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Radiological Case Report / Caso Clínico

Malignant Peripheral Nerve Sheath Tumor in a Patient with Neurofibromatosis 1: Case Report

Tumor Maligno da Bainha de Nervo Periférico em Doente com Neurofibromatose Tipo 1: Caso Clínico

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Abstract

Neurofibromatosis type 1 is an autosomal dominant disease, with neurofibroma being the hallmark of this disease. Malignant peripheral nerve tumors are more frequent in neurofibromatosis type 1 and may result from the transformation of neurofibromas, arising de novo or post-radiotherapy. There are several features in the imaging studies, primarily in Magnetic Resonance, that may help differentiate benign lesions, such as neurofibromas, from malignant peripheral nerve tumors, namely their larger dimensions, dimensional increase over time, signal heterogeneity with intratumoral cystic change or perilesional edema.
We report a case of a 29-year-old patient with neurofibromatosis type 1 who presented with a lesion in the proximal right thigh with a progressive increase over several months. Imaging and pathologic studies of the biopsy and post-chirurgic revealed a malignant tumor of the peripheral nerve sheath.

Keywords

Peripheral nervous system malignant neoplasm; Thigh; Neurofibromatosis.

Resumo

A neurofibromatose tipo 1 é uma doença autossómica dominante em que o neurofibroma é a lesão mais característica. Os tumores malignos de nervo periférico são mais frequentes na neurofibromatose tipo 1 e podem resultar da transformação de neurofibromas, surgir de novo ou após-radioterapia. Existem várias características nos estudos imagiológicos, principalmente em Ressonância Magnética, que podem auxiliar na diferenciação de lesões benignas, como os neurofibromas, dos tumores malignos de nervo periférico, nomeadamente as dimensões, o aumento dimensional ao longo do tempo, a heterogeneidade de sinal com degenerescência quística ou o edema perilesional.
Descrevemos um caso de uma doente de 29 anos com neurofibromatose tipo 1 com uma lesão no segmento proximal da coxa direita com crescimento ao longo de vários meses. O estudo imagiológico e anatomopatológico da biópsia e após a cirurgia revelaram um tumor maligno da bainha do nervo periférico.

Palavras-chave

Neoplasia maligna do sistema nervoso periférico; Coxa; Neurofibromatose.

Case Report

A 29 years old female with the diagnosis of neurofibromatosis type 1 and multiple neurofibromas scattered throughout their body complained of a mass in the right thigh with progressive increase in size for several months. She also referred pain over the mass. Physical examination revealed a firm mass in the proximal right thigh. There were also other small cutaneous nodules over the entire body (probably neurofibromas) and several café-au-lait spots. Her blood tests were unremarkable.
A CT (figure 1) was performed and showed a well-defined heterogeneous mass with cystic and solid components located lateral to the sartorius and rectus femoris and anterior to the vastus intermedius.
The Positron Emission Tomography–Computed Tomography (PET-CT) reveals an intense uptake of the mass (figure 2).
On Magnetic Resonance images (figures 3 and 4) the mass was isointense to muscles in T1-weighted-images and heterogeneous high signal in T2-weighted-images. It has a fusiform shape and well-defined contours, without invasion of the adjacent muscles that were displaced by the mass effect of the lesion. Administration of gadolinium revealed solid and cystic areas. Note the enlargement of the mass on the MR study performed 2 months after the CT.
A tumor with origin in the peripheral nerve and with malignant nature was the most probable diagnosis. The pathologic studies of the biopsy and the surgical specimen confirmed a malignant peripheral nerve tumor. The patient underwent surgery, but the margins were positive. Adjuvant radiotherapy and chemotherapy was then performed. On a follow-up CT performed 6 months after surgery, hepatic metastasis were detected without evidence of local recurrence.

