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1**Title:** Localized Juvenile Spongiotic Gingival Hyperplasia: A Report of 27 Cases.

2

3**Abstract**

4**Background:** Localized juvenile spongiotic gingival hyperplasia (LJSGH) is a poorly
5understood but distinctive inflammatory hyperplasia occurring in children and
6young adults. Less than 100 cases have been reported since its initial description.

7

8**Methods:** During the period of 2015-2018, cases of LJSGH were identified, retrieved
9and their clinical and histopathological data reviewed.

10

11**Results:** There were 27 cases with a median age of 13 years (range 7-72 years).
12Twenty-four of 27 patients were less than 20 years old, and in 3 cases the patients
13were over 60 years of age. The most commonly affected site was the anterior
14maxillary gingiva presenting as a solitary, red, and papillated lesion. Typical
15microscopic findings included elevated areas of variably acanthotic, spongiotic non-
16keratinized epithelium with elongated rete ridges, accompanied by a neutrophilic
17rich infiltrate. An abrupt transition between epithelium affected by LJSGH and
18normal mucosa was characteristic. LJSGH typically exhibited full thickness epithelial
19expression of CK19 without expression of estrogen and progesterone receptors.

20

21**Conclusions:** The clinical and histopathologic characteristics of LJSGH are unique
22and consistent. Despite the name, the condition is not limited to juveniles and can
23occur in adults. LJSGH in adults and juveniles shares the same spectrum of
24histopathologic and immunohistochemical findings.

25

26**Keywords:** Oral disease, gingival lesion, gingivitis, inflammatory gingival
27hyperplasia

28Introduction

29Localized juvenile spongiotic gingival hyperplasia (LJSGH) is a rarely encountered,
30poorly understood but distinctive form of inflammatory hyperplasia with less than
31100 cases reported in the literature. In 2007, Darling et al. [1] first described the
32condition using the monicker of “juvenile spongiotic gingivitis” to highlight its
33spongiotic and inflammatory nature. The term “localized juvenile spongiotic
34gingival hyperplasia” (LJSGH) was subsequently introduced by Chang et al. [2] to
35emphasize its localized clinical nature and hyperplastic morphology seen on
36microscopy.

37

38Affecting the gingivae, LJSGH most often occurs in children and young adults [1,2].
39In contrast to conventional plaque-associated gingivitis and puberty-associated
40gingivitis, LJSGH is typically resistant to oral hygiene measures [1,2]. The diagnosis
41of LJSGH requires a high index of suspicion on the part of the clinician and
42pathologist alike to exclude similar appearing inflammatory gingival lesions.
43However, no previous report of LJSGH was found in previous dermatology
44publications. To increase awareness, further describe this condition, and offer
45additional insights, we identified 27 cases of LJSGH and reviewed the clinical,
46microscopic, and immunohistochemical findings.

47

48Methods

49This study was approved by our Institutional Review Board (IRB). From the period of
502015-2018, we identified cases of LJSGH from the files of our institution. Clinical and
51demographic information including age, gender, anatomical location, and clinical
52features were collected. Hematoxylin and eosin stained slides and corresponding
53immunochemical stained sections were reviewed. All cases had been
54immunostained with cytokeratin 19 (CK19), estrogen receptor, and progesterone
55receptor as described previously [1].

56

57Results

58We reviewed slides that were diagnosed as LJSGH, and identified 27 patients who
59met the criteria for LJSGH described by Darling et al. [1] and Cheng et al. [2]. The
60demographic information and clinical findings are summarized in Table 1. Twenty-
61four patients were less than 20 years of age, and 3 patients were older than 60
62years of age. The median age was 13 years (range 7-72 years) with a predominance
63of males (17/27; 63%). Reported duration of the condition prior to biopsy ranged
64from 3 months to greater than 7 years. The most commonly involved site was the
65anterior maxillary gingiva, and it most commonly present as a red, bleeding, and
66papillated lesion without pain. Additional reported features included ulceration,
67bleeding, soreness, an intermittent clinical course, irregular margins, firmness, and
68exophytic or hyperplastic quality. The largest reported size was 1 cm lesion in the
69greatest dimension. The clinical diagnoses included developmental gingivitis,
70plasma cell gingivitis, pyogenic granuloma, giant cell granuloma, granulation tissue,

71gingival hyperplasia, hemangioma, peripheral ossifying fibroma, and fibroma not
72otherwise specified.

