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Intranodal Hemorrhagic Spindle Cell Tumor with Amianthoid Fibers – Report of a Case with Emphasis to Mast Cell Reaction and D2-40 Expression

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Abstract. *Aim: Intranodal palisaded myofibroblastoma (IPM) is a rare benign mesenchymal tumor restricted to the lymph nodes. Here, we report the case of a 44-year-old male patient with an IPM confined to the left laterocervical area. Case Report: After an accurate microscopic evaluation of morphological and histochemical stains, immunohistochemistry was performed for vimentin, smooth muscle actin vascular markers, S100 protein, D2-40, Ki67, lymphoid and melanoma markers, keratin and desmin on sections obtained from a paraffin-embedded surgical biopsy. Results: Spindle cell proliferation was positive for vimentin, smooth muscle cell actin and D2-40 and negative for the other markers. Low proliferative index, assessed by Ki67, was found. Based on morphological and immunohistochemical findings we diagnosed this case as intranodal palisaded myofibroblastoma and we highlighted a D2-40 expression in the tumor spindle cells. The presence of mast cells and their particular distribution inside the tumor are also, together with D2-40 expression, original findings of this study. No therapy was recommended after surgical and histopathological evaluation. The evolution of the patient was favorable with no other relapse following surgical removal of the lymphadenopathy. He has a normal life and no other changes of clinical and biological parameters were registered. Conclusion: To the best of our knolwedge, this is the first report regarding a D2-40-positive reaction in the spindle cells of intranodal palisaded myofibroblastoma. Thus, D2-40 could be added to the panel of antibodies used for immunohistochemical diagnosis of such types of tumors.*

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Described and characterized for the first time by two independent groups in 1989 (1, 2), intranodal palisading myofibroblastoma (IPM), intranodal hemorrhagic spindle cell tumor with amianthoid fibers is a rare, benign mesenchymal tumor of lymph node, usually diagnosed in the inguinal area. Unusually, this tumor develops in the submandibular or cervical lymph nodes. No more than 50 cases are described in the literature; most cases are solitary, but the involvement of more than one lymph node or reccurent behaviour have so far been reported only by two publications (3, 4).

Based on current data, the tumor seems to arise from smooth muscle cells or myofibroblasts (5). Microscopically, the tumor consists of areas of low proliferative spindle cells mixed with hemosiderin-laden histiocytes and very fine collagen fibers known as amianthoid fibers. Metaplastic bone formation and calcification have also been reported (4, 6). The tumor appears to be benign and local excision is adequate and curative.

Here, we report the case of a 44-year-old man with IPM in the left laterocervical area with a particular immunophenotype.

Case Report

A 44-year-old man with a previous history of a spontaneously-regressed 3-cm solitary, inguinal lymphadenopathy, was admitted to the hospital because of a slow-growing tender mass in his left laterocervical area. Surgical excision and histopathology were performed to establish the diagnosis. The patient was discharged and no relapses have been registered to date (10 months after the treatment).

The first histopathological and immunohistochemical findings excluded lymphoma and the pathologist suspected the lesion to be silicosis. A second diagnostic opinion was recommended and the patient came to our Department for further investigations.

Macroscopically, the unique lymph node was encapsulated and measured 2×2.2×3 cm in size. The sectioned lymph node had a tan, solid cut surface, with patchy red-brown areas. Tumor tissue specimens were fixed in 10% buffered formalin

