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Neurothekeoma in the Axilla Causing Persistent Shoulder Pain: Case Report*

Neurotecoma na axila causando dor persistente no ombro: Relato de caso

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Abstract

Neurothekeomas, also known as neural sheath myxomas, are rare benign tumors of the neural sheath affecting most commonly the head, arms and shoulder of women in their 2nd and 3rd decades of life. Due to the low prevalence and undefined clinical picture, they are hardly considered in the initial differential diagnosis of skin tumors. We report the case of a 24 year-old woman who was seen in 2016 reporting > 1 year of moderate pain and limited mobility of her left shoulder. Clinical evaluation revealed restricted mobility of the affected shoulder and nuclear magnetic resonance imaging showed a T2-weighted contrast-enhanced multilobular mass in the quadrilateral area apparently invading the adjacent humeral cortical region. Histopathology of a needle sample material revealed loose fibroconnective tissue with no signs of invasion, mitosis or atypical figures. Successful surgical excision was performed and the diagnosis of neurothekeoma was confirmed after detailed histopathology, including immunohistochemistry. The patient was asymptomatic at 18 months of follow-up, with full recovery of shoulder movement and no signs of relapse.

Keywords
- neurothekeoma
- shoulder
- tumors

Resumo

Neurotecomas, tambémconhecidoscomomixomas da bainha neural, sãotumoresbenignosraros da bainha neural afetandomaiscomumente a cabeça, braços e ombros de mulheres entre 20 e 40 anos de idade. Devido à baixaprevalência e quadroclínico mal definido, essaslesõessãoraramenteconsideradas no diagnósticodiferencial de tumorescutâneos. Relatamos o caso de umamulher de 24 anos de idadequeprocurouatendimentoem 2016 relatandodormoderadapormais de um ano e limitação dos movimentos do ombroesquerdo. Aoexame, foiconstatadarestrição da mobilidadedessaarticulação e umaressonânciamagnéticarevelouimagemmultilobular com aumento de sinalem T2 naregião

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Palavras-chave
- neurotecoma
- ombro
- tumor

quadrilateral, aparentandoinvasão da região cortical do úmerosubjacente. A histopatologia de umabiópsia incisional mostroulesãocompostaportecidoconjuntivofrouxo, semsinais de invasão, figuras de mitoseouatipias. Foirealizadaexcisãocompleta da lesão e o diagnóstico de neurotecomafoiconfirmadoapósanálisehistopatológicaqueincluiupainelimunohistoquímico. À revisão de 18 meses, a pacienteestavaassintomática com recuperaçãocompleta do movimento e semevidência de recidiva da lesão.

Introduction

Neurothekeoma is a rare benign skin tumor of the neural sheath, also known as neural sheath myxoma. It originates from the endoneurium of peripheral nerves and is characterized by abundant mucoid matrix. The rarity and noninvasive character of neurothekeomas probably account for them not being remembered as a diagnostic possibility, which led us to prepare the present case report.[1] Usually, neurothekeomas appear as solitary fibroelastic nodules on the skin localized in the head and neck regions and in the upper extremities.[1,2]

Case Report

A 24 year-old woman sought specialized care on August 2016 for pain and restricted mobility of her left shoulder during the previous year. There was no history of repetitive use or isolated trauma, as well as no systemic manifestations. Pain was escalating in intensity in the last 2 months. Family history was negative and there were no comorbidities. She was using analgesics on demand. Physical and neurological examination revealed a mild restriction of external rotation of the left shoulder reaching up to 60° in active motion. Rotator cuff tests as well as neurovascular exam of the affected shoulder were normal. Shoulder radiographies were normal (►**Fig. 1**) whereas magnetic resonance imaging (MRI) of the left shoulder revealed a T2-weighted contrast-enhanced nonspecific solid lobular lesion ($3.3 \times 2.6 \times 1.7$ cm) in the quadrilateral area close to the adjacent humeral cortical region (►**Fig. 2**). A bone scintigraphy scan was negative.

An incisional biopsy was inconclusive, and the apparent invasive characteristic seen in the MRI prompted surgical planning for complete excision. The histopathological analysis description after hematoxylin-eosin (H&E) staining revealed fusiform-shaped cells in a storiform arrangement with no atypia, forming nodules interspersed within a collagen stroma in a plexiform appearance together with some epithelioid foci, rendering definition of the histogenesis impossible (►**Fig. 3**).

