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SCIENTIFIC LITERATURE

CASE REPORT

Neurofilament Expression in a Dermatofibroma

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ABSTRACT

Dermatofibroma is a benign tumor of dermal fibroblasts frequently observed in limbs. A case of dermatofibroma in the forearm is presented, with a strong and diffuse expression of vimentin and neurofilament. No neural, schwannian, endoneurial or perineurial elements were demonstrated with immunohisto chemistry.

The case has positive and negative internal control. The co-expression of both intermediate filaments was limited to the tumor, suggesting that the dermatofibroma´s vimentin filaments are different from the other mesenchimal vimentin filaments.

Introduction

Dermatofibroma, also known as benign fibrous histiocytoma, is regarded as a benign tumour or reactive inflammatoryprocess that may uncommonly recur locally1. They are usually secondary to a history of trauma, blunt, piercing or insect bite. Dermatofibromais mostly observed in inferior extremities in women [1]. Incidence in upper extremities is very low [2].

Histologically, the skin has 2 subsets of fibroblasts in base of the expression of CD34, which can give rise to well-differentiated tumors. Dermatofibroma is a benign tumour composed by CD34 negative dermal fibroblasts; in contrast dermatofibrosarcoma protruberans is a low grade malignant tumour composed by CD34 positive fibroblasts [2]. Their intermediate filament is vimentin [2]. Although muscular differentiation has been observed on some occasion, no desm in expression was reported in dermatofibromas [3].

Intermediate filaments are the main cytoskeletal structural proteins, and are classified into 5 categories plus laminin 4. Neurofilament protein is classified in IV group of intermediate filaments, and vimentin is classified in the III group [4,5]. Neurofilament replaces vimentin as main intermediate filament in the neural system (both central and peripheral) during development [5]. Intermediate filaments are regarded in the peripheral nervous system as regulators of several processes including myelination [6], and are required for development [7].

A high grade of homology has been observed within the different families of intermediate filaments, and thus occasional recognition of 2 intermediate filaments by the same monoclonal antibody has been observed [8].

Cross-reactivity has been observed with antineurofilament antibodies, troponin-T9 and glial fibrillary acidic protein [10]. It has also been observed in thymus11, CD3 lymphocytes [12,13] and even the human sperm cell [14]. Co expression of vimentin with anti neurofilament antibodies has not been described in non tumoral skin [15].

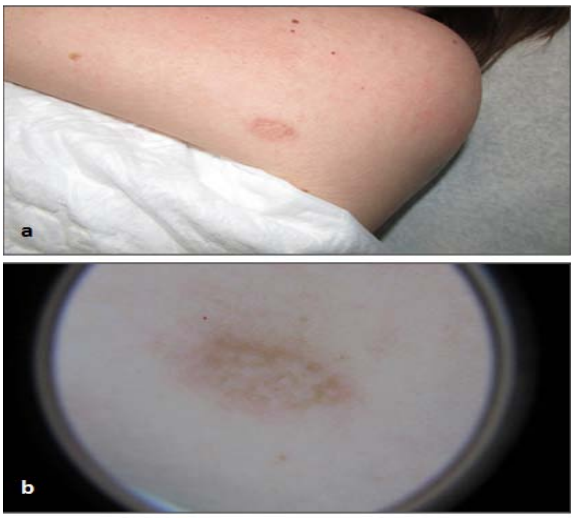

Figure 1: (a) A weakly pigmented ovoid plaque is observed in the proximal left arm. (b) Dermatoscopy was also employed.

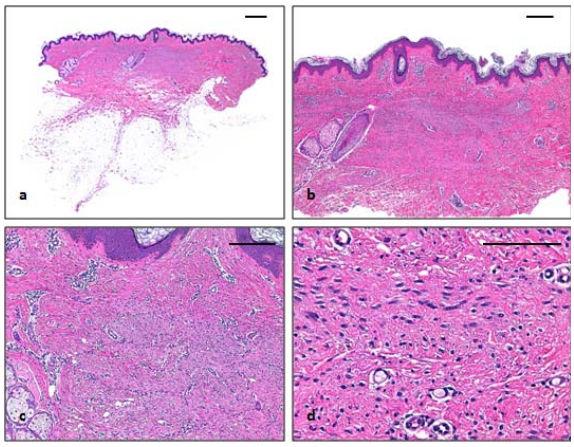

Figure 2: Tumor section stained with haematoxilin-eosin. Panoramic view (a – 2x – scale bar 500 µm) depicts a well excised tumor beneath the papillary dermis. Cutaneous adnexae are preserved (b – 4x – scale bar 250 µm). The tumor has irregular contour (c – 20x – scale bar 50 µm) and wavy cellular disposition (d – 40x – scale bar 50 µm).

Case Report

One 37 year old woman was submitted to Dermatology department due to a mass on her left arm (Figure 1). The patient had the lesion removed with local anesthesia and discharged the same day.

