Case report

Lumbar malignant peripheral nerve sheath tumor: a rare case in a young patient

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Abstract. Malignant peripheral nerve sheath tumor (MPNST) is a rare soft tissue sarcoma that originates from peripheral nerves or from cells associated with the nerve sheath. We report the case of a 30yearold male patient with a history of neurofibromatosis type I (NF-1) and a MPNST located in the lumbar region. The mass was resecated but surgical margins weren't clear. Recurrence of disease was observed after a few months. A close monitoring of subjects with NF-1 is crucial to diagnose MPNST at an earlier stage and allow a complete surgical resection (www.actabiomedica.it).

Key words: malignant peripheral nerve sheath tumors (MPNSTs), soft tissue sarcomas (STS), neurofibromatosis type I (NF-1), prognosis

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are soft tissue sarcomas (STS) that originate from peripheral nerves or from cells associated with the nerve sheath, such as Schwann cells or perineural cells [1]. MPNSTs account for about 5–10% of STS with an incidence of 0.001% in the general population [2], rendering them rare tumors with a poor prognosis [3]. About one half of cases are related to neurofibromatosis type 1 (NF-1) that represents a major risk for the development of malignancies, particularly MPNSTs [4]. This paper presents a rare case of a lumbar MPNST in a 30-year-old male patient with NF-1 from the diagnosis to its clinical course, showing the malignancy of this tumor in terms of a rapid local recurrence and therefore the importance of an early diagnosis to allow the best therapeutic strategy.

Case presentation

A 30-year-old male patient presented to our department with a four-month history of paraesthesia and worsening low back pain not responding to nonsteroidal anti-inflammatory drugs. There was no history of preceding trauma or accident but the physical examination revealed dark colored spots on the skin (café-au-lait spots) and sporadic subcutaneous nodules referring to his history of NF-1. Laboratory findings, including leukocyte and platelet counts, hemoglobin, serum creatinine, liver function did not reveal abnormalities. Lumbar spine Magnetic Resonance Imaging (MRI) was performed, revealing a heterogeneous mass of cystic appearance extending medially to the right psoas muscle at L4-L5 level. The lesion showed low signal intensity on T1-weighted images, while high and inhomogeneous signal on T2-weighted images (Figure 1, A-B).

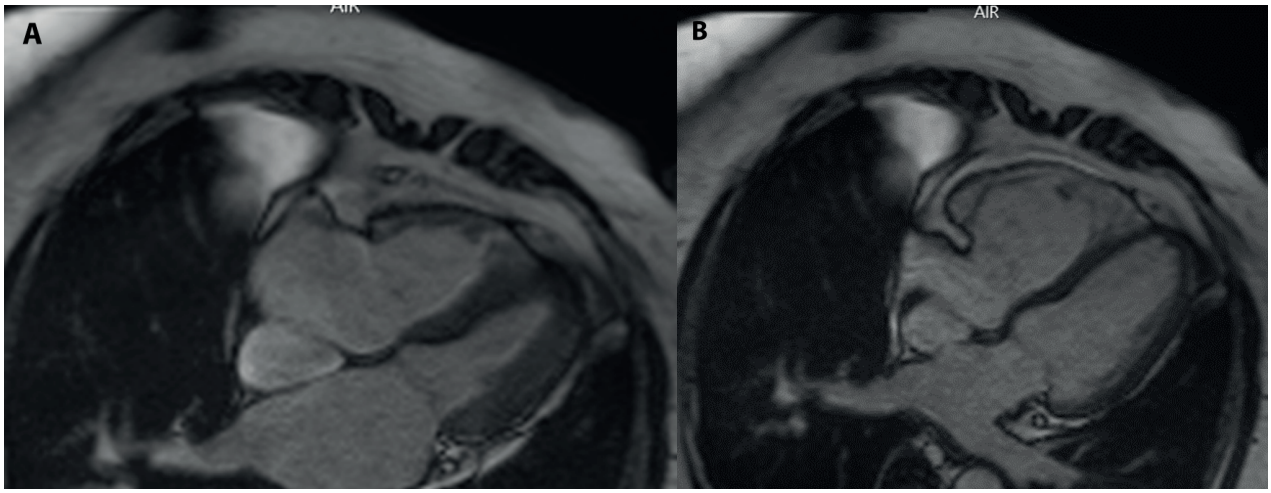

Figure 1. Lumbar spine MR images show a heterogeneous mass of cystic appearance extending medially to the right psoas muscle at L4-L5 level that is (A) hyperintense on axial T2-weighted image, (B) hypointense on sagittal T1-weighted image.

