

Case Presentation

Intravascular papillary endothelial hyperplasia of the vulva: report of a patient with Masson tumor of the vulva and literature review

Bryce David Beutler¹, Philip R. Cohen²

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¹ University of Nevada School of Medicine

² University of California, San Diego

Correspondence:

Bryce D. Beutler, BS
1060 Wiegand Road
Encinitas, CA 92024
Email: brycebeutler@hotmail.com

Abstract

Background: Intravascular papillary endothelial hyperplasia -- also known as Masson tumor -- is a rare, benign vascular condition that manifests on the skin as a firm, blue-black colored nodule or papule. Lesions range in size from 0.25 to 5 centimeters in diameter and may be tender or painless. In some individuals, nodules appear red colored, mimicking hemangioma or pyogenic granuloma. Histologically, intravascular papillary endothelial hyperplasia is characterized by the presence of an organizing thrombus in the vascular lumen with accompanying hyperplastic endothelial cell proliferation. Common sites of presentation include the head, neck, and extremities. However, albeit rarely, lesions may also appear in the genital region.

Purpose: We describe the clinical and pathologic findings of a woman who developed intravascular papillary endothelial hyperplasia of the vulva. We also review the characteristics of other patients with intravascular papillary endothelial hyperplasia of the vulva and summarize the differential diagnosis and treatment options for this condition.

Materials and methods: The features of a woman with intravascular papillary endothelial hyperplasia of the vulva are presented. Using PubMed, the following terms were searched and relevant citations assessed: intravascular papillary endothelial hyperplasia, IPEH, labia majora, Masson hemangioma, Masson pseudoangiosarcoma, Masson tumor, and vulva. In addition, the literature on intravascular papillary endothelial hyperplasia is reviewed.

Results: A 32-year-old woman presented with a 3 x 2 millimeter painless, black colored submucosal papule on her left labia majora. The lesion was removed by excisional biopsy. Microscopic examination revealed a re-canalizing thrombus and a proliferation of erythrocytes within a dilated vascular structure. Based on correlation of the clinical presentation and histopathologic findings, a diagnosis of intravascular papillary endothelial hyperplasia was established. The patient applied mupirocin 2% ointment to the biopsy site, which subsequently healed without complication or recurrence.

Conclusion: Intravascular papillary endothelial hyperplasia -- also known as Masson tumor -- is a rare, benign vascular eruption. Cutaneous lesions typically present as red colored or blue-black colored nodules ranging in size from 0.25 to 5 centimeters in diameter. The most common sites of presentation include the head, neck, and extremities. However, albeit rarely, lesions may also appear in the genital region. The histologic hallmark of intravascular papillary endothelial hyperplasia is an organizing thrombus in the vascular lumen with associated hyperplastic endothelial cell proliferation. Lesions often appears similar to other neoplastic

and non-neoplastic cutaneous tumors, including hemangiomas, pyogenic granulomas, and cutaneous angiosarcomas. Therefore, pathologic examination is required to confirm the suspected diagnosis and exclude malignancy. The condition can usually be treated with simple local excision.

Keywords: intravascular papillary endothelial hyperplasia, IPEH, labia majora, Masson hemangioma, Masson pseudoangiosarcoma, Masson tumor, vulva

Introduction

Intravascular papillary endothelial hyperplasia -- also known as Masson tumor -- is a benign vascular lesion caused by hyperplastic endothelial cell proliferation occurring in association with a re-canalizing thrombus in a blood vessel. It most commonly presents on the skin as a red colored or blue-black colored nodule affecting the head, neck, or extremities. However, albeit less commonly, lesions may also appear at other sites, including the genital region and oral mucosa. Nodules typically range in size from 0.25 to 5 centimeters in diameter and may be either tender or non-tender. Intravascular papillary endothelial hyperplasia is characterized histologically by the presence of an organizing thrombus in the vascular lumen with accompanying hyperplastic endothelial cell proliferation. Fibrin deposition may also be present. Lesions frequently appear similar to other cutaneous tumors, including angiosarcoma, lymphangioma, melanoma, and pyogenic granuloma. Therefore, pathologic examination is required to distinguish intravascular papillary endothelial hyperplasia from other neoplastic and non-malignant skin conditions. Treatment usually involves simple surgical excision, but radiation therapy has been utilized for some patients who develop recurrent lesions [1].

