

Case Report

Malignant Peripheral Nerve Sheath Tumor Relapse Detected by Positron Emission Tomography

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REZUMAT

Tumoră malignă de teacă nervoasă recidivată diagnosticată prin tomografia cu emisie de pozitroni

Introducere: Tumorile maligne de teacă nervoasă periferică (MPNST) sunt tumori rare agresive, reprezentând 5-10% din totalul tumorilor maligne mezoteliale. Tratamentul MPNST este complex, multimodal implicând excizia chirurgicală a tumorii primare, urmată de tratament oncologic. Evoluția naturală este spre recidivă locală și metastazare pulmonară. Urmărirea postoperatorie este esențială pentru supraviețuire.

Material și metodă: Pacientul, bărbat în vârstă de 41ani, internat în clinică pentru o formațiune tumorală de părți moi coapsă stângă operată, recidivată cu nodul pulmonar lob inferior drept. După efectuarea investigațiilor paraclinice și imagistice, se intervine chirurgical, practicând ablația recidivei, cu margini de rezecție libere. Pacientul este referit la oncolog pentru chimio și radioterapie. La 6 luni postoperator examenul IRM relevă o formațiune inghinală stângă fără criterii de malignitate. Se decide efectuarea PET-CT ce evidențiază un nodul captant inghinal stang. Se practică excizia acestuia. Examenul histopatologic confirmă diagnosticul de recidivă MPNST.

Concluzii: Recidivele tumorale îmbracă varii forme histopatologice, cu aspect clinic și imagistic echivoc. Pet-ct-ul oferă informații despre activitatea metabolică tisulară permițând detecția precoce a celulelor neoplazice.

Cuvinte cheie: tumoră malignă de teacă nervoasă periferică, excizie, recidivă, PET-CT, terapie oncologică

ABSTRACT

Malignant peripheral nerve sheath tumors are rare aggressive tumors that account for 5-10% of soft tissue sarcoma. The treatment is complex, involving surgical excision of the primary tumor and oncologic therapy. The natural evolution of MPNST is towards relapse and pulmonary metastasis. Careful postoperative follow-up is essential for long term survival.

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Materials and Method: The patient, a 41-year old man, was admitted to our clinic for an operated, relapsed soft tissue mass in his left thigh. At admission he had a nodule in his inferior right pulmonary lobe. After undergoing imagistic investigations, the patient is operated, the mass is removed, with negative microscopic margins. The patient is referred to the oncologist for chemotherapy and radiotherapy. After 6 months, the MRI investigation detects a soft tissue mass in the inguinal region, without any suspicion of malignancy. Fortunately, a full body PET-CT showed a “hot” nodule in the inguinal region. The mass was surgically removed. The pathologic examination confirms the clinical suspicion: relapse of MPNST.

Conclusion: Tumor relapse, due to the subsequent diversity in their histology may vary in clinical and imagistic appearance. Pet-Ct offers valuable information on the metabolic activity of a suspicious mass, allowing rapid detection of neoplastic cells.

Key words: malignant peripheral nerve sheath tumor, surgery, oncologic therapy, relapse, PET-CT

BACKGROUND

Malignant peripheral nerve sheath tumors (MPNST) are soft tissue tumors showing neuroectodermal differentiation. They arise in connection to a major nerve trunk, a peripheral nerve or a pre-existing neuroma in patients with hereditary neurofibromatosis type 1. [1, 2]

They usually develop in the deep soft tissue between anatomic compartments, the root of the limbs (inguinal region, the axilla) being one of the most common sites of occurrence.

MPNST occurs in individuals between 20-50 years of age, unrelated with gender. They cause minimal discomfort making clinical diagnosis a challenge. [3]

MPNST are aggressive tumors, prone to relapse after excision and hematologic spread, the most common site being the lungs. Distant metastasis to the bones has also been described.

The treatment protocol includes a multimodal therapy involving primary tumor wide excision, chemo- and radiotherapy. These tumors are generally resistant to adjuvant oncologic therapy, so the complete surgical resection remains the mainstay of successful therapy.

Unfortunately, MPNST hold a poor prognosis, the overall survival rate being 30-60%. The most important prognostic factor is considered to be tumor resectability. [4, 5, 6, 7]

Other negative prognostic factors associated to decreased survival are tumor size exceeding 5cm, more than 6/10 fields cell mitotic rate at microscopical examination, associated NF1, high grade tumor, central location and tumor relapse.[8,9,10]

This article presents the case of a rare MPNST in a 41 year old man, with 3 subsequent tumor relapses, despite the presence of negative surgical margins and correct complete oncological therapy. The relapse was suggested by the MRI examination, but the confirmation was possible after PET-CT of the tumor bed.

