Case Report

Malignant peripheral nerve sheath tumor mimicking an adnexal mass: a radio-pathologic correlation

Paulo Santos Correia, MD,†, Filipa Rosa, MD, Vera Sousa, MD, Filipe Barros Alves, MD, João Pedro Caldeira, MD, Joana Ferreira, MD, Carmo Martins, BSc, PhD, Teresa Margarida Cunha, MD

†Department of Radiology, Centro Hospitalar e Universitário de Lisboa Central, Rua José António Serrano, 1150-199 Lisbon, Portugal
bDepartment of Pathology, Instituto Português de Oncologia de Lisboa Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisbon, Portugal
cDepartment of Gynaecology, Instituto Português de Oncologia de Lisboa Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisbon, Portugal
dDepartment of Radiology, Centro Hospitalar Universitário de S. João, Alameda Professor Hernâni Monteiro, 4200-319 Oporto, Portugal
eDepartment of Radiology, Instituto Português de Oncologia de Lisboa Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisbon, Portugal
fMolecular Pathology Research Unit (UIPM), Instituto Português de Oncologia Francisco Gentil, Rua Prof. Lima Basto, 1099-023 Lisbon, Portugal

A B S T R A C T

We report the case of a pelvic malignant peripheral nerve sheath tumor mimicking an adnexal mass. A 59-year-old postmenopausal woman presented with a 3-month history of diffuse abdominal bloating and urinary frequency. Laboratory tests revealed an increased CA 125. Radiologic evaluation depicted a large, heterogeneous solid mass located right to the uterus, pushing it to the left. After a multidisciplinary board discussion, the diagnosis of a right adnexal lesion was assumed, and the patient was referred to surgery. The final diagnosis was only achieved after pathology examination, which prove to be a malignant peripheral nerve sheath tumor. This paper highlights some clinical, radiologic and pathologic features of malignant peripheral nerve sheath tumors, a rare entity that should be considered as a differential in patients presenting with pelvic tumors of uncertain origin.

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Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are rare and aggressive soft tissue sarcomas with a poor prognosis, that generally arise from major peripheral nerves [1,2]. MPNST can also arise in the pelvis and mimic a gynecological tumor, however, this is remarkably rare, and only a few cases are reported in the literature [3].

Given the lack of specific clinical criteria, distinctive imaging features, and conclusive immunohistochemistry, the diagnosis of MPNSTs is especially challenging and can mimic other entities.

Here, we report a case of a large MPNST mimicking an adnexal mass in a post-menopausal woman.

Case report

We describe the case of a 59-year-old postmenopausal woman referred to a tertiary center with a 3-month history of diffuse abdominal bloating and urinary frequency.

The patient's past medical and surgical records included inguinal hernia repair, bladder surgery, and endometrial polypectomy.

Physical examination showed a bulky abdominal and pelvic mass. No adenopathies were identified. The gynecologic evaluation revealed bulging of the vaginal cul-de-sac and left deviation of the uterine cervix, with no additional relevant findings. The digital rectal examination was unremarkable.

Laboratory results revealed a slight increase of CA 125 (89 U/mL – Normal < 35 U/mL).

The abdominal and pelvic computed tomography (CT) featured a large heterogeneous pelvic tumor, mostly necrotic, presenting with peripheric solid enhancing areas (Fig. 1). The ovaries were not properly depicted on this exam. Assessment of the upper abdomen revealed right hydronephrosis. A magnetic resonance (MR) was performed for further characterization. It revealed an ill-defined, voluminous, and intraperitoneal pelvic tumor, arising from the right parametrium, measuring 24 × 15 × 21 cm of greatest diameters (Figs. 2 and 3). On MRI the tumor was markedly heterogeneous. The upper part of the tumor displayed a predominantly central necrotic component, with a high signal on T2-weighted (T2-W) images, and peripheral solid areas, with an intermediate signal on T2-W images. The solid areas featured diffusion restriction (Fig. 4) and avid contrast enhancement (Fig. 5). The lower part of the tumor was almost completely solid, presenting with avid enhancement on contrast-enhanced sequences. A time signal-intensity curve was performed, revealing a type 3 pattern (rapid rising followed by plateau) (Fig. 6), suggestive of malignancy.

The left ovary was depicted, presenting with normal post-menopausal features. Bilateral hydronephrosis and pelvic ascites were documented.

After a multidisciplinary board discussion, the diagnosis of a right adnexal lesion was assumed, and the patient was referred to surgery. During surgery, the tumor was found to arise from the right parametrium, being adherent to the right ovary, right fallopian tube, bladder dome, and sigmoid colon. It was successfully removed, together with the uterus, right adnexa, and bladder dome, followed by left salpingo-oophorectomy and sigmoidectomy.

Pathologic gross examination of the surgical specimen revealed a large yellowish multinodular tumor, with a gelatinous cut surface and extensive necrosis (around 60% of the tumor volume). Histologically, the tumor showed alternating hypercellular and hypocellular areas (Fig. 7A). It was composed of fusiform cells and rhabdomyoblasts with a large vesicular nuclei and abundant deeply eosinophilic cytoplasm (Fig. 7B). Immunohistochemical analysis showed diffuse nuclear loss of H3K27me3 and myogenin staining in rhabdomyoblasts (Figs. 7C and D). Complementary FISH analysis was performed, revealing deletion on CDKN2A gene (Fig. 8). These findings were concordant with a MPNST with rhabdomyoblastic differentiation, also known as malignant Triton tumor.

After 3 months of follow-up, the patient presented at our institution with abdominal bloating. CT was performed revealing diffuse peritoneal bloating.
Fig. 2 – Sagittal (A) and coronal (B) T2-weighted images show a large heterogeneous pelvic tumor (*) anterior to the uterus (arrow). Pelvic ascites is depicted (arrowhead).

