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Riga-Fede Disease: A Rare Clinical Entity

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Abstract

Riga-Fede disease is a traumatic, ulcerative oral condition affecting infants and new-borns.

Since the early 1900s, there have been several case reports documenting this condition. The literature reports an association with congenital and developmental abnormalities, including global developmental delay and universal pain loss, suggesting that an underlying neurosensory disturbance may be present in affected children. Timely diagnosis and management can prevent potentially severe consequences including malnourishment, dehydration and permanent deformity. This article describes a case of Riga-Fede affecting an 11-month-old girl, with a review of the literature and discussion of the management options to better inform clinicians about this rare clinical entity.

Introduction

Riga-Fede disease was first described in 1881 by Antonio Riga, an Italian physician, and Francesco Fede who in 1890 furthered knowledge on the disease through histological studies and case reports (Riga 1881; Fede 1890). One of the earliest published case reports was by Amberg in 1902 in which a seven-month-old infant presented with a "tumour" under the tongue after eruption of the lower incisors, with the lesion resolving following excision (Amberg 1902).

In almost all cases to date, lesions affect the ventral surface of the tongue due to natal, neonatal or newly erupted mandibular central incisors and a tongue thrust is a frequent oral finding. Just under one-third of cases have an underlying developmental or neurosensory disturbance, including global developmental delay (GDD), familial dysautonomia and congenital autonomic dysfunction with universal pain loss (CADUPL).

The overall prevalence of Riga-Fede is unknown and to date, there have been no published case reports in New Zealand.

Case Report

An 11-month-old girl (LS) presented to the Emergency Department, Wellington Hospital in February 2020 with intermittent, high-grade fevers of unknown cause. She had presented on two occasions in the previous month for severe episodes of oxygen desaturation, a viral upper respiratory tract infection and otitis media. During these admissions, her parents reported an increase in agitated behaviours and a distinctive "tongue grinding" habit. Her GP had also noticed an enlarging ulcer on her tongue which appeared shortly after the eruption of her lower dentition. The paediatricians had observed a minimal increase in her height or weight in the previous three months, which were below the third centile for her age. An urgent dental assessment was requested to investigate a possible oral cause for her systemic symptoms.

LS had a complex medical history, including the following:

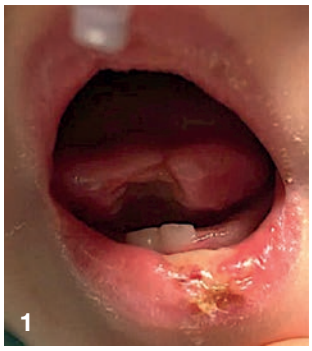
- Born at 34 weeks' gestation with intra-uterine growth restriction following maternal pre-eclampsia
- Global developmental delay, dysmorphic features and poor growth
- Dystonia
- Severe gastro-oesophageal reflux disease (GORD) and accompanying Sandifer syndrome
- Gastro-intestinal (GI) dysmotility
- Percutaneous endoscopic gastrostomy (PEG) feeding
- Severe scoliosis
- Multiple episodes of hypoxia
- Bilateral sensorineural hearing loss, with cochlear implants
- Nystagmus

LS was receiving EleCare and Calogen 3% (*Nutricia*) nutritional supplements via PEG feeding and had no known allergies.

Initial Presentation

During initial assessment, LS displayed repetitive, uncontrolled movements of the head and eyes, poor muscle tone, and was unable to sit up unaided. Extra-orally, there was no swelling, regional lymphadenopathy, asymmetry or lesions. An intra-oral assessment revealed a two-centimetre lesion on the ventral surface of the tongue extending from the tip to the lingual fraenum (Figure 1). The lesion had an ulcerative surface with a yellow slough, irregular margins, and bleeding towards the anterior border. The mandibular primary central incisors (teeth 71 and 81) were fully erupted. LS had a continuous tongue-thrust and did not respond to pain on palpation of the lesion.

Based on the clinical presentation, the provisional diagnosis was a traumatic ulcer. Multiple investigations were undertaken to exclude other possible causes. On admission, routine blood tests, a faecal calprotectin test to detect intestinal inflammation, and Coeliac screening test were completed. Results showed raised inflammatory markers, including white blood cells and C-reactive protein (CRP), consistent with a reactive inflammatory process, and elevated metabolic parameters (lactate and pyruvate). Further blood tests during the same admission showed these levels return to normal, with no consistent pattern and no changes in the clinical appearance of the lesion over this time.



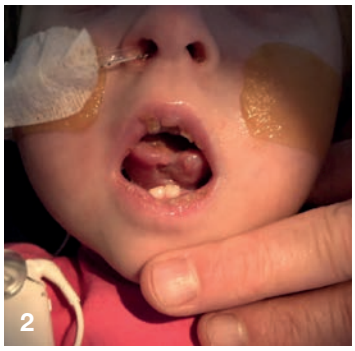


Figure 1. Initial assessment (February) – lesions on ventral tongue and lower lip.
Figure 2. Final assessment (May) – lesions visible on ventral tongue, upper and lower lips.

Oral swabs requested by the Paediatric medical team produced no isolated cultures of candida or detection of herpes simplex or varicella-zoster viruses. A full septic screen, including blood, urine and cerebrospinal fluid (CSF) cultures, were normal. Radiological exams including an abdominal ultrasound, a chest radiograph and a CT of the head showed no abnormalities. A video fluoroscopy conducted by a speech language therapist identified a high risk of aspiration.

Having excluded an infectious aetiology, a "central neurodegenerative condition," known as mitochondrial disease, was thought to be the cause of her systemic symptoms. Mitochondrial disease refers to a group of disorders affecting energy metabolism caused by gene mutations in the nuclear DNA (nDNA) and mitochondrial DNA (mtDNA) encoding mitochondrial proteins (Gorman et al. 2016; Kunungo et al. 2018). Mitochondrial disease is divided into childhood and adult-onset groups, with about 16 disease entities having been identified (Gorman et al. 2016). The diseases typically have multi-system involvement, with neurological deficits including sensorineural hearing loss, developmental delay, dystonia, ataxia, nystagmus, and non-neurological manifestations including respiratory failure, GI dysmotility and elevated metabolic markers (Edmonds et al. 2002). Diagnosis of mitochondrial diseases is based on genetic testing. In the present case, the mtDNA was fully sequenced and the results are yet to be confirmed.

Management

Having excluded infectious, haematological and gastrointestinal causes of her oral ulcers, LS was diagnosed with Riga-Fede disease. Following consultation with a Specialist Paediatric Dentist, it was recommended to extract the contributory teeth. The primary concerns were the risk of systemic spread of infection, poor healing capacity, and the involuntary tongue thrust which may increase the likelihood of persisting or recurring lesions.

The parents did not give consent to extract the offending teeth, and conservative treatment options were preferred. Based on the literature, a recommendation was made to smooth the incisal edges and apply topical corticosteroid cream to the lesion (triamcinolone acetonide 0.1% in *Orabase*), until improvement was observed.

After a few weeks, new lesions had developed on the mid-line of the lower lip near the now partially erupted maxillary central incisors (51 and 61). There was minimal healing of the tongue lesion and a 'bifid' defect remained at the tip (Figure 2).

Due to the failure of conservative approaches, extraction of the maxillary and mandibular central incisors under a general anaesthetic (GA) was deemed necessary. The parents declined and continued the use of *Orabase* for a further month. During this time, decline of the patient's general health resulted in another hospital admission. On a final assessment, new lesions at the midline of the upper and lower lips and further tissue loss of the ventral tongue had occurred involving almost the entire thickness. The maxillary lateral incisors (52 and 62) could now be palpated (Figure 3).