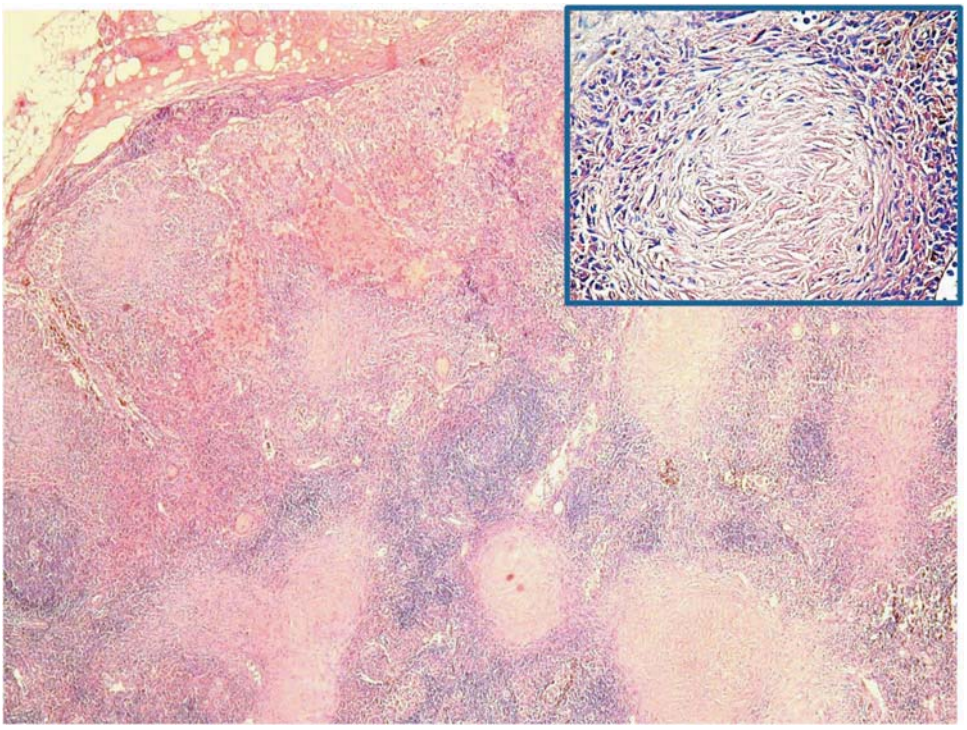

Figure 1. *Low-power magnification of the tumor (×20). Lymph node structure can be seen to have been replaced by a well-encapsulated tumor mass composed of large fibrous areas, hemorrhagic zones and hemosiderin pigment mixed with remnant lymphoid follicles. Early stage of the lesion is characterized by collagenous areas centered by a small blood vessel (inset, ×200).*

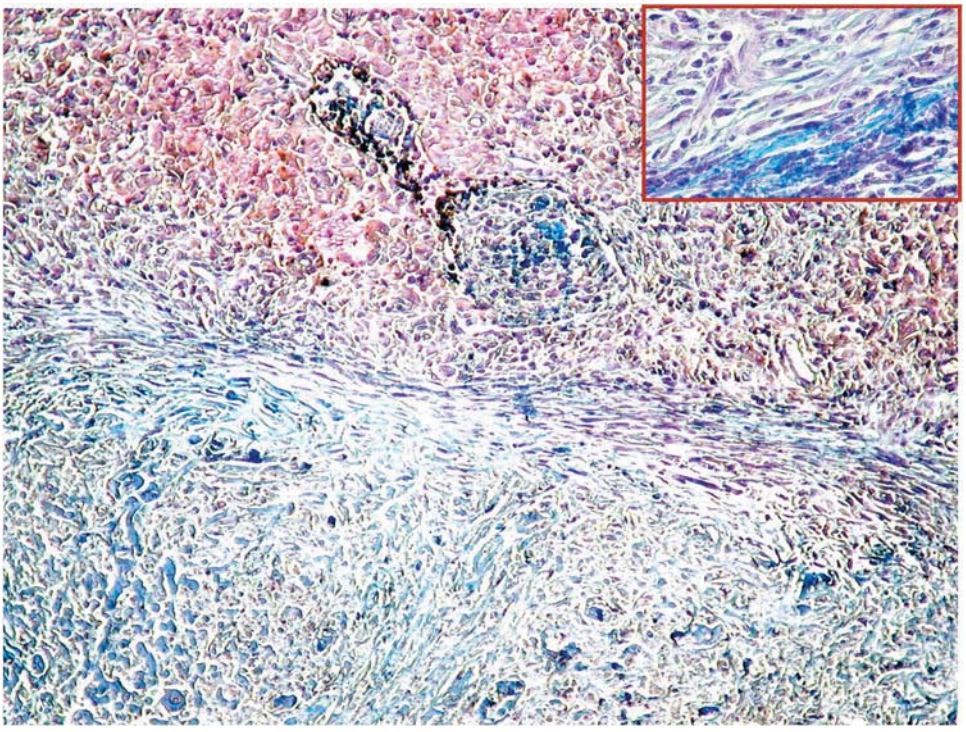

Figure 2. *Large collagen-rich areas stained with Masson's trichrome method. Note the thickness of the blue-stained collagen fibers (inset, longitudinal section, ×400).*

