could have been adequate for the maxillary right primary cuspid and lateral incisor that had minimal clinical crowns (Figure 4a); the patient will continue to be under follow-up and will be scheduled for gingivectomy if required.

Children and adolescents who are unable to meet their nutritional needs orally and depend on GT ~~tube~~ feeding at a significantly increased risk of poor oral health, specially tartar, accumulation an subsequent gingivitis.[10, 41, 46] In the present case, the possibilities of recurrence of calculus accumulation are high. ~~Based on our search of the literature, it appears that this is the youngest case reported with severe generalized calculus accumulation~~.

Aspiration of exfoliating primary teeth is apparently ~~most uncommon or non-reported since our review of the literature disclosed only one~~uncommon. A case of aspiration of a maxillary primary cuspid by a 9 year 11 month old child with cerebral palsy was reported, the authors have -emphasized ~~ing the fact that~~ the possibility of aspiration of primary teeth is ~~exacerbated~~ in debilitated patients.[47] A~~a~~lso, avulsion of primary teeth due to trauma and their aspiration is possible.[48] This emphasizes the need to ~~consider the need~~ to investigate ~~refer~~ children who “lost” a primary tooth that cannot be found ~~to~~using a chest radiograph, especially in children with developmental disturbances, and a history of aspiration pneumonia which involves the entry of infectious pharyngeal contents into the lower airway.[41] Relevant is the fact that low salivary flow associated with gastric tube (GT) feeding may predispose the growth of salivary bacteria that, when mixed with food or liquid, provide a substantial inoculum to the lungs if aspirated.[41]

In conclusion , LGS in young children presents a significant challenge to the dental professional including GA consideration, G-tube issues, poor oral hygiene and gingival hyperplasia , both The neurologist and the pediatric dentist should be aware of the potential complication and work as team on behalf of the patient and the family of the LGS patient.

References

1. Heiskala H: Community-based study of Lennox-Gastaut syndrome. Epilepsia 38: 526-31, 1997.
2. Crumrine PK: Lennox-Gastaut syndrome. J Child Neurol; Suppl 1: S70-75, 2002.
3. Shields WD: Diagnosis of Infantile Spasms, Lennox-Gastaut Syndrome, and Progressive Myoclonic Epilepsy. Epilepsia 45: 2-4, 2004.
4. Abu Saleh T, Stephen L. Lennox Gastaut syndrome, review of the literature and a case report. Head Face Med. 9;4:9. 2008. http://www.ncbi.nlm.nih.gov/pubmed/18541034. Accessed February 26, 2016.
5. Archer JS, Warren AE, Jackson GD, Abbot DF. Conceptualizing Lennox-Gastaut syndrome as a secondary network epilepsy. Front Neurol 30: 225, 2014. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4214194/ Accessed February 26, 2016.
6. Markand ON: Lennox-Gastaut syndrome (childhood epilepticencephalopathy). J Clin Neurophysiol 20: 426-41, 2003.
7. Berg AT, Berkovic SF, Brodie MJ et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE commission on classification and terminology. 2005-2009. Epilepsia 51: 676-85, 2010.