Consent was eventually given for extractions under GA. An acute multidisciplinary GA was arranged along with a gastroenterology procedure, involving a Paediatric surgeon and Paediatric anaesthetist. Dental treatment was completed by a Senior Dentist, with assistance from a Dental House Surgeon. Pre-operative radiographs showed all the incisors present with incomplete root development. The procedure involved local anaesthetic infiltrations (1.1mL 2% lignocaine with 1:100,000 adrenaline), incisions to expose the unerupted 52 and 62, simple extractions of the maxillary incisors and mandibular central incisors and placement of resorbable sutures (*Velosorb* 4-0).

Follow-Up

24 hours post-operatively, the mother reported that the child had been settled with

minimal bleeding from the extraction sites. At a three-week review by telephone, the parents reported a marked improvement in the lesions with their child seeming less distressed. They had also noticed the primary mandibular molars erupting with new ulcerative lesions.

At the seven-week review, the lesions on the lips and ventral tongue had completely resolved, though a residual defect remained at the tip of the tongue.

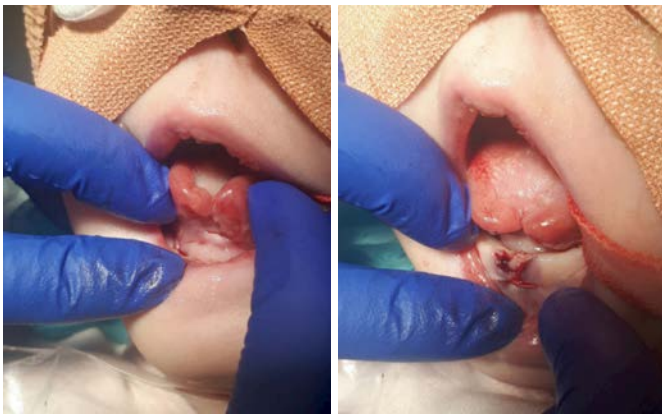


Figure 3. Teeth 52 to 62, 71 and 81 extracted under general anaesthetic with *Velosorb* sutures placed. The lesion has left a 'bifid' defect at the tip of the tongue.

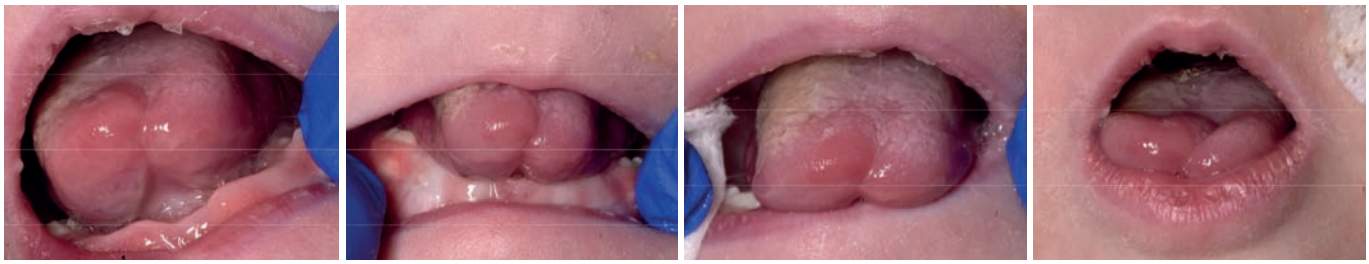


Figure 4. Post-operative review (July): healing of the tongue and lip lesions, with a defect remaining at the tip of the tongue.

The primary mandibular molars (74 and 84) were partially erupted and no further lesions were identified (Figure 4).

Three months later, her mother noticed new ulcers on the right cheek and tongue. LS had been showing signs of distress, including pressing her hand against her right cheek and she had developed a fever. On assessment there was a 1.5 cm diameter lesion on the right buccal mucosa adjacent to the newly erupted primary molars (54 and 84) and recurrence of a 1 cm lesion on the ventral tongue near the erupted mandibular lateral incisor (82). All primary molars were partially erupted and 72 and 82 were fully erupted.

Table 1. Summary of Case Reports

Author, Year	Study Type	Sex	Age at presentation	Presenting Complaint	Medical History	Site of lesion
Amberg, 1902	Case Report	M	7 months	"Tumour" under tongue	Nil	Ventral tongue
Bray, 1927	Case Report	M	9 months	-	Nil	Ventral tongue
Bradley, 1932	Case Report	F	8 months	-	Nil	Ventral tongue
Moncrieff, 1933	Case Report	M	6 months	-	Nil	Ventral tongue
		M	6 months	-	'Mentally deficient'	Ventral tongue
Newman, 1935	Case Report	M	8 months	-	Nil	Dorsal tongue
		F	11 months		Nil	Ventral tongue
Abramson, 1944	Case Report		11 months	Growing lesion under tongue, speech interference, "tongue scraping"	Nil	Ventral tongue
			9 months	Referred for suspected malignancy	Pertussis, scurvy	
Jacobs, 1956	Case Report	-	1 week	-	-	Ventral tongue
McDaniel & Morano, 1978	Case Report	M	6 months	Ulcer on tongue	Febrile illness, diarrhoea	Dorsal tongue
Rakocz et al. 1987	Case Report	M	10 months	Extensive ulceration of tongue	Familial dysautonomia, perinatal complications (aspiration, pneumonia, failure to thrive)	Ventral & dorsal tongue
Eichenfield et al. 1990	Case Report	F	6 months	Growing lesion on tongue after eruption of teeth, poor weight gain	Familial dysautonomia	Ventral tongue
Goho, 1996	Case Report	F	21 days	Difficulty feeding, pain, poor weight gain	Nil	Ventral tongue
		F	10 days	Teeth present at birth	Nil	Ventral tongue

A neurological assessment indicated reduced pain sensitivity with results of genetic testing yet to confirm an underlying diagnosis. LS continues to receive both medical and dental input into her care. Ongoing dental management is likely to include further extractions in order for new lesions to resolve, and continued reviews thereafter as remaining teeth erupt.

Literature Review

A literature search of PubMed and the University of Otago Library was conducted. A total of 71 studies were identified consisting of 68 case reports and three literature reviews, the majority of which were published within the last 25 years. A summary of all cases is listed in Table 1.

A male predilection was found, and children affected were on average nine months at presentation, with ages ranging from three days to nine years.

The most common presenting complaint was difficulty during feeding or teeth present at birth (natal) or shortly after birth (neonatal teeth). Patients were often referred by Paediatricians to Paediatric Dentists, Ear Nose & Throat (ENT) Specialists or Dermatologists after observing poor weight gain, nutrient intake or dehydration.

Twenty case reports included patients with congenital or developmental abnormalities, including familial dysautonomia, congenital autonomic dysfunction with universal pain loss (CADUPL), Down Syndrome, encephalopathies, cerebral palsy, developmental delay and pre- or perinatal complications. Three case reports mentioned a family history of natal/neonatal teeth.

The ventral surface of the tongue was the most commonly affected site and often associated with natal or neonatal mandibular incisors, a tongue-thrust or exaggerated sucking reflex.