A woman who developed intravascular papillary endothelial hyperplasia involving her vulva is described. The characteristics of other patients with intravascular papillary endothelial hyperplasia of the vulva are also reviewed and the differential diagnosis and treatment options for this condition are summarized.

Case synopsis

A 32-year-old woman, who had delivered a baby via vaginal birth six weeks earlier, presented for evaluation of a small, dark lesion on her vulva. The vulvar lesion initially appeared six months earlier -- during the fourth month of her pregnancy; it subsequently increased in size. She has a family history of melanoma. She also has a history of genital herpes simplex infection; she began to receive oral (one gram daily) valacyclovir at 36 weeks gestation.

Cutaneous examination revealed a painless, 3 x 2 millimeter black submucosal papule affecting her left labia majora (Figure 1).



Figure 1. (a and b). Distant (a) and close (b) views of the vulva of a 32-year-old woman. A solitary black colored papule measuring 3 x 2 millimeters -- which was later diagnosed as intravascular papillary endothelial hyperplasia -- can be seen on the left labia majora.

The lesion was removed by excisional biopsy. Microscopic examination revealed a large dilated vessel containing a thrombus. The thrombus is re-canalizing. There are numerous erythrocytes within a proliferation of spaces lined by endothelial cells (Figure 2).

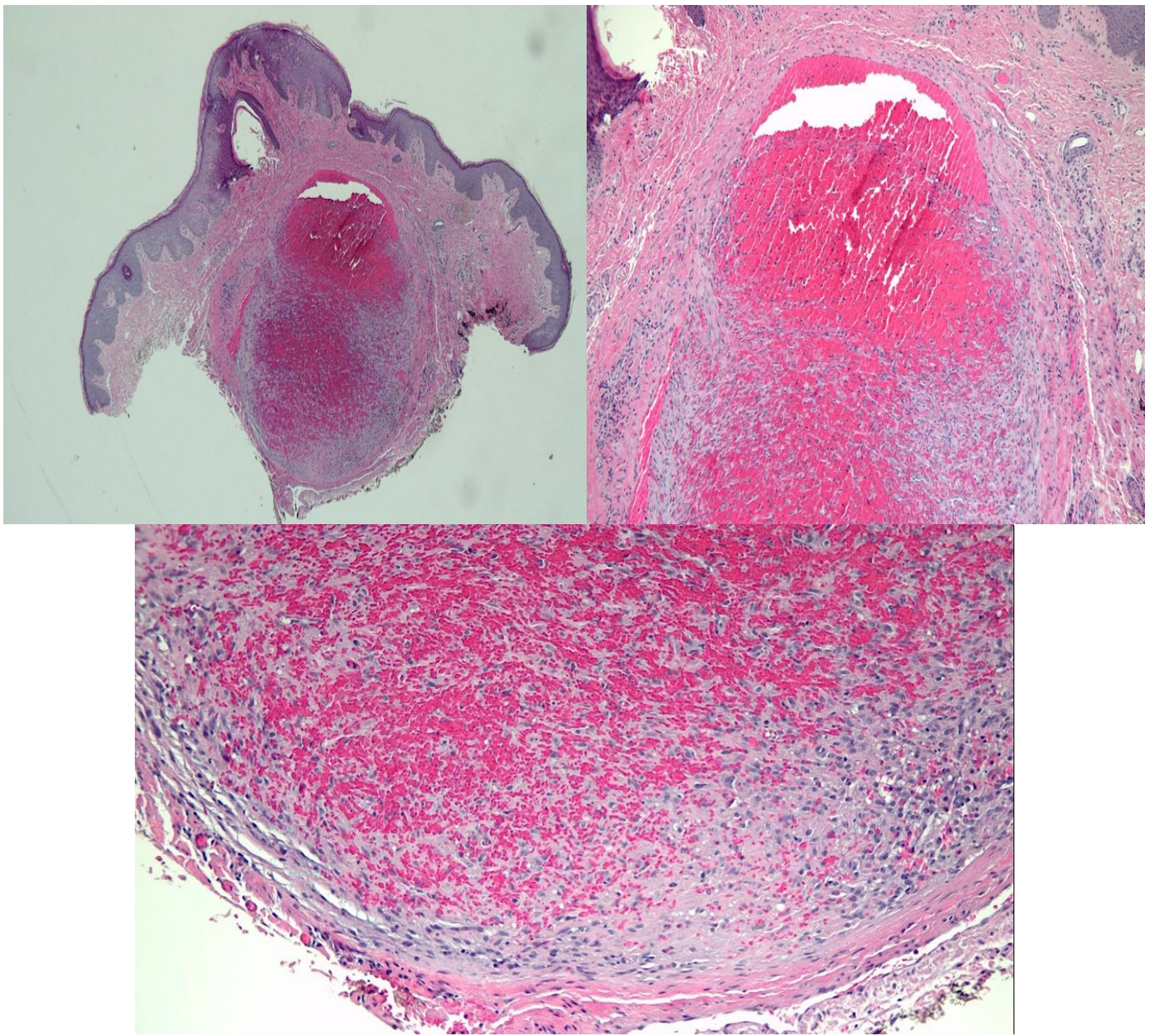


Figure 2 (a, b, and c). Low (a), intermediate (b), and high (c) magnification views of intravascular papillary endothelial hyperplasia. There is a large dilated vessel which contains a thrombus. There is recanalization of the thrombus. Within the vessel, there is a proliferation of small vascular spaces lined by endothelial cells and containing erythrocytes. [Hematoxylin and eosin; a = x4, b = x10, c = x20].

Based on correlation of the clinical presentation and histopathologic findings, a diagnosis of intravascular papillary endothelial hyperplasia was established. The patient applied mupirocin 2% ointment to the biopsy site, which subsequently healed without complication or recurrence.

Discussion