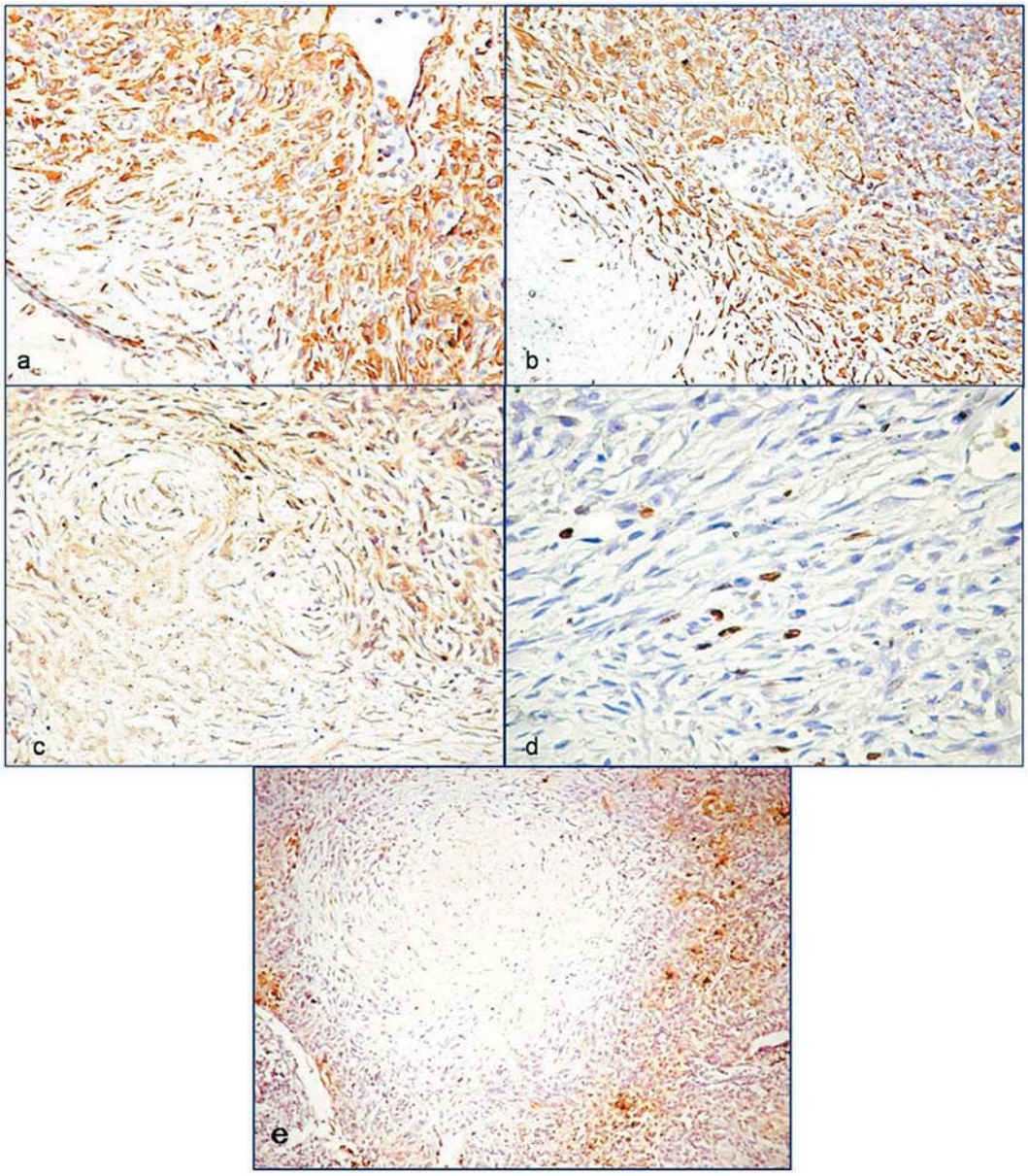

Figure 3. *Positive immunostaining for smooth muscle actin (a), vimentin (b) and D2-40 (c) in tumor cells surrounding collagenous areas. Low expression of Ki67 (d). Numerous mast cells can be seen grouped around collagenous areas and near blood vessels (e).*

and were paraffin embedded. Five micrometer-thick sections were stained with hematoxylin-eosin (H&E) and Masson's trichrome (MT) stains. Immunohistochemistry was performed by a streptavidin biotin system. All immunohistochemical steps were performed in an automated fashion with a PT Link antigen retrieval System (DakoCytomation, Carpinteria, CA, USA) and a Dako Autostainer (DakoCytomation, Carpinteria, CA, USA). Antibodies used and their characteristics are shown in Table I. The procedures were in accordance with the ethical standards of the institution and the Helsinki Declaration of 1975, as revised in 1983 (7).

