Intravascular Fasciitis: Report of an Intraoral Case and Review of the Literature

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Abstract Intravascular fasciitis (IF) is an unusual variant of nodular fasciitis. It is characterized by intraluminal, intramural, and extramural involvement of small to large arteries or veins. Only three cases involving the oral cavity have been reported previously in the literature. Here we present an additional case of oral IF arising in the submucosa of the upper lip of a 20-year old female. Microscopic examination showed a well-circumscribed, nodular proliferation of spindle cells arranged in intersecting fascicles. Occasional multinucleated giant cells also were noted. The tumor was present within the lumen of an intermediate-sized artery and extended into adjacent smaller vessels, thereby creating a multinodular appearance. Extramural extension into the surrounding connective tissue also was observed. Among the 31 cases of IF reported thus far (including the present case), the majority ($n = 23$) arose in individuals in the 1st through 3rd

decades, with a 1.4:1 male:female ratio. The most common sites of involvement were the head and neck ($n = 11$) and upper extremity ($n = 11$), followed by the lower extremity ($n = 6$) and trunk ($n = 3$). Conservative excision is standard treatment, although local recurrence has been reported in three cases. It is important for the pathologist to be aware of this lesion in order to avoid misdiagnosis as a sarcoma with angioinvasion.

Keywords Intravascular fasciitis · Nodular fasciitis · Head and neck · Oral cavity · Lip

Introduction

Intravascular fasciitis (IF) was first described in 1981 by Patchefsky and Enzinger [1] as an unusual variant of nodular fasciitis. These authors presented a series of 17 cases, which exhibited typical microscopic features of nodular fasciitis but were notable for an intimate association with veins and/or arteries. In addition, these investigators warned that the presence of intravascular growth may lead to a false impression of a sarcoma with angioinvasion.

Among the original cases reported by Patchefsky and Enzinger, the most commonly involved site was the upper extremity ($n = 7$, 41%), followed by the head and neck ($n = 5$, 29%), lower extremity ($n = 3$, 18%), and trunk ($n = 2$, 12%). Since this initial description, several additional cases have been reported [2–12], including three within the oral cavity [3, 5] and two within periorbital soft tissue [6]. With these additional reported cases, both the head and neck region and upper extremities are now the most commonly involved anatomic locations.

Here we report an additional case of intravascular fasciitis arising within the oral cavity. In addition, we review

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the literature regarding the clinical and histopathologic features of this unusual entity.

Case Report

A 20-year old Caucasian female presented to an oral and maxillofacial surgeon for removal of an upper lip nodule. The patient reported that the lesion first appeared 3 weeks prior and was enlarging rapidly. She denied any history of pain or tenderness. Upon oral examination, a firm, smooth-surfaced, bluish nodule was observed in the submucosa of the right upper lip. The nodule measured 0.5 cm in maximum diameter and was moveable. The clinical impression was that the lesion likely represented an area of chronic sialadenitis. An excisional biopsy was performed.

The gross specimen consisted of a soft, tan portion of tissue measuring $0.7 \times 0.5 \times 0.4$ cm. Microscopic examination showed a proliferation of spindle cells arranged in intersecting fascicles. The spindle cells exhibited plump, vesicular nuclei without significant pleomorphism. Scattered multinucleated giant cells also were present (Fig. 1). Mitotic activity was noted, with as many as 11 mitotic figures per 10 high power fields. No atypical mitotic figures were identified. The lesion was fairly well circumscribed in areas, although in other foci the tumor infiltrated adjacent skeletal muscle. Immunohistochemical stains showed the lesional cells to be diffusely positive for smooth muscle actin (1A4, 1:2,500, Dako Corporation, Carpinteria, CA, USA) and negative for S-100 protein (1:800, Dako Corporation, Carpinteria, CA, USA). The multinucleated giant cells were positive for CD68 (KP1, 1:2,560, Dako Corporation, Carpinteria, CA, USA). Immunohistochemical stains for CD31 (JC70, 1:80, Dako Corporation, Carpinteria, CA, USA) and CD34 (QBend10, 1:320, Dako Corporation, Carpinteria, CA, USA) exhibited a prominent capillary network within the background but no reactivity among the lesional cells (Fig. 2a–c). The diagnosis was uncertain at this point. The differential diagnosis included nodular fasciitis and myofibroma. Re-excision was recommended because the tumor extended to the surgical margins. In addition, although the cytologic features were bland, the prominent mitotic activity was somewhat disturbing, and the possibility of a benign but locally aggressive tumor was considered.