Discussion

Neurofibromatosis type 1 (NF1), or von Recklinghausen disease, is an autosomal dominant disorder due to a mutation or deletion of the NF1 gene on chromosome 17 and it affects multiple organ systems.[1]

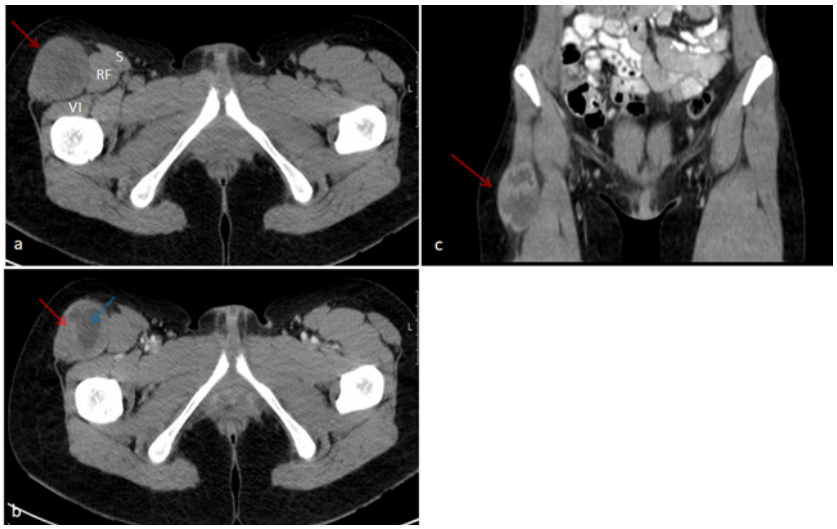

Figure 1 – Computed Tomography (CT) of the proximal thighs. Axial non-enhanced image (a) shows a low attenuation mass (red arrow) on the muscular plane of the proximal right thigh lateral to the sartorius (S) and rectus femoris (RF) and anterior to the vastus intermedius (VI). Axial contrast enhanced image (b) reveals solid (red arrow) and cystic (blue arrow) componentes of the mass. Coronal contrast enhanced image (c) shows that the mass has a fusiform shape with well-defined contours.

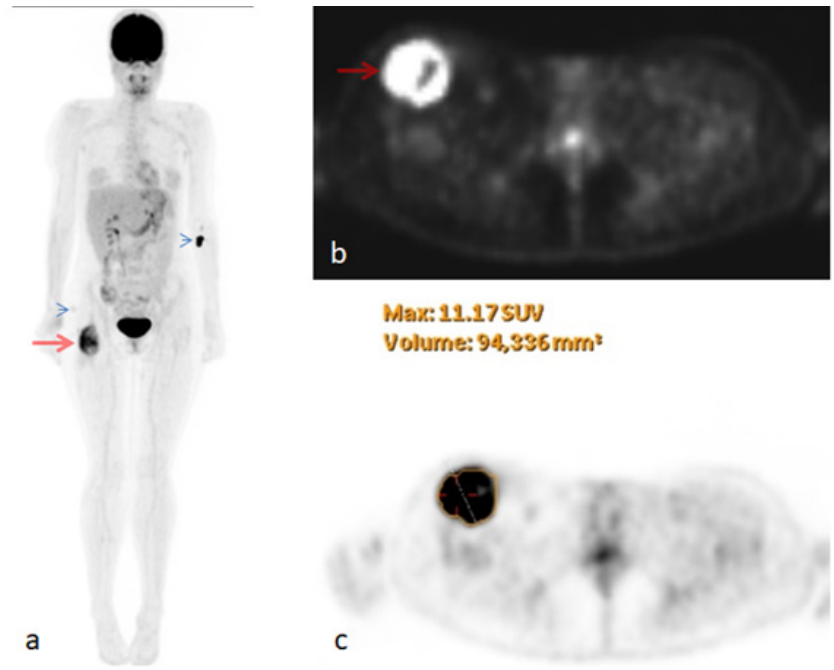

Figure 2 – Positron emission tomography–computed tomography (PET-CT) images show an intense uptake of the mass (arrow) with SUVmax=11,17. Note the smaller and with lower uptake lesions (arrowheads) compatible with neurofibromas.

