Intranodal Palisaded Myofibroblastoma: A Diagnostic Differential for Inguinal Lymphadenopathy

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Patient: Male, 48-year-old
Final Diagnosis: Intranodal palisaded myofibroblastoma
Symptoms: Inguinal lump
Medication: —
Clinical Procedure: Lumpectomy
Specialty: Pathology • Surgery

Objective: Rare disease
Background: Benign tumors of the lymph nodes are rare and are not usually considered in the differential diagnosis in cases of lymphadenopathy because reactive hyperplasia, lymphoma, and metastatic carcinoma are the most likely causes of enlarged nodes. Intranodal palisaded myofibroblastoma (IPM) is a very rare benign mesenchymal tumor of the lymph nodes most often affecting but not limited to the inguinal region, with up to 92 cases reported in the English literature. The cell of origin is the intranodal differentiated smooth muscle cell or myofibroblast. Although the pathophysiology of IPM remains unclear, theories about viral oncogenesis and mutational changes in the β-catenin gene with subsequent abnormal expression of β-catenin and cyclin D1 have been raised.

Case Report: We report a case of IPM in a 48-year-old man who presented with a mass in the left groin, with inconclusive imaging. The typical histologic findings of smooth muscle actin, cyclin D1, and β-catenin positive intranodal spindle cell proliferation with characteristic palisades, amianthoid fibers, collagenous bodies, lack of atypia, and very low mitotic count, together with characteristic profile on ancillary testing, confirmed the diagnosis. In addition to staining with smooth muscle actin, cyclin D1 and β-catenin, immunohistochemical studies showed focal positivity with desmin, a finding previously reported in 2 of the published cases. Surgical excision is usually curative, with a 6% recurrence rate and no reported cases of locally aggressive disease or malignant transformation.

Conclusions: Although rare, IPM should be included in the differential diagnosis of isolated lymphadenopathy.

Keywords: beta Catenin • Lymphadenopathy • Soft Tissue Neoplasms

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Background

Intranodal palisaded myofibroblastoma (IPM), also known as intranodal hemorrhagic spindle cell tumor with amianthoid fibers, is a benign tumor of the lymph node. Originally thought to be of neural origin, more recent studies highlight characteristic immunohistochemical and molecular features, confirming myoid or myofibroblastic differentiation with a likely mutational activation of the β-catenin gene [1].

It was described concurrently in 1989 by Weiss et al as “palisaded myofibroblastoma” [2] and Suster et al as “intranodal hemorrhagic spindle cell tumor with amianthoid fibers” [3], followed by Lee et al who called it “solitary spindle cell tumor with myeloid differentiation” [4] in the same year. Earlier reports of lesions with identical characteristic morphology have been considered intranodal leiomyoma or schwannoma, with the earliest description by Deligdish et al in 1968 referring to it as an identical tumor to malignant neurilemmoma [5].

Case Report

A 48-year-old man presented with a 2-month history of a 2-cm firm and mobile lump in the left groin with no associated generalized lymphadenopathy or other symptoms. The results of full blood examination and chemistry panels were within normal limits. On ultrasound, the mass was thought to represent an unusual infection with abscess formation or a necrotic lymph node. Magnetic resonance imaging (MRI) confirmed a 2-cm mildly heterogeneous lesion with a hypointense rim demonstrating minimal enhancement following contrast administration, perilesional T2 hyperintensity, and probable intralesional calcification, likely a calcified lymph node or other entity warranting excision.

The specimen was a 2-cm tan nodule with attached fat and a hemorrhagic cut surface. Microscopic examination showed a spindle cell proliferation surrounded by a well-defined collagenous capsule and a thin rim of lymph node tissue perforated by amianthoid fibers highlighted with elastic stain (Van Gieson), marked hemorrhage, and pigmented macrophages (Figure 1). The spindle cells were quite monotonous, with oval nuclei, granular cytoplasm, and round eosinophilic bodies, the latter also seen extracellularly (Figure 2). The tumor stained with cyclin-D1, β-catenin, smooth muscle actin, myosin, and vimentin and focally with desmin (Figure 3). It showed a Ki-67 proliferative fraction averaging 4%. Immunohistochemical stains for S100, keratin, EMA, CD31, and HHV8 were negative. The lesion was diagnosed as IPM. The main differential diagnosis was schwannoma, which was excluded based on the absence of amianthoid fibers, characteristic hypocellular and hypercellular “biphasic” pattern, and immunohistochemical profile, particularly positive S100.
Discussion

IPM is a relatively rare intranodal mesenchymal tumor of smooth muscle fibers or myofibroblasts, typically presenting in the inguinal nodes and infrequently at other sites such as cervical [6], submandibular [7,8], supraclavicular [9], axillary [10], mediastinal [11], and retroperitoneal nodes [12]. Although mostly seen in middle-age, IPM can affect a broad age group (19-71 years) [10], with a single case reported in an infant [13]. IPM is more commonly reported in males than females (ratio 2:1), with no ethnic predisposition and with reports in White, Black, and Asian populations [14].

