Case Report

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Dentistry Section

Gingival Giant Cell Fibroma in Three-year-old Patient: A Case Report with Review of Literature

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ABSTRACT

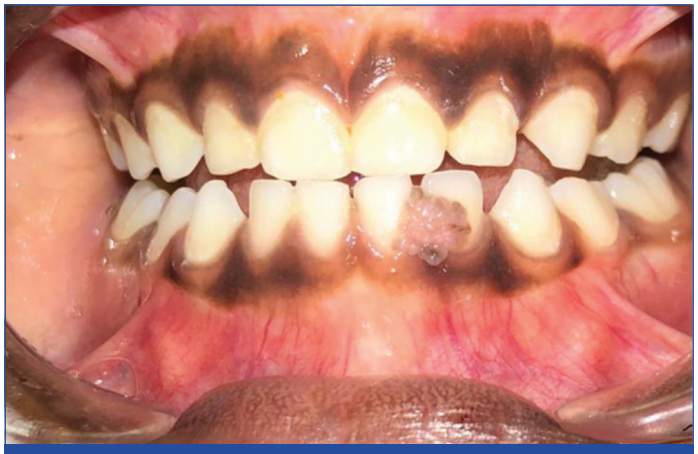
Gingival diseases are commonly observed in children and young adults. However, Giant Cell Fibroma (GCF) is a rare occurrence in children, accounting for only 2.2-7.3% of oral fibrous tumour cases. Clinically, these lesions often resemble squamous papillomas, and a definitive diagnosis can only be confirmed through histopathological {Haematoxylin and Eosin (H&E)} examination. Hereby, the authors present a rare case of gingival GCF in a three-year-old boy who presented with a pebbly growth on the mandibular gingiva. Initially, the lesion was clinically diagnosed as a papilloma and subsequently excised. The final diagnosis of GCF was established through histological examination. It is crucial for paediatric dentists to consider GCF as a differential diagnosis for lesions, particularly those with a papillary surface. Additionally, submitting all excised specimens for histopathological examination is recommended.

Keywords: Fibrous tumor, Giant cell, Papilloma

CASE REPORT

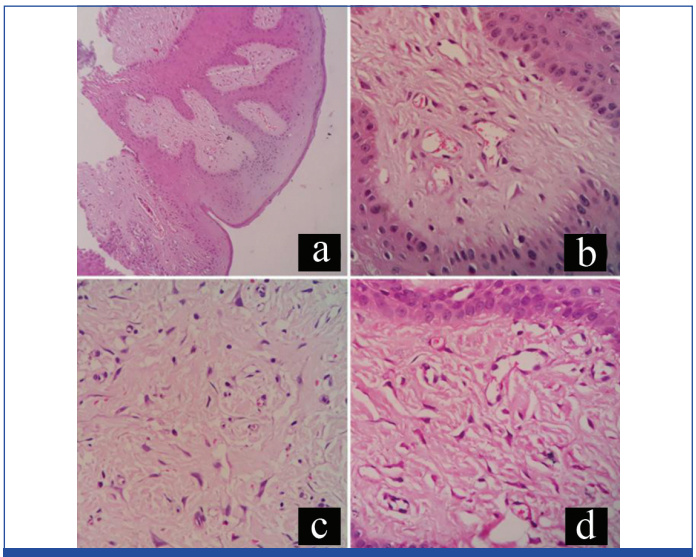
A three-year-old boy of Dravidian (linguistically Tamil) background presented to the Department of Paediatric Dentistry with a chief complaint of painless swelling in the lower jaw, since he was eight months old. The parents noticed a small growth between the lower front teeth while brushing his teeth, but it did not significantly affect his oral functions. Over the course of two years, the swelling gradually increased in size, causing slight discomfort, prompting them to seek medical consultation. The patient had received vaccinations and had no other notable medical history.