8. National Institute of Neurological Disorders and Stroke. Leukodystrophy Information Page. http://www.ninds.nih.gov/disorders/leukodystrophy/leukodystrophy.htm. Accessed February 26, 2016.
9. American Academy of Pediatric Dentistry. Reference manual. Resource section, 2 to 20 years: Girls. Stature-for-age and weight-for-age percentiles. 36: 381, 2015
10. Norwood KW, Slayton RL. Oral health for children with developmental disabilities. Pediatrics 131: 614-9, 2013.
11. Gastaut H, Roger J, Soulayrol R, Tassinari CA, Regis H, Dravet C: Childhood epileptic encephalopathy of children with diffuse slow spike-waves (otherwise known as "petit mal variant") or Lennox syndrome. Epilepsia 7: 139-179, 1966
12. Trevathan E: Infantile Spasms and Lennox-Gastaut Syndrome. J Child Neurol 17:9-22, 2002
13. Goldsmith IL, Zupanc ML, Buchhalter JR. Long-term seizure outcome in 74 patients with Lennox-Gastaut sundrome: effects of incorporating MRI head imaging in defining cryptogenic subgroup. Epilepsia 41: 395-9, 2000.
14. Arzimanoglou A, French J, Blume W T et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. Lancet Neurol 8: 82–93, 2009.
15. Tao JX, Ray A, Hawes-Ebersole S, Ebersole JS. Intracranial EEG substrates of scalp EEG interictal spikes. Epilepsia 46: 669-76, 2005.
16. Van Rijckevorsel K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. Neuropsychiatr Dis Treat 4: 1001–19, 2008.
17. Breen GH, Addante R, Black CC. Early onset of hereditary gingival fibromatosis in a 28-month-old. Pediatr Dent 31; 4:286-8, 2009.

18. Rees TD. Drugs and oral disorders. Periodontol 1998; 18:21-36, 2000.

19. Mariotti AJ. Gingival Diseases. In: Bimstein E, Needleman HL, Karimbux N, Van Dyke TE, eds. Periodontal and gingival health and diseases. Children, adolescents and young adults. Martin Dunitz Ltd; 2001: 31-48.

20. Davidovich E, Schwarz Z, Davidovitch M, Eidelman E, Bimstein E. Oral findings and periodontal status in children, adolescents and young adults suffering from renal failure. J Clin Periodontol 32: 1076-82, 2005.

21. Ferrendel JA, Kinscherf DA. Phenytoin: effects on calcium flux and cyclic nuceotides. Epilepsia 18: 331-6, 1977.

22. Seymour RA, Heasman PA. Drugs and the periodontium. J Clin Periodontol 1988;15:1-16.

23. Brown RS, Arany PR. Mechanism of drug-induced gingival overgrowth revisited: a unified hypothesis. Oral Dis 21:e51—61, 2015.

24. Li WL, Wu CH, Yang J, Tang M, Chen LJ, Zhao SL. Local Inflammation Alters MMP-2 and MMP-9 Gelatinase Expression Associated with the Severity of Nifedipine-Induced Gingival Overgrowth: a Rat Model Study. Inflammation 38: 1517-28, 2015.

25. Doufexi A, Mina M, Ioannidou E. Gingival overgrowth in children: epidemiology, pathogenesis, and complications. A literature review. J Periodontol 2005;76: 3-10, 2005

26. Nishikawa S, Nagata Toshihiko, Morisaki I, Oka T, Ihida H. Pathogenesis of drug induced gingival overgrowth. A review of studies in the rat model. J Periodontol 67: 463-71, 1996.

27. Rx list. The internet Drug index, http://www.rxlist.com/fycompa-side-effects-drug-center.htm. Accessed February 26, 2016.

28. Katz J, Givol N, Chaushu G, Taicher S, Shemer J. Vigabatrin-induced gingival overgrowth. J Clin Periodontol 24: 180-2, 1997.