CASE PRESENTATION

The patient, a 41-year old man was admitted to the Clinic of Plastic Surgery and Reconstructive Microsurgery of the Emergency Hospital Bucharest for an operated, relapsed soft tissue mass of the upper left thigh and a subsequent nodule in the inferior right pulmonary lobe.

First surgical intervention for MPNST

His medical history described a previous hospital admission in the general surgery department 10 months ago for a soft tissue mass in the upper left thigh. He denied family history of peripheral stigmata of NF-1. The clinician initially suspected a hematoma or lipoma of the thigh. The patient underwent surgical excision of the mass, described by the operator as a cystic-like lesion of 7/6.5/3 cm, shabby and friable. The mass was excised.

The pathological examination described a large tumor surrounded by a pseudo-capsule, with fleshy, opaque, white-tan surface marked by areas of secondary hemorrhage and necrosis. The microscopical evaluation showed cells arranged in sweeping fascicles, densely cellular fascicles alternate with hypocellular, myxoid zones which swirl and interdigitate with one another, creating a marble-like effect.

More than 30 mitoses/field were identified suggesting increased tumor aggressiveness. The preliminary result was spindle cells sarcoma.

Immunohistochemical findings

Immunohistochemical findings were necessary for diagnostic purposes. The investigation showed diffuse positive reaction for Vimetine, and weak focal positive reaction for neural differentiation markers such as S100 protein and myelin-associated glycoprotein Leu7. Blood vessels tested positive for CD34 and Actin. Ki76 marker of cell proliferation was positive in 60% confirmed the tumors aggressive behavior.

The patient was diagnosed with aggressive malignant peripheral nerve sheath tumor. Radical excision was confirmed by the pathologist.

3 month check-up

After 3 month the gadolinium enhanced MRI detected a small nodule 40/15/45 mm between the vastus medialis muscle and the sartorius of the left thigh. The nodule is located in the adductor channel, superficial to the femoral artery. A central area of 40/15mm of intense vascularization and invasion of sartorius muscle are described. A tumor relapse is suspected, and several ultrasound evaluations of the abdomen and pelvis rule out distant metastasis. A chest x-ray describes a small solitary pulmonary nodule without clinical significance.

Elastography

A soft tissue ultrasound elastography of the proximal left thigh showed increased fibrosis in the tumor bed: oblique surgical scar, parallel to the medial border of the sartorius muscle, subsequent tumor relapse with small neoplastic nodules, of liquid content infiltrating the surrounding adipose tissue and muscle fascia UNFO score 4-5 and up to 62 FLR suggestive of malignancy. All nodules presented increased blood flow. Inguinal lymph nodes are enlarged, without obvious signs of tumor invasion. After analyzing the data, a re-excision of the scar and an additional surgical margin of 2.5 cm are recommended.

Clinical findings

Postoperative oblique scar measuring 4 cm, reddish, slightly elevated parallel to the medial border of the left Sartorius muscle, adherent to the deep structures. No other pathologic findings.



Figure 1. CT scan of the thorax reveals no pathologic masses [11]

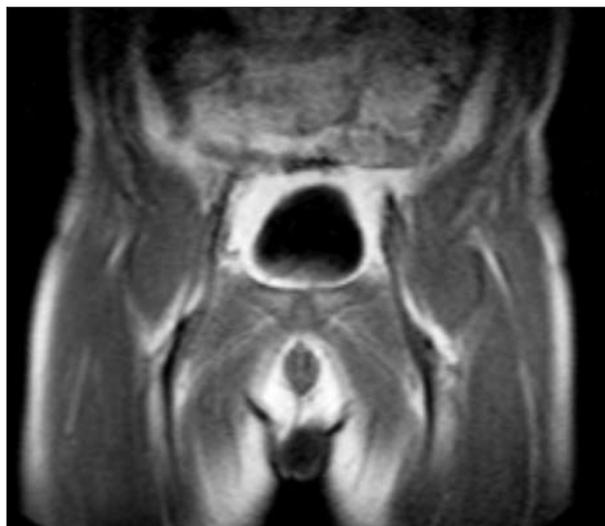


Figure 2. MRI coronal view showing enlarged left inguinal lymph nodes [11]

CT-scan of the abdomen and thorax reveal no abnormal masses. (Fig. 1)

A MRI of the abdomen and root of the left limb detect inguinal node enlargement, without any other pathologic findings (Fig. 2). Tumor relapse not visible.

Second surgical intervention for MPNST

After the initial evaluation, the patient is operated under general anesthesia. The scar was removed, as well as the underlying nodule measuring 0.5 cm and the fibrous mass invading the sartorius muscle. Frozen section histology was suggestive of a malignant peripheral nerve sheath

tumor. Negative surgical margins were achieved.

Subsequent histological examination of formalin-fixed tissue confirmed MPNST relapse. The patient had no immediate surgical complications and was discharged and referred to the oncologist for adjuvant therapy.