Upon intraoral examination, a pedunculated, painless, soft growth was observed originating from the facial aspect of teeth 71 and 72 (According to Federation Dentaire Internationale tooth numbering system). The swelling, with a pebbly surface, appeared pink in colour and measured 1.7×1.5 cm [Table/Fig-1]. There was no associated bleeding or pus discharge. The teeth were free of cavities, and no other abnormalities were detected in the soft tissues or teeth. The overall oral hygiene was good. Based on the clinical appearance of a painless growth with a papillary surface, a provisional diagnosis of squamous papilloma was made. An excisional biopsy was performed under local anaesthesia, and the mass was easily removed.



[Table/Fig-1]: Clinical presentation of the lesion in relation to teeth 71 and 72.

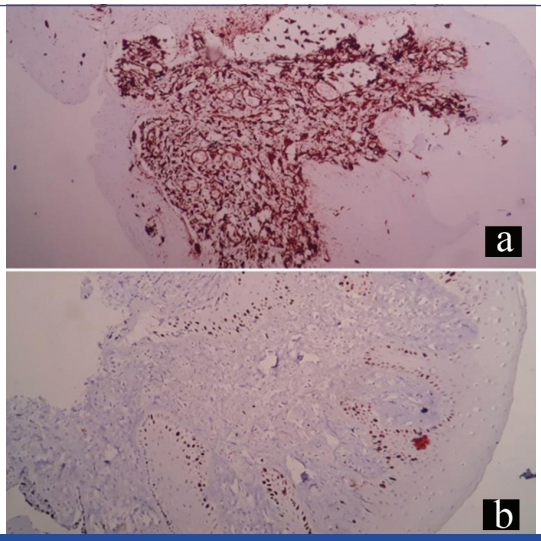
The excised specimen was submitted to the Department of Oral Pathology and Microbiology in 10% buffered formalin. Grossly, the specimen consisted of multiple small creamy white bits with a soft consistency. Microscopic examination revealed hyperplastic hyperparakeratinized stratified squamous epithelium covering the tissue, with numerous surface crypts reminiscent of papillary surface and elongated confluent rete pegs [Table/Fig-2a]. The juxtaepithelial connective tissue exhibited fibrovascular connective tissue stroma with numerous enlarged, stellate-shaped fibroblasts, occasionally displaying multiple nuclei [Table/Fig-2b,c]. Characteristic retraction spaces were observed around these cells [Table/Fig-2d].



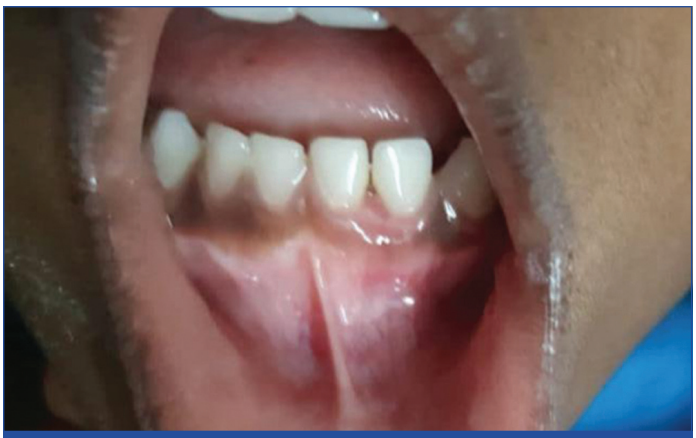
[Table/Fig-2]: Photomicrographs showing: a) Tissue covered by hyperplastic stratified squamous epithelium with confluent rete pegs and loose underlying stroma (H&E, 40X); b) Fibrovascular sub epithelial connective tissue with numerous stellate-shaped cells (H&E, 400X); c) Prominent stellate-shaped cells and occasional large cells (H&E, 400X); and d) Artefactual retraction space around stellate cells (H&E, 400X).