Intravascular papillary endothelial hyperplasia is a rare, benign vascular tumor caused by the presence of an organizing thrombus and associated hyperplastic endothelial cell proliferation within the lumen of a blood vessel. It was first described in 1923 by the French physician Pierre Masson, who observed an intravascular papillary proliferation within the ulcerated hemorrhoidal vein of a 68-year-old man [2]. The condition has since been reported in the medical literature under various eponyms, including Masson tumor, Masson hemangioma, and Masson pseudoangiosarcoma [3].

Cutaneous manifestations of intravascular papillary endothelial hyperplasia occur most commonly among adults between the ages of 30 and 40 years [3,4]. However, the condition has also been described in infants [4], children [5], and the elderly [6]. There is a slight female predominance [4,5,7] and no known ethnic predilection.

In 1983, Hashimoto et al. reviewed the clinical and histopathologic features of 91 patients with intravascular papillary endothelial hyperplasia; they developed a classification system based on the unique presentation of various lesions [4]. The "pure form" lesion

is consistent with Masson's original description: papillary endothelial hyperplasia within a dilated vascular structure. In contrast, the "mixed form" lesion appears superimposed on a pre-existing vascular neoplasm, such as a hemangioma, lymphangioma, or pyogenic granuloma [4,8]. Lastly, Hashimoto et al. observed a third type of lesion that did not fit into either category, which they referred to as "unclassifiable." Unclassifiable lesions are rare extravascular forms that typically arise in hematomas. It has been suggested that these lesions may occur only secondary to trauma [8].

Pure form lesions have a predilection for the fingers, upper extremities, and head while mixed form lesions commonly appear on the trunk [4,5,9]. Both pure and mixed form lesions affecting the oral mucosa have also been described [10]. Unusual sites of presentation include the tongue [11], eyelid [12], and plantar foot [13]. Intravascular papillary endothelial hyperplasia affecting the genital region is rare. Indeed, only four individuals with genital lesions have been described in the medical literature: an 82-year-old man with a tumor on his penis [6] and three women, including our patient, with intravascular papillary endothelial hyperplasia of the vulva (Table 1) [14,15].