The excised material measured 2, 7 x 0, 9 x 0, 7 cm and was sent to Pathology department in order to confirm the clinical diagnosis. No lesion was observed in the routinary macroscopic examination. The microscopic study revealed a nonencapsulated lesion showing dermal extension with benign appearing spindle cell proliferation displaying a storiform arrangement (Figure. 2a,b). The cells presented scant cytoplasms and thin elongated nuclei with pointed ends (Figure 2c,d). No necrosis or mitotic figures were found.

In the differential diagnosis the possibility of neurofibroma was considered on a rapid assessment, and thus immunohistochemistry was performed.

Immunohistochemistry showed no expression off actor XIII or S100 protein, but strong and diffuse vimentin and neurofilament positivity was observed (Figure 3a-c). A second round of immunohistochemistry was performed due to the surprising neurofilament expression, and no PGP 9.5 or neuron specific enolase was observed, nor actin, desmin, CD34 or HMB45 (Figure 3d-f). The neurofilament technique was repeated with the same result.

The final diagnosis was dermatofibroma due to the morphological appearance combined with the inconspicuous immunohistochemical results.

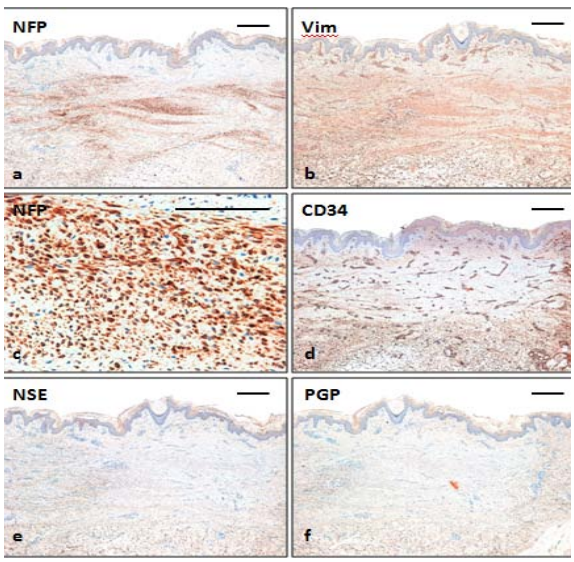

Figure 3: Immunohistochemistry results: consecutive slides demonstrate expression of neurofilament protein (a – 4x – scale bar 250 µm) and vimentin (b – 4x). On close inspection the neurofilament expression ir related to the celullar cytoplasm (c – 40x – scale bar 50 µm). Other antigens were negative, including CD34 (d – 4x), neuron-specific enolase (e – 4x) and protein gene product 9.5 (f – 4x).

Discussion

Dermatofibromas can show some morphological variation3, but neural differentiation in a cutaneous fibrous tumor usually means it is a neurofibroma [2]. In this case tumor cells showed on occasion a clear wavy cytoplasm, and dermatofibroma and neurofibroma were considered in the differential diagnosis on a rapid assessment basis.

Although dermatofibroma diagnosis was clear in a detailed inspection, the aberrant neurofilament expression was followedup with a deeper immunohistochemical study revealing no expression of other neuronal markers. In addition no schwannian, endoneurial or perineurial elements were noted.

Neurofilament expression has been described in some malignant tumors which can be observed in the skin like squamous carcinoma [16], melanoma [17] or malignant fibrous histiocytomas [18-20]. Vimentin and neurofilament co-expression was noted specifically on some of these tumors [18,19]. We have not found benign cutaneous tumours with neurofilament expression in the literature [1,2].

As neurofilament replaces vimentin during neural development [5,7], coexpression of both intermediate filaments in normal tissue or benign tumors seems hard to believe. The case presented also lacks expression of other axonal or peripheral nerve components, so neurofilament expression seems to be a cross-reaction of the antibody employed. Our laboratory has long experience with no previous issues using this particular antibody (Biocare Medical, clone 2F11).

A possible reason for the observed coexpression could bethepresence of common epitopes on several intermediate filaments, specially vimentin filaments [8,21], or a mere cross-reaction between antibodies. These assumptions seem unlikely due to the existence of a positive and negative control on the neurofilament technique, with no intermediate filament co-expression outside the dermatofibroma. Extratumoral components in our case are positive for vimentin and negative for neurofilament in the same slide, meaning that the neurofilament stain has a negative control; the positive control was performed thanks to the presence of small nerves in the non affected skin.

Vimentin and neurofilament co-expression could be better explained by a different state of phosphorylation of the intermediate filaments [4], which play an important role on their function [22]. Vimentin state of phosphorylation has regulatory importance in several cell processes like cell adhesion [23] or even controlling other intermediate filaments function [24]. As intermediate filaments are proteins with significant homology [22], a different phosphorylation state of vimentin filaments may cause neurofilament expression with the clone employed in our case. In any case, neurofilament expression could be an immunohistochemical marker of a specific phosphorilation pattern on vimentin intermediate filaments, which should be further confirmed in broader studies.

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