29. ONFI® (clobazam) CIV, https://onfi.com Accessed February 26, 2016.
30. Rx list. The internet Drug index, http://www.rxlist.com/topamax-drug.htm. Accessed February 26, 2016.
31. http://www.drugs.com/pro/diastat.html. Accessed February 26, 2016.
32. Ferruca E. Cloyd J, Critchley D, Fuseau E. Rufinamide: Clinical pharmacokinetics and concentration-response relationships in patients with epilepsy. Epilepsia 49:1123-41, 2008.
33. Kluger G, Kurlemann G, Haberlandt E et al. Effectiveness and tolerability of rufinamide in children and adults with refractory epilepsy: Firs European experience. Epilepsy Behav 14: 491-5, 2009.
34. Guerrini R, Zaccara G, la Marca G, Rosati A. Safety and tolerability of antiepile[ptic drug treatment in children with epilepsy. Drug Saf 35: 519-33, 2012
35. Gillham R, Baker G, Thompson P, Birneck K et al. Standardisation of a self-report questionnaire for use in evaluating cognitive, affective and behavioural side-effects of anti-epileptic drug treatment. Epilepsy Res 24; 47-55, 1996.
36. Suri L, Gagari E, Vastardis H. Delayed tooth eruption: pathogenesis, diagnosis and treatment. A literature review. Am J Orthod Dentofacial Orthop 126: 432-45, 2004.
37. Katz J, Guelmann M, Barak S. Hereditary gingival fibromatosis with distinct dental skeletal and developmental abnormalities. Pediatr Dent 24: 253-6, 2002.
38. Rodriguez dos Santos MT, Masiero D, Ferreira Novo N, Lorenzetti Simionato MR. Oral conditions in children with cerebral palsy. J Dent Child 70:40-6, 2003.
39. Staufer K, Hanadeh S, Gesch D. Failure of tooth eruption in two patients with cerebral palsy and bruxism – a 10-year follow up: a case report. Spec Care Dentist 29:169-74, 2009.

40. American Academy of Pediatric Dentistry. Reference manual. Resource section, Dental growth and development 36: 371, 2014

41. Jawadi AH, Casamassimo PS, Griffen A, Enrile B, Marcone M. Comparison of oral findings in special needs children with and without gastrostomyPediatr Dent 26: 283-8, 2004.

42. Delima AJ, Sjodin BE, Tonetti MS, Bimstein E. Newman HN, Van Dyke TE. Periodontal diseases in children, adolescents and young adults. In: Bimstein E, Needleman HL, Karimbux N, Van Dyke TE (eds.) Periodontal and gingival health and diseases. Children, adolescents and young adults. Martin Dunitz Ltd. 2001:75-105.

43. Martins C, Siqueira WL, Oliveira E, Nicolau J, Primo LG. Dental calculus formation in children and adolescents undergoing hemodialysis. Pediatr Nephrol 27: 1961–6, 2012.

44. Cardoso AMR, Gomes LN, Silva CRD, de S. C. Soares, de Abreu MHNG, Padilha WWN, Cavalcanti AL. Dental caries and periodontal disease in Brazilian children and adolescents with cerebral palsy. Int J Environ Res Public Health 12: 335-53, 2015.

45. Jin Y, Yip H-K. Supragingival calculus: formation and control. Crit Rev Oral Biol Med 13: 426-41, 202.

46. Hidas A, Cohen J, Beeri M, Shapira J, Steinberg D. Salivary bacteria and oral health status in children with disabilities fed through gastrotomy. Int J Paediatr Dent 20: 179-85, 2010

47. Steelman R, Millman E, Steiner M, Gustafson R. Aspiration of a primary toth in a patient with tracheostomy. Spec care Dent 17:97-9, 1997.

