

Review

Intravascular Papillary Endothelial Hyperplasia: A Review of the Literature

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Abstract

Intravascular papillary endothelial hyperplasia (IPEH), also known as Masson's tumor, is a rare benign vascular lesion first described in 1923. Its pathogenesis involves thrombus formation influenced by stasis, trauma, hormones, or radiation, followed by endothelial proliferation and papillary formation. IPEH occurs in various anatomical locations, including the hand and wrist, with a predilection for the skin and subcutaneous tissues. Clinical presentation varies according to the site, ranging from asymptomatic slow-growing masses to syndromes caused by the compression of surrounding structures. Diagnosis relies on histopathology, supported by immunohistochemistry. Complete surgical excision remains the treatment of choice, with excellent prognosis and low recurrence rates.

Keywords: Intravascular papillary endothelial hyperplasia (IPEH); Masson's tumor; intravascular papillary hyperplasia; vascular lesion

1. Introduction

Intravascular papillary endothelial hyperplasia (IPEH), historically known as Masson's tumor, is a benign vascular lesion that accounts for approximately 2% of vascular tumors, primarily involving the skin and subcutaneous vessels [1]. It is more common in women (1.3:1), with a peak incidence in the fifth decade, although all ages can be affected [2–4]. Contributing factors include trauma, radiation, and prior thrombotic events [5,6], as IPEH originates from an organizing thrombus.

However, when IPEH occurs in the upper extremity, specifically within the hand and wrist, its clinical relevance changes drastically. The intricate anatomy of the hand, characterized by confined spaces, dense anatomical structures, and the immediate proximity of noble neurovascular bundles, makes the clinical presentation of IPEH highly confounding. In this district, IPEH frequently presents as an ambiguous soft-tissue mass, often mimicking more common pathologies such as ganglion cysts, lipomas, hemangiomas, or neurofibromas. Most importantly, its deceptive histopathological appearance can closely resemble malignant vascular conditions, particularly angiosarcoma. Misinterpreting a benign IPEH of the hand can lead to either inappropriately aggressive radical surgery, jeopardizing digital function, or incomplete marginal excisions that predispose to local recurrence.



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Therefore, understanding the specific clinical behavior, radiological features, and surgical management of IPEH within the hand is paramount for hand surgeons to ensure complete marginal excision while preserving digital function.

Objective: To present two illustrative cases of IPEH localized in the hand and wrist, detailing the diagnostic pathway and specific surgical nuances, and to provide a systematic literature review following PRISMA methodology to clarify the diagnostic pitfalls and optimize clinical outcomes.

2. Case Presentation

2.1. Case 1

A 44-year-old right-handed female presented to our department with a 5-month history of a painful, slowly growing subcutaneous nodule located on the radial aspect of her left wrist. Physical examination revealed a well-demarcated, firm, and tender mass, which was initially suspected to be a tenosynovitis of the first extensor compartment tendons (De Quervain's disease) due to its specific anatomical location. An initial ultrasound examination revealed an elongated cystic lesion, which was subsequently aspirated, yielding 3 mL of blood.

To further investigate the lesion, a dedicated baseline soft-tissue Magnetic Resonance Imaging (MRI) scan was performed. Coronal images demonstrated a well-defined subcutaneous lesion on the radial side of the distal forearm/wrist (Figure 1). To better define the depth and anatomical boundaries, axial MRI slices were evaluated (Figure 2). On the axial T1-weighted image (Figure 2a), the superficial, well-demarcated nodular lesion was confirmed to be strictly confined to the subcutaneous compartment. The corresponding axial T2-weighted image (Figure 2b) showed a brilliant, homogeneous hyperintensity of the mass, demonstrating a safe dissection plane completely superficial to the first extensor compartment tendons (abductor pollicis longus and extensor pollicis brevis), without any signs of deep fascial or osseous invasion.

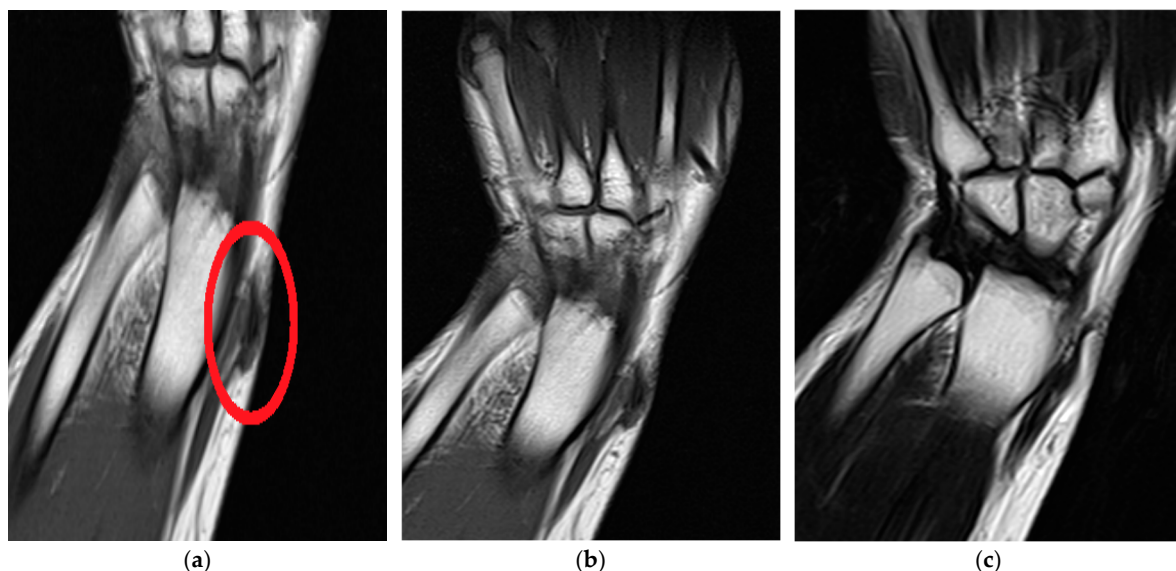


Figure 1. Cont.