Adjuvant therapy

The patient received immediately after surgery a total of 6 series of polichimiotherapy with Farmorubicin and Ifofosfamide, followed by radiotherapy sessions of 20 fractions of 5 Gy each, 5 fractions per week to a total dose of 40 Gy for the targeted volume comprising the postoperative scar and drainage tube scar.

Due to the tumor aggressiveness, monthly imagistic evaluations of the abdomen, pelvis and initial tumor were recommended. All came back negative.

3 month and 6 month check-up: contrast MRI

The MRI examination describes inflammatory changes in the tumor bed, without malignant characteristics: postoperative scar and subsequent area of increased STIR signaling, decreased T1 signal, diffuse contour of the adductor channel consistent with postoperative inflammatory changes. No tumor relapse detected. The 6 month follow-up describes a 31/21 mm soft tissue mass on the anterior aspect of the upper left thigh showing increased T2 signal, decreased T2 signal, with subsequent muscular edema. A new tumor relapse is suspected. As a conclusion of the two MRI examinations, interpreted by the same doctor, using the same MRI and technician, the supposition can be made that the first examination failed to detect tumor relapse, because of subsequent inflammatory changes. The malignant characters became obvious after 3 months.

PET-CT

A PET-CT using 18F-FDG is recommended after the MRI, 6 months after surgery. In the upper aspect of the left thigh, superior to the Sartorius and Adductor muscles, a small metabolically active oval nodule measuring 3.6/2.8/4.5 cm is detected, the nodule is invasive in the subcutaneous tissue. Several nodular images of variable size in both pulmonary lobes, inactive metabolically (Fig. 3, 4,5).

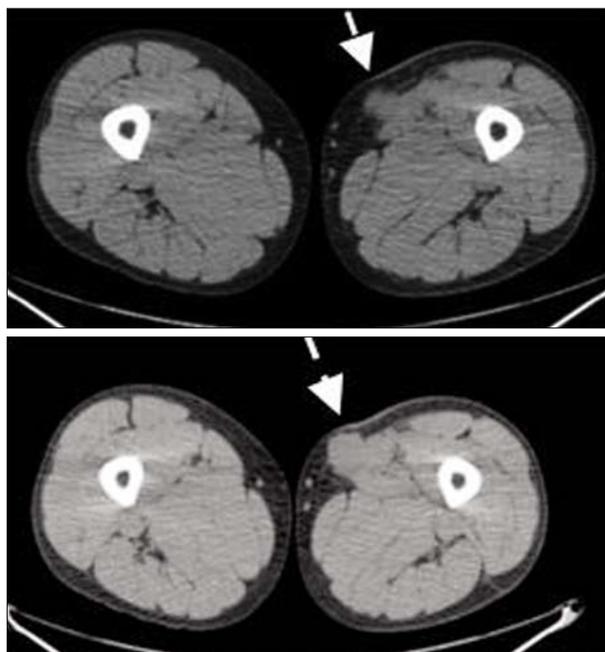


Figure 3. Pet-Ct transverse aspect showing left thigh soft tissue mass invasive in the underlying muscle (arrow)[11]

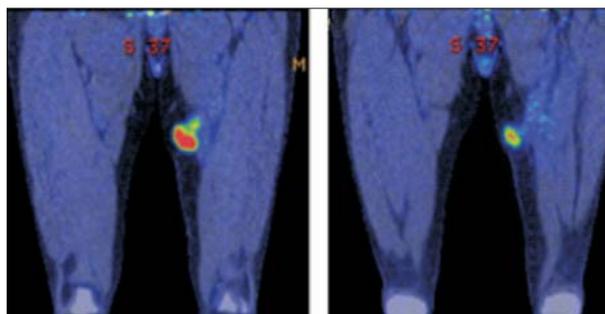


Figure 4. Pet CT coronal view showing increased uptake of 18F-FDG in a "hot" inguinal node and surrounding inflammation [11]

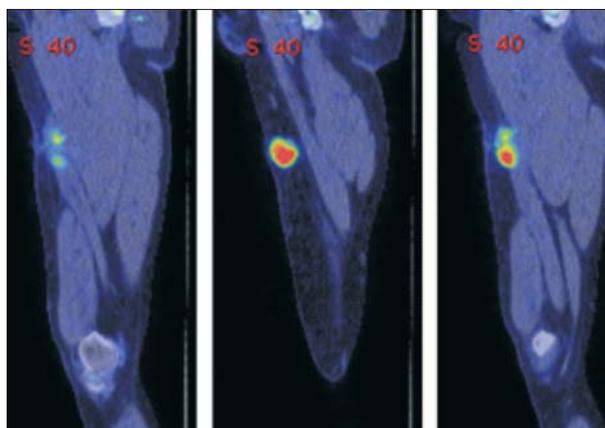


Figure 5. Pet-CT: sagittal view of the left thigh and subsequent metabolic active nodule[11]

Third surgical intervention

The patient is admitted in our clinic with the diagnosis of malignant peripheral nerve sheath tumor of the left upper thigh relapse.