Immunohistochemical (IHC) analysis using a panel of markers was conducted to assess histogenesis. Vimentin showed diffuse positivity, while Ki-67 demonstrated a proliferation index of less than 1%. CD34 (Clusters of Differentiation), S100, and CD68 markers were negative [Table/Fig-3a,b] (only positive markers shown). Based on the histopathology findings, a final diagnosis of Gingival Giant Cell Fibroma (GCF) was established. Subsequent follow-up appointments were scheduled every four months for the next year, during which no signs of recurrence or residual disease were

observed [Table/Fig-4]. Since, the lesion was excised using laser ablation, causing minimal discomfort to the patient, syrup Ibugesic Plus was prescribed at a dosage of 2.5 mL twice a day for three days to alleviate pain.



[Table/Fig-3]: a,b) Photomicrographs showing showing diffuse cytoplasmic vimentin immunopositivity, Ki-67 immunoreactivity <1% (basal layer of epithelium served as a positive internal control) (IHC, 100X).



[Table/Fig-4]: Clinical presentation at eight months follow-up.

DISCUSSION

Gingival diseases in children and young adults encompass a wide range of conditions, including infectious, reactive, developmental, and neoplastic lesions. Often, these lesions exhibit such close clinical resemblance that it becomes challenging, if not impossible, to make a definitive diagnosis based solely on clinical presentation. Papillary or pebbly lesions commonly observed in children include vascular malformations like lymphangiomas and virally induced lesions such as squamous papilloma, verruca vulgaris, Heck's disease, and occasionally condyloma acuminatum [1].

Gingival Giant Cell Fibroma (GCF), a term coined by Weathers DR and Callihan MD in 1974, is considered a distinct fibrous tumour with unique clinical and histopathological features [2]. GCF accounts for 2.2-7.3% of all oral fibrous tumours submitted for biopsy [3-6]. Typically, this lesion is more prevalent in the second to third decade of life, with a slight female predominance [5-7]. In the absence of histopathological confirmation, GCF is often clinically diagnosed as papilloma or fibroma [5]. GCF is a rare diagnosis in infants and young children, and the final diagnosis can only be established through histological examination. As mentioned earlier, GCF is an uncommon entity, most commonly seen in individuals in their second to third decade of life, with a slight female predominance [3,5,8].

Clinically, GCF can resemble fibroma, squamous papilloma, verruciform xanthoma, or even lymphangioma, depending on whether it appears sessile or pedunculated with a smooth or papillary surface [9]. Although rare, oral focal mucinosis may also be considered in the differential diagnosis. However, definitive diagnoses for all these lesions can only be made through histopathology. A clinicopathological analysis of 464 cases revealed that 44.6% of the clinically diagnosed cases were fibromas, followed by papillomas in 28.9% of cases [5]. The lower concordance between clinical and histopathological diagnoses emphasise the fact that clinicians might be less familiar with GCF [5].

Review of literature: A detailed clinicopathological data of GCF in individuals younger than 18 years is presented in [Table/Fig-5] [7,10-25]. Individuals older than eighteen years were excluded from the clinicopathological review. Additionally, papers written in languages other than English and papers for which the full text could not be obtained were also excluded. The youngest reported patient was a

Author and year	Ethnicity	Age	Sex	Location	Laterality	Size (in cm)	Appearance and colour	Treatment and follow-up
Takeda Y et al., (1986) [10]	Japanese	3 y	F	Posterior palatal gingiva	Right	1.5×0.5×0.4	Nodular, Normal	Excision No recurrence
Fadavi S et al., (1987) [11]	-	11 y	M	Maxillary gingiva	-	-	-	Excision
Swan RH (1988) [12]	Caucasian	6 y	M	Posterior maxillary facial gingiva	Left	1×0.5	Bosselated, Pink	Excision 2 years No recurrence
Braga MM et al., (2006) [13]	Caucasian	3 y	M	Anterior palatal gingiva	Right	0.5	Nodular and pedunculated, normal	Excision 3 month No recurrence
Campos MS et al., (2009) [14]	Caucasian	11 y	F	Anterior palatal gingiva	Midline	1.5	Nodular and pedunculated, normal	Excision 1 year No recurrence
Kuo RC et al., (2009) [15]	-	10 y	F	Lateral border of tongue	Left	4×3	-	Excision No recurrence
		18 y	F	Lateral border of tongue	Left	6×4	-	Excision No recurrence
		7 y	M	Anterior labial gingiva (maxillary)	Midline	2×1	-	Excision No recurrence
		10 y	M	Anterior palatal gingiva (maxillary)	Right	5×4	-	Excision No recurrence
		18 y	F	Hard palate	Left	9×5	-	Excision No recurrence
		18 y	F	Retromolar area	Right	4×3	-	Excision No recurrence
		13 y	F	Retromolar area	Right	4×3	-	Excision No recurrence
		15 y	F	Retromolar area	Left	4×4	-	Excision No recurrence