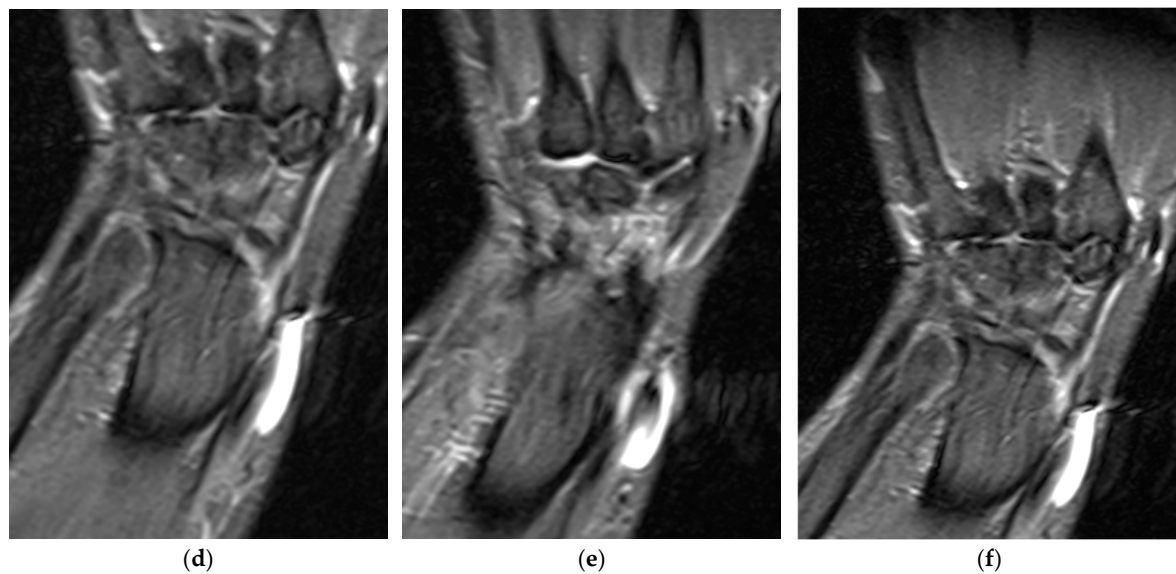


Figure 1. Preoperative coronal Magnetic Resonance Imaging (MRI) of the left wrist (Case 1). (a–c) Coronal T1-weighted images showing an elongated, well-circumscribed subcutaneous mass along the radial aspect of the wrist (red circle). (d–f) Coronal fluid-sensitive, fat-suppressed T2-weighted images highlighting a sharp, homogeneous hyperintensity of the lesion, characteristic of an intravascular slow-flow vascular proliferation.

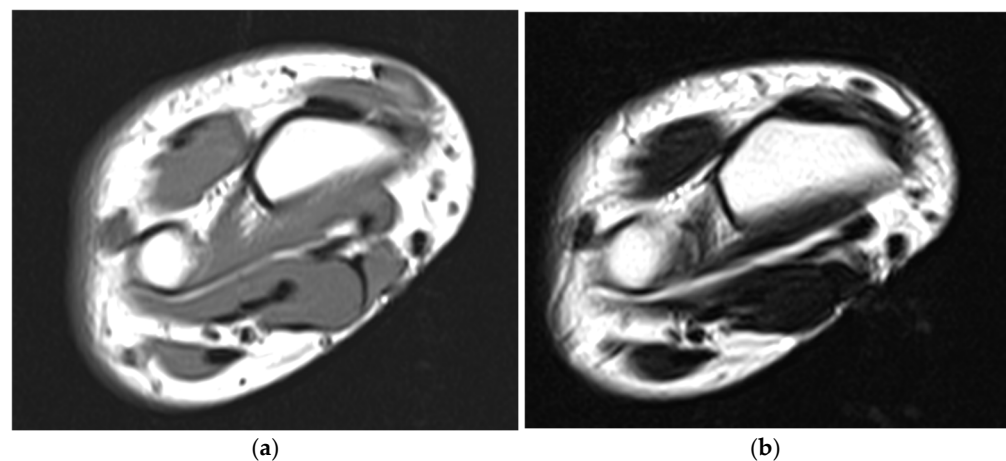


Figure 2. Preoperative axial Magnetic Resonance Imaging (MRI) of the left wrist (Case 1). (a) Axial T1-weighted baseline sequence showing the superficial, well-demarcated nodular lesion confined to the subcutaneous compartment on the radial side. (b) Corresponding axial T2-weighted sequence showing a brilliant, homogeneous hyperintensity of the mass, confirming its safe dissection plane superficial to the first extensor compartment tendons.