In the suspicion of a dermoid cyst, fine-needle aspiration (FNA) biopsies were performed but no histopathological diagnosis was reached on the basis of the samples obtained. Three months later Computed Tomography (CT) confirmed the presence of a hypodense mass in lumbar paravertebral region on the right side which pushed anterolaterally psoas muscle, characterized by inhomogeneous enhancement. There was no evidence of associated lymphadenopathy in the scanned area, thus the patient underwent surgery and a subtotal removal of the mass was performed. On gross examination, the tumor measured 6×5×3,5 cm and its weight was 100 gr. The cut surface appeared firm and whitish with a translucent area, hemorrhagic and necrotic foci. Microscopically, the tumor was composed by interlacing fascicles of spindle cells with wavy, elongated hyperchromatic nuclei and displayed highly cellular areas alternating with less cellular one (Figure 2, A–C).

There was both an increased mitotic index (>10 and <20 per 10 high-power field) and necrosis in less than 50% of the tumor (Figure 2, D). Another characteristic of the tumor was some areas with chondrosarcomatous differentiation (Figure 2, E-F). Immunohistochemistry demonstrated positive staining for S-100. Based on these findings, the diagnosis of a MPNST was confirmed. According to the Fédération Nationale des Centres de LutteContre le Cancer (FNCLCC) grading system of STS [5], the tumor was classified as grade 2 (a total score of 5: 2 MPNST, 2 for 10-19/10HPF and 1 for <50% tumor necrosis). Microscopically, the margins showed residual tumor. Radiation therapy was proposed to the patient but he refused it. The postoperative course was initially smooth; lumbar pain disappeared, remaining only a minimal reduction of psoas muscle strength and the following CT examination was negative. Nevertheless after one year, the follow-up CT demonstrated a local recurrence of the tumor; a heterogeneous hypodense mass was found in the right paravertebral side (Figure 3, A-B) at the same level of the excised lesion.

The patient received three cycles of systemic chemotherapy with ifosfamide and epirubicin but that was ineffective because the tumor grew up, occupying almost the entire right lumbar region and reaching the inferior border of the liver (Figure 4, A-C).

The lesion showed necrotic-colliquative areas and infiltration of both the proximal part of right ureter and right iliac arteries. Moreover, enlarged retroperitoneal lymph nodes were found in the interaortocaval and paraaortic regions. He died two weeks later, fourteen months after the histological diagnosis of MPNST.

Discussion

MPNSTs account for 5-10% of all STS, arising in the peripheral nerves and characterizing by a high