Shapira M M and Akrish S (2011) [16]	-	6 y	F	Tip of tongue	Midline	0.3×0.3	Exophytic, white	Excision
Uloopi KS et al., (2012) [17]	Indian	12 y	F	Lateral border of tongue	Left	1.8×0.7×0.6	Sessile growth, normal	Excision 6 months No recurrence
Sabarinath B et al., (2012) [18]	Indian	9 y	F	Anterior gingiva (maxillary)	Midline	6×5	-	-
Vergotine RJ (2012) [7]	African-American	17 m	F	Anterior palatal gingiva	Right	0.75	Sessile, normal	Excision 1 week No recurrence
Nikitakis NG et al., (2013) [19]	Caucasian Caucasian	7 y 6 y	M M	Anterior gingiva (mandibular) Anterior interproximal gingiva (mandibular)	Right Left	0.4×0.3 0.7×0.5	Pedunculated, white Pedunculated, papillary, white	Excision 2 years No recurrence Excision 4 years No recurrence
Reddy VK et al., (2015) [20]	Indian	10 y	M	Anterior lingual gingiva (mandibular)	Right	NA	Pedunculated	Excision 3 months No recurrence
Mello-Moura AC et al., (2016) [21]	Caucasian	2 y	F	Anterior lingual gingiva (mandibular)	Midline	0.5×0.5×0.3	Pedunculated, white	Excision 20 months No recurrence
Patankar SR et al., (2016) [22]	Indian	5 y	M	Posterior facial gingiva (mandibular)	Right	1×0.7	Papillary, pinkish	Excision 6 months No recurrence
Sanjeeta N et al., (2018) [23]	Indian	18 y	F	Posterior gingiva (maxillary)	Right	1.2×0.9	Pedunculated, lobulated, normal	Excision
Razi MR et al., (2020) [24]	Malay	1 m	M	Posterior gingiva facial (maxillary)	Left	1.5×1.5	Sessile, normal	Excision 1 year No recurrence
Irani S et al., (2022) [25]	-	4 y	F	Anterior gingiva facial (mandibular)	Right	0.5	Sessile, papillary surface	Excision
Present case	Indian	3 y	M	Anterior gingiva facial (mandibular)	Left	1.7×1.5	Pedunculated, pebbly surface, pink	Excision 8 months No recurrence

[Table/Fig-5]: Clinico-demographic profile of Giant Cell Fibroma (GCF) cases in individuals younger than 18 years [7,10-25].
y: Years; m: Months; F: Female; M: Male

newborn [24]. Including the present case, only six cases of GCF in children aged 3 years or younger have been reported [Table/Fig-6] [7,10,13,21,24].

The present patient is a young male, in contrast to the overall trend of females being more commonly affected than males (female to male ratio was 2.36: 1), which is consistent with the gender distribution in adults. These findings align with the literature [5,6]. The gingiva was the most commonly affected site in children, followed by the tongue, retromolar region, and palate in descending order. The literature consistently mentions the gingiva as the most common site [3,5], although a study in the Brazilian population found the tongue to be the most frequently affected site [6]. Overall maxillary cases were more prevalent than mandibular lesions and, the lesions were more frequent in the anterior segments, contrasting with the literature [3]. In the present case, the patient presented with a lesion in the anterior mandibular gingiva. Racial details were available for 15 cases (including the present case), and an equal distribution was found among Caucasians and Indians, contrary to the literature [Table/Fig-5] [5]. The present case is the youngest reported case in the Indian population, possibly due to under reporting and lack of awareness of the entity.