The patient underwent surgical excision under local anesthesia. A meticulous marginal surgical resection was performed through a longitudinal incision directly over the radial aspect of the left wrist. Intraoperatively, the mass was found to arise from a superficial subcutaneous venous structure, presenting a reddish-blue, encapsulated appearance. The lesion was fully dissected and removed en bloc while carefully preserving the adjacent superficial radial nerve branches and the underlying first extensor compartment tendons.

Postoperative clinical photographs obtained during follow-up (Figure 3) document an excellent cosmetic outcome and perfect skin healing. Histopathological examination confirmed the definitive diagnosis of Intravascular Papillary Endothelial Hyperplasia (Masson's tumor) arising from a venous vessel. At the final 3-month follow-up, the pa-

tient demonstrated complete, painless extension, flexion, and adduction of the first digit, alongside a full functional recovery of the wrist with no signs of local recurrence.



Figure 3. Postoperative clinical photographs of Case 1 at 3 months follow-up. (a) Palmar view showing optimal healing of the longitudinal surgical scar along the radial aspect of the wrist, with complete and painless extension and flexion of the digits. (b) Lateral view demonstrating full, unrestricted adduction and opposition of the thumb, showcasing complete functional recovery of the first ray and resolution of the previous mass.

2.2. Case 2

A 15-year-old male presented to our department with pain and swelling over the thenar eminence of the right hand, with mechanical pain exacerbated during thumb adduction, flexion, and opposition. No history of trauma or other underlying systemic pathologies was noted. The patient had a complex clinical history: 7 months prior, he had undergone a primary surgical excision of a suspected vascular lesion at another institution without a definitive histopathological diagnosis.

We retrieved and reviewed his initial preoperative Magnetic Resonance Imaging (MRI) from that primary onset (Figure 4). The multi-panel coronal images demonstrate a large, well-circumscribed mass deeply situated within the right thenar eminence. The lesion presented a characteristic low-to-isointense signal on baseline T1-weighted sequences (Figure 4f) and a brilliant, prominent hyperintense signal on fluid-sensitive T2-weighted sequences (Figure 4b–d), typical of an intravascular slow-flow vascular proliferation expanding within the thenar compartment.

After an asymptomatic postoperative period of approximately 7 months following first surgery, the patient experienced a rapidly growing, painful local recurrence. A secondary baseline MRI was performed at our institution (Figure 5), confirming a recurrent, multilocular, and lobulated vascular lesion infiltrating the thenar muscles. On coronal and axial fluid-sensitive sequences (Figure 5a,c), the recurrent mass exhibited a prominent, heterogeneous hyperintense signal with internal septations, typical of an active vascular fluid-enhanced tumor. Conversely, on the corresponding coronal T1-weighted baseline sequence (Figure 5b), the lesion appeared predominantly hypointense to isointense relative to the adjacent hand musculature, defining its boundaries prior to our revision surgery.