The immunohistochemistry panel was positive for the S100 protein and epithelial membrane antigen (EMA) staining in areas of the proliferating fusiform cells, along with CD68 and smooth muscle actin (SMA) staining. The cell proliferative index, evaluated by K_i-67 marker staining, was $< 1\%$.

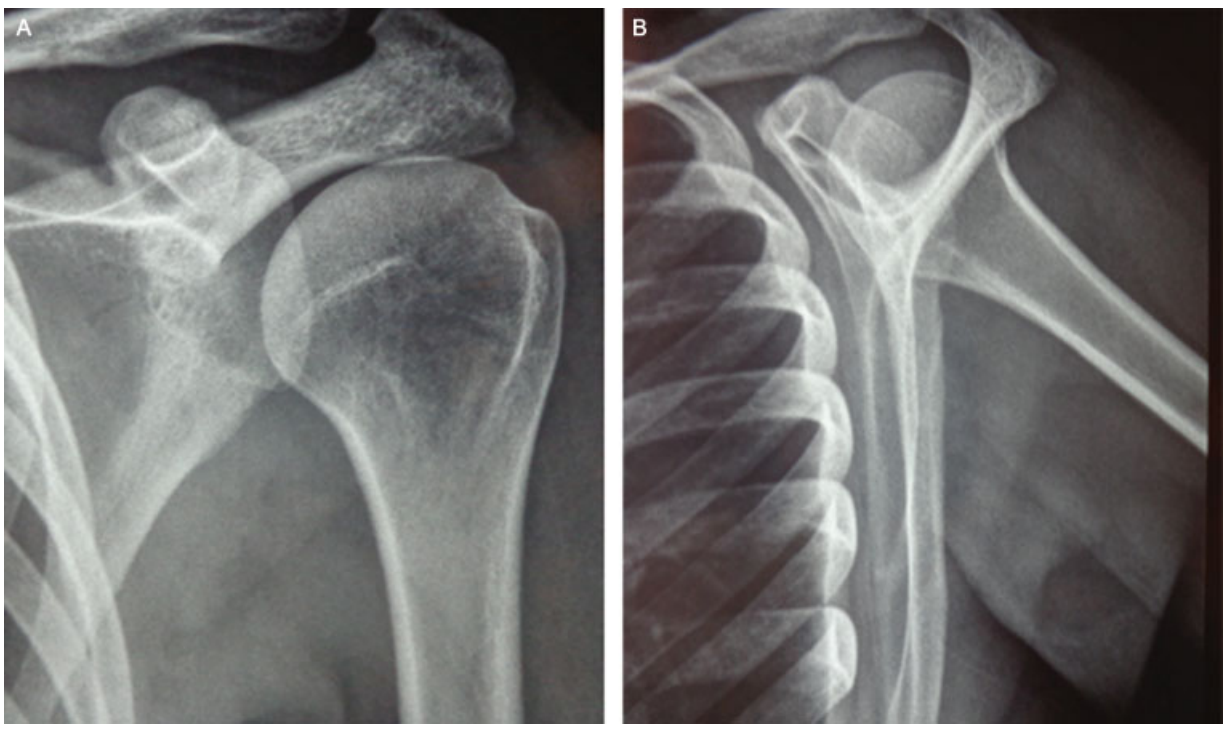

Fig. 1 Presurgical radiological shoulder, anteroposterior (A) and left scapula profile (B) images.