	Teeth present, natal/neonatal	Associated factors	Investigations	Treatment	Follow-up	Outcome
	Lower incisors	Bleeding	Nil	Excision	2 months	Resolution
	*Yes	-	Biopsy	Excision	-	-
	*Yes	-	Biopsy	Excision	-	-
	*Yes	-	Biopsy	Weaning	-	-
	*Yes	-	Nil	Smoothing incisal edges		
	*Yes	-	Nil	Extraction	-	-
	*Yes	-	Biopsy	Excision		
	Upper central and lateral incisors, *3 lower incisors	Tongue-tie, tongue-thrust, bleeding	Blood test (CBC), urine test, tuberculin & Wasserman tests, biopsy (excisional)	Excision	-	Resolution
	Lower central incisors		Blood tests (CBC), Tuberculin & Wasserman tests, biopsy (excisional)	Excision	-	Resolution
	Lower central incisors (natal teeth)			Extraction		Resolution (with defect)
	Yes	Nil	Biopsy	Excision	1 year	Resolution
	Upper & lower central incisors, lower right lateral incisor	Tongue thrust	Biopsy (excisional)	Composite covering of incisal edges (central incisors)	9 weeks	Recurrence
				Composite covering (lateral incisor)	2 weeks	Resolution
	Lower central incisors	-	Biopsy (excisional), histamine challenge, pilocarpine test	Excision	-	-
	Lower left central incisor (natal)	Pain on palpation	Radiographs	Extraction	5 days	Resolution
	Lower central incisors (natal)	-	Radiographs	Smoothing incisal edge, composite covering	1 week	Resolution

Buchanan & Jenkins, 1997	Case Report	M	4 weeks	Persistent tongue ulcer, poor feeding & sleeping	Family history of natal teeth	Ventral tongue
Slayton, 2000	Case Report	M	10 months	Non-healing tongue ulcer, poor weight gain	Down Syndrome, repaired aortic septic defect	Ventral tongue
Toy, 2001	Case Report	M	20 months	"Oral plaques" after teething, tongue thrusting, lip biting	GDD, congenital autonomic dysfunction with universal pain loss	Ventral tongue, lower lip
Baghdadi, 2001	Case Report	M	10 months	Inflammatory tongue lesion, failed treatment, child distressed inflammatory lesion the tongue which had not healed following penicillin therapy.	Nil	Ventral tongue
Baghdadi, 2002	Case Report	F	12 months	Non-healing ulcer, poor sleep, feeding, dehydration and malnutrition	Delayed speech development, microcephaly	Ventral tongue
Terzloğlu et a., 2002	Case Report	M	7 months	Progressing tongue ulcer, "tongue raking"	-	Ventral tongue
Zaenglein et al. 2002	Case Report	M	10 months	"Extensive oral plaque"	Congenital autonomic dysfunction with universal pain loss	Ventral tongue, lower lip
Ahmet et al. 2002	Case Report	F	6 years	Tongue-biting habit, ulcer forming	-	Ventral tongue
Ahmet et al. 2003	Case Report	M	7 months	Deformity and "clefting" of tongue	-	Ventral tongue
Hegde, 2005	Case Report	F	28 days	Tongue ulcer, pain during breastfeeding, poor weight gain	-	Ventral tongue
Campos-Munoz et al. 2006	Case Report	M	11 months	Tongue ulcer, pain, difficulty feeding	Nil	Ventral tongue
Baroni et al. 2006	Case Report	M	11 months	Painful tongue ulcer	Nil	Ventral tongue
Domingues-Cruz, 2007	Case Report	M	2 years	Indurated lesion on lower lip	Down Syndrome, post-anoxic encephalopathy	Lower lip
Machuca et al. 2007	Case Report	F	12 months	Painful tongue ulcer, poor feeding, dehydration	Hypoxic-ischaemic encephalopathy	Ventral tongue
Narang et al. 2008	Case Report	M	9 months	Painful tongue ulcer, difficulty feeding, poor weight gain	Nil	Ventral tongue

	Lower central incisors (neonatal)		Radiograph	Initial: smoothing incisal edges, antifungal gel, (parents declined extraction)	-	Persisting lesion
				Final: covering incisal edges (Stomahesive Wafers)	1 day	Feeding & sleeping normally
					2 days	Healing
					8 days	Further healing
					14 days	Near complete resolution
					21 days	Resolution
					1 month	No recurrence
					4 months	No recurrence, scarring
	Lower central incisors	Tongue- thrust		Initial: topical corticosteroid (Orabase)	-	Persisting lesion
				Final: smoothing incisal edges, modifying feeding	1 week	Healing
					1 month	Resolution (risk of recurrence)
	Lower teeth	Tongue- thrust, lip biting	Neurological exam, biopsy	-	-	-
	Lower central incisors	"Nocturnal" tongue-biting	Nil	Smoothing incisal edges, topical corticosteroid (Orabase)	1 day	Reduced pain and swelling
					Few days	Resolution
	Lower central incisors	Macroglossia, tongue thrust, mandibular prognathism, pain on palpation	Head circumference, neurological exam (incl CT)	Smoothing incisal edges, topical corticosteroid (Orabase)	Few days (telephone)	Healing, feeding and sleeping normally
					1 week (clinical)	Healing
					25 days	Near complete resolution
	Lower central incisors	Tongue thrust	Nil	Advice–use of feeding bottles/toys		-
		Tongue thrust, lip biting	Biopsy (punch)			-
	Lower central incisors	Tongue thrust	-	(Parents declined extraction)	1 year	Resolution (with defect)
	Lower central incisors	Tongue thrust	Nil	Use of feeding bottles/ toys, reconstructive surgery planned	-	*Improvement
	Lower incisors (neonatal)	Pain on palpation	Radiographs	Extraction	10 days	Resolution, feeding normally
	Yes	"Nocturnal" tongue thrust	Blood tests (CBC, biochemistry, coagulation), X-rays (thorax and digestive tract), neurological exam, EEG, immunological study, biopsy	NG feeding	3 months	Healing (with scarring)
					11 months	Resolution, regaining weight
	Lower central incisors		Blood tests	Composite covering, topical odontologic cream, 0.2% CHX mouthrinse, use of a teething ring	3 weeks	Resolution
	Lower central and lateral incisors	Frequent "lip sucking"	Nil	Initial: *conservative treatment	-	Persisting lesions
				*Later: Extraction (lower central incisors only)	-	Recurrence
				Final: extraction (lower lateral incisors)	3 weeks	Resolution (with scarring)
	Lower central incisors	Tongue-thrust, continuous "sucking reflex"	(Parents declined biopsy)	Acrylic mouthguard, topical cicatrising gel (Aloclair gel)	1 week	Improvement, reduced pain, feeding normally
					3 weeks	Resolution
	Lower incisors	Angular cheilitis, partial tongue-tie	Neurological exam, blood tests	Use of a teething ring, surgical repair of tongue-tie	2 months	Resolution
					6 months	Regaining weight

Jariwala et al. 2008	Case Report	F	6 weeks	Discomfort, difficulty feeding	Nil	Ventral tongue
Ceyhan et al. 2009	Case Report	M	15 months	Non-healing ulcer, difficulty feeding, bleeding from tongue, failed treatment	Low weight (<5th percentile) and height (10-25th percentile), mild anaemia	Ventral tongue
Taghi & Motamedi, 2009	Case Report	M	8 months	Large tongue lesion, difficulty feeding	Cerebral palsy	Ventral tongue
Choi et al. 2009	Case Report	M	8 months	Tongue biting, bleeding, difficulty feeding	Nil	Ventral tongue
		F	2 months	Tooth present at birth, tongue biting, difficulty feeding		Ventral tongue
Eley et al. 2010	Case Report	F	11 months	Pyrexia, coryzal symptoms, bleeding from oral cavity	Nil	Ventral tongue
Basavanthappa et al. 2011	Case Report	M	8 days	Tooth present at birth, difficulty feeding, child distressed	Nil	Ventral tongue
		M	18 days	Tooth present shortly after birth, difficulty feeding	Nil	Ventral tongue
		M	20 days	Tooth present shortly after birth, difficulty feeding	Nil	Ventral tongue
Deep et al. 2011	Case report	F	20 days	Tongue ulcer, difficulty feeding, poor weight gain	Familial dysautonomia	Ventral tongue
Yacovone et al. 2011	Case Report	F	12 months	Tongue ulcer, pain, bleeding, failed treatment	Premature birth, central hypertension	Ventral tongue
van der Meij et al., 2012	Case Report	M	6 months	Tongue ulcer	Nil	Ventral tongue
Costacurta et al. 2012	Case Report	F	2 months	Progressing tongue ulcer, bleeding, inadequate nutrient intake, difficulty feeding	Nil	Ventral tongue
Sharma et al. 2012	Case Report	-	20 days	Tongue ulcer, pain and difficulty feeding	-	Ventral tongue
Bafna et al. 2013	Case Report	F	1 year	Ulcer below tongue, pain, difficulty feeding/drinking, dehydration	-	Ventral tongue
Dunlop et al. 2013	Case Report	F	2 months	Tongue ulcer, pain and difficulty feeding, inadequate nutrient intake	-	Ventral tongue
Ghimire et al. 2013	Case Report	M	27 days	Pain during feeding	Nil	Ventral tongue
Praveen Kumar PS et al. 2013	Case Report	M	20 days	Tooth present at birth	Nil	Anterior border tongue
		-	4 days	Tongue ulcer, pain during feeding	-	Anterior border tongue
		M	24 days	Teeth present at birth, pain during feeding	Nil	Ventral tongue
Baldiwala & Nayak, 2014	Case Report	M	2 ½ years	Teeth present at birth, difficulty feeding, tongue ulcer.	Nil	Ventral tongue