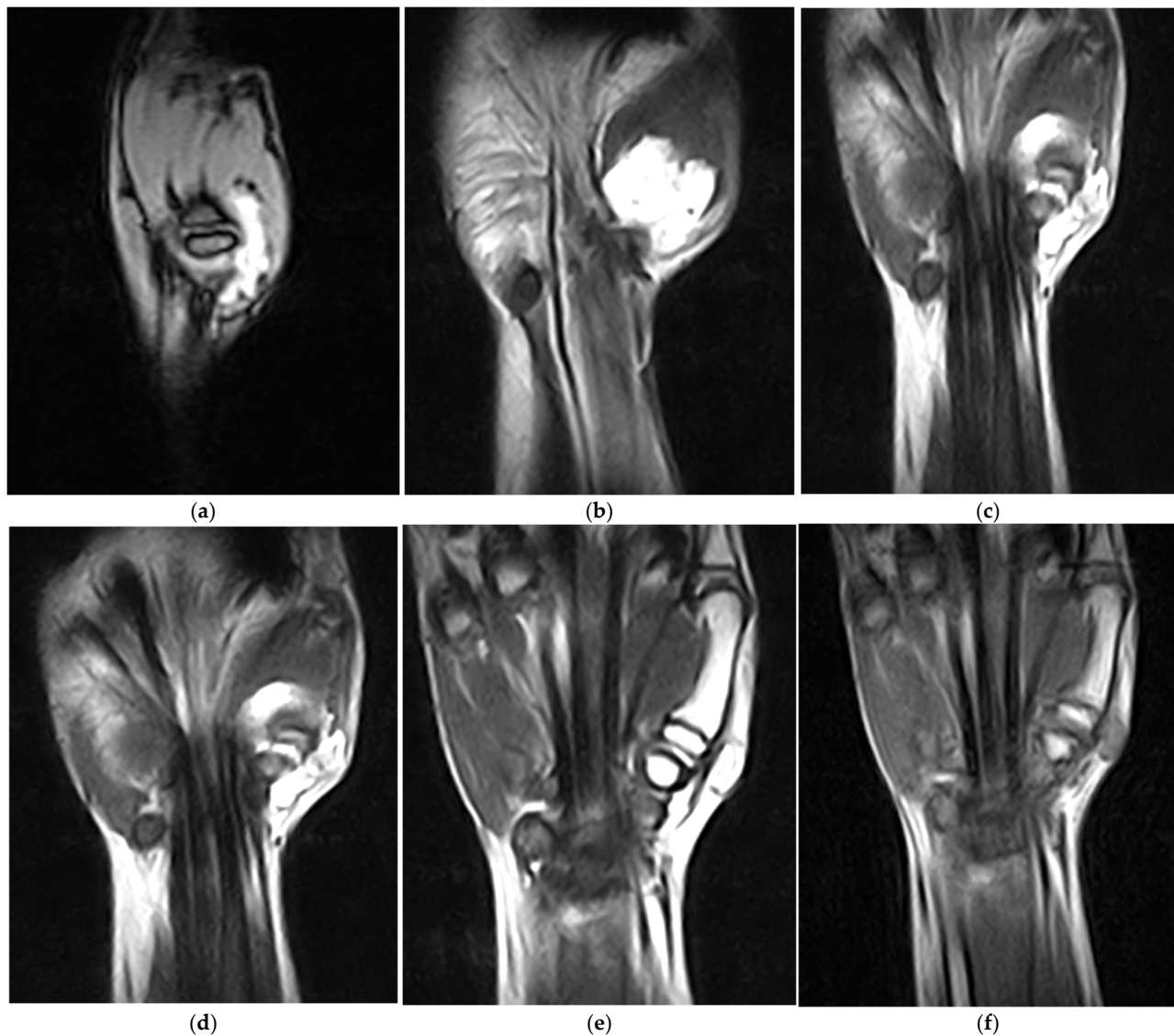


Figure 4. Preoperative coronal MRI of Case 2 from the primary onset, performed at an external institution. Fluid-sensitive T2-weighted sequences show: (a) the anterior aspect of the multi-lobulated, hyperintense lesion; (b) its central, maximum volumetric expansion within the thenar musculature; and (c) the posterior margins demonstrating relationships with surrounding tissues. Corresponding baseline T1-weighted sequences show the same lesion as predominantly hypointense-to-isointense relative to adjacent hand muscles, defining: (d) its anterior projection; (e) its central deep boundaries; and (f) its posterior limits within the thenar compartment prior to the primary surgery.

A meticulous radical marginal excision was performed by our surgical team through a dedicated surgical approach to fully clear the recurrent mass and protect the adjacent digital neurovascular bundles. Histopathological examination of the resected specimen confirmed the definitive diagnosis of Intravascular Papillary Endothelial Hyperplasia (Masson's tumor) originating from an arterial vessel, characterized by an organized thrombus with characteristic endothelial papillary projections and an absence of cellular atypia.

Postoperative clinical photographs obtained during follow-up (Figure 6) document an excellent cosmetic and functional outcome. The palmar and clinical movement views (Figure 6a,b) showcase a complete, painless recovery of general hand mobility and grasp strength, fully comparable to the contralateral healthy side. Furthermore, lateral examination (Figure 6c) demonstrated an unrestricted range of motion (ROM) during thumb extension, while close-up evaluation (Figure 6d) confirmed optimal skin healing with a

soft, stable, and pliable surgical scar over the thenar eminence, with no further clinical or radiological signs of local recurrence at the final 3-month follow-up.