73

74The histological and immunological findings are summarized in Table 2. LJS�GH has a
75consistent histopathology showing elevated areas of non-keratinized, variably
76acanthotic stratified squamous epithelium that exhibited spongiosis, elongation of
77rete pegs, atrophy of the epithelium overlying long connective tissue papillae, and a
78neutrophilic infiltrate. Depending on orientation of the specimen there was a
79characteristic sharply demarcated border between lesional tissue and adjacent
80unaffected gingiva. All cases showed full thickness epithelial expression of CK19,
81but were uniformly negative for estrogen and progesterone receptors. All three
82adult cases demonstrated identical microscopic findings and immunohistochemical
83staining properties compared to those seen in the juvenile cases (Figures 2, 3).

84

85Discussion

86LJS�GH is a distinct entity limited to the gingiva with, to date, less than 100 cases
87reported in the literature. This rarity is likely an underestimation due to its clinical
88and microscopic similarity to other diseases and is also likely impacted by clinicians'
89and pathologists' unfamiliarity with this relatively newly described entity. Here, we
90report 27 additional cases of LJS�GH to offer additional insights into the disease. A
91total of 27,901 oral cases were reviewed by our institution between 2015 and 2018,
92during the study time period. To our knowledge, this is the first report of LJS�GH in
93the dermatology literature.

94

95As its name suggests, LJS�GH is most often described in juveniles. Darling et al. [1]
96reported that 17 of their 24 (71%) patients were between 10 and 14 years old, while
97Chang et al. [2] and Allon et al. [3] reported that 28 of 51 (55%) patients and 7 of
9810 (70%) patients were between 11 and 15 years old, respectively. In this current
99study, we found that all but 3 patients were less than 20 years of age with 29.6% of
100the patients younger than 10 years old, and 44.4% of the patients between 11 and
10115 years. The majority of patients within other prior publications are also between
10211 and 15 years [4-6]. Vargo et al. [7] reported a large age range between 3 to 64
103years old, with the median to be 14.5 years old. The median age in our series was
10413 years old. Together with the previous case series [1-8], we conclude that LJS�GH
105is most common to but not limited to the juvenile age range.

106

107Cases of LJS�GH have been reported in adults but there have been no other reports
108of this disease in patients over 40 years old. Darling et al. [1], Chang et al. [2],
109Argyris et al. [4], and Siamantas et al. [8] each reported the condition in one adult
110between the ages of 19 to 40. Vargo et al. [7] described ten adults between the
111ages of 18 to 64. In our study, we identified 3 adults with ages of 65, 66, and 72,
112who presented gingival lesions that were clinically, morphologically, and
113immunohistochemically identical to LJS�GH. Hence, the age range of LJS�GH is likely

much wider than previously believed, and we expect that as further cases in adults are described the recognized age range of the condition might increase.

116

Prior reports have described varying female to male ratios of 1:1 in one series of 24 patients, 2.3:1 in a series with 51 patients, 1:1 in a series of 10 patients, 1.25:1 in a series of 28 patients, 0.5:1 in a series of 21 patients, and 0.5:1 in a series of 3 patients [1-4, 6, 7]. In our series of 27 patients, we found a slight male predominance with a female to male ratio of 0.6:1. When prior reports are aggregated with our series a balanced gender ratio emerges, with a female to male ratio of 1:1, suggesting that sex hormones are likely unrelated to the etiology of LJSGH.

125

Similar to previous reports [1-8], the most commonly affected oral site for LJSGH was the anterior maxillary gingiva. The reason for this localization in the anterior maxilla is unknown. In a new finding, we identified patients with LJSGH affecting other intraoral sites including the posterior maxillary and posterior mandibular gingivae. We can offer no explanation for this but increased awareness of the condition and enhanced vigilance on the part of the clinicians might be a factor.