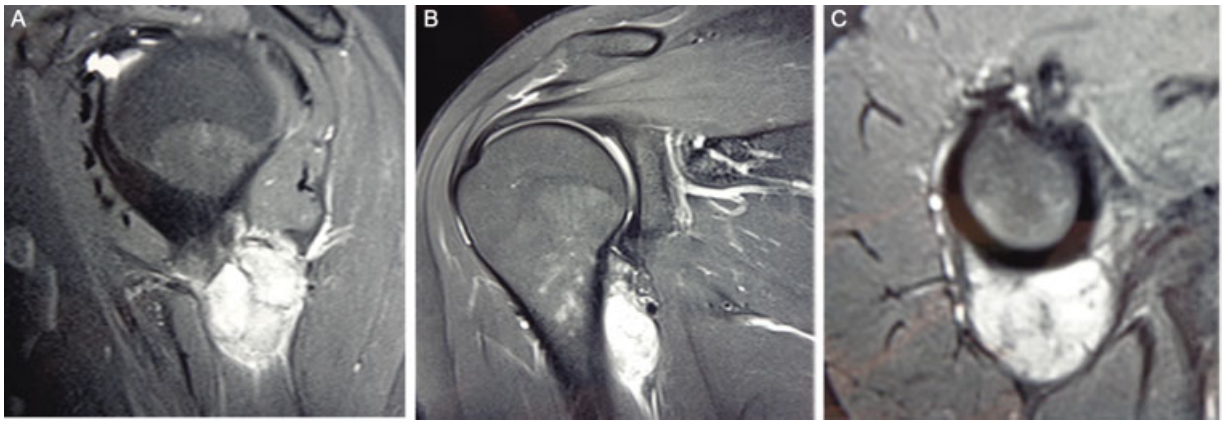

Fig. 2 T2-weighted Nuclear Resonance Imaging, sagittal (A), coronal oblique (B), and axial (C) fat-suppressed MRI images of the left shoulder showing a large lobular mass with internal septations, well-defined contours, near the proximal humeral diaphysis, with no signs of invasion.

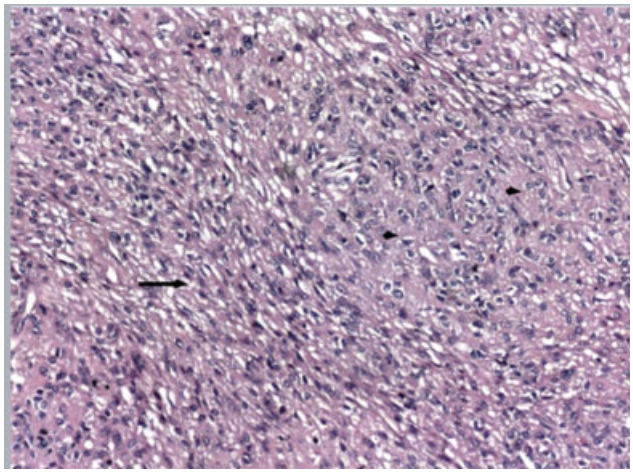

Fig. 3 Histologic appearance of the surgically excised mass. There is predominance of fusiform (arrow) and scattered epithelioid (arrowhead) cells with no signs of atypia or mitotic figures (H&E staining; Original x100).

The analysis of clinical and imaging data coupled to the histopathological evaluation led to the conclusion of a neurothekeoma diagnosis.

The surgical planning was for total mass excision, performed in April 2017, rendering the patient asymptomatic with no limitation of shoulder movement after 18 months follow-up. An MRI postsurgical exam showed no signs of relapse (►**Fig. 4**).

Histopathology

Briefly, histopathological examination was performed on routinely prepared resected samples after paraffin-embedding with 4-µm sections stained with H&E. Immunohistochemistry was performed using a Ventana Benchmark apparatus (Ventana Medical Systems; Tucson, AZ, USA) after deparaffinization with EZprepbuffer (Ventana Medical Systems, Tucson, AZ, USA) (04 minutes). Antigen recovery was done with Cell Conditioning (Ventana Medical Systems, Tucson, AZ, USA) buffer (30 minutes; pH 8.4) followed by washings with the reaction buffer and amplification using UltraView, Hematoxylin and Bluing reagents (Ventana Medical Systems, Tucson, AZ, USA). Commercially available primary antibodies were as follows: S100 (Clone S1/61/69 1:1000; Leica Biosystems, Buffalo Grove, IL, USA), EMA (E29 1:5000; CellMarque Darmstadt, Germany), CD34 (QBEnd/10 Ready-to-use; Roche, São Paulo, SP, Brazil), CD68 (514h12 Ready-to-use; Roche, São Paulo, SP, Brazil), SMA (1A4 1:5000; CellMarque, Darmstadt, Germany) and KI67 (SP6 1:300 CellMarque, Darmstadt, Germany).

Discussion

Neurothekeomas are typically restricted to the skin and subcutaneous tissue, with lesions involving the axillary hollow being extremely unusual. Up to 35% of neurothekeomas are localized in the upper extremities.[2] The age range includes 15 month-old children as well as elderly up to 84 years old, with an 18 years old mean age incidence. Usually, the diameter of the lesions measures 1.2 cm. Local trauma and estrogen use have been proposed as trigger factors, probably because of the predominance in females1.[1,2]

