

## Sciatic Nerve Tumor: Malignant Peripheral Nerve Sheath Tumor: Case Report

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### ABSTRACT

**Background:** Malignant peripheral nerve sheath tumour (MPNST) is rare. It is a type of peripheral nerve sheath tumour that is cancerous (malignant). Most peripheral nerve sheath tumours are not cancerous (benign). A tumour is a lump or growth in the body.

**Objective:** This paper reports a case of a malignant peripheral nerve sheath tumour revealed from the Magnetic Resonance Imaging (MRI) examination and other processes, with remarkable unusual size of the tumour.

**Case report:** A 36 years old male patient with a three months history of massive right-thigh medial side swelling came to the clinic. The patient reported that he fell while walking before the beginning of the symptoms. He then visited the clinic with medial side thigh pain, limping, and massive swelling in the medial side of his right thigh. The provider recommended a triple assessment; 1- clinical, 2- laboratory, and 3- radiological. The clinical evaluation showed that the swelling was about 20 cm x 10 cm diffuse fusiform swelling, with tense stretched skin over cystic to a firm consistency.

**Conclusion:** There is usually a poor MPNST prognosis, so the doctors must be sure about the diagnosis before treating the condition. Typically, there are three ways to treat MPNST: surgery, chemotherapy and radiotherapy.

**Keywords:** Sciatic Nerve Tumor, Malignant Peripheral Nerve Sheath Tumor.

### INTRODUCTION

Malignant peripheral nerve sheath tumour (MPNST) is a cancer type that occurs in the lining of the nerves that spread out from the spinal cord into the body. This type of cancer is a rare condition known as neurofibrosarcomas. Cancer can also occur anywhere in the body, but in most cases, it appears in the deep tissue of the legs, arms, and trunk. They cause weakness and pain in the affected area, and many also grow a mass or a lump. Function loss mutations characterise MPNST occurrences to the tumour suppressor neurofibromin <sup>(1)</sup>. The prognosis is usually poor with increased relapse rates and other multimodality therapy in early disease, low propensity for rapid disease progression and high mortality and low response rates to cytotoxic chemotherapy for advanced disease <sup>(2)</sup>.

This paper reports a patient case of a malignant peripheral nerve sheath tumour revealed from the Magnetic Resonance Imaging (MRI) examination and other processes. MRI showed 20 cm of swelling on the medial side thigh with possible sarcomatous changes. The issue was then approached by a multidisciplinary team consisting of a radiologist, histopathologist and orthopedic surgeon. A surgery excision was then completed, and the histopathological assessment showed high-grade spindle cell sarcoma compatible with high-grade malignant peripheral nerve sheath.

### OBSERVATION

A 36 years old male patient with a three months history of massive right-thigh medial side swelling came to the clinic. The patient reported that he fell while walking before the beginning of the symptoms. He then visited the clinic with medial side thigh pain, limping, and massive swelling in the medial side of his right thigh. The provider recommended a triple assessment; 1- clinical, 2- laboratory, and 3- radiological. The clinical evaluation showed that the swelling was about

20 cm x 10 cm diffuse fusiform swelling, with tense stretched skin over cystic to a firm consistency. In addition, the results showed a non-mobile mass, mild tenderness with pressure, and intact distal neurovascular status. Also, the results indicated a non-pulsatile mass and no other palpable mass. From the patient's report, the clinician stated an adverse family history, no palpable lymph nodes, and no history of smoking or exposure to radiation. Next, the laboratory procedure for basic tests, CBC, CRP, and ESR, was conducted. The third procedure followed with radiology included an ultrasound and X-ray (Figures 1 and 2), then, Magnetic Resonance Imaging (MRI) examination with contrast (Figures 3, 4 and 5), which showed a 20 cm swelling on the medial side of the thigh with possible sarcomatous changes.