The gross specimen of the re-excision consisted of an elliptical wedge of mucosa with an associated firm, submucosal nodule measuring $0.6 \times 0.5 \times 0.2$. Histopathologic examination showed a multinodular proliferation of spindle cells with microscopic features similar to that of the previous specimen. However, an additional finding consisted of a distinctly recognizable vessel wall, with elastic lamina and smooth muscle, partially surrounding the tumor

Fig. 1 Photomicrographs of the initial biopsy: (a) There is a proliferation of spindle cells arranged in intersecting fascicles. (hematoxylin and eosin, original magnification 200 $\times$) (b) Scattered multinucleated giant cells and occasional mitotic activity also were evident. (hematoxylin and eosin, original magnification 400 $\times$)

(Fig. 3a). A Verhoeff van Gieson stain confirmed that the tumor was present within an artery (Fig. 3b). Indeed, the tumor appeared to be present within the lumen of an intermediate-sized artery, with extension into the perivascular connective tissue. Additional smaller tumor nodules were noted within capillaries emanating from the main tumor mass (Fig. 3c), thereby creating a multinodular appearance. A diagnosis of intravascular fasciitis was rendered. Unfortunately, the patient was lost to follow-up.

Review of the Literature

A summary of the clinical findings for the 30 previously reported cases and the current case is provided in Table 1. Data for the 17 cases reported by Patchefsky and Enzinger [1] were reported in aggregate, whereas findings for individual cases were provided by subsequent studies.

Fig. 2 Immunohistochemical stains: **(a)** The spindle cells are diffusely positive for smooth muscle actin. **b** The multinucleated giant cells are positive for CD68. **c** Immunohistochemical staining for

CD31 is negative for the spindle cells but demonstrates a prominent network of small, delicate vessels within the background

Fig. 3 Photomicrographs of the re-excision: **(a)** There is a distinct vessel wall, with elastic lamina and smooth muscle, surrounding the main tumor mass. (hematoxylin and eosin, original magnification 200 $\times$). **b** Verhoeff van Gieson stain demonstrates elastic fibers within

the wall of the artery surrounding the tumor (original magnification 200 $\times$). **c** Smaller tumor nodules are present within capillaries emanating from the main tumor mass. (hematoxylin and eosin, original magnification 100 $\times$)

Although there was a broad age range (6 months to 66 years), the majority of cases. ($n = 23$) arose in individuals in the 1st through 3rd decades. There were slightly more males than females (male-to-female ratio 1.4:1). The most commonly involved anatomic locations were the head and neck region ($n = 11$) and upper extremity ($n = 11$), followed by the lower extremity ($n = 6$), and trunk ($n = 3$). Among the head and neck cases, the most common site was the oral cavity ($n = 4$), with additional cases

involving the ocular region, face, scalp, and neck. Maximum diameter ranged from 0.6 to 5 cm. Most lesions presented as a solitary nodule or swelling, although multiple lesions were found in the case reported by Wang et al. [10]. Three cases appeared elongated or “sausage-shaped” [1, 10] and one case appeared multilobulated [8]. The lesion color or color of the overlying skin/mucosa was reported as yellow, white, red, blue, or “hyperpigmented.” Pain was a variable finding, with 8 cases exhibiting pain,

Table 1 Features of previously reported cases and current case of intravascular fasciitis

