Cutaneous intravascular papillary endothelial hyperplasia of the hand: A case report and review of the literature

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Intravascular papillary endothelial hyperplasia (IPEH) is a rare benign endothelial proliferation that bears a remarkable resemblance to angiosarcoma. We report a case of cutaneous IPEH in the thumb of a seven-year old girl which was successfully treated with excision. The relevant literature is reviewed and histopathological features, differential diagnosis and natural history of the lesion are discussed.

Key words: hand, histopathology, intravascular papillary endothelial hyperplasia, skin.

Intravascular papillary endothelial hyperplasia (IPEH) was first described in 1923 by Masson as a neoplastic proliferation of the endothelium, a condition which he termed “hémangio-endothéliome végétant intravasculaire”¹. Since then this peculiar tumor-like process has been described under different names including intravascular endothelial proliferation, intravascular angiomatosis, Masson’s pseudoangiosarcoma and vegetant intravascular hemangioendothelioma. Similar papillary endothelial proliferations have been reported in thrombotic blood vessels². It was stated that these lesions are probably the examples of unusual organizing thrombi with reactive proliferation of endothelial cells. Due to the histopathological resemblance, IPEH must be distinguished from angiosarcoma in order to avoid unnecessary additional surgery or irradiation³.

In this report, a female patient with cutaneous IPEH in her thumb is presented and the clinical and pathologic features of the lesion are described. The relevant literature is reviewed and the details concerning the histological features, differential diagnosis and natural history of the lesion are discussed.

Case Report
A seven-year-old girl presented with a painless bluish mass in her right hand. The lesion first appeared when she was one-year old and had since increased in size. There was no history of previous trauma or bleeding. As she was right-handed, she complained of tenderness when holding a pencil to write. Physical examination revealed a 1 cm bluish mass in the volar aspect of the metacarpophalangeal joint of her right thumb with thinning in the skin but no sign of ulceration (Fig. 1). No thrill was palpated and there was blanching with pressure. As she could not use her right hand for writing due to the pain, her parents expressed concern that this might lead to failure in schoolwork, and it was decided to excise the lesion. On surgical exploration, the lesion was easily distinguishable from adjacent tissues. It was not connected with the underlying digital

Fig. 1. Preoperative view of the lesion on the volar aspect of first metacarpophalangeal joint.
neurovascular bundle and could be totally excised. Postoperative period was uneventful. No evidence of recurrence has been noted one year after excision.

The excised specimen consisted of non-encapsulated, 1 cm in diameter, purplish-red ovoid nodule partially covered with skin. Microscopically, the lesion was composed of a superficial (cavernous) hemangioma and a deeply located dilated thin-walled vein appearing to contain a thrombus (Fig. 2). High-power magnification revealed anastomosing vascular channels in the latter part of the lesion. In a focal area, along the contours of the thrombus, there were coarse papillary fronds with fibrin cores (Fig. 3). The endothelial cells appeared plump but lacked pleomorphism and mitotic figures. The surrounding stroma featured focal hemorrhage with scattered hemosiderin pigment and mononuclear inflammatory cells. Histochemically, Gomori’s reticulin and Verhoeff’s elastic fiber stains were performed. It was observed that reticulin fibers were distributed around vascular spaces. Vessels were devoid of well-formed elastic fibers. Immunohistochemical stain by the streptavidin-biotin peroxidase method demonstrated vascular spaces lined by plump endothelial cells, which were focally immunoreactive for factor VIII-related antigen. Our findings led us to the diagnosis of superficial hemangioma and IPEH.

Discussion

Intravascular papillary endothelial hyperplasia (IPEH) comprises approximately 2% of the benign and malignant vascular tumors of the skin and subcutaneous tissues. Its histogenesis is still under debate. IPEH arises primarily within a preceding angioma or some type of vascular anomaly, including hemorrhoids, as in Masson’s original description. Its presentation with other associated lesions, such as hemangioma, and its pattern of growth suggest that it is not a true neoplasm, but rather a reactive lesions. It remains to be elucidated whether the proliferation is primary and the thrombosis secondary, as Masson postulated, or whether the proliferation reflects an exuberant phase of growth of an organized thrombus, in which channels covered with proliferating endothelial cells are formed.