Fig. 3 – (A, B) Axial T2-weighted images shows an ill-defined heterogeneous tumor in the pelvis. The tumor features central cystic areas (*) consistent with necrosis and solid peripheral nodules with intermediate signal (arrow).

Fig. 4 – Axial diffusion-weighted image b-1000 (A) showing peripheral solid areas (arrow) with high signal intensity and corresponding low signal intensity on apparent diffusion coefficient (ADC) map (B), compatible with restriction.
Discussions

MPNSTs are rare malignant spindle cell tumors, accounting for approximately 5% of soft-tissue sarcomas [1,2]. They often arise from a pre-existing benign nerve sheath tumor, from a peripheral nerve, or in association with neurofibromatosis type 1 (NF1) [2]. MPNSTs have no gender predilection and are commonly diagnosed in the third to sixth decades of life [4]. NF1 is the most important risk factor for developing MPNSTs since up to 50% of cases are linked to NF1 [4,5]. MPNSTs usually arise in the proximal upper and lower extremities, as well as in the pelvis. Nevertheless, MPNST presenting as a gynecological tumor is exceptionally rare, and only a few cases are reported in the literature [3].

Clinically, this tumor presents as a painful/painless mass that may be palpable on physical examination. Neurologic deficits such as weakness, radicular pain, or paraesthesia are common, whenever the tumor directly involves the nerve [2,6]. The diagnosis and differentiation of MPNSTs from neurofibromas may be particularly challenging, since the symptoms and imaging features of these 2 entities may overlap, especially in patients with NF1 [1,5].

Although both CT and MR imaging can detect and characterize the tumor location and size, MR remains the preferred modality for imaging MPNSTs given its excellent soft tissue contrast and its ability to assess the local invasiveness of the tumor. Still, their imaging features lack specificity, and the diagnosis may be challenging since they can overlap those of neurofibromas.

On MR, the presence of a large infiltrative mass with peripheral enhancement suggests MPNST. Intratumoral cystic areas can be found, as a result of hemorrhage or necrosis [5]. All these features were depicted in our case. Another clue is the presence of perilesional edema-like zone, more frequently found in MPNSTs [5].

The target sign, described by Bhargava et al. [7], may be useful in differentiating MPNSTs from neurofibromas, since the former usually lack this appearance. This sign is depicted on T2-weighted images and is characterized by a round central hypointensity surrounded by a hyperintense rim [7].

On gross examination, MPNST usually presents as a large mass with a tan white gray, firm, gelatinous to fleshy cut surface, often with areas of hemorrhage and necrosis [8].

The classical histological findings of MPNST are a fascicular growth pattern with a branching hemangiopericytoma-like vascular pattern and alternating hypercellular and hypocellular areas. They are generally composed of cells with spindled, buckled, or comma-shaped hyperchromatic nuclei and pale cytoplasm. There is often necrosis and conspicuous mitotic activity [8]. Heterologous differentiation occurs in up to 15% of these neoplasms, the most common being towards skeletal muscle. A malignant Triton tumor is an MPNST with rhabdomyoblastic differentiation [2]. These tumors usually show focal and patchy positivity for S100, SOX10, and GFAP. The complete loss of staining for H3K27me3 is supportive of the diagnosis. Rhabdomyoblasts express desmin, myogenin, and MyoD1 [8,9].

From a molecular point of view, genomic analyses of signaling regulation genes can support the diagnosis of MPNSTs.
Fig. 6 – Time signal-intensity curve of the solid areas showed a type 3 pattern (rapid rising followed by plateau), suggesting malignancy.

Fig. 7 – (A) The tumor is arranged in fascicles with a marbled appearance due to alternating hypocellular and hypercellular areas. (H&E); (B) The neoplasm is composed of neural fusiform cells and rhabdomyoblasts with large vesicular nuclei with nucleoli and abundant deeply eosinophilic cytoplasm. Mitotic activity is noted. (H&E); (C) Tumor cells demonstrating nuclear loss of H3K27me3. (H3K27me3 antibody); (D) Rhabdomyoblasts showing a strong nuclear myogenin expression. (myogenin antibody).
The inactivation of CDKN2A, a tumor suppressor gene, is one of the genes proven to be linked to MPNSTs progression [10]. Surgical resection with tumor-free margins remains the gold-standard treatment [11].

Despite not having significant effect on long-term survival, adjuvant radiotherapy is recommended to decrease local recurrence. Neoadjuvant radiotherapy may be indicated if the tumor is larger than 5 cm [12,13]. Chemotherapy is reserved for the treatment of metastatic disease [13].

The prognosis of MPNSTs is usually poor, presenting the highest recurrence rates of all sarcomas. Metastases to the lung, liver, bone, or regional lymph nodes are common [13].

**Conclusion**

MPNSTs are rare aggressive soft tissue sarcomas that mostly arise from major peripheral nerves. Their unspecific clinical and imaging features usually overlap those of other entities, making it challenging for the multidisciplinary team.

There are some imaging findings on MR that may suggest the diagnosis of MPNSTs. These features include intratumoral cystic areas, infiltrative borders, peripheral enhancement, the presence of perilesional edema-like zone, and the lack of a target sign. However, pathologic and molecular analysis remains crucial to establish a definitive diagnosis. Surgery remains the mainstay treatment of MPNSTs and the prognosis is usually poor.

While rare, MPNSTs should be considered as a differential diagnosis in patients presenting with pelvic tumors of uncertain origin. Therefore, radiologists should be aware and familiarized with this tumor and with its most common imaging features in order to avoid misdiagnoses.

**Patient consent**

The patient’s informed consent for the publication of this case was granted. There are no ethical issues for the publication of this case report according to the standard of our institution.

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