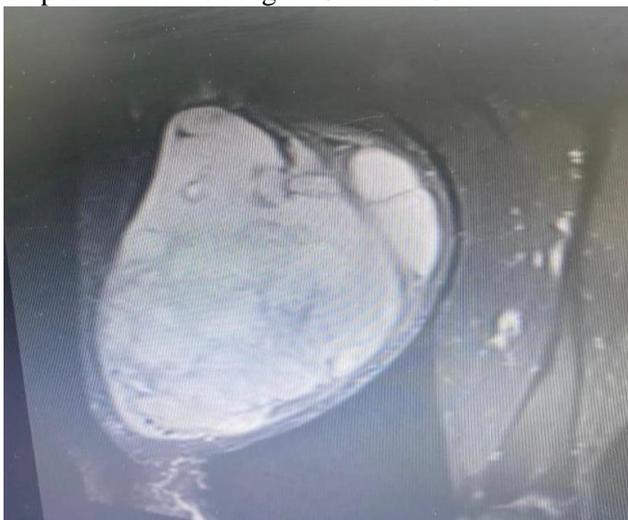
**Figure (1):** X-ray lateral view of the right femur showing no bone abnormalities



**Figure (2):** X-ray AP view of the right femur showing no bone abnormalities



**Figure (3):** MRI with contrast of the right thigh Sagittal plane showing a mass involving the posterior compartment measuring 21.6x12.2x13 cm



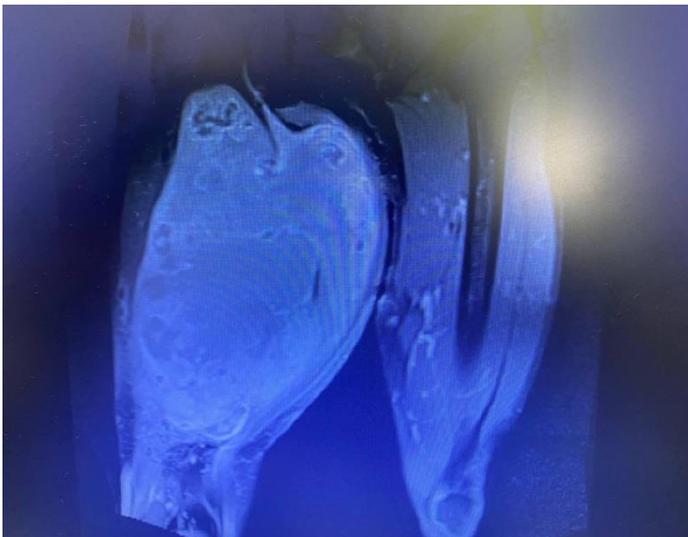
**Figure (4):** MRI with contrast of the right thigh coronal plane showing a mass involving the posterior compartment measuring 21.6x12.2x13 cm



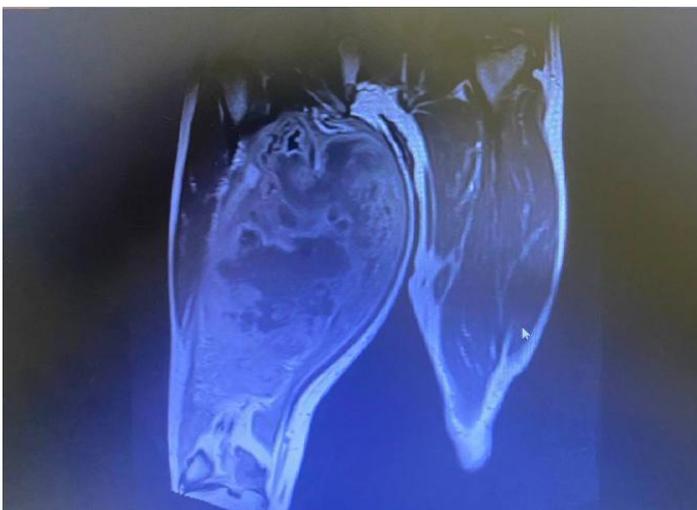
**Figure (5):** MRI with contrast of the right thigh axial plane showing a mass involving the posterior compartment measuring 21.6x12.2x13 cm