	Lower R incisor (natal/neonatal – not stated)	Tongue slightly raised at rest	Nil	Extraction	10 days	Resolution, feeding normally
	Lower central incisors	Nil	Neurological exam, blood tests, chest X-ray, Gram stain, culture, Syphilis screening, tuberculin skin test, HIV (ELISA) test, (Parents declined biopsy)	Topical corticosteroid (Orabase), (parents declined extraction)	1 year (telephone)	Near complete resolution
	Lower incisors		Biopsy (incisional)	Composite covering	2 weeks	Resolution
					2 years	No recurrence
	Lower incisors	Nil	Nil	Composite covering, topical corticosteroid (Orabase)	2 months	Resolution
					6 months	Regaining weight
	Lower right central incisor (neonatal)	Nil	Nil	Smoothing incisal edges, topical corticosteroid (Orabase)	1 month	Resolution, feeding normally
	Lower central incisors	-	Biopsy (incisional)	(Parents declined extraction)	6 months	Healing (with defect)
					1 year	Recurrence on bilateral borders of tongue (adjacent to lower first molars)
					10 years (telephone)	Resolution
	Lower right central incisor	-	Radiographs	Extraction (with prophylactic IM Vitamin K)	-	-
	Lower left central incisor	-	Radiographs	Extraction	-	-
	Lower right central incisor	-	Radiographs	Extraction	-	-
	Lower central incisor	Pain on palpation	-	Smoothing incisal edges, composite covering, topical corticosteroid	-	Resolution, feeding normally
	Lower central and lateral incisors	-	Biopsy	Smoothing incisal edges	-	Recurrence
					9 days	Healing
					1 month	Resolution
	Lower central incisors	Nil	Biopsy (excisional)	Excision	3 months	Resolution
	Lower central incisors (neonatal)	Pain on palpation	Blood tests, neurological exam, histological analysis of extracted teeth	Extraction	4 weeks	Resolution
					1 year	No recurrence
	Lower incisor (neonatal)	Pain on palpation	Nil	Extraction	-	Resolution, feeding normally
	Lower central and lateral incisors (partially-erupted)	Tongue-thrust, continuous “sucking reflex”	Nil	Composite covering, analgesic gel	1 day	Feeding normally
					2 days	Healing
					8 days	Healing, composite removed
					14 days	Near complete resolution
					1 month	Resolution
	Lower central incisors (neonatal)	Tongue-thrust	Neurological exam	Extraction	7 days	Healing
					1 month	Resolution, feeding normally
	Lower left central incisor (neonatal)	Pain on palpation	Radiograph	Smoothing incisal edges	1 month	Resolution, feeding normally
	Lower central incisor (natal)	Nil	Nil	Extraction	2 weeks	Resolution, feeding normally
	Lower central incisor (natal)	Nil	Radiographs	Extraction	1 week	Healing, feeding normally
	Lower central incisors (natal)	Nil	Radiographs	Extraction	2 weeks	Resolution, feeding normally
	Lower incisors (natal)	Nil	Radiograph (undiagnostic)	Initial: smoothing incisal edges	-	(Unable to complete procedure)
				Final: soft mouthguard	1 week	Healing, feeding normally
					3 weeks	Resolution

Jingarwar et al. 2014	Case Report	M	17 days	Teeth present at birth, pain during feeding	-	Ventral tongue
Lee & Mandel, 2014	Case Report	F	9 months	Ulcer on floor of mouth, difficulty feeding	Nil	Ventral tongue, floor of mouth
Mohan et al. 2014	Case Series	M	30 days	-	Nil	Lower lip
		M	42 day	-	Nil	Ventral tongue
		M	34 day	-	Nil	Ventral tongue
		M	15 days	-	Nil	Ventral tongue
		M	20 days	-	Nil	Ventral tongue
		M	30 days	-	Nil	Left lateral tongue
		M	46 days	-	Nil	Right lateral tongue
		M	34 days	-	Nil	Tip of tongue, alveolar ridge
		M	50 days	-	Nil	Ventral tongue
Moura et al. 2014	Case Report	M	14 days	Presence of teeth at birth, difficulty feeding	-	Ventral tongue
		M	3 days	Presence of teeth at birth	-	Ventral tongue
Picciotti et al. 2014	Case Report	F	37 days	Fever, inadequate nutrient intake, difficulty feeding, bleeding from tongue	Meningitis	Ventral tongue
Senanayake & Karunatratne, 2014	Case Report	M	18 months	Persisting tongue lesion	Down Syndrome, developmental delay, recurrent URTIs	Ventral tongue
Bhatt et al. 2015	Case Report	F	28 days	Pain and difficulty feeding, poor weight gain	-	Ventral tongue
Hong, 2015	Case Report	F	6 months	Enlarging intra-oral lesion, gradual growth of child	-	Ventral tongue
Ozmen & Acar, 2015	Case Report	M	9 years	Tongue ulcer	Nil	Ventral tongue
Sachdeva & Vengal, 2015	Case Report	M	15 days	-	-	Ventral tongue
Volpato et al. 2015	Case Report	F	1 month	Presence of teeth at birth, difficulty feeding, child irritable	Nil	Ventral tongue
Li et al. 2016	Case Report	M	6 years	Tongue ulcer, habit of “sticking out tongue”	Nil	Ventral tongue
Alahmari & Alahmari, 2017	Case Report	F	20 days	Tongue ulcer, difficulty feeding	Nil	Ventral tongue
Cavus & Ozmen, 2017	Case Report	F	11 months	Difficulty feeding, sensitivity and child distressed	Nil	Ventral tongue
Da Silva et al. 2017	Case Report	F	43 days	Difficulty feeding, pain, weight loss, child irritable, unable to sleep	-	Ventral tongue

	Lower incisors (natal)	Tongue-thrust, continuous "sucking reflex," pain on palpation	Nil	Smoothing incisal edges, topical corticosteroid (Orabase)	1 month	Healing
					6 months	Resolution, feeding normally
	Lower central incisors	Tongue-thrust	Nil	Smoothing incisal edges	5 weeks (telephone)	Resolution
	Lower central incisors (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower central incisors (natal)	-	Neurological exam	Extraction, topical corticosteroid	-	*Improvement
	Lower left central incisor (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower right central incisor (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower central incisors, right lateral incisor (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower left lateral incisor (natal)	-	Neurological exam	Extraction, topical corticosteroid	-	*Improvement
	Lower central incisors (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower right central incisor (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower central incisors (natal)	-	Neurological exam	Smoothing incisal edges, topical corticosteroid	-	*Improvement
	Lower right central incisor (natal)	-	Nil	Smoothing incisal edges, 0.12% CHX applied topically	2 weeks	Resolution
	Lower right central incisor (natal)	-	Nil	Smoothing incisal edges	1 month	Resolution
	Lower left central incisor	-	Blood tests (CBC, biochemistry, immunological study), neurological exam, CSF culture	Extraction	1 day	Fever resolved
					1 week	Healing
					3 weeks	Resolution
	Lower incisors (natal)	Nil	Nil	Extraction	-	-
	Lower incisors (neonatal)	Nil	Nil	Smoothing incisal edges	15 days	Resolution
					*Later	Feeding normally
	Lower central incisors	-	-	-	-	-
	Lower left canine & lateral incisor	Nil	-	Extraction (canine), smoothing incisal edge (lateral incisor)	3 months	Resolution
	Lower incisor (natal)	-	-	*Conservative treatment	-	-
	Lower incisors (natal)	-	(Parents declined biopsy), 1-year post-op radiograph	Extraction (mobile tooth), GIC covering incisal edge (non-mobile tooth), cleaning with saline	-	Feeding improved
					5 days	Healing
					15 days	Resolution
					1 year	No recurrence
	*Yes	Tongue-thrust	Blood tests, neurological exam	Topical rbşbFGF gel, Advice – discourage habit	1 week	Resolution, ceased tongue-thrusting
					3 months	No recurrence
	Lower incisor (natal)	Tongue-thrust	-	Extraction	-	Resolution, feeding normally
	Lower central incisors	-	Nil	Analgesic + anti-inflammatory topical gel (Dentinox), smoothing incisal edges	2 weeks	Resolution
					4 months	No recurrence (ongoing reviews)
	Lower left central incisor	-	Radiograph	Topical corticosteroid, 0.12% CHX applied topically, low-level laser	1 day	Feeding improved
					4 days	Healing
					10 days	Resolution, feeding normally, weight gain

