

Neurofibroma with psammoma bodies

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Summary. Neurofibromas are benign tumours of the nerve sheath. Histologically they vary depending on their contents of cells, myxoid stroma and collagen. A 41-year old male with radicular pain had a tumour involving the posterior chest wall. Microscopically it resulted to be a neurofibroma with abundant psammoma bodies. Although these bodies are very frequent in some neoplasias, to our knowledge they have not been described in neurofibromas to date.

Key words: Neurofibroma, Psammoma

Introduction

Neurofibromas are benign, heterogeneous peripheral nerve tumours arising from the connective tissue of the nerve sheath that may assume one of three growth patterns, localized, diffuse or plexiform. Localized neurofibromas occur most often as sporadic lesions and are composed of Schwann cells and fibroblasts with perineurial cells, axons and mast cells embedded in an extracellular matrix. So they may vary histologically depending on their content of cells, collagen and mucin. The most frequent type shows interlacing bundles of fusiform cells with wavy nuclei that are intimately associated with strands of ropey collagen and small to moderate myxoid matrix. Other neurofibromas are highly cellular with elongated cells in a collagen stroma devoid of mucin. The cells may be arranged in short fascicles or even in a storiform pattern resembling Antoni A areas of schwannomas. Nevertheless they are not encapsulated and small neurites can be demonstrated throughout these lesions. Less frequently they are highly myxoid and so may be confused with myxomas. Rare variants of neurofibroma include epithelioid change, presence of skeletal muscle or benign glands (Enzinger and Weiss, 2001), pseudorosettes (Michal et al., 2002) or melanin laden pigmented cells (Fetsch et al., 2000). So

within the medical literature, a large number of variants of neurofibroma have been reported. We describe the clinical features and histopathologic findings associated with a neurofibroma with abundant psammoma bodies, and discuss the differential diagnosis.

Material and methods

Case report

A 41-year old male patient with radicular pain had a tumour involving the posterior thoracic wall. It was located under the arch of the 7th rib. The lesion was solitary and the patient had no other tumours, "café au lait macules" or other criteria for neurofibromatosis. After surgical resection hematoxylin and eosin (H&E), Fontana-Masson for melanin pigment and Perls for iron were performed on sections of formalin-fixed and paraffin-embedded tumor specimen. Immunohistochemistry was performed with the Techmate (DakoCytomation) staining machine. The following monoclonal antibodies and dilutions were used: vimentin (Novocastra, 1:500), actin (DakoCytomation, 1:50), desmin (DakoCytomation, 1:200), S-100 protein (DakoCytomation, 1:1000), CD57 (Becton-Dickinson 1:10), neurofilament (DakoCytomation, 1:200), membrane epithelial antigen (DakoCytomation, 1:300) and anti-ki67 (Master Diagnostica 1:100). Binding of the primary antibodies was visualized using the peroxidase-antiperoxidase method. After completion of the immunoreaction, sections were counterstained with hematoxylin.

Results

The specimen submitted showed a glistening tan-white nodule that measured 2x0.6 cm. Microscopically the tumour is not encapsulated, is highly myxoid with scarce elongated cells immersed in a mucoid material. Abundant psammoma bodies are present dispersed throughout the lesion (Fig. 1). Some histiocytes with xanthomatous changes and haemosiderin-laden macrophages (positive staining with Perls), are also