Afterwards, a multidisciplinary team (MTD) approach was involved, including a radiologist, histopathologist, and orthopedic surgeon. The plan was as follows: First, a malignancy workup was done, including CT abdomen and pelvis with contrast, bone scan, and then ultrasound-guided biopsy from the thigh lesion and histopathological assessment. Myxofibrosarcoma was suspected, and a second lesion on the contractual side in the left iliac fossa, about 4 cm by 4 cm, was found in the abdominal CT. Therefore, a general surgical oncologist was consulted. After the second ultrasound-guided biopsy, abdominal lesion excision was done, which showed the same tumour pathology—consequently, the tumour board team aimed for curative therapy for the patient.

The patient was prepared for surgery, and his plan was finalised after the oncology workup and blood preparation. Three weeks later, the patient's mass markedly increased in size. Therefore, a new MRI was done (Figures 6 and 7), which showed that the mass was then 30 cm by 15 cm with the engulfed sciatic nerve. From the gross picture, the mass weighed 5.5 kg and measured 30x20x17cm surrounded by the muscular tissue. The cut sections appeared nodular, yellowish-white cut sections with scattered necrosis foci.



**Figure (6):** MRI with contrast of the right thigh T1 coronal plane showing a mass involving the posterior compartment measuring 30 cm x 20 cm x 16 cm englobing the sciatic nerve.



**Figure (7):** MRI with contrast of the right thigh T2 coronal plane showing a mass involving the posterior compartment measuring 30 cm x 20 cm x 16 cm englobing the sciatic nerve

The surgery was done starting with wide excision of the right thigh mass for which: first, an anteromedial thigh incision was performed; secondly, a complete dissection of the femoral artery, vein, and nerve from the mass was done; third, the sartorius muscle was preserved, fourth, a complete dissection of the mass with a safety margin about 2 to 3 cm surrounding the tumour was done, and lastly, the sciatic nerve was engulfed inside the tumour. The scarification of the sciatic nerve was proximally and distally about 20 cm of its length. The complete dissection of a large mass was size 30 cm by 15 cm by 10 cm (Figure 8). Later, the excised tumour was sent for a histopathological assessment that showed high-grade spindle cell sarcoma compatible with a high-grade malignant peripheral nerve sheath tumour.



**Figure (8):** Soft tissue mass post resection from right thigh measuring 30x20x16 cm.

#### **Declaration of patient consent:**

An approval of the study was obtained from Saudi German Hospital, Jeddah (Saudi Arabia) Academic and Ethical Committee. The patient was informed that the case would be published as case report and this was accepted. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

#### **DISCUSSION**

Peripheral nerve tumours are unusual conditions that arise from the nerve sheath, which originates from the neural crest and neurectoderm. Malignant peripheral nerve sheath tumour is less common, but it can happen to people. It accounts for 5% to 10% of all tissue sarcoma. Additionally, 50% to 60% of the patient with the condition are connected to neurofibromatosis type 1 (NF1), while others are sporadic or radiation-induced. MPNST manifest as badly aggressive and associated with a high local recurrence rate and meagre survival. Systemic chemotherapy and radiation are used for MPNST patients, but resection surgery is the primary therapy used as it is more effective. In addition, radical therapy surgery is combined with adjuvant therapy. The prognosis of MPNST remains poor, with five years overall survival rate of 15% to 66%, five years local recurrence rate of 20% to 85.7%, five-year event-free survival of 25 to 53% <sup>(3)</sup>.

Nerve sheath tumours are mostly diagnosed through medical imaging, including ultrasound, MRI, and positron emission tomography (PET) scans to see cancer. A biopsy is done to identify the kind of cells in the tumour to determine whether it is cancerous. The general complication can be scarring, pain, local

infection, and bleeding. In some instances, the surgery involving the nerves can damage the nerve and cause permanent disability; thus, the multidisciplinary team works with the patient after surgery to manage ongoing disability challenges. Different types of therapy, including occupational, physical, and speech, may help the patient regain function <sup>(4)</sup>.