Kanumuri, 2017	Case Report	M	4 days	Difficulty feeding, teeth present at birth	-	Ventral tongue
Mehta et al. 2017	Case Report	F	2 months	Enlarging tongue ulcer, pain, bleeding, difficulty feeding, dehydration	-	Ventral tongue
		F	20 days	Pain, difficulty feeding	-	
Paranna & Kamath, 2017	Case Report	F	16 days	Teeth present, difficulty feeding	-	Ventral tongue
Ekinci et al. 2018	Case Report	M	14 months	Tongue ulcer, difficulty feeding, failed treatment	Down Syndrome, cachectic, neurodevelopmental delay	Ventral tongue
Jamani et al. 2018	Case Report	F	1 month	Tooth present shortly after birth, difficulty feeding, tongue ulcer, bleeding	Family history of natal teeth	Ventral tongue
Shivpuri et al. 2018	Case Report	F	27 days	Difficulty feeding, teeth present shortly after birth	Nil	Ventral tongue
Kumari & Singh, 2019	Case Report	F	45 days	Difficulty feeding, tongue ulcer, tooth present since birth	Nil	Ventral tongue
Lee et al. 2019	Case Report	F	8 months	Pain, poor feeding, weight loss, failed treatment	Nil	Ventral tongue
Sakulratchata, 2019	Case Report	F	25 months	Enlarging tongue ulcer, bleeding, discomfort	Birth asphyxia and hypoxic ischemic encephalopathy, recurrent pneumonia, GDD, low weight, hypotonia, abnormal involuntary movements, moderate hearing loss, otitis media, PEG feeding	Ventral tongue
Sivamurukan et al. 2019	Case Report	F	7 months	Difficulty feeding	GDD, dystonia, glutaric aciduria Type I	Ventral tongue
Yureki & Dincer, 2019	Case Report	M	9 years	Persisting tongue ulcer, failed treatment	Nil	Ventral tongue

Key

* = not specified
\- = not reported
GIC = glass ionomer cement
rb-bFGF = recombinant bovine basic fibroblast growth factor
CHX = chlorhexidine gluconate
IM = intramuscular
NG = nasogastric
GDD = global developmental delay

Treatment varied from conservative to more invasive approaches, including one or a combination of preventive techniques, protective mouthguards, topical corticosteroids, composite covering or smoothing of incisal edges, extraction of the contributory teeth and excision of the lesion. Excision was the treatment of choice in earlier case reports, while extraction was considered in cases of malnourishment or dehydration, recurring or persisting lesions, or mobile teeth. In four cases, the parents did not consent to extraction.

Biopsies were completed in 16 cases. Histopathology assessments showed granulation tissue,

fibroblastic and histiocytic proliferations, and a predominantly mixed inflammatory cell infiltrate including eosinophils. No biopsies showed evidence of malignancy. In two case reports, treatment also included surgical procedures, namely repair of a ‘tongue-tie’ and reconstructive surgery on a full-thickness lesion of the ventral tongue. These patients were managed by Dermatologists and Plastic Surgeons, respectively.

	Lower incisors (natal)	-	Radiograph	Extraction (with prophylactic IM Vitamin K)	1 week	Resolution, feeding normally
	Lower left central incisor (neonatal)	Pain on palpation	-	Extraction	3 days	Healing
					1 week	Pain reduced, feeding normally
					3 weeks	Resolution
	Lower central incisors	-	-	Extraction	-	-
	Lower incisors (natal)	Pain on palpation	-	Extraction	10 days	Resolution, improved feeding
	Lower incisors (neonatal)	Tongue-thrust	Blood tests, sonography	Extraction	2 weeks	Resolution
	Lower left incisor (neonatal)	-	(Parents declined radiographs and biopsy)	Extraction	2 days	Healing, resumed breastfeeding
					1 week	Resolution, feeding normally
	Lower central incisors (neonatal)	-	-	Extraction	1 month	Improved feeding
	Lower incisor (natal)	Pain on palpation	Nil	Extraction	3 weeks	Resolution, feeding normally
	Lower central incisors	Bifid uvula	Bloods tests, full-body imaging, biopsy (excisional)	Smoothing incisal edges, excision, changing to NG feeds	2 days	Improved oral intake, ceased NG feeds
					2 weeks	Healing
					1 month	Healing
					2 months	Resolution, weight gain
	Lower central incisors	Tongue-thrust	-	Smoothing incisal edges, topical corticosteroid	1 week	Healing, child less distressed, feeding normally
					2 weeks	Further healing (with defect), feeding normally
					1 year	Resolution (with defect)
					1 ½ years	No recurrence
					2 years	No recurrence, upper and lower lateral incisors erupted
	Lower central incisor	-	Head circumference	Extraction	-	Resolution
	Lower left canine	Nil	Blood tests, neurological exam	Smoothing incisal edge	6 months	Resolution

Advice given to parents included the use of teething rings or feeding bottles to reduce trauma from incisal edges against the ventral tongue. Nasogastric (NG) feeding was introduced in two cases as a way of minimizing trauma caused by the teeth and ensuring adequate nutritional intake. In two cases, protective mouthguards were used to minimize trauma. Machuca et al. (2007) used a "soft silicone relining material" to create a tongue protector which covered the mandibular central incisors and alveolar ridge, in conjunction with a topical cicatrising gel (*Aloclair* gel). Baldiwala and Nayak (2013) used a "soft elastic foil" (*Bioplast*) covering the mandibular incisors and ridge, following failed attempts at smoothing incisal edges and with difficult isolation precluding the use of composite. In both cases the parents were instructed on how to correctly use the appliance, which involved daily insertion for the maximum time tolerated by the infant. By the three-week follow-up, complete healing was observed in both cases.

Discussion

Riga-Fede disease is a rare traumatic ulcerative disease of childhood, characterised by mechanical irritation of newly erupted, natal or neonatal teeth, typically against the ventral surface of the tongue. With repetitive tongue-thrusting or reduced pain sensitivity, lesions can become severe with the potential to cause tongue deformity and involve other regions of the mouth with further eruption of teeth. More seriously, as the lesion can impact feeding, nutritional deficiency, dehydration and poor growth often accompanies the clinical presentation (Ceyhan et al. 2009).

Similar cases to the one presented have been reported. Abramson and Dowrie in 1944 reported an 11-month-old girl with a rapidly progressing ulcer on the ventral tongue after eruption of her mandibular teeth. The child frequently 'scraped' the tongue over the teeth, causing bleeding and resulting in a defect at the tip. Zaenglein et al. (2002) describe a 10-month-old infant with an extensive "oral plaque" affecting the ventral

tongue and lip. The clinical findings included a repetitive tongue-thrust and lip-biting behaviour. The medical history revealed poor feeding since birth with recurrent post-prandial vomiting, GI dysmotility, developmental delay, poor muscle tone and an abnormal pain response. The child was diagnosed with congenital autonomic dysfunction with universal pain loss (CADUPL).