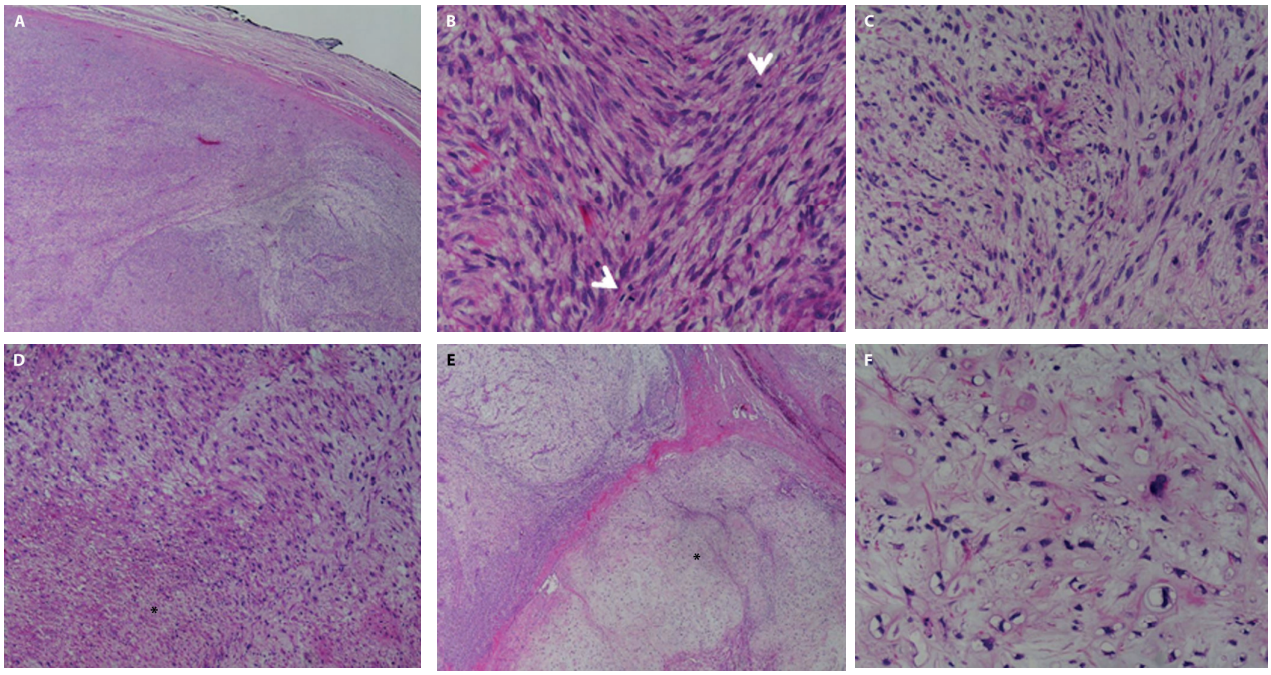

Figure 2. A) Typical appearance of MPNST with highly cellular areas alternating with less cellular ones (magnification 2X); B) Higher magnification of dense cellular area with spindle cells fascicle and mitotic figure (arrowhaeds) (magnification 20X); C) Higher magnification of hypocellular area with myxoid extracellular matrix (magnification 20X); D) Tumor area with geographic necrosis indicated with asterisk (magnification 20X); E) Tumor area with heterologous mesenchymal differentiation indicated with asterisk (magnification 2X); F) Higher magnification of chondrosarcomatous area (magnification 20X)

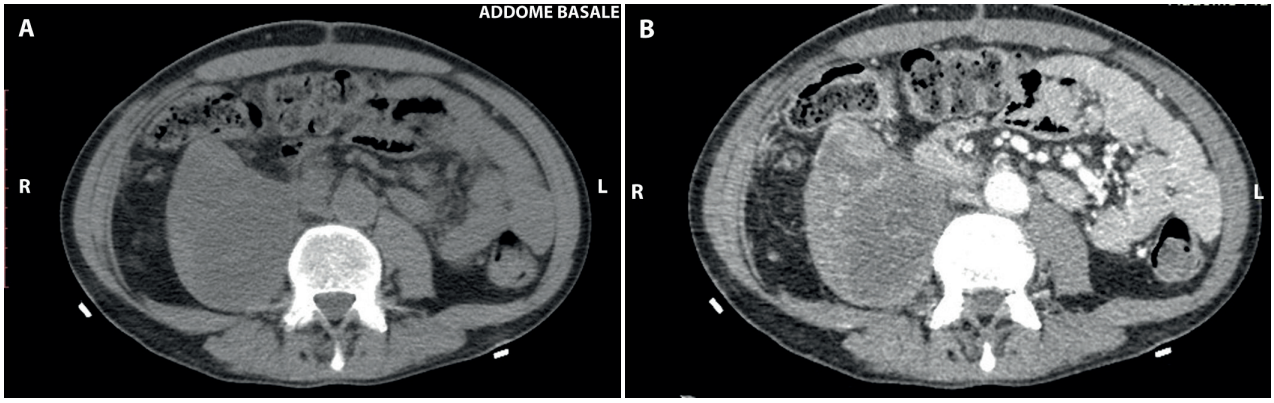

Figure 3. Follow-up CT scans demonstrate a heterogeneous hypodense mass in the right paravertebral side; (A): axial unenhanced CT scan, (B): axial enhanced CT scan.

risk of recurrence and poor outcome [6]. Approximately 50% of cases occur in the context of NF-1, because of the loss of function of NF-1 gene that codifies neurofibromin, an important negative regulator of cellular proliferation [7]; the remaining cases arise sporadically or following radiation therapy [8]. NF-1 has been associated with an increased risk of MPNST, displaying in this association male predominance, young age and infrequent head and neck presentation. Moreover, NF-1 can be considered a negative prognostic factor [9] together with large tumor size, truncal location, high grading and a mitotic index of greater