48. Holan G, Ram D. aspiration of an avulsed primary incisor. A case report. Int J Paed Dent 10: 150-2, 2000.

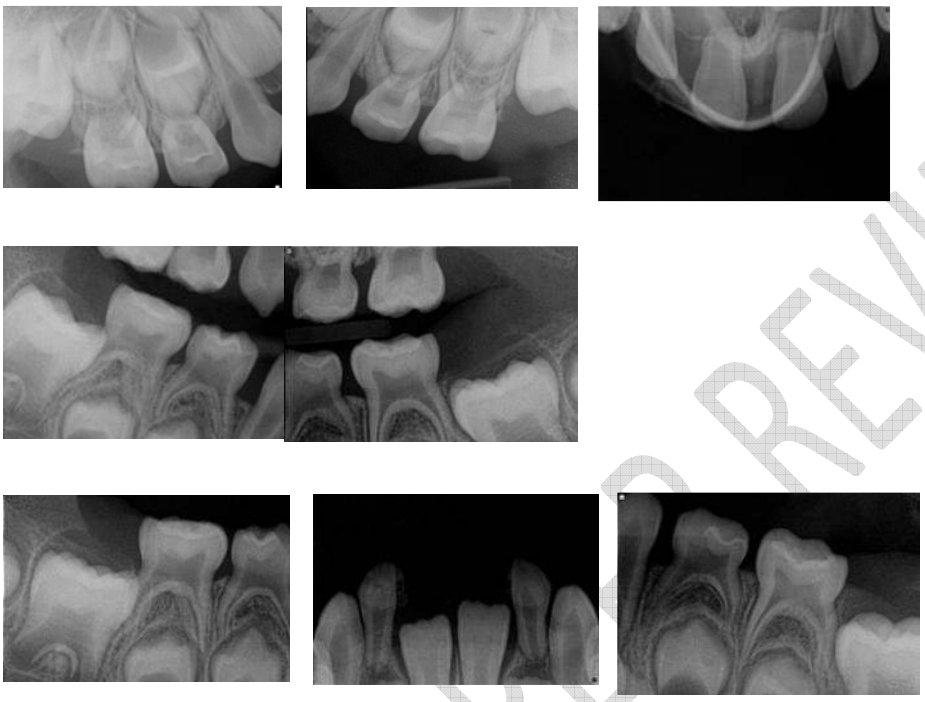

Fig1: a radiographic examinations of the patient achieved during general anesthesia revealed no caries, and no evidence of dental pulp pathology. The lower deciduous incisors are missing

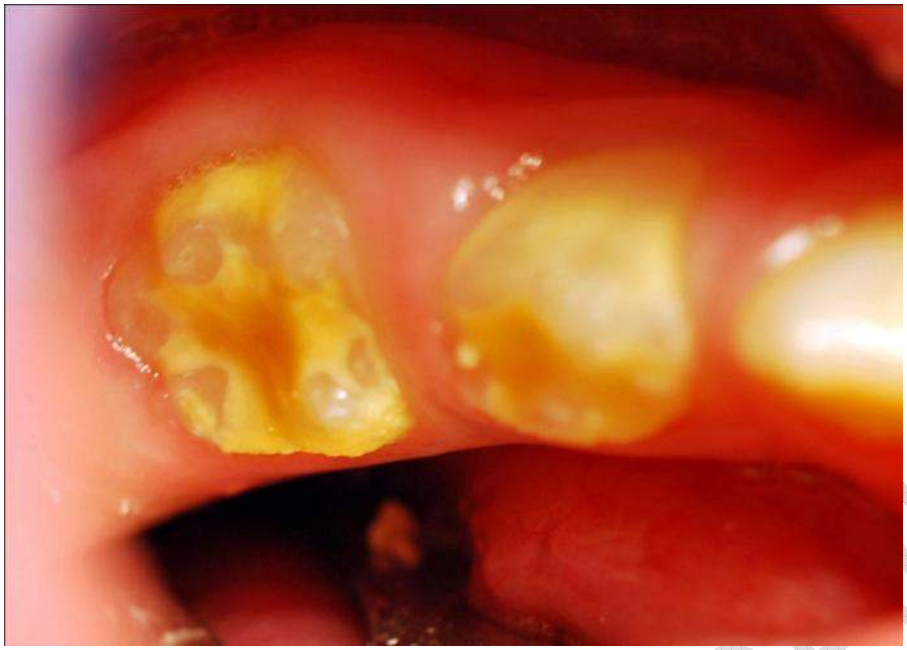

Figure-2

Teeth covered with heavy plaque and calculus.