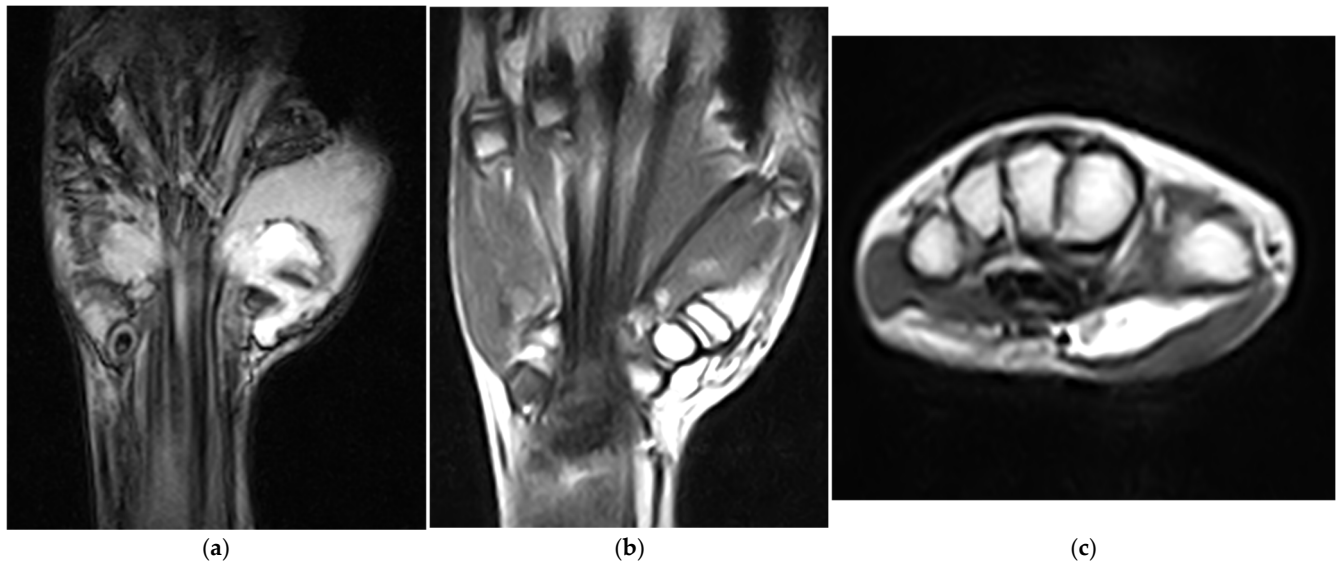


Figure 5. Secondary baseline Magnetic Resonance Imaging (MRI) of Case 2, performed 7 months after the primary surgery, demonstrating a prominent local recurrence [1]. (a) Coronal fluid-sensitive sequence showing the recurrent mass presenting with a characteristic multilobulated, lobulated appearance and prominent hyperintensity [1]. (b) Coronal T1-weighted sequence showing the lesion as hypointense-to-isointense relative to the adjacent thenar muscles [1]. (c) Axial fluid-sensitive view demonstrating the cross-sectional volumetric expansion of the hyperintense recurrent mass strictly within the thenar compartment [1].

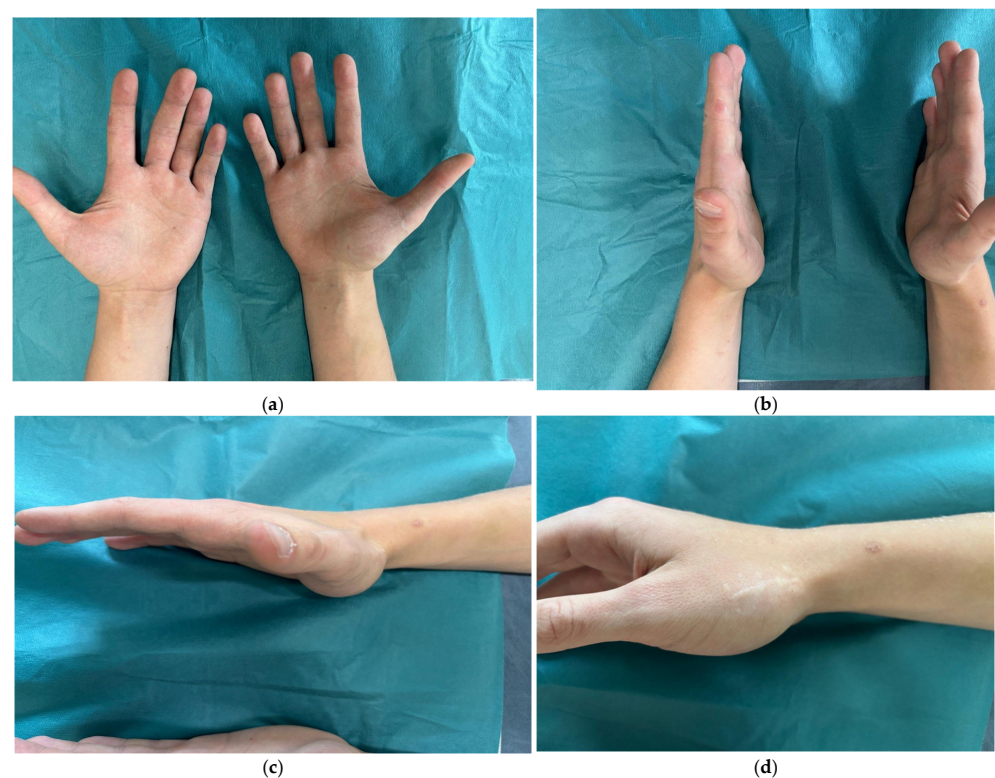


Figure 6. Postoperative clinical photographs of Case 2 at 3 months follow-up, demonstrating complete functional recovery and optimal wound healing. (a) Palmar view of both hands showing excellent cosmetic

outcomes, symmetrical appearance, and full extension of the fingers. (b) Clinical photographs demonstrating complete, active, and painless flexion-extension range of motion of both hands. (c) Lateral view highlighting perfect radial extension and full alignment of the first digit without functional impairment. (d) Close-up clinical photograph showcasing a well-healed, pliable, and minimal surgical scar over the right thenar eminence with complete resolution of the previous mass-related swelling.

3. Literature Review

3.1. Methods

Studies reporting clinical cases or case series of Intravascular Papillary Endothelial Hyperplasia (Masson's Tumor) were included. Both adult and pediatric populations, all anatomical sites, and only studies published in English were considered when sufficient clinical information was provided. Reviews without primary cases or with insufficient clinical or histopathological data were excluded.

A systematic literature search was conducted in February 2020 using the PubMed database. Additional sources included reference lists of relevant papers. No restrictions by publication year were applied. The last database consultation occurred in February 2020.

Search terms included: "Masson's Tumor" and "Papillary Endothelial Hyperplasia".

The combination of these terms yielded 2501 results (2095 for "Masson's Tumor" and 406 for "Papillary Endothelial Hyperplasia"). No filters or language limits were used.

Titles and abstracts were screened for relevance. A total of 2501 records were screened; 2120 were excluded due to irrelevant or insufficient data. Full-text evaluation was performed for 381 articles, of which 309 were included. Screening and selection were independently verified by two reviewers.