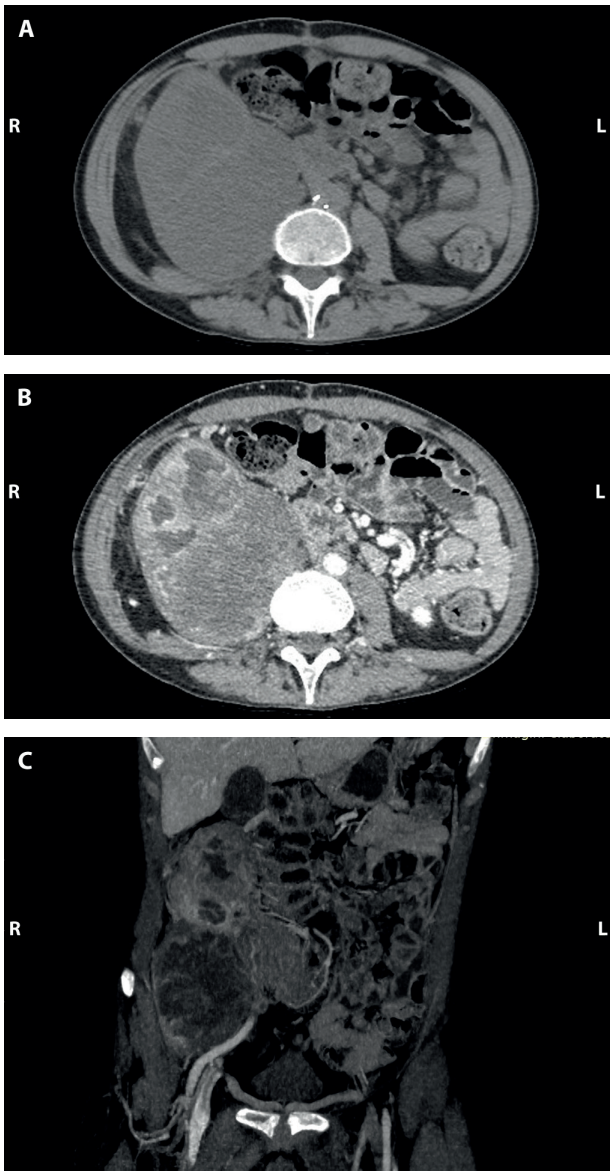

Figure 4. Last CT scans show an enlargement of the mass which occupies the entire right lumbar region and reaches the inferior border of liver. (A): axial unenhanced CT scan, (B): axial enhanced CT scan shows necrotic-colliquative areas within the mass, (C): coronal enhanced CT scan shows the extention of the lesion till the inferior border of the liver.

than 6/10 high-power fields [10]. MPNST, as STS arising in the abdomen and pelvis, are usually clinically silent so that they can rapidly enlarge until they invade or compress adjacent organs [11]. MRI is the most useful diagnostic tool in the examination of soft tissue malignancies [12]. MPNST usually is hyperintense on T2- weighted images and low or isointense on T1-weighted images. In our case the tumor shows low intensity on T1-weighted images and high intensity on T2-weighted images. The histopathogenesis of MPNST is still unknown but the most important theory is that Schwann cell is the major contributor to the development of both benign and malignant tumors of the nerve sheath [2]. This neoplasm rarely can arise from a preexisting benign nerve sheath tumor such as neurofibroma or schwannoma. Microscopically, most tumors are highly cellular and are made of spindle cells with hyperchromatic nuclei and indistinct cytoplasm. Divergent differentiation can be seen in about 25 % of the tumors and may include osteoid, chondromatous (our case), angiosarcomatousand rhabdomyosarcomatous areas (malignant triton tumor). Nerve sheath differentiation is confirmed by S-100 protein; basing on histological and immunohistochemical findings, the diagnosis of MPNST can be made. It is generally staged according to the FNCLCC grading system of STS [13] which is based on 3 factors: differentation, mitotic count and tumor necrosis. Each factor is given a score and the results are added to determine the grade of the tumor. The grade of tumor is one of the most important factors which influence patient survival together with the extention of excision. Complete surgical resection with negative (wide) margins is the optimal treatment for this tumor according to standard protocol for managing STS [14], improving the prognosis through decreased rates of local recurrence and distant metastases. Radiotherapy can be useful to decrease the incidence of local recurrences [3] but it has not a meaningful role in reduction in both rates of distant metastases and overall survival [15] while chemotherapy has no role in the initial treatment of MPNST for patients without metastases in whom radical resection is accomplished [16]. Prognosis of patients with MPNST has always been poor with a 5-year survival rate of 16% to 52% [17]. The 5-year survival rates of patients with MPNST who received surgical resection with and without negative margins have been 67 and 22%, respectively [18]. All this information shows the malignancy and poor outcome that characterize this tumor. Future approaches could involve genomics and proteomics in order to identify molecular biomarkers as targets for biological therapies [19]; they are not yet well documented for STS, therefore a better

understanding of the cellular and molecular mechanisms could in future play an important role in the management of soft tissue masses. In conclusion, in this report we presented a rare case of a young patient with MPNST. It is a malignant sarcoma often associated with NF-1. Histopathology and immunohistochemistry are fundamental tools to establish the diagnosis. Poor outcome of this tumor is related to its high incidence of local recurrence and distant metastases. A complete excision of the lesion represents the best therapeutic strategy to improve the prognosis of the patient. Therefore, a close monitoring of subjects with NF-1 and a multidisciplinary approach to management of this lesion is crucial to diagnose MPNST at an earlier stage and allow a complete surgical resection.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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