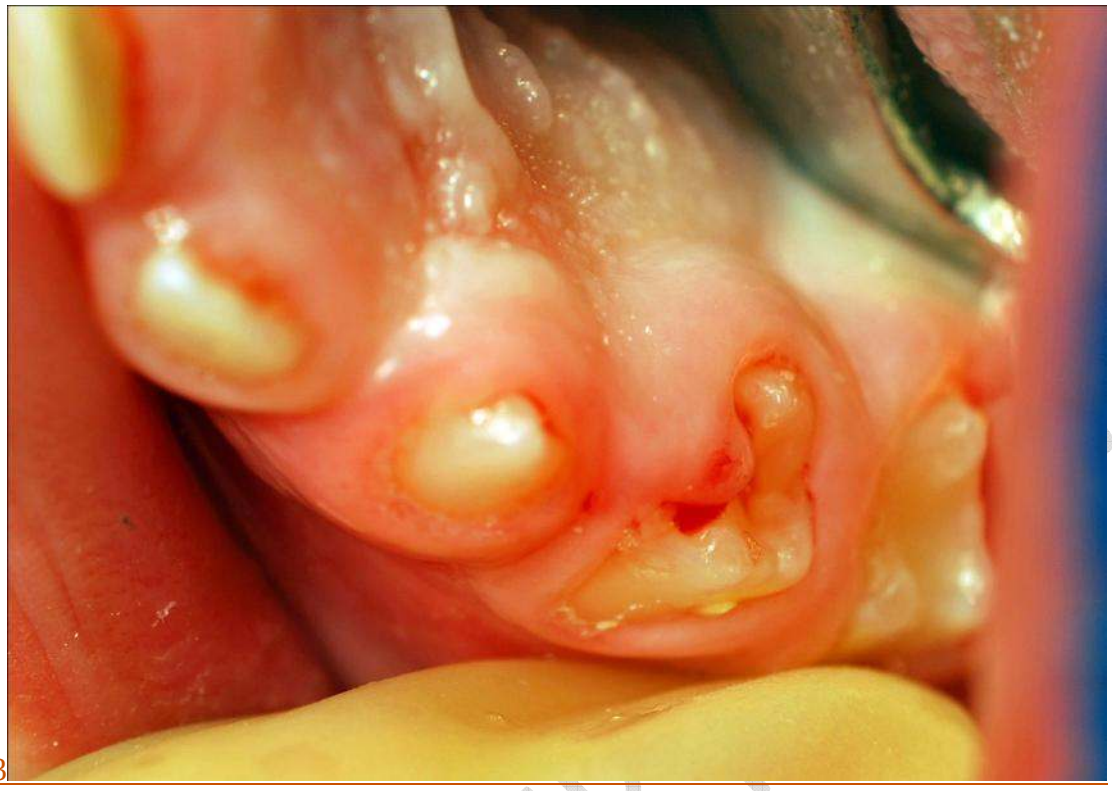

Fig3

Gingival overgrowth and gingivitis affecting the maxillary R quadrant

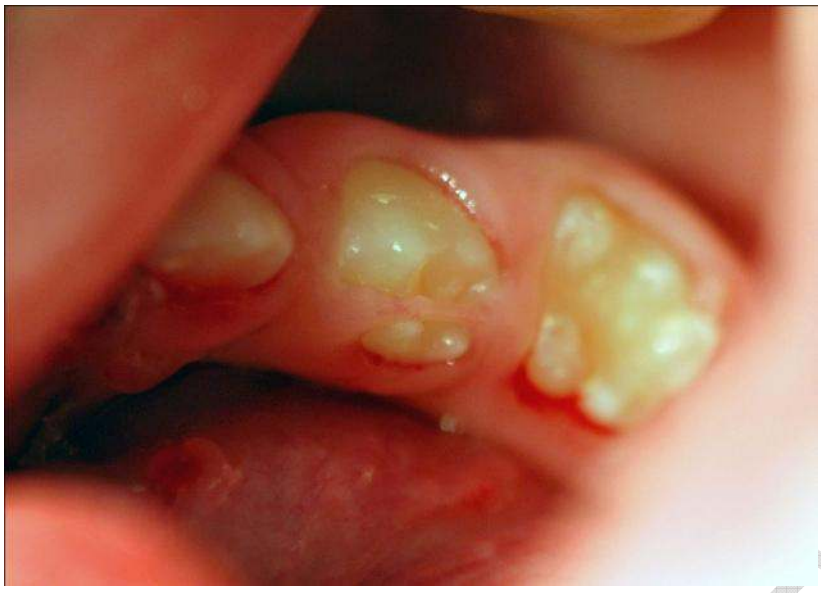

Figure-~~43a~~

generalized moderate gingival hyperplasia, and a band of gingiva over the occlusal surface of the mandibular right first primary molar

