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Case Report

Mixed malignant peripheral nerve sheath tumor in the inguinal region: a case report

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Abstract: Malignant peripheral nerve sheath tumor (MPNST) is a rare malignant soft tissue tumor that accounts for approximately 5% of all soft tissue sarcomas. This tumor originates from the peripheral nerves and occurs mainly in the limbs, head and neck, and spine. As a more aggressive tumor, it has higher recurrence and metastasis rates, and patient prognosis is poor. MPNST has a variety of histologic subtypes such as classic MPNST and epithelioid malignant peripheral nerve sheath tumors (EMPNSTs). Due to the diversity of histologic types, these tumors have a high histologic similarity to other benign and malignant soft tissue tumors. Due to the lack of specific diagnostic criteria, pathologic diagnosis is extremely difficult, since these tumors should be differentiated from other sarcomas according to the site of tumor occurrence and morphologic characteristics, which can be determined using immunohistochemical staining. The specific pathogenesis of MPNST is not well understood. Studies have shown that approximately 50% of MPNSTs are closely related to neurofibromatosis I (NF1), while other causes of these tumors include radiotherapy. Herein, we report the first case of a mixed tumor composed of classic MPNST and EMPNST elements in the inguinal region.

Keywords: Malignant peripheral nerve sheath tumor, classic type, epithelioid, immunohistochemistry

Introduction

Malignant peripheral nerve sheath tumor (MPNST) is a peripheral nerve sheath neoplasm originating from peripheral nerve. This tumor type is also known as neurogenic sarcoma, neurofibrosarcoma, or malignant neurilemmoma [1]. As a rare malignant tumor, MPNST accounts for only 3%-10% of all soft tissue sarcomas [2, 3].

MPNST includes a variety of histologic subtypes, including epithelioid malignant peripheral nerve sheath tumors (EMPNSTs), those with adenoid differentiation and rhabdomyoblast differentiation, and tumors of the classical type [4]. Although MPNST has been extensively studied clinicopathologically, it is difficult to distinguish MPNST from malignant melanoma, fibrosarcoma, leiomyosarcoma, and other soft tissue sarcomas due to its lack of tissue specificity. Moreover, even the subtypes of MPNST are difficult to distinguish effectively, and thus its diagnosis is usually difficult. This report describes the clinicopathologic features of a rare case of mixed MPNST in the right inguinal region an elderly man. The diagnosis, differential diagnosis, and treatment of mixed MPNST are discussed in detail in combination with relevant literature.

Clinical summary

A 79-year-old man was admitted to the hospital with a painless rapidly growing mass in the right inguinal region. Ten months prior, an oval mass approximately the size of a quail egg was unexpectedly found on the right side of his inguinal region; the mass, however, rapidly changed to the size of a goose egg. The patient had no history of smoking or malignant tumors and had not experienced fever, night sweats, or weight loss. By physical examination, a nontender nodule approximately 8.0*4.0 cm in size could be palpated on the right side of the inguinal region; the nodule had an unclear

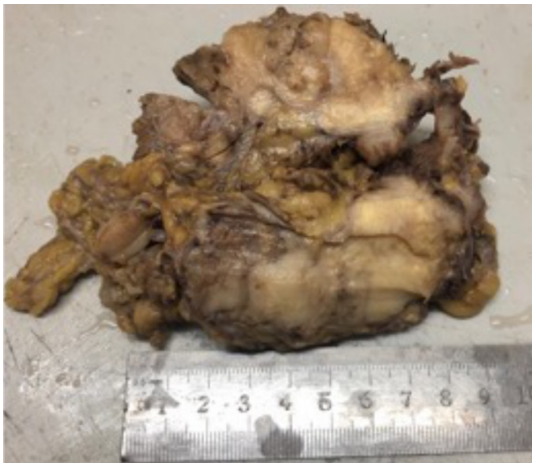

Figure 1. Gross photograph of tumor showing the diffuse cut surface of MPNST.