An earlier study showed that MPNST incidence is 1.46 per million person-years and is more prevalent among the elderly. It is higher in post-pubertal children around 10 to 19 years. Also, the incidence among the pediatric population was 0.56 million person-years <sup>(5)</sup>. MPNST is a rare sarcoma type amounting to 5% to 10% of sarcoma cases. It is common in young and middle-aged adults. It is also more prevalent in people with a genetic condition known as neurofibromatosis type 1 (NF1). It is generally reported that about 8% to 13% of people with NF1 will get MPNST in their lifetime <sup>(6)</sup>. Another recent piece of literature approximates MPNST cases to be about 20% of the pediatric population. Tumours occur primarily among adults between 20 and 60 years. Approximately 45% of MPNST happen sporadically with unidentified genetic anomalies, and the other 10% of cases are iatrogenically congenital anomalies <sup>(7)</sup>.

The genotypic hallmark of NF1 encompasses mutations to or other loss of the 350 kilobase gene NF1 on the chromosome 17 long arm. This cytoplasmic protein possesses a guanosine triphosphatase (GTPase) associated protein-related domain that inhibits the RAS proto-oncogene activity by catalyzing the conversion of active RAS-GTP to its inactive GDP bound conformation. The consequent molecular path from neurofibroma to MPNST in NF1 syndrome is indeterminate. However, NF1 deficiency is insufficient because only approximately 10% of all NF1 patients eventually develop MPNST <sup>(2)</sup>.

The clinical presentation of MPNST shows that the symptoms and signs of peripheral nerve tumours are caused by direct nerve invasion, mass effect, or involvement of surrounding tissues. For instance in the scenario, the clinical examination showed that the swelling was about 20 cm in 10 cm diffuse fusiform swelling, with tense stretched skin over cystic to a firm consistency. There is no specific clinical presentation of peripheral nerve or a suggestive tumour except for schwannomatosis and neurofibromatosis type 1 and type 2. The symptoms of nerve sheath tumours include muscle weakness, tingling feeling, lump or mass under their skin that may be painful when pressed, numbness, and pain that is aching, sharp, or burning. MPNST can occur anywhere in the body, but the most vulnerable places are the legs, arms, and the trunk. Although the cause of the condition is not well known, clinicians know that it begins when the cell in the protective lining around the nerve mutates in its DNA <sup>(1)</sup>.

The risk factors that increase the chances of getting MPNST include previous radiation cancer therapy, noncancerous nerve tumours, and an inherited

condition that increases the risk of nerve tumours. If an area is treated with radiation for 10 to 20 years, the person may develop a sheath tumour in that area. They can also develop from noncancerous or benign nerve tumours like neurofibroma. It further occurs more frequently in people with neurofibromatosis 1 <sup>(1)</sup>.

A patient undergoes tests to diagnose malignant peripheral nerve sheath tumours, including blood tests, ultrasound, biopsy, MRI, CT, and X-rays <sup>(8)</sup>. For instance, an outpatient has undergone a biopsy, MRI, and CT scans. Blood tests are used to determine whether a benign tumour is cancerous. People with neurofibromatosis type 1 usually develop noncancerous tumours growing along the nerves. However, a doctor cannot determine whether the transformation to cancer has occurred. National cancer institute's researchers, in collaboration with the Washington University School and part of the National Institute of Health, have developed blood tests believed to be highly inexpensive and sensitive to detect cancer early in people with NF1 <sup>(9)</sup>. In addition, blood tests can help clinicians monitor the patient to determine the patient's response after the cancer treatment <sup>(10)</sup>.

On the other hand, nerve ultrasound can visualise the extensive mass growth of a tumour non-invasively. Furthermore, it effectively monitors stable disease and detects sub-clinical nerve involvement, avoiding overwhelming MRI acquisition. The method is effective because it sees sonomorphological patterns, including tumour mass and load, which plays a significant role as a prognostic marker concerning MPNST. Nevertheless, if nerve growth is revealed by ultrasound, it might be challenging to distinguish between benign mass and malignant transformation. Thus, MRI or CT scans can be used <sup>(11)</sup>.