132

The clinical presentation of LJSGH in our series was as a solitary, red, and papillated lesion that may be ulcerated or bleed. The course can be waxing and waning or progressively enlarging. LJSGH can be otherwise asymptomatic or be associated with soreness. Other clinical features include irregular margins, firmness, and exophytic or hyperplastic qualities. Due to these findings, the clinical differential diagnosis can include puberty related gingivitis, plaque-related gingivitis, pyogenic granuloma, giant cell granuloma, hemangioma, and peripheral ossifying fibroma.

140

In our series, the microscopic findings of LJSGH from both child and adult patients included elevated areas of spongiotic and variably acanthotic, non-keratinized stratified squamous epithelium, with elongated rete ridges and atrophy of the epithelium overlying long connective tissue papillae. While a neutrophilic infiltrate is invariably present, a plasma cell-rich infiltrate sometimes containing eosinophils can be observed. The abrupt transition between epithelium affected by LJSGH and normal mucosa was characteristic, and this is a histopathological observation that has not been previously described. There are morphological similarities between LJSGH and cutaneous clear cell acanthoma, including sharp margination, acanthosis, thin supra-papillary plates, and intraepithelial neutrophils. However, clear cell acanthoma is characterized by glycogen-rich squamous epithelium, whereas LJSGH is characterized by a spongiotic squamous epithelium that lack PAS-staining (Figures 2D, 3D).

154

CK19 is expressed in all layers of the epithelium in the absence of estrogen and progesterone receptor expression in LJSGH. By contrast, the more common puberty gingivitis is CK19 positive but also expresses progesterone and estrogen receptors

158while plaque-related gingivitis is negative for all three markers. Additional
159differences between pyogenic granuloma and these disease processes are
160summarized in Table 2 [9-12]. [CK19 expression is not present within clear cell](#)
161[acanthomas \[13\]](#). It has been hypothesized that the CK19 expression is due to the
162odontogenic origin of LJS GH [1]. CK19 expression has been theorized to be a sign of
163impending carcinogenesis of oral mucosa, due to its increased expression in
164hyperplastic lesions, and its expression continues in dysplastic and malignant
165lesions [13,14]. Epithelial dysplasia is absent in LJS GH from all of our juvenile and
166adult patients, thus LJS GH is not likely to be a premalignant condition. Furthermore,
167evidence presented by Argyris et al. concluded that human papillomavirus does not
168participate in the pathogenesis of LJS GH [4].

169
170Unlike puberty and plaque-related gingivitis, LJS GH is reported to not respond to
171conventional oral hygiene measures such as brushing and flossing [1,2]. There is
172potential for LJS GH to recur after biopsy procedures. Localized ablative procedure
173such as cryotherapy has been reported effective for the treatment [14,15], which
174would be reasonable to consider when the lesion is symptomatic or is cosmetically
175unsightly. The therapeutic effect of topical steroid therapy has been reported to be
176transitory [15,16]. For cases of asymptomatic lesions, observation would be viable
177for this benign entity.

178

179Conclusions

180LJS GH is an infrequently encountered entity that is commonly a lone, red, papillated
181lesion located on the anterior maxillary gingiva. It can affect both children and
182adults over a wide range of ages, and has no strong predilection towards a gender.
183Microscopically, LJS GH is characterized by epithelial acanthosis and spongiosis, with
184neutrophilic infiltrate and sharp marginations from the surrounding tissue. Full-
185thickness epithelial CK19 expression is a constant finding, and when coupled with
186progesterone and estrogen receptor findings, LJS GH can be differentiated from
187puberty and plaque-related gingivitis.

188

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232

233

234**Tables**

235

236**Table 1:** Localized juvenile spongiotic gingival hyperplasia (LJSGH) demographic
237and lesional characteristics

238

Age group	Numbers (% , N=27)
<=10	8 (29.6%)
11-15	12 (44.4%)
16-20	4 (14.8%)
21-60	0 (0.0%)
>=61	3 (11.1%)
Median age	13 years
Average age	18 years
Gender	Numbers (% , N=27)
Male	17 (63.0%)
Duration prior to biopsy†	3 months to over 7 years
Anatomical location	Numbers (% , N)
Maxilla	23 (85.2%, N=27)
Anterior	24 (92.3%, N=26)
Right	18 (72%, N=25)
Left	5 (20%, N=25)
Midline	2 (8%, N=25)
Clinical features‡	Numbers reported§
Red color	20
Papillated	6
Asymptomatic	5
Growth	3
Bleeding	2

239

240† Duration prior to biopsy is reported in nine patients.