Our patient presented at the average age reported in the literature and with the typical clinical features of the disease, namely ulceration of the ventral tongue caused by the primary mandibular incisors and a continuous tongue thrust. The patient also displayed some of the well-documented medical features associated with Riga-Fede, including GDD, prenatal complications and reduced sensitivity to pain associated with an undiagnosed genetic condition, suspected to be mitochondrial disease.

Riga-Fede can often be one of the first indications of an underlying neurological condition. Baghdadi (2001) and Sivamurukan et al. (2019) reported cases diagnosed with microcephaly and glutaric aciduria Type I, respectively. In both cases, these diagnoses were made after a history and examination revealed developmental regression and an oral traumatic ulcer. A referral for neurological assessment confirmed the diagnosis. The relationship between neurological abnormalities and the development of Riga-Fede has thus far not been explored in the medical or dental literature, and is an area requiring further research. One possible explanation is that a reduced pain response and involuntary muscle contractions, which are characteristic features of CADUPL and familial dysautonomia, both affecting the autonomic nervous system, contribute to persistence and severity of the traumatic ulcers.

Although diagnosis of Riga-Fede is made based on the typical clinical presentation and seldom requires biopsy, in cases of unresolving lesions and inconsistencies between the clinical appearance and causative factor, systemic involvement or medically compromised patients, further investigations may be required. Differential diagnoses of oral ulcerations are listed in Table 2.

In general, the principles of a thorough history, assessment and prompt diagnosis are paramount to minimising the risk of complications associated with Riga-Fede and may obviate the need for invasive procedures. The presence of multiple anomalies, dysmorphic features or involuntary movements may support a clinician's decision to refer for neurological examination or genetic testing (Hallett et al. 2016).

The literature states that a conservative approach is preferable due to the sequelae of early extraction of deciduous teeth, such as space loss (Slayton 2000; Choi et al. 2009; Jingarwar et al. 2014). However, space loss is less likely to occur in the anterior region, with a greater risk the earlier the extraction, prior to eruption of the primary canines, if more than one tooth is extracted and in crowded dentitions. The premature loss of one or more primary incisors has also been reported to be a causative factor in tongue thrusting and contribute to abnormal eruption of the permanent successor, but there is little evidence to support this (Holan et al. 2013).

The various treatment options are summarised in Table 3. In the present case the risk of systemic involvement, higher risk of recurrence, severity of the lesions and later, failure of conservative treatment, supported the decision to extract the offending teeth. Other reasons supporting extraction include mobile teeth nearing exfoliation or posing an aspiration risk, impaired feeding resulting in dehydration or malnutrition or slow resolution of the lesion (Baroni et al. 2006; van der Meij et al. 2012; Li et al. 2015). Although frequently carried out in earlier case reports, biopsy is rarely indicated as the clinical presentation if often sufficient to confirm the diagnosis.

Novel approaches of laser therapy and recombinant bovine basic fibroblast growth factor (rb-bFGF) have been reported in the literature (Li et al. 2016; da Silva et al. 2017). Da Silva et al. (2017) used a low-level laser in addition to extractions and topical corticosteroid use. The laser treatment was applied directly to the lesion on three consecutive days after extraction. After the third day, there was evidence of healing of the lesion. It is difficult to conclude whether the laser therapy alone or in combination with other treatment modalities resulted in the outcome. Li et al. (2016) applied rb-bFGF topically to the lesion and advice was given to the parents to reduce soft tissue trauma. Clinical healing was observed within one week and

Table 2: Differential Diagnoses for Oral Ulcerations (Neville et al. 2016)

Aetiology	Example
Trauma	Traumatic ulcer – mechanical, heat, chemical
Nutritional deficiency	Iron, Vitamin D, folate
Haematological disease/disorders	Pernicious anaemia, leukaemia, neutropenia
Viral	Herpes simplex virus – primary herpetic gingivostomatitis
Bacterial	Tuberculous ulcer
Malignancy	Oral squamous cell carcinoma

Table 3: Treatment Options

Preventive	Modifying feeding, weaning
	Teething rings
	Mouthguard
Pharmacologic	Topical corticosteroids (e.g. 0.1% triamcinolone acetonide in Orabase)
	Topical recombinant-fibroblastic growth factor
Restorative	Covering incisal edges (e.g. composite)
	Smoothing incisal edges
Surgical	Laser therapy
	Extraction
	Excision

no recurrence at the three-month follow-up. Rb-bFGF and laser therapy are understood to promote tissue repair. rb-FGF, a cytokine, stimulates angiogenesis, cell division and differentiation to accelerate wound healing (Lie et al. 2017; Fu et al., 2000). Laser irradiation increases microcirculation in the affected tissue and triggers a pro-inflammatory cytokine response, stimulating proliferation of fibroblasts and inflammatory cells to form granulation tissue (Aggarwal et al. 2014; Spanemberg et al. 2016; da Silva et al. 2017). Currently there is limited evidence about the effectiveness on these therapies, with few long-term studies assessing their independent therapeutic effect on oral ulcerative lesions.

The treatment of choice should take into consideration the medical status of the patient, the severity and risk of recurrence of lesions and the presence of mobile teeth. In the present case, and frequently noted in the literature, was the parents' reluctance consenting to tooth extraction. Combined with often late identification of the disease by clinicians, this can impact timely delivery of care. Greater clinician awareness and their role in educating parents about the potential complications of untreated Riga-Fede, which may be facilitated by joint discussions with GPs or Paediatricians, may improve this. Multidisciplinary management, such as combined general anaesthetics for dental and other surgical procedures and ongoing communication with a patient's medical team, are more likely to result in greater parent confidence and treatment outcomes.

Future directions include exploring the association with congenital neurological and developmental conditions, which may allow clinicians to identify 'high risk' patients, and the development of definitive diagnostic criteria. More research is required to assess the prevalence of the disease in New Zealand, how it is being managed, and the current awareness of Riga-Fede amongst medical and dental professionals considering the complex medical histories of affected patients, and the potential systemic complications if left untreated. It is clear that Riga-Fede disease presents several opportunities for further research.

Conclusion

Riga-Fede disease is a rare clinical entity affecting children and can have a significant impact on quality of life if not effectively managed with early detection and intervention. This can be achieved by a comprehensive history and examination, including screening for neurological conditions, which may warrant referral for further investigations and reveal risk factors supporting treatment decisions. As dentists, it serves as a reminder to take a 'whole person' approach to care in order to achieve optimal outcomes for both the child's oral and general health.

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References

Abramson M, Dowrie JO (1944). Sublingual granuloma in infancy (Riga-Fede's disease). *The Journal of Pediatrics.* 24: 195–198.

Aggarwal H, Singh MP, Nahar P, Mathur H, GV S. (2014). Efficacy of low-level laser therapy in treatment of recurrent apthous ulcers–sham controlled, split mouth follow up study. 8(2): 218-221.

Ahmet T, Ferruh B, Gurcan A (2002). Lingual traumatic ulceration (Riga-Fede disease). *Journal of Oral and Maxillofacial Surgery*. 60(4): 478.

Ahmet T, Ferruh B, Gurcan A (2003). Lingual traumatic ulceration (Riga-Fede disease). *British Journal of Oral and Maxillofacial Surgery.* 41(3): 201.

Amberg S (1902). Sublingual growth in infants. *The American Journal of Medical Sciences*. 126: 257-269.

Alahmari A, Alahmari AS (2017). Management of Riga-Fede disease: A Case Report. *Dentistry.* 7: 2.

Bafna Y, Khandelwal V, Bafna M, Nayak PA (2013). Management of sublingual ulceration in a 12-month-old child. *BMJ Case Reports.* Aug 2013.

Baghdadi ZD (2001). Riga-Fede Disease: Report of a Case and Review. *Journal of Clinical Pediatric Dentistry.* 25(3): 209-213.