Four MRI features help distinguish an MPNST from neurofibromas. They include the presence of an enhanced peripheral pattern, the increased largest dimension of the mass, the presence of an intratumoral cystic lesion, and the presence of a perilesional oedema-like zone. It is also effective for cases connected to heterogeneity on the weighted images. From the current case the first MRI examination with contrast, showed a 20 cm swelling on the medial side of the thigh with possible sarcomatous changes. After the mass had grown for three weeks, the MRI scan showed that the mass was then 30 cm by 15 cm with the engulfed sciatic nerve. From the gross picture, the mass weighed 5.5 kg and was measured 30x20x17 cm surrounded by the muscular tissue. Researchers have noticed these factors, although many patients with malignant peripheral nerve sheath have rare soft-tissue sarcoma <sup>(12)</sup>. CT scans apply standardised uptake values (SUVs) tumour-to-liver ratios as semi-quantitative metabolic imaging markers, and it has been used as a diagnostic tool for MPNST. However, there are variations in scanning tools; thus, there are variations in the literature regarding the CT scan tool <sup>(13)</sup>.

Radiological features have various aspects, including size, boundary, relation with adjacent tissue, signal or density, and enhancement. The average length of MPNST is usually above 5 cm and more extensive than benign peripheral nerve sheath tumours (BPNST). For example, from the scenario, the complete dissection of a large mass was size 30 cm by 15 cm by 10 cm. The boundary usually is unclear because MPNST can infiltrate the surrounding soft tissue and cause peritumoral oedema. The benign neurogenic tumour is surrounded by a capsule and tends to be well defined<sup>(13)</sup>. MPNST may be well margined when it grows deeply. The spilt-fat emblem is often seen in benign neurogenic tumours. In the scenario, the patient's details of scans, including the subcutaneous tissue, were not included because it was easy to identify the condition after all examinations.

MPNST signals can become a diagnostic indicator through the presence of T1W1 MRI images. There are different types of signals, including single or multiple cystic appearances, target signs, and homogenous signals. MPNST typically shows in homogenous signal mainly in the NF1 context. MPNST indicates a poor prognosis due to the malignance nature of that sign. Peripheral high signal and central low signal on T2W1 is a neurogenic tumour feature sign. It is attributed to peripheral myxomatous tissue and central fibro collagenous tissue. It is uncommonly seen in MPNST. In the scenario, this feature is not captured because it is rare, and thus it does not matter. Intratumoral lobulation can also be detected in MPNST, initiated by a network-line growth of plexiform neurofibromas, which encompasses multiple fascicles and nerve branches, causing a diffuse thickened nerve mass. The enhancement is seen in contrast showing peripheral enhancement on contrast-enhanced T1 weighted images<sup>(14)</sup>. The MRI scan differs in our clinical scenario to enhance the image. It also has a significant effect on the image to improve the review.

As in the scenario, primarily MPNSTs are treated through surgery, but other methods like chemotherapy and other therapies are applied. The patient in the scenario was prepared for the surgery because it was the most effective treatment. The clinicians ensure that they routinely monitor the nerve sheath tumours to reveal whether it is growing or changing. For instance, the patient was prepared for surgery in the clinical scenario. After three weeks, the tumour had increased its mass, and thus surgery had to be done immediately because it would possibly have continued growing. Surgery is mostly the only option if the patient wants the tumour removed for cosmetic reasons, primarily for symptomatic tumours. Some neurofibromas, primarily plexiform neurofibromas, are challenging to remove because they grow between the insulation layers and into the nerve. The healthcare team monitor a patient closely if the surgery results in incomplete removal because it can come back<sup>(4)</sup>.