Microscopically, we observed a disorganized architecture of the lymph node, with most of the lymphoid mass being replaced by the tumor (Figure 1). The lesion was composed of spindle cells distributed around small blood vessels (Figure 1, inset) or surrounding large, round fibromyxoid hypocellular areas mixed with numerous hemorrhagic areas

Table I. *Antibody features and methods used for each immunostain.*

Antibody	Manufacturer	Dilution	Antigen retrieval	Incubation time (minutes)	Chromogen
Vimentin	Dako Glostrup, Denmark, clone V9	Ready to use	5', MW, citrate buffer pH 6	30, RT	3,3' Diaminobenzidine
Smooth muscle cell actin	Dako clone 1A4		5', MW, citrate buffer pH 6		
Desmin	Dako		5', MW, citrate buffer pH 6		
Ki67	Dako, clone MIB1		30', MW, citrate buffer pH 6		
S-100 protein	Dako, polyclonal,		5', MW, citrate buffer pH 6		
Melan A	Dako		30', MW, citrate buffer pH 6		
MAGE1	Dako		30', MW, citrate buffer pH 6		
D2-40	Dako, clone D2-40		30', MW, citrate buffer pH 6		
CD31	Dako, clone JC70		30', MW, citrate buffer pH 6		
CD34	Dako, clone, QBEnd10		30', MW, citrate buffer pH 6		
FVIII related antigen	Dako, polyclonal		30' MW, citrate buffer pH 6		
EMA	Dako		None		
CD68	Dako		30', MW, citrate buffer pH 6		
Keratin AE1/AE3	Dako, clone AE1/AE3		Proteinase K, 5', RT		

MW: Microwave antigen retrieval procedure; RT: room temperature.

and histiocytes with hemosiderin pigment. Between spindle cells, we observed acidophilic bands interposed in a disorganized manner. These acidophilic bands were found to be stained blue following MTs stain, illustrating their high collagen content (Figure 2). Tumor cells shared bland nuclear features and no significant mitotic activity. Immunohistochemical analysis showed strong positive reaction for smooth muscle actin (Figure 3a) and vimentin (Figure 3b). Immunostains for melanoma markers as melan A, melanoma associated antigen-1 (MAGE-1) as well as for cytokeratin, Epithelial Membrane Antigen (EMA), desmin, S100 protein, CD68 and vascular markers were negative in tumor cells.

A particular finding for this tumor was the positive reaction observed for podoplanin (D2-40) in the tumor spindle cells. Its expression had a cytoplasmic pattern with moderate intensity and this was a constant finding in all spindle tumor cells (Figure 3c).

The proliferative index as assessed by Ki67 antibody was less than 1% in the tumor cells (Figure 3d). Between amianthoid fibers and tumor cells, a high number of tryptase-positive mast cells were detected by immunohistochemistry. Mast cells were focally distributed (Figure 3e), usually grouped around amianthoid collagen fibers surrounding blood vessels.

Discussion

Non-lymphoid pathology of the lymph node includes a group of rare primary diseases, most of them of mesenchymal origin (8). IPM is a distinctive benign spindle cell tumor arising exclusively from the lymph nodes. The microscopic resemblance of IPM with schwannoma of the lymph node previously led to numerous mis-diagnoses.

IPM usually occurs in the inguinal area but a few other locations have been also reported (9). We report here a case of IPM located in a latero-cervical lymph node following a history of single inguinal lymphadenopathy that spontaneously regressed. To the best of our knowledge, this is the first case in the literature with this particular location and evolution.

Spindle cells were characterized by a consistent expression of smooth muscle actin, myosin and vimentin and a lack of desmin. The origin of tumor cells from IPM is still controversial. One of the most accepted hypotheses is that spindle tumor cells arise from myofibroblasts. It is well-known that myofibroblasts are positive for D2-40 expression (10). This evidence together with our finding concerning D2-40 expression, in tumor cells, and in addition, positivity for actin and vimentin support the hypothesis that IPM is a tumor derived from myofibroblasts.

A high number of mast cells surrounding the sclerosing regions and between amianthoid fibers of IPM was described here. The role of mast cells in the pathogenesis of IPM is not yet known. Bigotti *et al.*, hypothesized that mast cells may have a crucial role, in both the formation of amianthoid fibers and in the proliferation of myofibroblasts in myofibroblastoma (11). In the final diagnosis, differential diagnosis of IPM from Kaposi sarcoma, schwanomma and metastatic melanoma lesions is mandatory. In the case reported here, the lack of reaction for vascular markers, S100 protein and melanoma markers excluded all these conditions.

In the present study, we present a case of IPM with cervical location and with expression of D2-40 in tumor

cells. To our knowledge, this is the first report highlighting-D2-40 expresion in tumor cells from IPM in addition to mast cell reaction.

Competing Interests

None.

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