The three women with intravascular papillary endothelial hyperplasia of the vulva ranged in age from 32 to 56 years (Table 1) [14,15]. The two younger women developed solitary papules while the oldest woman presented with multiple cystic lesions on the mons and labia majora. The condition was asymptomatic in two women; one woman reported tenderness and intermittent vulvar pain. All three women were successfully treated with simple surgical excision without complication or recurrence.

Table 1. Characteristics of patients with vulvar intravascular papillary endothelial hyperplasia

C	Age	Location	Size	S/M	Color	Symptoms	Treatment	Comments	Ref
1	32y	Left labia majora	3x2 mm	S	Black	None	Excision	Lesion developed during fourth month of gestation	CR
2	37y	Vulvar surface	3x2 cm	S	NS	Tender	Excision	Tenderness developed suddenly after menstruation	14
3	56y	Mons and labia majora	<1 cm	M	Brown	None	Excision	Lesion developed following treatment with external radiation therapy	15

*Abbreviations: C = case; CR = current report; M = multiple lesions; NS = not stated; S = single lesion; y = years. The oldest woman had a history of vaginal cancer; she had been treated with external radiation therapy prior to the development of the condition. Although this association is interesting, there is no previous etiologic link between radiation therapy and the development of intravascular papillary endothelial hyperplasia [15].

Our patient's lesion first appeared during the fourth month of her pregnancy. It is therefore conceivable that a pregnancy-associated thrombus contributed to the subsequent development of her vulvar intravascular papillary endothelial hyperplasia. Although there is currently no established association between pregnancy and intravascular papillary endothelial hyperplasia, Susini et al. recently described a 40-year-old pregnant woman who developed intravascular papillary endothelial hyperplasia in the uterine cervix at 15 weeks' gestation [16].

Intravascular papillary endothelial hyperplasia presents as a firm, dome-shaped, red or blue-black vascular papule or nodule. Lesions may be tender or painless and typically range in size from 0.25 to 5 centimeters in diameter; the pure form variant tends to be significantly smaller than the mixed form [4]. Although a solitary tumor is most commonly observed, individuals presenting with multiple lesions have also been described [15]. Histologically, intravascular papillary endothelial hyperplasia is characterized by the presence of an organizing thrombus in the vascular lumen with an accompanying hyperplastic endothelial cell proliferation. Fibrin deposition may also be observed.

Intravascular papillary endothelial hyperplasia may appear similar to other neoplastic and non-malignant cutaneous tumors, including hemangiomas, lymphangiomas, and pyogenic granulomas. The clinical and pathologic differential diagnosis is listed in Table 2 [5,8,10,17]. It includes not only local conditions, but also systemic disorders whose skin lesions can mimic those of intravascular papillary endothelial hyperplasia.

Table 2. Clinical and pathologic differential diagnosis of intravascular papillary endothelial hyperplasia.

Clinical	Pathologic
Angiokeratoma	Angiosarcoma
Angiosarcoma	Dabska tumor

Basal cell carcinoma	Hemangioma
Cysticercosis	Intravascular endothelioma
Hemangioendothelioma	Mucocele
Hemangioma	Spindle cell hemangioendothelioma
Kaposi's sarcoma	
Lymphangioma	
Melanoma	
Mucocele	
Neurofibroma	
Pyogenic granuloma	

Cutaneous angiosarcoma -- a rare, malignant vascular tumor -- bears a striking resemblance to intravascular papillary endothelial hyperplasia. Indeed, intravascular papillary endothelial hyperplasia is occasionally referred to as "Masson pseudoangiosarcoma" [18]. The two conditions can be differentiated only by careful histopathologic evaluation. Distinguishing histologic features of intravascular papillary endothelial hyperplasia include the following: 1) Papillary endothelial hyperplasia that is well-circumscribed and confined to intravascular spaces; 2) Papillae that are composed of fibrohyalinized tissue of multiple endothelial cell layers; 3) Thrombotic material within the vessel; 4) Minor or nonexistent nuclear atypia; and 5) The absence of necrosis [3,4].