Baghdadi ZD (2002). Riga-Fede Disease: Association With Microcephaly. *International Journal of Paediatric Dentistry.* 12(6): 442-445.

Baldiwala M, Nayak R (2014). Conservative management of Riga-Fede disease. *Journal of Dentistry for Children.* 81(2): 103-106.

Baroni A, Capristo C, Rossiello L, Faccenda F, Satriano RA (2006). Lingual traumatic ulceration (Riga–Fede disease). *International Journal of Dermatology.* 45: 1096-1097.

Basavanthappa NN, Kagathur U, Basavanthappa RN, Suryaprakash ST (2011). Natal and neonatal teeth: a retrospective study of 15 cases. *European Journal of Dentistry.* 5(2): 168–172.

Bhatt R, Dave B, Sheth M (2015). Riga-Fede Disease: Report of a Case with Literature Review. *Advances in Human Biology.* 5(1): 52-55.

Buchanan S, Jenkins CR (1997). Riga-Fedes syndrome: Natal or neonatal teeth associated with tongue ulceration. Case report. Australian Dental Journal. 42(4): 225-227.

Campos-Muñoz L, Quesada-Cortés A, Corral-De la Calle M, Arranz-Sánchez D, Gonzalez-Beato M, De Lucas R, Vidaurrázaga C (2006). Tongue ulcer in a child: Riga-Fede disease. *Journal of the European Academy of Dermatology and Venereology.* 20: 1357-1359.

Cavus S & Ozmen B (2017). Riga-Fede Disease in the Upper Jaw in an Infant. *Dermatology and Therapy.* 30(5).

Ceyhan AM, Yildirim M, Basak PY, Akkaya VB Ayata A (2009). Traumatic lingual ulcer in a child: Riga–Fede disease. *Clinical and Experimental Dermatology.* 34: 186-188.

Choi SC, Park JH, Choi YC Kim GT (2009). Sublingual traumatic ulceration (a Riga-Fede disease): report of two cases. *Dental Traumatology.* 25: 48-50.

Chotai PN, Nollan R, Huang EY, Gosain A (2017). Surgical informed consent in children: a systematic review. *Journal of Surgical Research*. 213: 191-198.

Compilato D, Corsello G, Campisi G. (2012). An Unusual Traumatic Ulceration of the Tongue. *Journal of Paediatrics and Child Health*. 48(12): 1104-1105.

Costacurta M, Maturo P, Docimo R (2012). Riga-Fede disease and neonatal teeth. *ORAL & Implantology.* 5(1): 26-30.

da Silva DC, de Freitas PM, Calvo AF, Gimenez T, Zanola M, Imparato JC (2017). Treatment of Riga-Fede disease using laser therapy: clinical case report. *Revista Gaúcha de Odontologia.* 65(1): 87-91.

Deep SB, Ranadheer E, Rohan B (2011). Riga-Fede Disease: Report of a case with Literature Review. *Journal of Advanced Dental Research.* 2(2): 27-30.

Dezan CC, Walter LRF, Weber-Gasparoni K, Sangiorgio JPM, Nogari B, Fernandes KBP (2011). Sublingual Traumatic Ulcerative Lesions Caused by the Eruption of First Primary Mandibular Molars: a Case Report. *International journal of morphology*. 29(4): 1136-1138.

Domingues-Cruz J, Herrera A, Fernandez-Crehuet P, Garcia-Bravo B, Camacho F (2007). Riga-Fede Disease Associated with Postanoxic Encephalopathy and Trisomy 21: A Proposed Classification. *Pediatric Dermatology.* 24: 663-665.

Dunlop R, Barton D, Jones J (2013). Riga-fede Disease: A Case Report. *Journal of Pediatric Health Care.* 27(2): 155-157.

Edmonds JL, Kirse DJ, Kearns D (2002). The Otolaryngological Manifestations of Mitochondrial Disease and the Risk of Neurodegeneration With Infection. *Archives of Otolaryngology – Head & Neck Surgery.* 128(4): 355-362.

Eichenfield LF, Honig PJ, Nelson L (1990). Traumatic granuloma of the tongue (Riga-Fede disease): Association with familial dysautonomia. *The Journal of Pediatrics.* 116(5): 742-744.

Ekinci AP, Kilic S, Kobaner GB (2018). Early-onset and persistent traumatic granuloma of the tongue (Riga-Fede disease) associated with neonatal teeth and Down syndrome. *Journal of the European Academy of Dermatology and Venereology.* 33(3): 131-132

Eley KA, Watt-Smith PA, Watt-Smith SR (2010). Deformity of the Tongue in an Infant: Riga- Elzay RP (1983). Traumatic ulcerative granuloma with stromal eosinophilia (Riga-Fede's disease and traumatic eosinophilic granuloma). Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 55(5): 497-506.

Fede Disease*. Paediatrics & Child Health.* 15(9): 581-582.

Fede F (1890). Della produzione sottolinguale, o malattia di Riga. *Atto Congresso italiano di pediatria*. Napoli, 1891: 251.

Fu X, Shen Z, Chen Y, Xie J, Guo Z, Zhang M, Sheng Z (2000). Recombinant bovine basic fibroblast growth factor accelerates wound healing in patients with burns, donor sites and chronic dermal ulcers. *Chinese Medical Journal.* 113: 367–71.

Ghimire N, Maharajan IK, Kumar A, Koirala B (2013). Riga-Fede Disease. *Health Renaissance.* 11: 174-176.

Goho C (1996). Neonatal sublingual traumatic ulceration (Riga-Fede disease): reports of cases. *ASDC Journal of Dentistry for Children.* 63(5): 362-364.

Gorman G, Chinnery P, DiMauro S et al., (2016). Mitochondrial diseases. *Nature Reviews Disease Primers.* 2: 16080

Hallett KB, Alexander S, Wilson M, Munns C, Cameron AC, Widmer RP (2016). Medically compromised children. In Cameron AC & Widmer RP, editors *Handbook of Pediatric Dentistry (Fourth Edition)*: Mosby (pages 329-383).

Hegde RJ (2005). Sublingual traumatic ulceration due to neonatal teeth (Riga-Fede disease). *Journal of Indian Society of Pedodontics and Preventive Dentistry.* 23(1): 51-52.

Holan G, Needleman HL (2013). Premature loss of primary anterior teeth due to trauma – potential short- and long-term sequelae. *Dental Traumatology.* 30(2): 100-106.

Hong P (2015). Riga-Fede Disease: Traumatic Lingual Ulceration in an Infant. *The Journal of Pediatrics*. 167(1): 204.

Inagaki LT, Sullcahuamán JAG, Lara, SMH, Dezan CC, de Figueiredo Walter LR (2009). Tongue Granulomatous Lesion Caused by Mandibular Primary Incisors Eruption. *Pediatric Dermatology*. 26(5): 640-641.

Jamani NA, Ardini YD, Harun NA (2018). Neonatal tooth with Riga-Fide disease affecting breastfeeding: a case report. *International Breastfeeding Journal*. 13: 35.

Jariwala D, Graham RM, Lewis T (2008). Riga-Fede Disease. *British Dental Journal.* 204(4): 171.

Jingarwar MM, Bajwa NK, Pathak A (2014). Riga Fede Disease: Fibrous Hyperplasia Associated with Natal Teeth in an Infant – A Case Report and Clinical Update. *Indian Journal of Neonatal Medicine and Research*. 2(1): 11-13.

Kanumuri PK (2017). Riga Fede Disease. *Journal of Neonatal Surgery.* 6(1) 20.

Kanungo S, Morton J, Neelakantan M, Ching K, Saeedian J, Goldstein A (2018). Mitochondrial disorders. *Annals of Translational Medicine.* 6(24): 475.

Kariya PB, Shah S, Singh S, Buch A (2019). Riga-Fede Disease Associated With Syndactyly and Oligodactyly: A Rare Occurrence. *Journal of Clinical Pediatric Dentistry.* 43(5): 356-359.