The clinical examination of the upper left thigh shows a postoperative scar and a subsequent soft tissue mass of 3/2 cm, invasive in the surrounding tissue, adherent to the muscle plane. Left inguinal nodes enlarged.

After preoperative workup the patient is operated under general anesthesia. The scar is

excised. After careful dissection, a small 3/2 cm nodule is seen. The nodule invades the surrounding adipous tissue as well as the muscle fascia that is removed, the mass is excised with a margin of 3 cm of macroscopically healthy tissue. (**Fig. 6**)

A small oblique 3 cm long incision was made on the projection of the inguinal ligament. After dissection, an infiltrated lymphatic nodule was excised. (**Fig. 7**) The two pieces were send for pathological examination (**Fig. 8**).

Afterwards, a perforated drainage tube was left in place, followed by an anatomically-layered surgical suture.

Postoperative evolution was favorable. The patient was discharged after 4 days (**Fig. 9**).

Current status

The patient is still under oncologic surveillance, being investigated every 3 months by clinical examination, pelvis and abdomen ultrasound and a gadolinium enhanced MRI of the left lower limb. Because of the prolonged need for surgical and oncologic therapy, the patient was forced to retire on medical grounds. The inferior limb function is maintained, no functional impairment resulted after repeated surgery and radiotherapy. The pulmonary nodule is being observed by plain chest x-rays every 3 months.

DISCUSSION

Malignant peripheral nerve sheath tumors (MPNSTs) are sarcomas which originate from peripheral nerves or cells associated with the nerve sheath, such as Schwann cells, perineural cells, or fibroblasts. MPNSTs comprise approximately 5-10% of all soft tissue sarcomas. They can occur spontaneously or in conjunction with hereditary syndromes such as neurofibromatosis-1. The etiology is idio-



Figure 6. Postexcisional defect after the resection of the soft tissue mass [11]



Figure 7. Enlarged lymph node excised [11]



Figure 8. Resected MPNST relapse and inghinal lymph node [11]



Figure 9. Immediate postoperative aspect [11]

pathic but several studies showed a higher incidence in patients with a history of radiation exposure. [1-4] MPNSTs generally occur in adulthood, between the ages of 20 and 50 years of age without a predilection towards gender.

Approximately 10-20% of cases have been reported to occur in the first 2 decade of life. [5] MPNSTs present as an enlarging palpable mass. MPNSTs arising from peripheral nerves may result in a variety of clinical patterns, including radicular pain, paresthesias or motor weakness. Pain is an inconstant finding. Most MPNSTs occur in conjunction with large peripheral nerves such as the sciatic nerve, brachial or sacral plexus. They are usually deep-seated and often involve the proximal upper and lower extremities as well as the trunk.

Magnetic resonance imaging is the imaging modality of choice. Large tumors (>5 cm), invasion of fat planes, heterogeneity, ill-defined margins, and edema surrounding the lesion are more suggestive of MPNSTs. MPNSTs are most likely to metastasize to the lungs. For this reason, a simple chest x-ray or a computer tomography of the chest is the preferred imaging study to screen for distant disease. FDG PET is a dynamic imaging modality which evaluates metabolic activity by quantitatively assessing intracellular glucose use. [8-14] FDG PET has proven useful in detecting metastatic or recurrent disease its value in differentiating malignant nerve sheath tumors from benign ones remains unclear. More recently, it has been suggested that 18FDG PET technology has prognostic relevance. As experience with FDG PET technology grows clarification of its diagnostic and prognostic implication is expected. [6-17]

The mainstay of treatment is surgical resection. The goal of the operation is to achieve complete surgical excision of the tumor with negative (wide) margins. This offers the best outcome with respect to both local recurrence and distant metastases. [10,12] Together with wide surgical excision, radiation therapy offers local and overall survival rates similar to those following more extensive procedures. The combined modality treatment often allows patients the option to undergo successful limb-salvage surgery.

The use of chemotherapy is only employed in high-grade disease, in which metastatic disease is likely. For this reason, the decision to treat with chemotherapy is tailored to an individual patient. The prognosis is reserved, with frequent relapse and disease related mortality and morbidity.

CONCLUSIONS

MPNST are aggressive sarcomas that arise from cells showing neural differentiation. They affect young adults and cause significant morbidity because of frequent relapse and associated oncologic therapy. Surgery is the mainstay of therapy. Careful post-operative surveillance is the key to relapse detection. Although gadolinium enhanced MRI is the golden standard in sarcoma investigation, PET-CT provides a more accurate diagnosis of atypical metabolically active masses. [13, 14, 15, 16, 17]

Acknowledgments

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