The histological appearance can be classified as myxoid, cellular, and mixed, based on cell predominance, presence of mucinous material, and abundance of myxoid matrix. Features to distinguish neurothekeomas from neural sheath myxomas are yet to be established.[3,4] Immunohistochemistry markers may help discriminate neurothekeoma subtypes, as follows: S100 protein, glial acidic fibrillary Protein (GFAP), nerve growth factor receptor, and melanoma-specific antigens (NKI/C3, K_i-M1p). The S100 A6 protein staining is highly positive in the cellular subtype. Histologically, neurothekeomas should be discriminated from other fibrohistiocytic tumors such as fibromyxomas.[4–6]

Benign tumors are amenable to surgery when localized in areas that restrict movement and/or cause other functional limitation. The pain and limitation of movement in this case justified surgical excision. Lesions $>$ 6 cm, involving the subcutaneous tissue, muscles and blood vessels, with

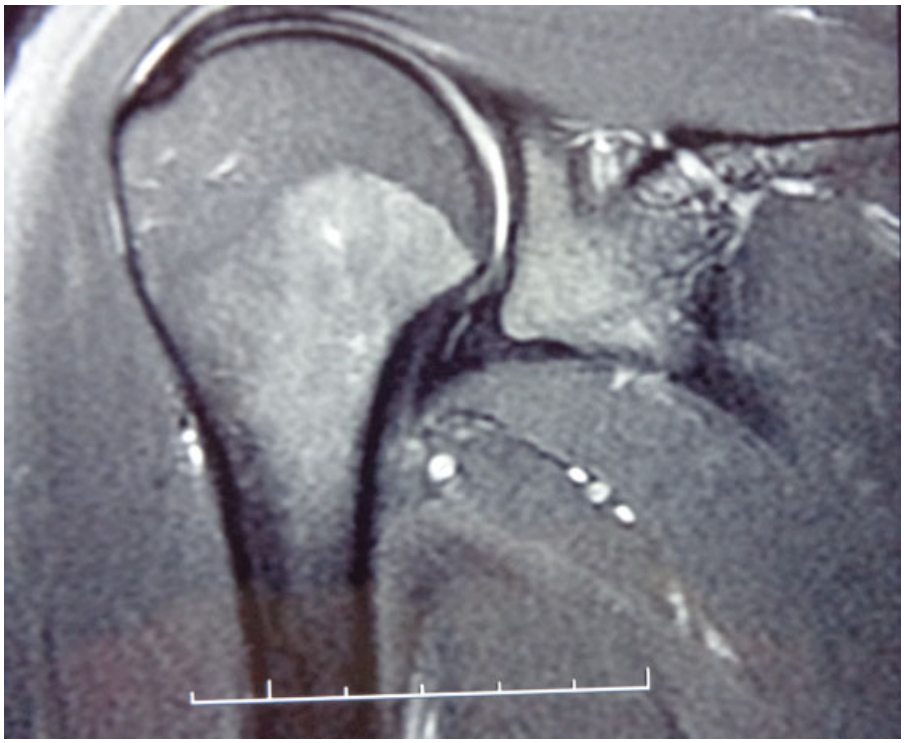

Fig. 4 Postsurgical (18 months) T2-weighted coronal MRI view of the left shoulder.

pleomorphic cytological appearance, are considered atypical neurothekeomas. Marginal infiltration and high mitotic index (>3 *per*hpf) have been associated with the atypical subtype. In a series of 10 patients classified as presenting the atypical pattern followed for 5 years there were no local relapses or metastasis leading the authors to suggest that apparent histological aggressive behavior is not associated to the clinical outcome.[7,8]

Neurothekeomas are rarely suspected prior to histopathology. There are no reports of malignant transformation or metastasis, but local recurrence, though uncommon, may happen, particularly in those presenting the cellular and mixed patterns. Complete surgical resection with clear margins, usually of some millimeters, is the appropriate treatment. Apparently, aggressive lesions have been subjected to resection with larger margins. Proposed risk factors for neurothekeoma relapse include: myxoid subtype, female gender, head localization, young age, compromised margins and absence of adipose tissue in the excised material. Presence of atypical cells and number of mitotic figures were not associated with recurrence.[1]

Despite being rare, neurothekeomas need to be remembered as a diagnostic possibility when lesions involve the head and neck, since early surgical removal is usually curative.

The rare occurrence in the axillary hollow justifies the present case report coupled to the clinical picture in a young patient with a normal radiography prompting MRI request. Diagnostic delay can be caused by confounding with more frequent causes of a painful shoulder, such as rotator cuff lesion and adhesive capsulitis. The surgical planning contributed to a successful, curative intervention, with virtually no sequelae.

Conflict of Interests
The authors have no conflict of interests to declare.

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