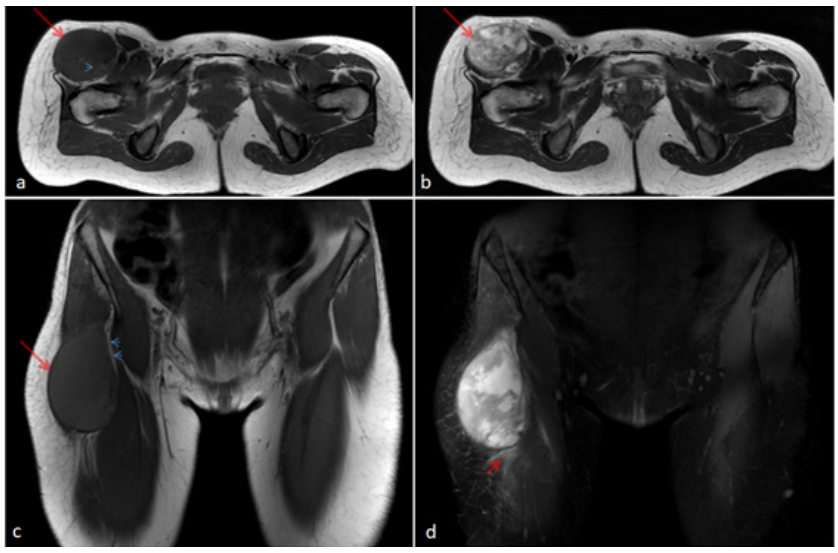

Figure 3 – Magnetic Resonance (MR) images of the proximal thighs. Axial T1-weighted-image (a) showing a mass (arrow) with intensity similar to that of muscle. Note also small hyperintense areas (arrowhead), probably reflecting hemorrhagic foci. Axial T2-weighted-image (b) reveals heterogeneous high signal of the mass (arrow). Coronal T1-weighted-image (c) shows that the mass (arrow) has a fusiform shape with well-defined contours and a rim of fat (arrowheads). Coronal T2-SPAIR image (d) reveals small perilesional area (arrow).

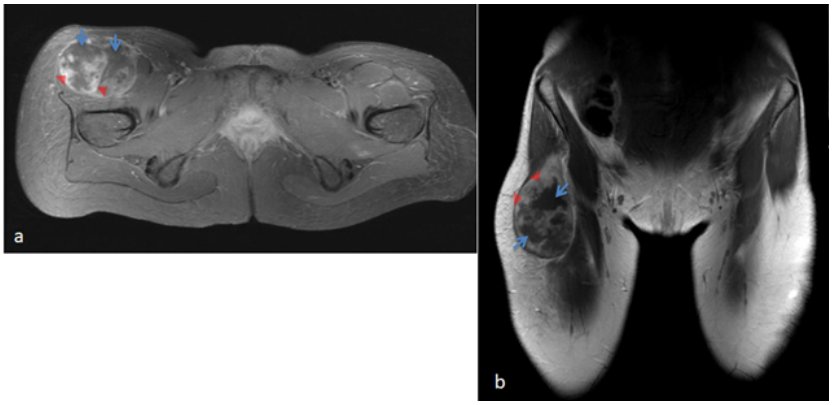

Figure 4 - Magnetic Resonance (MR) axial T1-SPIR image (a) and coronal T1 weighted-image (b) of the proximal thighs after gadolinium administration reveals a heterogeneous uptake of the mass with solid (arrowheads) and cystic (arrows) areas.