surface and tough texture and was not accompanied by enlarged, palpable lymph nodes. No obvious abnormality was found in the hemogram indexes. Pelvic contrast-enhanced MRI revealed multiple nodules with slightly longer T1 and slightly longer T2 signals in the right inguinal region and around the right iliac vessels, the larger of which was approximately 4.8×3.3×5.8 cm. The enhanced scan clearly demonstrated uneven enhancement. Malignant lesions were considered, and an ultrasound-guided right inguinal mass biopsy was then performed. Postoperative pathology showed that the lesions were likely malignant mesenchymal tumors, and more specifically, they were likely malignant peripheral nerve sheath tumors. Therefore, complete resection and biopsy of the tumors were recommended. The patient underwent surgical resection of the mass in the right inguinal region at our hospital on June 12, 2019. The tumor was located in the right inguinal region, was approximately 12.0×8.0×3.0 cm in size, and exhibited an irregular shape, toughness, an indistinct capsule, and wrapping of the femoral artery and femoral nerve. The tumor was completely removed, and routine histopathologic examination was performed.

Pathological findings

The specimen received in formalin consisted of the tumor, which measured 8.0×4.5×2.5 cm. The cut surface was solid, gray-yellow, gray-red and soft, and exhibited focal toughness; moreover, some areas were encapsulated (**Figure 1**). Microscopically, multiple cell morphologies were observed, most of which were spindle-shaped cells with bundle-like diffuse growth (**Figure 2**). Nuclear division was obvious, pseudopalisading necrosis was observed, and necrotic peripheral tumor cells resembled a fence-like structure; tumor cells were also denser around thick-walled blood vessels (**Figure 3**). The remaining portion consisted of a small number of epithelial-like cells that featured multinodular growth and that were surrounded by mucous-like or fibrous stroma. Tumor cells were large in size, rich in plasma cells, and contained irregular, prominent nuclei. A gradual migration process between the spindle cells and the epithelioid cells was observed, and it could be seen that the two cell types had intermixed and grew. Immunohistochemical examination showed that S-100 and SOX-10 protein expression in the spindle tumor cells was diffuse and strongly positive; diffuse S-100 staining and partial SOX-10 strong positive staining in the epithelioid tumor component was observed (**Figure 4**). In addition, the tumor was found to be Vimentin (+), Desmin (-), HMB45 (-), CK (-), SMA (-), CD34 (-), and the Ki67 positivity rate was approximately 70%. A diagnosis of mixed classic MPNST with EMPNST was made based on the findings described above. The patient recovered well, and the wound healed considerably before the patient was discharged.

Discussion

Classic MPNST occurs mostly in adults aged 30 to 60 years, with a median age of 37, and no significant difference is observed in the incidence between males and females. Most cases involve the peripheral nerve trunk, and specifically, the limbs, pelvis, and spine [5]. As a rare subtype of MPNST, EMPNST accounts for less than 5% of all MPNST cases [6]. The incidence of EMPNST peaks in individuals between 20 and 50 years of age, with a median age of 44 years [7]. EMPNST is similar to MPNST and predominantly occurs in the lower limbs and trunk, followed by the upper arm, neck, and inguinal region and some parenchymal organs such as the ileum, prostate, pleura, and mediastinum [8].

At present, the etiology and pathogenesis of MPNST are not clear. Studies have shown that

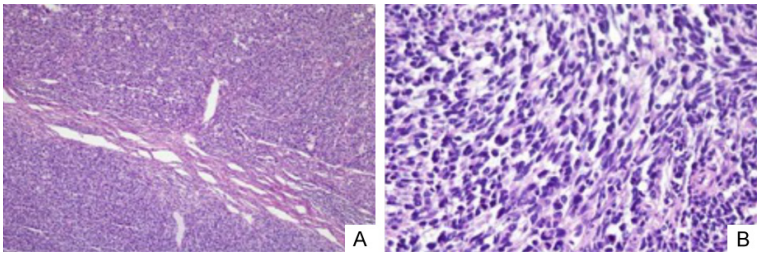

Figure 2. A. At low power (original magnification ×10), mixed spindle-shaped cells. B. Magnification at ×40 highlights spindle-shaped cells.