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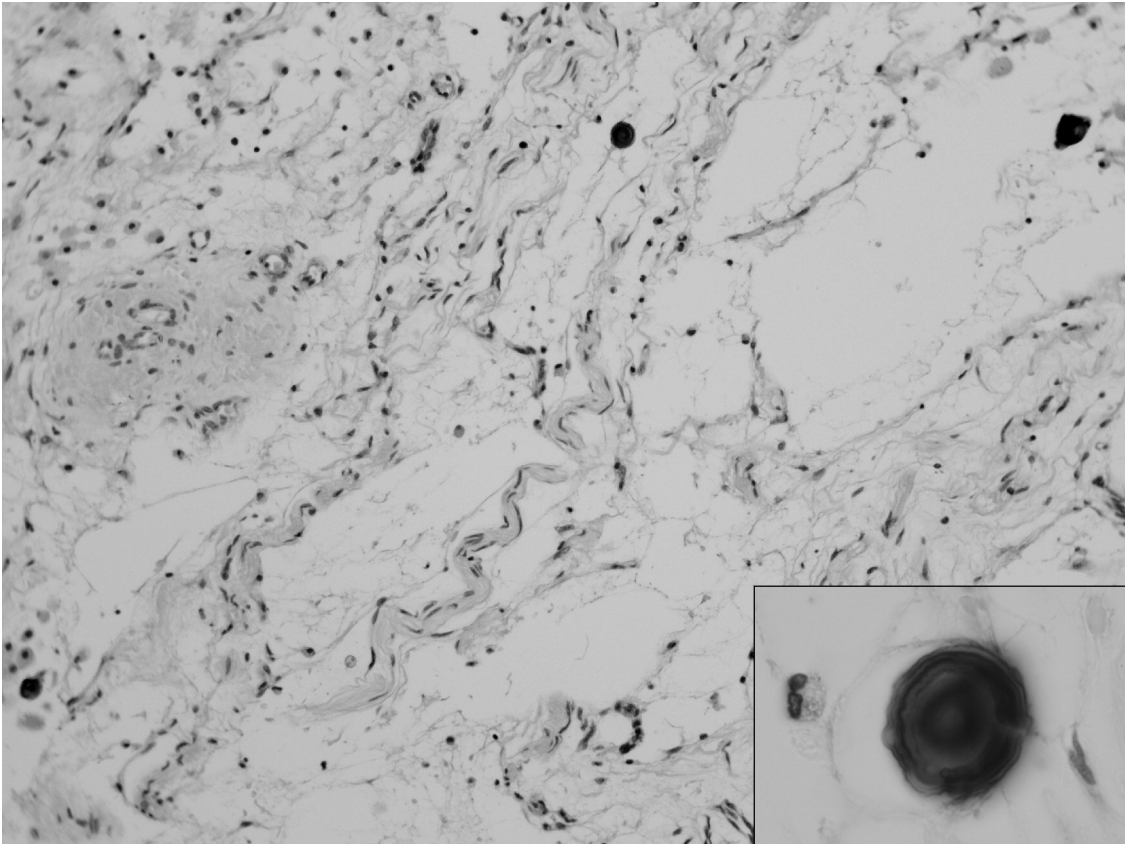


Fig. 1. Low-power view of the tumour. Numerous psammoma bodies are intermingled with scarce elongated cells in a myxoid background (HE, x50). Inset shows these psammoma bodies in detail. (HE, x500)