Intravascular papillary endothelial hyperplasia is thought to result from hyperplastic endothelial cell proliferation caused by the development and subsequent recanalization of a thrombus within a blood vessel. The putative role of thrombosis was recently substantiated by Kim et al., who observed that hypoxia-inducible factor 1-alpha (HIF-1 α) and vascular endothelial growth factor (VEGF) -- proteins associated with thrombus remodeling and angiogenesis -- are highly expressed within the cellular cores in regions affected by intravascular papillary endothelial hyperplasia. They postulated that an exaggerated recanalization response converts the thrombus into a mass of connective tissue which subsequently becomes integrated into the vascular wall [19].

Further evidence supporting the thrombosis hypothesis was presented by Levere et al. [20] and Pins et al. [21], who demonstrated that basic fibroblast growth factor (bFGF) -- which is found in association with thrombi and stimulates endothelial cell proliferation -- is highly elevated in tissues affected by intravascular papillary endothelial hyperplasia. Interestingly, basic fibroblast growth factor is secreted not only by macrophages, but also by endothelial cells. It is therefore plausible that the initial release of basic fibroblast growth factor could trigger a positive feedback loop resulting in excess endothelial cell proliferation.

In addition to the aforementioned hypotheses, some authors have also proposed that the slight female preponderance of intravascular papillary endothelial hyperplasia is suggestive of a hormonal influence [5,8]. However, to the best of our knowledge, there is no definitive data pertaining to the role of specific hormones in the development of this rare condition.

Simple local excision with a margin of normal-appearing skin or mucosa is an effective treatment for most patients with intravascular papillary endothelial hyperplasia. In addition, Cohen et al. reported excellent cosmetic results using sclerotherapy followed by dissection and excision [22]. Individuals with rare recurrent lesions may also benefit from radiation therapy [1].

Conclusion

Intravascular papillary endothelial hyperplasia -- also known as Masson tumor -- is a rare, benign, vascular lesion. It manifests on the skin as a red or blue-black dome-shaped papule or nodule ranging in size from 0.25 to 5 centimeters in diameter. It may be tender or non-tender. Solitary lesions are most common, but individuals presenting with multiple papules have also been described.

Intravascular papillary endothelial hyperplasia occurs more frequently in women than in men. Individuals between the ages of 30 and 40 years are most commonly affected, but the condition has also appeared in infants, children, and the elderly. There is no known ethnic predilection.

Lesions may take on three distinct forms: "pure," "mixed," or "unclassifiable." Pure form lesions feature papillary endothelial hyperplasia within a dilated vascular structure. The mixed variant appears superimposed on a pre-existing vascular neoplasm, such as a hemangioma or pyogenic granuloma. Unclassifiable lesions are rare extravascular tumors that typically arise within hematomas.

The most common sites of presentation of pure form lesions are the fingers, upper extremities, and head. Mixed form lesions often affect the same body sites, but also frequently develop on the trunk. Both pure and mixed form lesions occasionally affect the oral

mucosa. Intravascular papillary endothelial hyperplasia affecting the genital region is rare; only four individuals with genital lesions have been described in the medical literature.

Although cutaneous intravascular papillary endothelial hyperplasia often appears morphologically similar to other skin lesions -- including angiosarcomas, hemangiomas, and pyogenic granulomas -- it can be distinguished based on its unique histologic characteristics. Specifically, intravascular papillary endothelial hyperplasia features papillary endothelial hyperplasia that is well-circumscribed and confined to intravascular spaces. In addition, thrombotic material is typically present.

Intravascular papillary endothelial hyperplasia is thought to result from hyperplastic endothelial cell proliferation caused by the development and subsequent recanalization of a thrombus within a blood vessel. Hypoxia-inducible factor 1-alpha (HIF-1 α), vascular endothelial growth factor (VEGF), and basic fibroblast growth factor (bFGF) appear to play key roles in the processes that lead to the development of lesions.

Simple local excision with a margin of normal-appearing skin or mucosa is an effective treatment for most individuals with cutaneous intravascular papillary endothelial hyperplasia. However, sclerotherapy and/or radiation therapy may rarely be indicated.

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