Neurofibromas, which are benign peripheral nerve sheath tumors, are the hallmark of NF1.[1] Three subtypes of neurofibromas have been described: localized, diffuse, and plexiform.[2] The localized subtype is the most common (90%) and predominantly occur in patients without NF1, only up to 10% are associated with NF1.[1,2,3] The diffuse subtype is relatively rare and most commonly affects children and young adults.[4] Plexiform neurofibromas are pathognomonic of NF1, occurring in up to 40% of patients with NF1 and frequently appears in childhood.[1]

On ultrasound, localized neurofibroma is a homogeneous, hypoechoic mass that may simulate a cyst. On CT neurofibromas are well-defined, hypodense masses with little or no enhancement. Classic MR imaging findings include a fusiform shape with tapered ends, low-to intermediate signal intensity on T1-weighted-images and high signal intensity on T2-weighted-images, a target sign (high signal intensity in the periphery and low signal intensity in the central region of the lesion on T2-weighted-images) or fascicular sign (multiple small hypointense foci interspersed within a hyperintense area on T2-weighted-images).[3]

Imaging features most suggestive of diffuse neurofibromas are a plaquelike or infiltrative lesion isointense or mildly hyperintense on T1-weighted-images and hyperintense on T2-weighted-images with intense enhancement.[4]

Plexiform neurofibromas present as multinodular confluent masses and thickening of a long segment of the nerve and its branches with low-attenuation on CT and hyperintense on fat-suppressed T2-weighted-images often with multiple target signs.[2,3]

Malignant peripheral nerve sheath tumors (MPNST) are malignant neoplasms that have origin in peripheral nerves or demonstrate peripheral nerve differentiation. About 40%–60% of MPNST originates from patients with NF1 and present earlier (median age between 20 and 40 years) than sporadic ones (median age between 30 and 60 years).[5,6] MPNST arise from plexiform neurofibromas, de novo or secondary to radiation therapy and most commonly in the deep soft tissues.[5] The life time risk of developing a MPNST in patients with NF-1 is high, about 8% to 13%.[6] The clinical presentation MPNST include a mass with more than 2cm, rapid growth, pain and neurological symptoms such as weakness or paresthesia's.[5,6]

On imaging studies, MPNST usually present as a large (>5 cm), fusiform, heterogeneous soft tissue mass that may demonstrate ill-defined margins.[3,7,8,9] On unenhanced CT, MPNST have low attenuation and heterogeneous enhancement after the administration of iodate contrast.[7] These tumors have an intense uptake on PET-TC that is usually more intense than neurofibromas.[7]

A common diagnostic dilemma is that MPNSTs and neurofibromas may appear indistinguishable on imaging studies; however, there are several MR features that are useful for distinguishing them.[8,9] Wasa et al described the MR features that are useful for distinguishing malignant peripheral nerve sheath tumors from neurofibromas: tumor size, presence of peripheral enhanced pattern on gadolinium-enhanced T1-weighted images, presence of perilesional edema-like zone and intratumoral cystic change.[8] The presence of two or more of the four features suggestive of malignancy indicate malignant peripheral nerve sheath tumor with a sensitivity of 61% and a specificity of 90%.[8] Heterogeneity on T1-weighted images was also significant in differentiating neurofibroma from malignant peripheral nerve sheath tumor.[8]

In our case, the lesion had most of the above described features, namely, a large dimension, enlargement over time, heterogeneity on T1-weighted-images, intratumoral cystic change and perilesional edemalike zone.

MPNST has poor prognosis with 5-year survival ranging between 30% and 60%.[10] The prognosis is worse for MPNST arising in the setting of NF1 compared with sporadic disease.[6,10] Large tumor size at presentation (typically >5 cm), positive surgical margins, high pathologic grade (G3) and metastatic disease are the most important adverse prognostic factors.[10]

The treatment for localized disease is surgical resection.[6] Adjuvant radiation therapy may be performed in selected cases such as when the surgical margins are positive.[6,10] Neoadjuvant chemotherapy may be beneficial in localized disease.[6] In advanced or metastatic disease chemotherapy is performed, but outcomes are generally poor.[6] There are several molecular agents under clinical trials and the targeting of molecular pathways like TOR and hsp90 may change the course of patient care.[6]

In conclusion, it is very important for the radiologist to be aware of the imaging findings of the neurofibromas and MPNST in patients with NF1.

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Protection of human and animal subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).
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