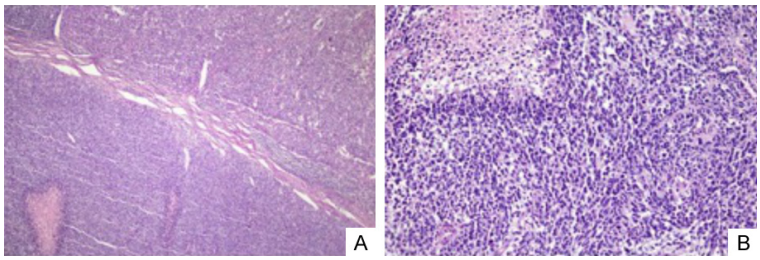

Figure 3. A. At lower magnification (×4), Tumor cells around necrosis presented as palisade structure. B. Magnification at ×20 highlights tumor cells.

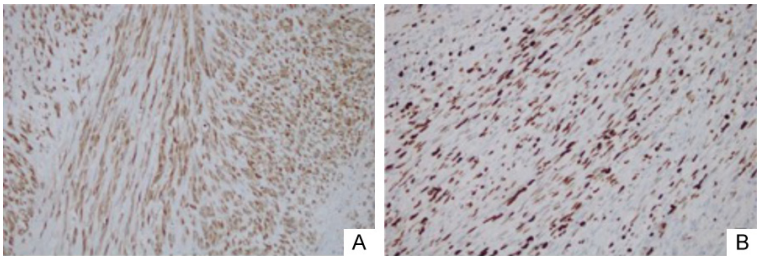

Figure 4. A. S-100 protein is diffusely positive in tumor cells. B. SOX-10 is focally positive.

approximately 50% of MPNSTs are closely related to neurofibromatosis I (NF1) [3]. Less than 10% of cases are induced by radiotherapy, while other causes are unknown [9, 10]. The clinical manifestations are primarily enlarged masses, accompanied by pain, compression symptoms, and motor and sensory dysfunction, especially in patients with NF1 [11].

The imaging manifestations are as follows: MPNST has no obvious characteristic manifestations on imaging, but it shares some common features with other malignant soft tissue tumors, such as the presence of a soft tissue mass with uneven density, an irregular shape, invasive growth, and enhancement to varying degrees after contrast-enhanced imaging. These changes indicate the malignant tendency of these tumors [12]. The CT manifestations of this case are similar to those of other malignant soft tissue tumors, which is consistent with the published literature.

MPNST lacks specific clinical and imaging manifestations, and thus the diagnosis still depends on pathologic and immunohistochemical examination. Most classical MPNSTs consist of tightly arranged spindle cells, which are often densely distributed around blood vessels in loose or mucoid areas; these spindle cells grow diffusely in rich intercellular areas that are interlaced with cell-sparse areas. The cytoplasm is lightly eosinophilic or dichroic [13]. The nuclei are darkly stained, irregular, and contain obvious mitotic figures. Approximately 1/3 of MPNSTs are composed of large cells with obvious pleomorphism and common multinucleated giant cells [5, 14]. EMPNSTs are mainly composed of groups of epithelioid cells arranged in a nodular pattern, with fibrous or mucoid stroma. Cells are usually round, oval, or polygonal in shape, and rich in cytoplasm, which is eosinophilic or dichroic [8]. The nucleus is large and vacuolated with obvious nucleoli and mitotic figures. In some cases, besides epithelioid areas, spindle cell areas similar to those in classical MPNST are seen, as is the migration of cells between the two areas [6, 15, 16]. Due to the lack of morphologic specificity of tumor cells, it is difficult to distinguish them solely by microscopic features. Therefore, further diagnosis requires a combination of immunohistochemical staining and microscopy [17]. Classical MPNST can often contain localized expression of S-100 to varying degrees. In addition, SOX-10 positivity is also an important diagnostic indicator. Tumor cells also express P53 and occasionally CK8 and CK18, but not CK7

or CK19 [18]. EMPNST cells are often diffusely and strongly positive for S-100, especially in the simple epithelial type, but HMB45, Melan-A, MiTF, and CK positivity are not observed [19]. Some cases can express GFAP and EMA [16].