Authors	Year	n	Age	Sex	Location	Clinical findings	Follow-up
Patchefsky and Enzinger [1]	1981	17	Mean 20.5 years	9M, 8F	7-upper extremity (including hand $n = 3$, shoulder $n = 2$, wrist $n = 1$, forearm $n = 1$); 5-head and neck (including scalp $n = 1$, subcutis of face $n = 4$; neck $n = 1$); 2-trunk (chest $n = 1$, breast $n = 1$); 3-lower extremity (lower leg $n = 1$, ankle $n = 2$)	Size range 0.6–5 cm; 2 lesions were elongated or sausage-shaped; most were painless and slowly growing; 6 patients were aware of lesion for 2 to several mos.; 2 patients reported a mass of 10–60 mos. duration; 2 patients noted rapid growth over 2–3 wks.; 4 patients had slight aching pain and 1 patient had no pain; 1 patient had possible preceding trauma; 4 denied trauma	alive and well $n = 7$; local recurrence $n = 2$ (first case occurred at 1 and 2 years, second case occurred at 3 mos.); lost to follow-up $n = 4$; too recent for follow-up $n = 4$
Freedman and Lumerman [3]	1986	2	19 years	F	Right posterior mucobuccal fold	2.5×1.2 cm firm swelling with surface ulceration; developed over 3 mos.	N.E.D. during initial recall period several mo. after excision
Kahn et al. [5]	1987	1	53 years	M	Left buccal mucosa	2.0×2.0 cm firm swelling, fixed, present for 2 mos.	N.E.D. several mos. after excision
Price et al. [6]	1993	2	17 years	M	Submucosa of left lower lip Outer canthus of eye	1.5 cm yellow, white nodule; 2.0×2.0 cm swelling, developed 6 weeks after an injury	N.E.D. 3 years
Beer et al. [2]	1996	1	18 years	F	Subcutis adjacent to eye and beneath oricularis oculi Subcutis of lateral thigh	1.0 cm firm, nontender, mobile nodule 1.5×2.0 cm tender, freely mobile, slowly growing nodule with radiating pain	N.S. N.E.D. 18 mos.
Sumaratunga et al. [7]	1996	1	49 years	M	Subcutis of left inguinal region	$3.0 \times 2.0 \times 1.5$ cm firm mass present for 3 mos.; some discomfort; slowly increasing in size; nontender; no history of trauma	N.E.D. 6 mos.
Sticha et al. [8]	1997	1	4 years	M	Subcutis of right foot in calcaneus region	$3.0 \times 1.0 \times 0.5$ cm multilobulated, well-demarcated nodule; developed 6 wks. prior to presentation; red and white mottled appearance; not mobile; tender with compression; no history of trauma except for new pair of boots	Recurrence after 10 wks; recurrent lesions remained asymptomatic and unchanged at 13 mos.
Ito et al. [4]	1999	1	26 years	M	Subcutis of proximal forearm	Tender lump; no history of trauma	N.S.
Anand et al. [12]	2007	1	20 years	F	Hypothenar eminence of the right hand; associated with the ulnar artery	2-mo. history of a slowly growing, painless mass; firm, non-tender, well-demarcated, and surrounded by mild erythema	N.E.D. 2 years
Sugaya and Tamaki [9]	2007	1	66 years	M	Subcutis of medial border of right foot	1.0×0.3 cm freely mobile, nontender nodule; slowly growing; first noticed 1 year prior; no preceding trauma	N.S.
Pantanowitz and Duke [11]	2008	1	17 years	M	Wrist	1.2 cm mass	N.S.
Wang et al. [10]	2009	1	28 years	F	Subcutis of calf of left leg	Multiple nodules present for 8 years; no discomfort; one nodule was elongated; slight phlebeurysm and hyperpigmentation	N.S.
Chi et al. (current case)	2011	1	20 years	F	Right upper lip submucosa	$0.6 \times 0.5 \times 0.2$ cm bluish, mobile, non-tender nodule; developed and enlarged rapidly over a 3-wk. period	Not available

n number of cases reported, M male, F female, $mo.$ month, $mos.$ months, $wk.$ week, $wks.$ weeks, $N.E.D.$ no evidence of disease, $N.S.$ not stated

discomfort, or tenderness and 8 lesions described as painless. In the current case and 2 previously reported cases [1], the lesion grew rapidly over a 2- to 3-week period, whereas in most other cases the lesions grew slowly over several months or years. A history of preceding trauma was present in 3 cases, denied by the patient in 7 cases, and not stated or known in the remaining cases.

The typical histopathologic findings included a proliferation of plump spindle cells arranged in short intersecting fascicles, a storiform pattern, or a haphazard manner. In all cases, the proliferation was present, at least in part, within the lumen and/or wall of a vessel; the vessels were either arteries or veins and ranged from small to large in size. Complete infiltration through a vessel into the surrounding connective tissue and infiltrative borders with entrapment of skeletal muscle were observed in some cases [6]. Patchefsky and Enzinger reported that among their cases, the soft tissue component often was more prominent than the vascular component [1]. In several cases, smaller vessels with intraluminal tumor emanated from the main tumor mass, thereby creating the appearance of multinodular growth or satellite nodules [1, 5, 7]. The tumor cells characteristically exhibited plump, vesicular nuclei; significant pleomorphism was reported in only a few cases [5]. The background stroma ranged from dense to myxoid and frequently exhibited a well-developed, slit-like capillary network. Cleft-like spaces were present in some cases, imparting a loosely textured appearance. Scattered lymphocytes and red blood cells frequently were evident within the background. Multinucleated giant cells were noted in some lesions as well [1, 4, 5, 7, 8]. Mitotic activity ranged from absent or scant to prominent, although atypical mitotic figures were not found.