IPM presents usually as a single unilateral painless mass, although large forms can cause discomfort and pain by local compression [10]. When palpable, IPM is firm, mobile, and well delineated from adjacent tissue. It is usually asymptomatic and can be associated with trauma [1]. Chief radiological investigations include static and functional ultrasound imaging; CT and MRI can also be used to better characterize the lesion or plan for surgical excision.

B-mode ultrasound used in the evaluation of superficial soft-tissue tumors confirms a homogenous or heterogenous echogenic solid lesion. Color Doppler ultrasound defines a single vascular pole, supportive of a benign tumor. CT scan shows a well-demarcated tumor separate from adjacent structures [15]. Most IPMs are subcutaneous and amenable to cytological assessment using fine needle aspiration technique [15], which presents diagnostic challenges for the inexperienced cytopathologist as cellular pigmented areas can be confused with other soft-tissue tumors, such as schwannomas or, more concerningly, sarcomas and melanomas.

Macroscopically, IPM is well circumscribed with a white cut surface and areas of hemorrhage. The characteristic histological features include a well-delineated encapsulated cellular tumor usually with a rim of residual lymph node, encompassing cellular areas of bland and monotonous spindle cells forming typical palisades of nuclei, amianthoid fibers, and extravasated red blood cells with evidence of old hemorrhage and hemosiderin pigment. On high-power magnification, intracellular perinuclear intracytoplasmic and extracellular fuchsinophilic or collagenous bodies are seen [1,14]. Mitotic figures are absent or sparse (up to 8 per 50 high-power field) [1], and abnormal forms have never been reported. No necrosis nor cellular atypia has been identified. The immunohistochemical profile of IPM is useful in confirming the diagnosis and to exclude other soft-tissue tumors with nuclear palisades, spindle cells, and pigment. Typically, the spindle cells stain with smooth muscle actin, vimentin, cyclin D1, and β-catenin, with a low Ki-67 proliferative index of less than 5%. Desmin is usually negative, although our case and 2 other previously reported cases were immunoreactive [16,17]. Epithelial, vascular, neural, and melanocytic markers including keratin, EMA, CD31, factor VIII, S100, synaptophysin, GFAP, and HHV8 are negative. Amianthoid fibers are highlighted on histochemical connective tissue stains, including trichrome, collagen, and elastic stains [5,14].

Molecular testing for mutations in the β-catenin gene glycogen synthase kinase-3 β phosphorylation mutational “hotspot” region in exon 3 using PCR amplification and Sanger sequencing identifies missense mutations due to single-nucleotide substitutions in 88% of cases analyzed, leading to abnormal expression of β-catenin and cyclin D1 [1,18].

Electron microscopy shows smooth muscle myofilaments and rough endoplasmic reticulum cisternae. The “amianthoid fibers” are in fact found to be collagen fibers with a smaller width (80-150 nm) than previously known amianthoid fibers (280-1000 nm) [14].

IPM must be distinguished from schwannoma, a spindle cell proliferation arranged in cellular areas (Antoni A) with palisades forming the so-called Verocay bodies, paucicellular areas (Antoni B), and, unlike IPM, stains with S100. Kaposi sarcoma can also mimic IPM with proliferating spindle cells and hemorrhage but is readily differentiated with the slit-like vascular network, PAS positive hyaline globules, absence of amianthoid fibers, and positive HHV8. Lymph node metastases from sarcomatoid carcinoma, melanoma, and sarcoma can be confused with IPM, especially in patients with a known past history of malignancy, and are readily excluded due to lack of amianthoid fibers and characteristic immunohistochemical profile with positive epithelial, melanocytic, and specific stromal markers, respectively.

Conclusions

IPM is a benign mesenchymal intranodal proliferation of spindle cells with amianthoid fibers and hemosiderin pigment. It is crucial to recognize the typical morphology to avoid diagnostic pitfalls. Although rare (less than 100 cases reported in the English literature), IPM should be considered in the differential diagnosis of localized lymphadenopathy, particularly of the inguinal region.

Declaration of Figures’ Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.
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