The multipotential origin of differentiated MPNST cells leads to the diverse histological morphology and tissues that are similar to various benign and malignant soft tissue tumors. However, due to the lack of specific diagnostic criteria, pathological diagnosis is more difficult. It is necessary to differentiate MPNST from the following diseases by immunohistochemistry: (1) Malignant Triton tumors: as another histologic subtype of MPNST, most of these tumors are round or spindle-shaped, with abundant cytoplasm and a strong eosinophilic appearance. Some of these tumors contain rhabdomyoblasts that are positive for S-100, CD56, myogenin, and desmin. (2) Synovial sarcoma: histomorphology can be divided into the biphasic, spindle cell, monophasic epithelial, and differential types. Tumor cells usually differentiate into cells with one of two immunophenotypes. CKI9 and Bcl-2 positivity are helpful in the diagnosis of synovial sarcoma, and approximately one third of synovial sarcomas can also express S-100. (3) Malignant melanoma: these tumor cells exhibit distinct atypia and various histologic structures and can be epithelioid. The cells are large and irregular, and the nuclei are large and darkly stained, with obvious nucleoli. These cells are positive for the specific markers HMB45 and S-100. (4) Epithelioid leiomyosarcoma: tumor cells are round, polygonal or spindle-shaped, with eosinophilic or dichroic cytoplasm. The growth of tumor cells is not nodular or nested. The tumor cells have an epithelioid morphology, and the cytoplasm is often transparent with perinuclear halos. The immunophenotype of these cells is characterized by desmin and actin positivity and S-100 negativity. (5) Epithelioid sarcoma: most of these tumors occur in adolescents aged 10-39 years, and most occur in the extensions of the fingers, hands, wrists and forearms. Tumor cells grow in a nodular or rosette-like pattern. The nodules are surrounded by collagen fibers, and the centers of the nodules are often necrotic, which is similar to what is observed in granulomas. The epithelioid tumor cells around the necrotic foci are arranged in a palisade shape. Multiple nodules can be fused in a map shape. The immunophenotype of these cells is characterized by positive CK, EMA, CK8, CKI9, and vimentin expression, while CD34 is expressed in 50%-70% of cases.

Most MPNSTs are highly malignant sarcomas that are highly invasive and usually spread along infiltrating peripheral nerves and blood vessels [10, 18]. The local recurrence rate can reach 50% [18], and therefore, surgical resection is the first choice for treatment. As the prognosis of patients is poor, some cases may be accompanied by lymph node metastasis as well as distant metastasis to the lungs, liver, and bone, among other sites [1]. The 5-year survival rate is less than 50%, and the survival rate of patients with neurofibromatosis type I is even lower. Therefore, adjuvant radiotherapy and chemotherapy after surgery is an important means to reduce recurrence. Studies have shown that NF1 is an independent factor that affects the prognosis of MPNST [20]. Patients with NF1 must consider the risk of recurrence and metastasis caused by radiotherapy, and thus long-term follow-up is required. Since only 2% of EMPNSTs are related to NF1, the prognosis of EMPNST is better than that of MPNST.

In summary, this case was diagnosed with a classical and epithelioid mixed type tumor. Its mixed growth pattern may be related to molecular genetic or microenvironmental changes. No literature has been published on this type of mixed malignant peripheral neurilemmoma. In this study, we reported a patient with mixed MPNST in the right inguinal region. The patient underwent surgery, which successfully relieved the symptoms. Postoperatively, the patient recovered well, but regular follow-up is still needed for the early detection of tumor recurrence. Our report illustrates the first example of a mixed malignant peripheral nerve sheath tumor in the inguinal region and suggests that we should not omit the possibility of this tumor type in future diagnoses.

Disclosure of conflict of interest

None.

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