Surgical management is essential in the treatment of MPNST. MPNSTs should be removed once there are clear margins to optimise survival and minimise local recurrence rates. Nerve-sparing surgery can facilitate the excision of atypical, conventional, and contrarily neurofibromas. Therefore, it is essential to have an accurate diagnosis before surgically excising a nerve sheath tumour in NF1 patients since it can lead to function loss that can graduate in a lifetime disability<sup>(8)</sup>. Sometimes resection of functional nerves might be inevitable, especially for pediatric patients. Reconstructions are purposed to restore lost function, although surgeons are primarily resistant to performing such operations since the outcome of reconstructions is sometimes questionable<sup>(8)</sup>.

On the other hand, radiotherapy and chemotherapy have good functional outcomes; therefore, doctors are not resistant to operating, including nerve reconstructions. Radiotherapy in MPNST patients is controversial, especially for pediatric patients. It has light potential side effects compared to surgery. It is administered to increase local MPNST local control, but it has not improved overall survival as in surgical methods. Radiation treatment is known to stunt tissue growth, and a reduced dose may be beneficial in decreasing side effects. Based on the evidence of various studies, clinicians are advised to apply radiation in pediatric MPNST. Chemotherapy has a limited role in MPNST, primarily in NF1-associated MPNST and has not yet been fully established. In a scenario where MPNST is estimated in negative margins, surgery alone cannot achieve desired outcomes, and radiotherapy and adjuvant chemotherapy are applied<sup>(15)</sup>.

There are various nerve sheath tumours, including schwannomas and neurofibromas<sup>(4)</sup>. Schwann cells serve as the primary glial cells of the peripheral nervous system. Every Schwann cell develops a single myelin sheath on the peripheral axon, each myelin sheath constituted by various Schwann cells. Schwannoma is an uncommon tumour type that forms in the nervous system. It grows from Schwann cells. Such tumours are often benign, meaning they are not cancer, although they develop into cancer in rare cases. Just like MPNST, schwannoma is a rare disease, and thus it affects less than 200,000 people<sup>(6)</sup>. It is the most common type of peripheral nerve tumour in adults.

Neurofibromas are tumours involving several nerve sheath tissue types, including endoneurium, Schwann cells, and perineurium. They usually appear under the skin as nodules or masses but can also impact deeper nerves. The tumours are not contained or encapsulated like schwannomas and penetrate between nerve bundles. Plexiform neurofibromas are web-like and surround multiple nerve bundles extending to nearby tissues. Like peripheral nerve sheath tumours, neurofibromas are noncancerous. But in some rare conditions, they can also grow into cancerous mass. Approximately 5% to 10% of tumours develop into

cancer that becomes malignant peripheral nerve sheath tumours. Neurofibromas and malignant peripheral nerve sheath tumours have similar symptoms in most cases, and therefore the doctors must run some tests to differentiate between the two conditions. Thus, misdiagnosis can harm patients diagnosed with neurofibromas instead of malignant peripheral nerve sheath tumours<sup>(4)</sup>.

## CONCLUSION

Malignant peripheral nerve sheath tumours are rare conditions that are more prevalent among young and middle-aged adults. The state also affects some people in the pediatric population. The tumour might grow in any place in the body, but they are more frequent in the legs, arms, and the trunk. Patients with MPNST have included blood tests, ultrasound scans, biopsy, MRI scans, CT scans, and X-rays as the tools for identifying a tumour. MPNST is a cancer type that occurs in the lining of the nerves that spread out from the spinal cord into the body.

There is usually a poor MPNST prognosis, so the doctors must be sure about the diagnosis before treating the condition. Typically, there are three ways to treat MPNST: surgery, chemotherapy and radiotherapy. Nevertheless, surgeries are more frequently used to treat the disease. However, surgeries can cause adverse side effects; thus, the clinicians must follow up the patient after the procedures. On the other hand, chemotherapy and radiotherapy are less effective. In addition, a multidisciplinary team including a radiologist, histopathologist, and orthopedic surgeon are consulted. At some point, an oncologist may be involved to advise on cancerous tumours.

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