Data were extracted manually from each eligible study. Two reviewers independently extracted the following variables: author, publication year, anatomical site, clinical presentation, treatment, and outcome. Any disagreement was resolved by consensus.

Primary data items included:

- Outcomes: Clinical presentation, type of treatment, recurrence, and prognosis.
- Other variables: Age, sex, lesion site, and associated conditions when available.

Due to the descriptive nature of the included studies (mostly case reports), a formal risk of bias assessment was not performed. However, the consistency of clinical, imaging, and histological data was verified for internal validity.

As this was a qualitative synthesis of case reports, no quantitative effect measures or meta-analysis were applicable.

A narrative synthesis approach was adopted. Data were tabulated to summarize the characteristics of individual cases by anatomical region. Quantitative synthesis was not performed due to heterogeneity in presentation and reporting.

Given the type of included evidence (case reports), no formal evaluation of publication bias was feasible.

The certainty of the evidence was considered low due to the predominance of isolated case reports and the limited sample size.

3.2. PRISMA Flow

Records identified through database searching: 2501 [7,8] (Figure 7).

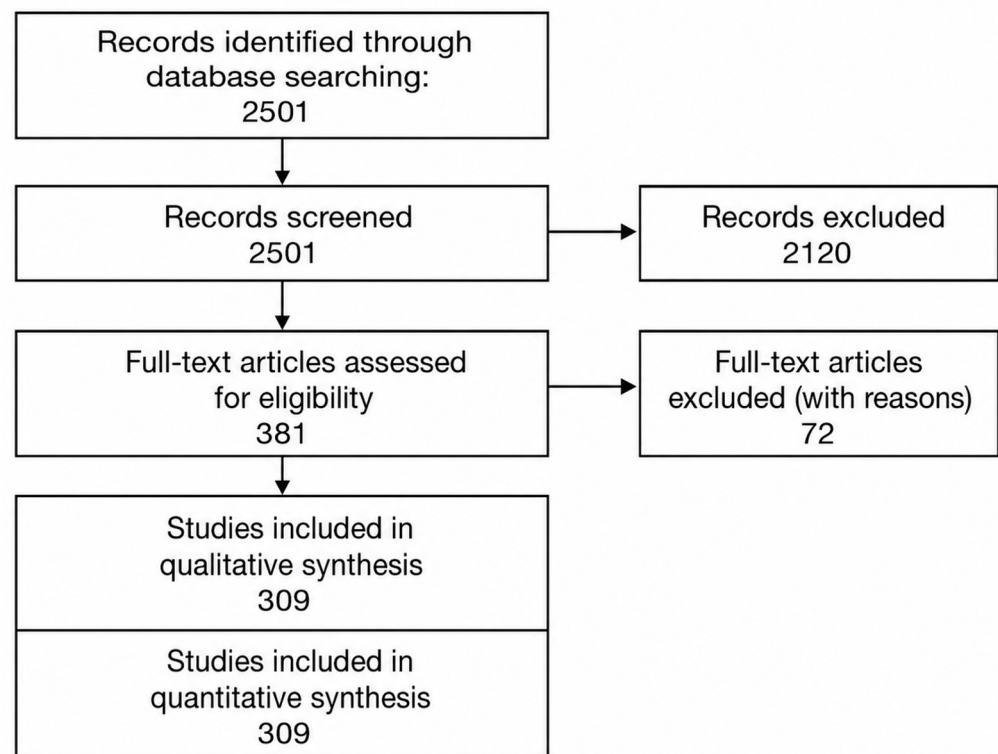


Figure 7. PRISMA flow diagram outlining the systematic literature search, screening, and selection process for cases of Intravascular Papillary Endothelial Hyperplasia (Masson’s tumor). The initial identification was conducted using the PubMed database according to standard screening guidelines. A total of 309 articles were thoroughly evaluated and included in the final qualitative synthesis.

Records after duplicates removed: 2501.

Records screened: 2501.

Records excluded: 2120.

Full-text articles assessed for eligibility: 381.

Full-text articles excluded (with reasons): 72.

Studies included in qualitative synthesis: 309.

Studies included in quantitative synthesis: 0.

3.3. Data Extraction

Key data were summarized from the included studies, including the authors, year, lesion site, clinical presentation, treatment, and outcomes [7,9–58].

4. Results

Most of the articles in the literature refer to case reports in particular locations associated with specific clinical pictures, while 52 reviews were identified as being associated with sectorial case reports on the area of specific onset of the neoplasm. In total, 309 articles referring to 428 particular cases were considered in the following evaluation:

In total, 151 articles were identified that affected the head and neck for a total of 225 cases (52.4%). The neoplasm has been identified intracranially [11–13], as well as in the skull [14], vocal cords [1], larynx [15], pharynx, tongue palate, oral mucous membranes, mandibular bones [16], sinonasal cavity [17], maxillary and paranasal sinus [18], parotid [19], auditory canal [20], lacrimal sac [21], eyelid [22], lips, thyroid [23], parapharyngeal region, and neck [24]. The overall cases involving the oral cavity totaled 109 (25.6%) [25].