Immunohistochemical stains showed the spindle cells to be typically positive for smooth muscle actin and vimentin and negative for cytokeratins, S-100 protein, desmin, CD31, and CD34 [4, 7, 9, 10, 12]. Despite lacking reactivity among the spindle cells, immunostains for CD31 and CD34 could be useful to demonstrate the highly vascular stromal background and the vascular location of the lesion [10]. In the current case and the case reported by Ito et al. [4], immunostaining for CD68 also was performed and exhibited positive reactivity among lesional multinucleated giant cells.

In addition, special stains for elastic fibers often have been used to exhibit the walls of associated vessels. Alcian blue staining has shown abundant acidic mucopolysaccharide within the stroma of a few cases [7, 10].

Discussion

The etiopathogenesis of intravascular fasciitis is poorly understood. Patchefsky and Enzinger theorized that the

lesion results from the proliferation of myofibroblasts indigenous to the walls of systemic arteries and veins. Furthermore, these authors commented that frequent extension into perivascular connective tissue, fascia, and smaller vessels at some distance from the main tumor mass is suggestive of a “field effect” of myofibroblastic transformation [1]. Indeed, the typical immunohistochemical profile—including reactivity for smooth muscle actin and vimentin and a lack of reactivity for desmin and CD34—supports a myofibroblastic origin for the spindle cells. However, the inciting stimulus for this myofibroblastic proliferation is uncertain. There is much speculation regarding the potential roles of trauma or thrombosis. Nevertheless, associated trauma or thrombosis has been reported in only a minority of cases [1, 4, 6]. The observation of intravascular fasciitis arising within a pregnant female led Anand et al. [12] to hypothesize that stimulation of estrogen receptors in myofibroblasts may be a contributing factor. In support of this theory, these authors cited previous studies showing weak expression of estrogen receptors in nodular fasciitis. However, no significant gender predilection is evident among cases of intravascular fasciitis reported thus far.

Although intravascular fasciitis is a rare lesion, it is important to recognize this entity in order to avoid a misdiagnosis of malignancy, which may lead to unnecessarily aggressive treatment. In fact, 6 out of 15 cases reported by Patchefsky and Enzinger initially were diagnosed as malignant by their contributors [1]. The intravascular growth characteristic of these lesions may be misinterpreted as vascular invasion by a sarcoma. Additional histopathologic features that might be mistaken as indicators of malignancy include infiltrative borders within soft tissue, envelopment of muscle, and increased mitotic activity. Accordingly, some authors have used the term “pseudosarcoma” to describe this lesion.

In the current case, vascular involvement was not readily apparent on the initial biopsy, and the diagnosis was not made until after the re-excision when a definite intact vessel wall was noted surrounding the main tumor mass. In fact, it is often the case that the soft tissue component comprises a much greater proportion of the tumor than the vascular component [1], and thus, small biopsy specimens may make diagnosis difficult. When intact or fragmented vessel walls cannot be easily appreciated, the recognition of a multinodular or serpentine growth pattern (reflecting the plane of section through a tumor with longitudinal intravascular extension) may be helpful. In such cases, special stains for elastic fibers and smooth muscle are essential in demonstrating the relationship between tumor and vessel walls.

A conspicuous feature in the current case was the presence of multinucleated giant cells. Multinucleated

giant cells are not a constant finding in intravascular fasciitis but have been noted in about one-third of cases reported by Patchefsky and Enzinger and nearly one-half of subsequently reported cases [1, 4, 5, 7, 8, 12]. Immunoreactivity for CD68, as demonstrated in the current case and the case described by Ito et al. [4], supports that these giant cells are histiocytic in origin. These cells are distinct from the multinucleated ganglion-like cells that may be found in proliferative fasciitis or proliferative myositis.

In conclusion, intravascular fasciitis is a rare variant of nodular fasciitis, with a predilection for the head and neck region and upper extremity. Although potentially missed in small biopsy specimens, recognition of intravascular growth is essential for diagnosis and may be facilitated by special stains for elastic fibers or immunohistochemical stains for vascular markers. The variable presence of multinucleated giant cells and often multinodular growth pattern also may aid in diagnosis. Intravascular growth, infiltrative borders, entrapment of muscle fibers, and increased mitotic activity are not indicative of malignancy. It is important to avoid a misdiagnosis of sarcoma, which may lead to overly aggressive treatment. Conservative excision is appropriate, and there is low recurrence potential.

Conflict of interest There is no financial conflict of interest.

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