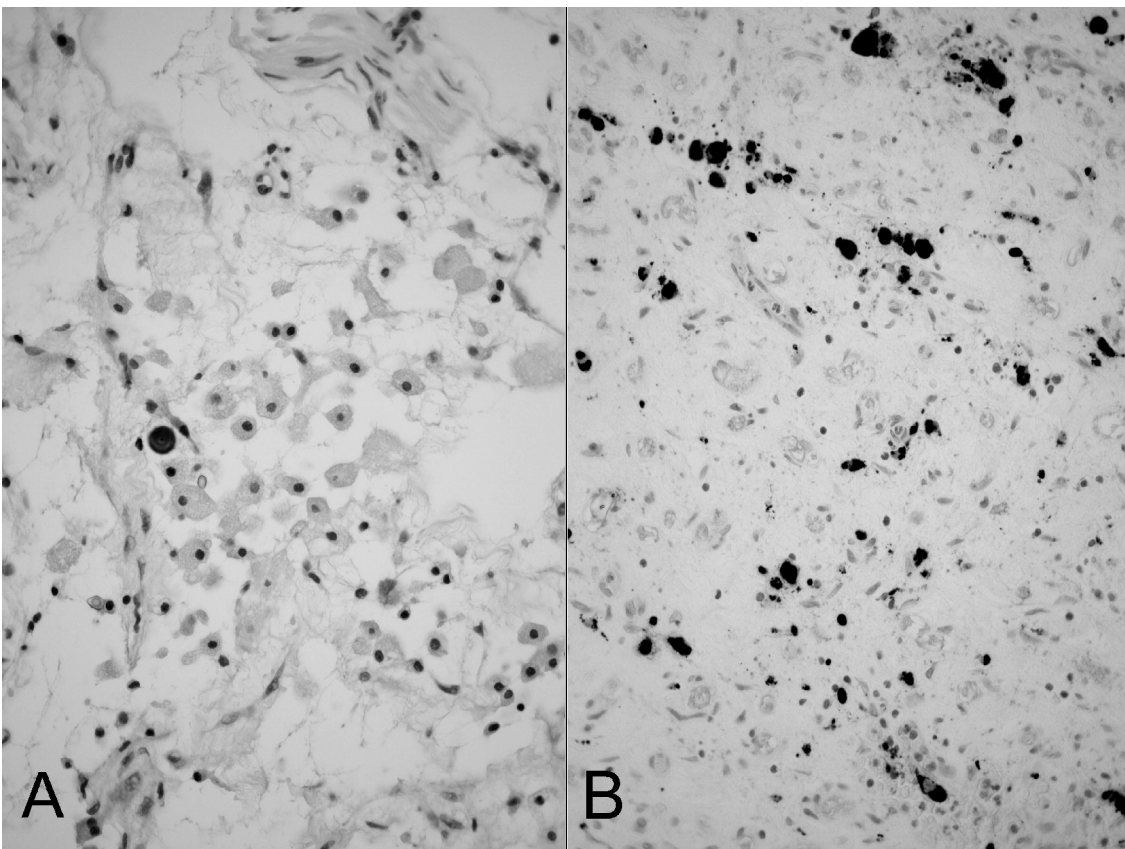


Fig. 2.A. Some histiocytes with xanthomatous changes are seen along with psammoma bodies (HE, x100). **B.** Abundant haemosiderin-laden macrophages are also seen (Perls, x100).

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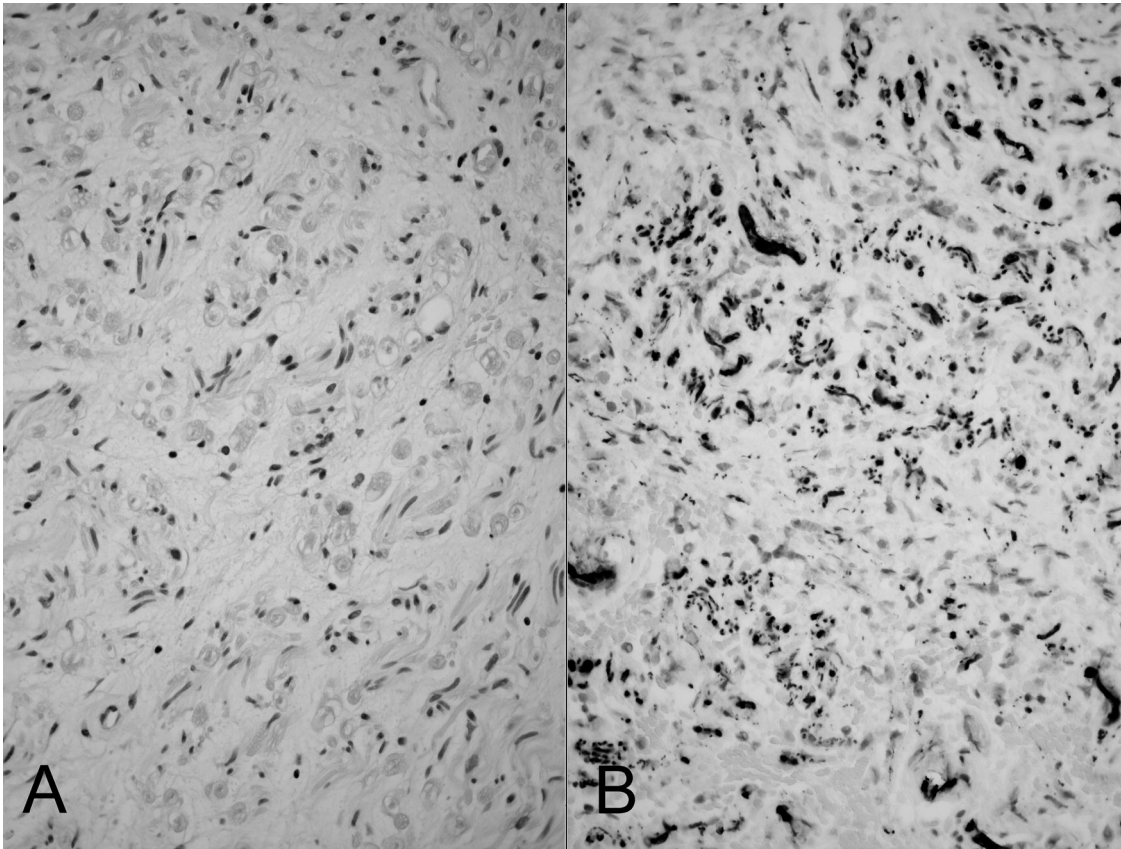