At the forearm and hand level, 43 articles were identified that presented a total of 53 cases (12.45%): subcutaneous lesions have been described at the level of the fingers [26], palm of the hand [27], radial and ulnar artery [28,29], sheaths of the flexor tendons [30], and syndromes that generated secondary compression at the carpal tunnel level [31]. In addition, nine articles were identified concerning limbs, which described nine cases (2.11%) in specific sections [triceps brachial [32], thigh [33], synovium of the knee [34]]. In total, ten articles for a total of 11 cases (2.58%) were described at foot level and ankle [35,36].

At the skin level, 26 articles were identified, which presented a total of 33 cases (7.75%) [37].

At the column level, 11 articles (2.58%) were identified that often reported myelo-compressive syndromes [38], while at the breast level, 22 cases (5.1%) were described in 6 articles [39], some of which were secondary to radiation therapy [40].

At the level of the digestive system, 12 articles were found that described as many specific cases (2.82%) in the stomach [41], jejunum [42], liver [43], anal region [44], and intra-abdominal region [45], sometimes due to occult bleeding.

At the level of the reproductive and urinary tract, 30 articles were found describing cases (7.28%) on the penis [46], kidney [47], vulva [48], cervix [49], bladder [50], urethra [51], adrenal gland [52], and periovaric and paratubular region [53], as well as chronic pelvic pain with erectile dysfunction [54].

In addition, six articles (1.41%) were identified at the chest level with lung [55] and rib involvement in multiple sites [56]; at the level of the large vessels, eight articles (1.88%) described involvement in brachial artery aneurysms [57], popliteal aneurysms [58], aortic pseudoaneurysms [59], aneurysmal aorta [60], iliac vein [61] and vena cava syndrome [62].

Finally, at the heart level, seven articles (1.64%) described lesions on the coronary arteries [63], atria [64], and ventricles [65].

5. Discussion

In 1922, Ewing [66] described a rare and obscure intravascular endothelioma located at the level of the corpus cavernosum. Subsequently, Masson, in 1923 [7], described an endothelial papillary neoplasm associated with thrombosis in a 68-year-old man, present at the hemorrhoid level. In 1932, Henschen [67] described a similar lesion at the level of the larynx and defined it as a benign intravascular lesion rather than a neoplasm. According to him, it represented the result of an unusual reparative reactive response of endothelial cells to inflammation and stasis in the vascular lumen. The current histological definition of IPEH was coined by Clerkin and Enzinger in 1976 [68], who described three typologies, and in 1993, Pins et al. [69] calculated the incidence of each typology: (1) pure (55.8%), occurring within a dilated vascular lumen; (2) mixed (39.9%), formed in pre-existing lesions such as hemangiomas, arteriovenous malformations, pyogenic granulomatosis, aneurysms, or chronic diseases with venous thrombosis; and (3) extravascular (4.3%), originating from previous hematomas secondary to trauma.

In addition to the reactive theory, the possibility that a thrombus associated with stasis and perivascular inflammation induces the formation of exuberant endothelial proliferations with papilla formation [7] has been considered.

In fact, while the degradation of newly formed thrombi can be easily obtained by the fibrinolytic cascade, the older thrombi tend to organize themselves because of the widely polymerized fibrin that is more resistant to fibrinolysis [70,71]. Macrophages, attracted to the thrombus, could induce endothelial cell proliferation by releasing basic fibroblast growth factor (bFGF) and triggering a vicious circle [9,72,73]. Channels could therefore form during the degradation process, which are then coated by endothelial and fibroblast cells, creating anastomoses that establish conduits within the thrombus, restoring the

continuity of the original structure. At this point, the thrombus would be transformed into richly vascularized connective tissue and incorporated into the sub-endothelial area or in the vessel wall itself. Such phenomena normally occur in our species [70,71].

However, this physiological process in IPEH, at a certain point, evolves into the intussusceptive process, which is also physiological, but is usually typical of neoangiogenesis processes. In fact, in the IPEH structure, the venous wall is affected focally (in patches) with invagination and the formation of folds. In these folds, most of the Smooth Muscle Cells [SMCs] of the venous wall acquire pericyte-like characteristics and form a subendothelial layer around the Endothelial Cells [ECs] of the growing vascular channels. Intimate venous ECs and those originating from them also participate in the papilla formation mechanism. At this point, ECs encircle the vein wall or thrombus components by a “piecemeal mode of angiogenesis”. These mechanisms combine the findings of sprouting and intussusceptive angiogenesis, and can be linked to hemodynamic conditions in the loops and mother vessels, as occurs in those described in vascular expansion and branching remodeling [2,74].

Histologic examination is necessary to confirm the diagnosis of IPEH. Microscopically, it is characterized by papillary projections of endothelial cells producing vascular channels, which can be attached to the walls or appear as multiple isolated papillae, apparently floating in the lumen [75]. The papillary projections contain a single layer of endothelial cells lining a dense hyalinized stroma that may represent capillaries. Sometimes, these papillary projections exhibit a large number of cells that appear to be coated by multiple layers of endothelial cells [25].

The microscopic differential diagnosis of IPEH is challenging. Some malignant and benign vascular tumors are involved, such as intravenous atypical vascular proliferation, also called epithelioid hemangioma, Kaposi sarcoma [76], malignant endovascular papillary angioendothelioma (or Dabska tumor), and angiosarcoma [77].