Kumari A, Singh PK (2019). Diagnosis of Riga-Fede Disease. *Indian Journal of Pediatrics.* 86(2): 191.

Lee J, Mandel L (2014). Rigo-Fede Disease: Case Report. *New York State Dental Journal*. 80(2): 36-37.

Lee JJ, Sarangam M, Feldman KW, Tieder JS (2019). Riga-Fede Disease: A Case of Sublingual Trauma Not Associated With Abuse. *Pediatric Emergency Care.* November 8, 2019.

Li J, Zhang YY, Wang NN, Bhandari R, Liu QQ (2016). Riga-Fede Disease in a Child. *Clinical and Experimental Dermatology.* 41(3): 285-286.

López-Cortés A, Zambrano AK, Guevara-Ramírez P, Echeverría BA, Guerrero S, Cabascango E, Perez-Villa A, Armendariz-Castillo I, Garcia-Cardenas JM, Yumiceba V, et al (2020). Clinical, genomics and networking analyses of a high-altitude native American Ecuadorian patient with congenital insensitivity to pain with anhidrosis: A case report. *BMC Medical Genomics* 13(1): 113.

Machuca G, Rordriguez S, Vargas MP, Suarez C, Bullon P (2007). Management of Riga-Fede disease: a case report. *Journal of Disability and Oral Health.* 8(1): 28-30.

Mhaske S, Yuwanati MB, Mhaske A, Ragavendra R, Kamath K, Saawarn S. (2013). Natal and neonatal teeth: an overview of the literature. *ISRN Pediatrics*. 2013: 956269.

Malhotra PU, Malhotra Y, Ohri N, Godara S (2020). Sublingual tongue deformity in infants: Riga-fede disease–A case report. *Journal of Advanced Medical and Dental Sciences Research.* 8(7): 143-145.

McDaniel RK, Morano PD (1978). Reparative lesion of the tongue. *Oral Surgery*. 45: 266–271.

Mehta A, Chaudhary S, Chaitra TR, Sinha A (2017). Riga-Fede Disease (Dentitia Praecox): Report of Two Cases with Literature Review. *Austin Journal of Dentistry.* 4(3): 1073.

Mohan RPS, Verma S, Gill N, Singh U (2014). Riga-Fede disease (Cardarelli's aphthae): A report of nine cases. *South African Journal of Child Health.* 8(2): 72-74.

Moura LF, de Moura LS, de Lima M, Lima CC, Barros N, Lopes TS (2014). Natal and Neonatal Teeth: A Review of 23 Cases. *Journal of Dentistry for Children.* 81(2).

Narang T, De D, Kanwar AJ (2008). Riga-Fede Disease: Trauma Due to Teeth or Tongue Tie? *Journal of the European Academy of Dermatology and Venereology.* 22(3): 395-396.

Neville BW, Damm DD, Allen CM, Chi AC (2016). Differential Diagnosis of Oral and Maxillofacial Diseases. In *Oral & Maxillofacial Pathology (Fourth Edition).* Missouri: Elsevier (pages 849-871).

Ozmen B and Acar O (2015). Persistent Untreated Riga-Fede Disease for 6 Years. *Pediatric Dermatology.* 32(3): 134-135.

Padmanabhan MY, Pandey RK, Aparna R, Radhakrishnan V (2010). Neonatal sublingual traumatic ulceration – case report & review of the literature. *Dental Traumatology.* 26: 490-495.

Paranna S, Kamath P (2017). Riga–Fede disease in association with natal teeth. *Journal of Dental Research and Review.* 4(3): 69-71.

Picciotti M, DiVece L, Viviano M, Giorgio A, Lorenzini G (2014). Meningitis and Riga-Fede disease: an unusual condition. *European Journal of Paediatric Dentistry.* 15(2): 245-246.

Praveen Kumar PS, Dhull KS, Dhull RS, Panda S, Yadav S, Indira MD (2013). Riga Fede Syndrome: A review of literature and report of three cases. *International Journal of Oral and Maxillofacial Pathology.* 4(2): 40-44.

Pujar, Pallavi (2014). Riga-Fede disease. *Indian Journal of Dental Advancements*. 6(1): 1475. *Gale Health and Wellness*. *https://link.gale.com/apps/doc/A378681991/HWRC?u=otago&sid=HWRC&xid=6958aa03 (accessed 2 October 2020)*.

Rakocz M, Frand M, Brand N (1987). Familial dysautonomia with Riga-Fede's disease: report of case. *ASDC Journal of Dentistry for Children*. 54(1): 57-59.

Riga A (1881). Di una malattia della prima infanzia, Probabilmente non trattata, di movimenti patologici. *Movimento medico-chirurgicoi*. XIII: 22.

Sachdeva SK, Vengal M (2015). Riga-fede disease: A rare case of traumatic sublingual ulceration. *Journal of Clinical Neonatology.* 4(1): 62-63.

Sakulratchata R (2019). Extensive sublingual ulceration leads to tongue deformity in a child with delayed development. *Pediatric Dental Journal*. 29(3): 164-166.

Samuel SS, Ross BJ, Rebekah G, Koshy S (2018). Natal and Neonatal Teeth: A Tertiary Care Experience. *Contemporary Clinical Dentistry.* 9(2): 218-222.

Senanayake MP, Karunaratne I (2014). Persistent lingual ulceration (Riga-Fede disease) in an infant with Down syndrome and natal teeth: a case report. *Journal of Medical Case Reports.* 8: 283.

Sharma N, Chander S, Soni S, Singh S, Chodhary MP (2012). Riga-Fede disease due to neonatal tooth: a case report. *International Journal of Oral and Maxillofacial Pathology.* 3: 43-44. Shivpuri, A, Mitra R, Saxena V, Shivpuri A (2018). Natal and neonatal teeth: Clinically relevant findings in a retrospective analysis. Medical Journal Armed Forces India. *https://doi.org/10.1016/j.mjafi.2018.07.001 (accessed 3 October 2020).*

Sivamurukan P, Chandrasekaran V, Biswal N (2019). Riga Fede Disease With Glutaric Aciduria Type I. *The Indian Journal of Pediatrics.* 87(6): 484-485.

Slayton RL (2000).. Treatment alternatives for sublingual traumatic ulceration (Riga-Fede disease) *Pediatric Dentistry Journal*. 22: 413–414.

Spanemberg JC, de Figueiredo MA, Cherubini K, Salum FG. (2016). Low-level laser therapy: A review of its applications in the management of oral mucosal disorders. *Alternative Therapies in Health and Medicine.* 22(6): 24-31.

Taghi A, Motamedi MH (2009). Riga-Fede Disease: A Histological Study and Case Report. *Indian Journal of Dental Research.* 20(2): 227-229.

Toy BR (2001). Congenital autonomic dysfunction with universal pain loss (Riga-Fede disease). *Dermatology Online Journal.* 7(2).

van der Meij EH, de Vries TW, Eggink HF, de Visscher JG (2012).Traumatic Lingual Ulceration in a Newborn: Riga-Fede Disease. *Italian Journal of Pediatrics.* 38: 20.

Volpato LE, Simoes CA, Simoes F, Nespolo PA, Borges AH (2015). Riga-Fede Disease Associated with Natal Teeth: Two Different Approaches in the Same Case. *Case Reports in Dentistry.* 1-4. Yacovone L, Robertson D, Ng MW (2011). Riga-Fede Disease: A Rare Sublingual Traumatic Ulcerative Lesion in a Child. *Otolaryngology – Head and Neck Surgery.* 146(2): 333-334.

Yurekli A, Dincer D (2019). Successfully Treated Riga-Fede Disease. *Dermatology Practical & Conceptual.* 9(3): 218-219.

Zaenglein AL, Chang MW, Meehan SA, Axelrod FB, Orlow SJ (2002). Extensive Riga-Fede Disease of the Lip and Tongue. *Journal of the American Academy of Dermatology.* 47(3): 445-447.

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