241‡ Other reported features include ulceration, soreness, waxing-waning course,
242irregular margins, firm, pedunculated, and exophytic/hyperplastic quality.

243§ Each of the clinical features is not reported in all twenty-five patients.

244**Table 2:** Comparison of localized juvenile spongiotic gingival hyperplasia (LJSGH)
 245with its differential diagnoses
 246

Disease	Age group	Archetypal location	Typical clinical appearance	Microscopic features	IHC properties	Response to oral hygiene
Localized juvenile spongiotic gingival hyperplasia	Primarily juveniles, with few presenting as elderly adults	Localized to attached anterior maxilla	Red, bleeding, asymptomatic, and papillated growth	Sharply marginated spongiosis and hyperplasia with elongation of rete pegs, atrophy of the epithelium overlying long connective tissue papillae, and a neutrophilic infiltrate	CK19+, ER-, PR-	No
Puberty associated gingivitis	Juveniles only	Generalized on marginal gingiva	Inflamed, bleeding, and tender gingiva, sometimes with hyperplasia	Spongiosis and acanthosis with elongation of rete pegs, atrophy of the epithelium overlying long connective tissue papillae, and a neutrophilic infiltrate	CK19+, ER+, PR+	Yes
Plaque-associated gingivitis	All age groups	Generalized, originates from gingival margin and spreads to the entire gingiva	Inflamed, bleeding, and tender gingiva, sometimes with hyperplasia	Inflamed fibrous and granulation tissue	CK19-, ER-, PR-	Yes
Pyogenic granuloma	All age groups, most prominently in young adults	Localized to marginal anterior maxilla	Red, bleeding, smooth or lobulated, and compressible growth	Vascular proliferation that resembles granulation tissue	N/A	No

247IHC, immunohistochemical; ER, estrogen receptor; PR, progesterone receptor; N/A,
 248not applicable.

249**Figure legends**

250

251**Figure 1:** Localized juvenile spongiotic gingival hyperplasia usually presents as a
252solitary, red, papillated lesion on the anterior maxillary gingiva.

253

254**Figure 2:** Localized juvenile spongiotic gingival hyperplasia (LJSGH) histological
255characteristics in pediatric patients. A, The slightly mamillated to papillated
256nonkeratinizing epithelium is spongiotic and acanthotic, with an abrupt transition
257between epithelium affected by LJSGH and normal mucosa (original magnification
258100x, H&E). B, Elongated connective tissue papillae are filled with neutrophils that
259infiltrate the spongiotic epithelium (original magnification 200x, H&E). C,
260Immunohistochemistry demonstrates full thickness epithelial Cytokeratin 19
261expression with an abrupt transition between epithelium affected by LJSGH and
262normal mucosa (original magnification 100x, CK19). D, Periodic acid-Schiff
263~~Progesterone-receptor A~~ stain is negative demonstrates a lack of glycogen
264deposition in LJSGH (original magnification ~~100x~~200x, PRA).

265

266**Figure 3:** Localized juvenile spongiotic gingival hyperplasia (LJSGH) histological
267characteristics in adult patients. A, The slightly mamillated to papillated
268nonkeratinizing epithelium is spongiotic and acanthotic, with an abrupt transition
269between epithelium affected by LJSGH and normal mucosa (original magnification
270100x, H&E). B, Elongated connective tissue papillae are filled with neutrophils that
271infiltrate the spongiotic epithelium (original magnification 200x, H&E). C,
272Immunohistochemistry demonstrates full thickness epithelial Cytokeratin 19
273expression with an abrupt transition between epithelium affected by LJSGH and
274normal mucosa (original magnification 100x, CK19). D, Periodic acid-Schiff
275~~Progesterone-receptor A~~ stain demonstrates a lack of glycogen deposition is-
276negative in LJSGH (original magnification ~~100x~~200x, PRA).

277