Histologically, GCF exhibits hyperplastic epithelium with abundant large stellate cells in the subepithelial fibrovascular stroma [2,26]. Binucleation/multinucleation is not uncommon, and retraction spaces around the stellate cells are frequently observed [26,27], as noted in the present case. Researchers have attempted to understand the histogenesis of GCF and have concluded that the stellate cells are of fibroblastic origin.

To gain further insight into histogenesis, a wide variety of immunohistochemical markers have been used in the literature. Among the markers used in the present case, only vimentin showed positive staining in the stellate stromal cells. The proliferation index was very low (<1%). S100, CD68, and CD34 were negative, consistent with previous studies, ruling out melanocytic, macrophage-monocytic, or endothelial origin [3,26]. It is now widely accepted that the stellate cells seen in GCF are fibroblastic in origin. There is uncertainty regarding whether these cells bear any relationship to similar cells found in angiofibroma, perifollicular fibroma, or fibrous papule of the nose [2]. The distinctive appearance and presence of multinucleated giant cells remain unclear. Based on ultrastructural study, Savage NW et al., suggested that these cells are relatively inactive compared to neighboring fibroblasts, supported by sparse rough endoplasmic reticulum, lack of pseudopodia, and central perinuclear concentration of microfilaments. They also proposed myofibroblastic differentiation [27]. However, subsequent studies have shown negative Smooth Muscle Actin (SMA) expression in all cases of GCF [26,28]. These studies also suggested that stellate and multinucleated giant cells are functional and participate in

Author and year	Ethnicity	Age	Sex	Location	Laterality	Size (in cm)	Appearance and colour	Treatment and follow-up
Takeda Y et al., (1986) [10]	Japanese	3 y	F	Posterior palatal gingiva	Right	1.5×0.5×0.4	Nodular, Normal	Excision No recurrence
Braga MM et al., (2006) [13]	Caucasian	3 y	M	Anterior palatal gingiva	Right	0.5	Nodular and pedunculated, normal	Excision 3 month No recurrence
Vergotine RJ (2012) [7]	African-American	17 m	F	Anterior palatal gingiva	Right	0.75	Sessile, normal	Excision 1 week No recurrence
Mello-Moura AC et al., (2016) [21]	Caucasian	2 y	F	Anterior lingual gingiva (mandibular)	Midline	0.5×0.5×0.3	Pedunculated, white	Excision 20 months No recurrence
Razi MR et al., (2020) [24]	Malay	1 m	M	Posterior gingiva facial (maxillary)	Left	1.5×1.5	Sessile, normal	Excision 1 year No recurrence
Present case	Indian	3 y	M	Anterior gingiva facial (mandibular)	Left	1.7×1.5	Pedunculated, pebbly surface, pink	Excision 8 months No recurrence

[Table/Fig-6]: Comparative clinico-demographic profile of six Giant Cell Fibroma (GCF) cases in individuals younger than three years [7,10,13,21,24].

collagen turnover. Multinucleation has been attributed to mitosis without cytokinesis or cell-to-cell fusion, with the latter being more widely accepted [29]. The role of Matrix Metalloproteinases (MMP), particularly MMP-1, has also been suggested to be involved in the pathogenesis of GCF [30]. The positivity for vimentin and the absence of immunoreactivity with CD34, CD68, and S100 reaffirm that stellate cells in GCF are fibroblastic in origin.

Conservative local excision is widely accepted as the treatment of choice for GCF. Recurrence is rare, with only two out of 464 cases in a series showing recurrence after complete excision (0.43%) [5].

CONCLUSION(S)

The GCF is a reactive soft tissue growth that primarily affects the gingiva. Although more common in adults, paediatric dentists should consider GCF in the differential diagnosis for lesions, especially those with a papillary surface. Furthermore, all excised specimens should be submitted for histopathological examination, as the actual incidence of GCF could be higher than reported.

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