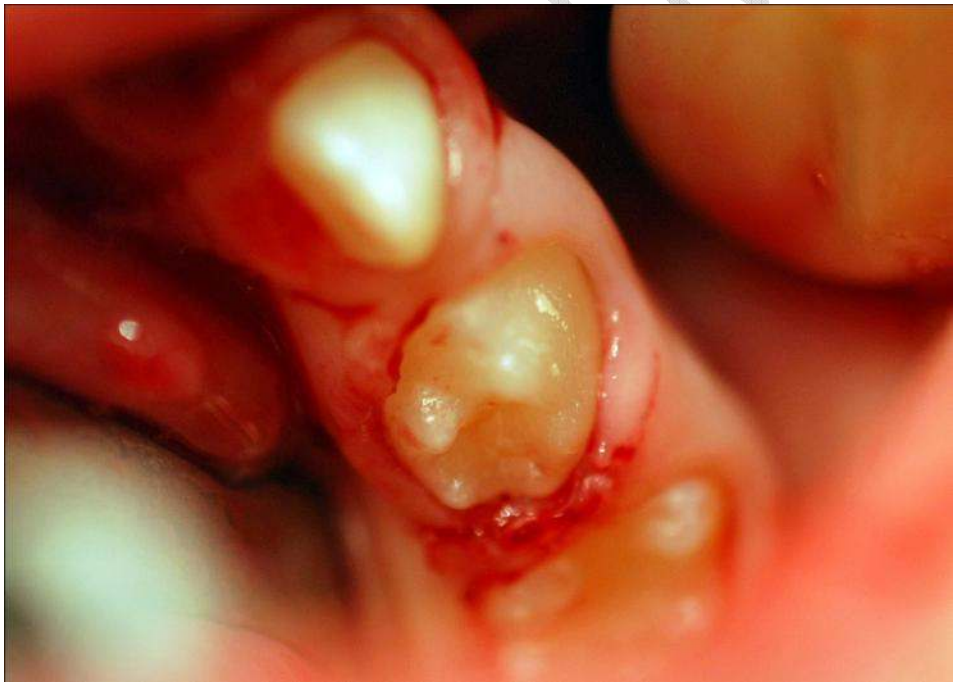

Fig 4b. gingival tissue over teeth B and S after removal with a surgical blade ~~gure-3b~~