At a histological level, several aspects make it possible to uniquely identify the IPEH with respect to other malignant neoplasms: (I) the endothelial proliferation remains limited to the vascular layer; (II) most of the papillary structures are associated with thrombi; (III) the lack of necrosis and solid areas; and (IV) the absence of mitotic figures and cellular pleomorphism [17].

Although histological findings may be sufficient for a diagnosis of IPEH, immunohistochemistry has gained increasing importance for further confirmation of IPEH diagnosis. The presence of CD31 and CD34 are among the most sensitive markers used to indicate the vascular origin of the lesion, even if they are not endothelial-cell-specific but commonly expressed by vascular endothelium, especially under pathological conditions. The presence of other vascular markers (FVIII, type IV collagen, SMA and MSA) was variable [71]. Additionally, IPEH lesions often show positive staining for ferritin, type VIII collagen, and vimentin [17].

Clinical findings are highly variable and depend on the site of onset. Chronic pelvic pain syndromes, vena cava syndromes, carpal tunnel syndromes, cauda equina syndromes, elevated intracranial pressure [78], aphasia [79], painful proptosis [80], massive myocardial infarction [63,81] and signs of intracranial compression were associated with specific IPEH frameworks. When the lesion is present in the subcutaneous tissues, IPEH appears as a mass of palpable soft tissue, often located within normal or dilated vascular spaces and characterized by a typically slow-growing nature.

Ultrasound (US) images, while not specific, allow us to identify vascular lesions, particularly when using color Doppler, which distinguish them from simple cystic areas. The neoplasm could be more easily found in the subcutaneous layer of the hand or within a muscle tissue associated with peripheral veins, thus resembling, at first feeling, an endovascular thrombus. US also helps us to determine whether the mass is confined or

locally extended, as well as the degree of compressibility. It can usually be used as a first diagnostic investigation for differential diagnosis of a small, well-defined, oval or elliptical, heterogeneous, hypoechoic soft tissue mass, showing a vascular pattern of one or more vessels in the lesion and variable vascularity [82].

Magnetic Resonance Imaging (MRI) basically shows a heterogeneous, iso- to slightly high signal intensity mass on T1-weighted images and a mass with a central heterogeneous, iso- to slightly high signal intensity area, completely or incompletely surrounded by peripheral high-signal-intensity areas on T2-weighted images. These imaging characteristics are due to the ratio of the mixture of organized thrombi, hyalinized thrombi, papillary endothelial proliferation, and vascular blood space that influences the signal intensity [83].

The prognosis of IPEH is generally favorable; however, fatal outcomes have been reported in rare cases, particularly in patients with intracranial hemorrhages [84]. The best treatment for IPEH is a complete surgical excision. Endoscopic surgery [85] and the use of beta-adrenergic antagonists related to the site involved have also been described [86]. For minimizing bleeding and improving esthetic results, Cohen et al. have utilized sclerotherapy with sodium tetradecyl sulfate prior to resection [87]. No reports of metastatic cases have been found, supporting the benign nature of IPEH. However, recurrence of IPEH has been observed in the recent literature in 15% of cases [88], likely due to incomplete removal. New cases have also been reported following brain and breast radiation therapy [40,89,90]. Follow-up from several large case series has shown no evidence of local invasion or metastasis [91].

Despite these well-defined histopathological mechanisms, clinical diagnosis of IPEH remains particularly challenging when localized in the hand and forearm. In these anatomical regions, the high density of noble neurovascular structures and limited subcutaneous space often leads to symptomatic presentations, even with small lesions.

The recent literature emphasizes that IPEH in the hand can frequently mimic more common pathologies, such as ganglion cysts or giant cell tumors of the tendon sheath (GCTTS), often leading to initial clinical misdiagnosis [92,93]. Furthermore, in the forearm, the hypervascular nature of IPEH, as seen on Doppler ultrasound or MRI, can mimic aggressive vascular neoplasms like hemangiopericytomas, potentially leading to over-treatment [27].

In our experience, the close relationship between the lesion and the small-caliber vessels of the hand requires a delicate surgical approach. Unlike IPEH in other sites, excision in the upper limb must be performed with meticulous dissection to prevent damage to digital nerves or tendons. Our cases confirm that complete surgical excision—balancing radicality with the preservation of motor and sensory function—is the treatment of choice, as the ‘pure’ form (Type 1) found in our patients shows excellent prognosis with no recurrence when the venous origin is correctly identified and managed.

6. Conclusions

IPEH (Intravascular Papillary Endothelial Hyperplasia) is a rare benign vascular lesion with a variable clinical presentation depending on the site involved. Although pain is not consistently present, it typically appears as a slowly growing mass in subcutaneous tissues or peripheral vessels.

Color Doppler ultrasound is a useful first-line imaging tool to identify the vascular nature of the lesion, but a definitive diagnosis requires histopathological examination.

The treatment of choice is complete surgical excision, which generally ensures excellent prognosis.

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Data Availability Statement: The clinical and radiological data supporting the reported results of the illustrative case presentations are contained within the patient medical records at the Department of Orthopaedics and Traumatology, Annunziata Hospital, Sulmona, Italy, and cannot be shared publicly due to strict institutional privacy regulations and patient confidentiality restrictions. The dataset for the systematic literature review was extracted entirely from primary data publicly indexed in the PubMed database. All data parsed, generated, and synthesized during the systematic evaluation are fully detailed and presented within the tables, figures, and reference list of this manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

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