Clearkin suggested that the thrombosis precedes the papillary proliferation and that the thrombotic material serves as a matrix for its development. In a typical case, the thrombotic material was fragmented and entrapped by the ingrowing endothelial cells and served as the initial core for the endothelium-linked, tuft-like structures. Slowing of blood flow, stasis, and thrombosis, therefore, appear to be the only prerequisites for the development of this lesion, and consequently, it may be encountered in a variety of vascular lesions following thrombosis. In clearkin’s study, which was based on 44 examples of this tumor-like process, the lesion was most common in small hemangiommas or vascular malformations, but also occurred in dilated veins. In any case, the papillary proliferations of endothelial cells are usually closely associated with a thrombus or with thrombotic material.

Albrecht and Kahn studied IPEH immunohistochemically and compared it to organizing thrombi. The results showed a similar
The progression of the immunophenotype of the endothelial cells in both entities: they are initially positive for a histiocytic marker, ferritin, then acquire vimentin positivity and only display factor VIII-related antigen in mature lesions. This also suggested that IPEH is closely related to organizing thrombi and is probably a peculiar form of it.

Clinically, IPEH usually manifests as a firm and sometimes tender mass that imparts a reddish-blue color to the overlying skin or mucous membrane. It may appear in the interval from nine months to 80 years of age, most commonly in the third and fourth decades of life (around 39 years of age) and has a greater incidence in women. The skin and subcutis of the fingers and the head-neck regions are its most common locations. The “pure” form is usually found in the extremities (particularly in the fingers) and the head and neck region, whereas the type associated with pre-existing vascular disorder (“mixed”) tends to be intramuscular.

The extremely rare extravascular forms of papillary endothelial proliferation were shown to develop from organizing hematomas. Intravascular papillary endothelial hyperplasia (IPEH) bears a considerable morphologic similarity to angiosarcoma. A helpful point in the differential diagnosis is its intravascular location, since angiosarcomas are almost never confined to a vascular lumen. Passive extension of this process into soft tissue may occur following vessel rupture. However, even in these cases, the intravascular location of most of the lesion, coupled with the reactive changes in the vessel wall suggesting rupture, aid in the proper identification. On very rare occasions, papillary endothelial hyperplasia occurs extravascularly as a result of organization of a hematoma. It also differs from angiosarcoma in that the endothelial cells lack necrosis, marked pleomorphism, significant mitotic activity, and solid sheets formation. Distinguishing IPEH from angiosarcoma is important in order to avoid unnecessary surgery or irradiation. Other conditions that should be considered in differential diagnosis include mucocele, intravenous pyogenic granuloma, Kaposi’s sarcoma, and vascular conditions such as hemangioma, angioendothelioma, papular angioplasia, Kimura’s disease, bacillary angiomatosis, and intravenous atypical vascular proliferation.

The prognosis of IPEH is excellent. Follow-up of some large series showed no evidence of metastasis. Essentially all cases are cured by simple excision. Nevertheless, IPEH may recur if it arises in a primary vascular lesion which may itself recur. The therapy in these cases should be planned according to the nature of underlying lesions.

The histopathogenesis of IPEH and cause of IPEH development in some thrombi still remain unclear. The female predilection may indicate a hormonal influence. The stimulation of the excessive endothelial proliferation by locally produced angiogenic growth factors has been suggested. Levere performed Northern blot studies and demonstrated elevated levels of basic fibroblast growth factor (bFGF) in cases of IPEH compared to non-IPEH organizing thrombi. bFGF was proposed to be released by macrophages in response to trauma or irritation leading to excessive proliferation of endothelial cells as an autocrine growth factor. As bFGF may also be secreted by endothelial cells, proliferation of endothelial cells will in turn lead to secretion of more bFGF which, by positive feedback, would cause a cascade of endothelial proliferation. It was stated that individual susceptibility to develop IPEH analogous to individual susceptibility to develop keloids needs to be investigated since individuals who develop IPEH may manifest an exaggerated release of bFGF by their venular endothelial cells, analogous to individuals who develop keloids and manifest an exaggerated synthesis of type 1 collagen by their dermal fibroblasts.

Intravascular papillary endothelial hyperplasia (IPEH) is a rare vascular tumor. The skin and subcutis of the fingers and the head-neck regions are its most common locations. We present here a case of IPEH located in the right thumb of a seven-year old girl. The lesion was totally excised. There is no evidence of recurrence one year after excision. Histopathologically, IPEH should not be confused with angiosarcoma. It is a perfectly benign condition.

REFERENCES