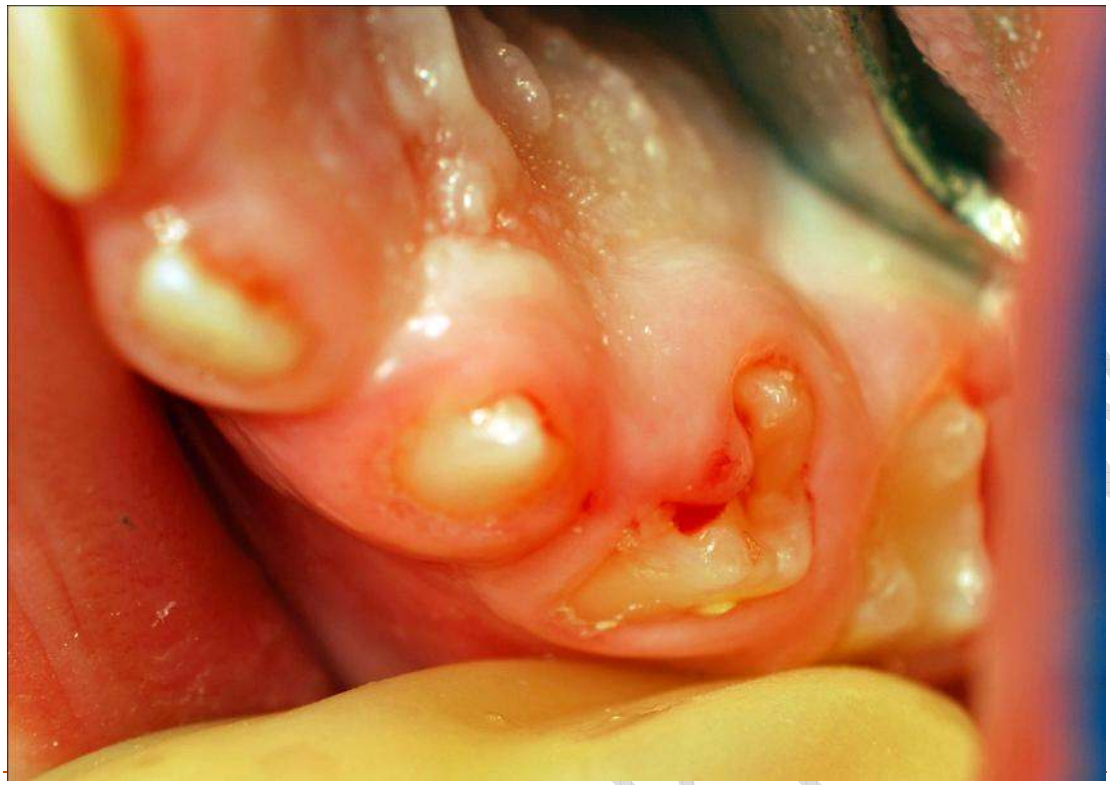

Figure-4a

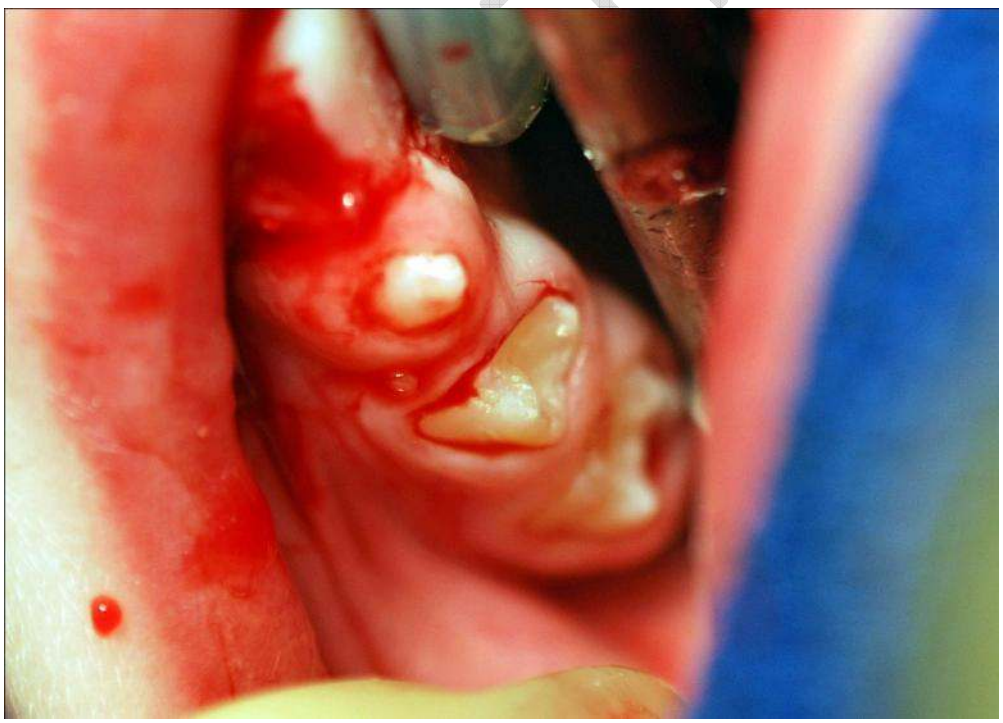

Figure-4b