Fig. 3.A. Small neurites can be demonstrated throughout the lesion (HE, x100). **B.** Immunostaining demonstrates the presence of neurofilaments intermingled with the proliferating cells. (PAP anti-neurofilaments, DakoCytomation 1:200, x100)

observed (Fig. 2). The proliferative index estimated by Ki-67 is low (less than 1%). Immunostaining reveals that the tumour cells are negative for actin, desmin, membrane epithelial antigen and that they are positive for vimentin, S-100 protein and CD57. Some small neurites can be demonstrated, with neurofilament immunostaining, throughout the tumour (Fig. 3). According to these features the diagnosis of neurofibroma with psammoma bodies was established.

Discussion

Psammoma bodies are spherical-shaped structures made of laminar deposits of calcium salts. Several tumours have been described to characteristically have psammoma bodies such as thyroid papillary carcinoma, ovarian papillary carcinoma, meningioma and psammomatous melanotic schwannoma (Carney, 1990).

Neurofibroma is a benign tumour of the nerve sheath characterized by proliferation of Schwann cells, perineurial cells, and endoneurial fibroblasts.

Many variants of neurofibroma have been reported to date such as classical, myxoid, cellular, hyalinized, plexiform, epithelioid, diffuse, pacinian, pigmented, granular, lipomatous, dendritic cell neurofibroma with pseudorosettes, and neurofibroma with rhabdo-

myomatous differentiation (Azzopardi et al., 1983; Megahed, 1994; Michal et al., 2002).

Neurofibromas must be distinguished from schwannomas. In contrast to schwannoma in which the remaining fascicles of the parent nerve are peripherally displaced and reside mainly on the tumour surface, in neurofibroma nerve fibres tend to be dispersed throughout or centrally located.

In the present case the morphological and immunohistochemical features are consistent with a benign tumour of the peripheral nerve. The main differential diagnosis must be made with the psammomatous melanotic schwannoma, which also has multiple psammoma bodies, although lacks neurites (Carney, 1990). In the present case, multiple centrally placed nerve fibres could be identified with neurofilament immunostaining. This central distribution of the neurofilaments favours the diagnosis of neurofibroma. Some morphological features present in this neoplasm such as psammoma bodies, haemosiderin and xanthoma cells are more frequent in schwannomas than in neurofibromas, so step sections were made to assure that neurofilaments were intermingled with the neoplastic cells and formed part of the lesion and that they were not entrapped neurofilaments in the perilesional tissue pushed aside by the neoplasm.

We also discarded a melanotic neurofibroma, in the later there are spindle or epithelioid pigmented cells with dendritic prolongations. These cells have melanin and therefore are positive with Fontana-Masson. In our case pigment was into macrophages, moreover it was iron, as could be proved because Fontana-Masson was negative and Perl's stain was positive. Xanthomatous cells are neither a frequent feature in neurofibromas, although they are described in schwannomas, especially if they have cystic changes (Gomez-Brouchet et al., 2001). In our case both the haemosiderin-laden macrophages and the xanthomatous cells could be degenerative changes.

The patient did not have any other feature of neurofibromatosis: café au lait spots, Lisch nodules, gliomas or other cutaneous or plexiform neurofibromas, he did not have any relative with neurofibromatosis. Carney's syndrome was also discarded. In this syndrome, patients have the complex of myxomas, spotty pigmentation, endocrine overactivity and psammomatous melanotic schwannoma localised in spinal nerve roots, alimentary tract or bone (Carney, 1990). This is of special interest, because, as has been aforementioned, the main differential diagnosis in our case must be made with psammomatous melanotic schwannoma.

The striking feature of our case is the presence of multiple spherical laminar structures reminiscent of psammoma bodies. These structures are dispersed throughout the tumour.

We would like to note that to the best of our knowledge there are no similar cases reported in the literature to date. In conclusion, a new histopathological

variant of neurofibroma is reported. We propose the term neurofibroma with psammoma bodies to name this new variant.

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