

# Metastatic malignant peripheral nerve sheath tumor in neurofibromatosis Type 1: a geriatric patient report

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**Abstract.** – Neurofibromatosis type 1 (NF1) (von Recklinghausen disease) is an autosomal dominantly inherited neurocutaneous disorder which affects many systems like ocular, cutaneous and nervous systems and seen in 1:3500 births. Cardinal diagnostic criteria of NF1 were established in 1987 by National Institutes of Health Consensus.

Early diagnosis and the findings of NF1 are unclear in childhood, but with age the clinical symptoms become apparent. NF1 is occasionally associated with mental retardation.

In this report, together a review of the literature, we present a quite elderly patient, 79-year-old-man, with NF1 suffering from metastatic malignant peripheral nerve sheath tumor in the axillary lymph node invading the brachial plexus and pleura. Moreover, this enormous metastatic mass had restricted movement of the extremity. He had multiple neurofibromas of different sizes almost covering his entire body, massively. To the best of our knowledge, our patient's malignant peripheral nerve sheath tumor and massive neurofibromatosis is a rare case to present in the eighth decade of life.

*Key Words:*

Neurofibromatosis type 1, Malign peripheral nerve sheath tumor, Geriatric.

## Introduction

Neurofibromatosis (NF) is an autosomal dominantly inherited neurocutaneous disorder which affects many systems like the ocular, cutaneous and nervous systems<sup>1</sup>. It was first published by Friedrich Daniel von Recklinghausen<sup>2</sup>. There are two major forms of neurofibromatosis: Neurofibromatosis type 1 (NF1, Von Recklinghausen disease)<sup>3</sup> and Neurofibromatosis type 2 (NF2, central form). It was shown that NF1 occurred as a result of a defect in 17<sup>th</sup> chromosome and NF2 occurred as a result of a defect in 22<sup>nd</sup> chromo-

some<sup>4</sup>. NF is seen in 1:3500 births<sup>3,4</sup>. Its clinical features begin to present during childhood and could be aggravated by puberty and pregnancy. Symptoms of NF1 are often unclear in early childhood, making diagnosis difficult, but with age the clinical symptoms become apparent<sup>5</sup>.

Malignant peripheral nerve sheath tumor (MPNST), malignant schwannoma, neurogenic sarcoma, or neurofibrosarcoma, is observed in 2-5% of NF1 patients with plexiform neurofibromas<sup>6</sup>. MPNST is a sporadic complication of NF1<sup>7</sup>.

In this report we present a quite elderly patient with NF1 suffering from metastatic malignant peripheral nerve sheath tumor in the axillary lymph node invading the brachial plexus and pleura. Moreover, this enormous metastatic mass had restricted movement of the extremity. We also present a review of the literature.

## Case

A 79-year-old-man presented to our Clinic with the complaint of a nonhealing and frequently bleeding wound on his left arm. He also had a painful swelling in his axilla, restricting his arm movements. He had multiple nodular masses of different sizes almost covering his entire body.

These masses were initially seen in the head, neck, and upper extremities when he was 9-10 years old, according to history taken from the patient and his first-degree relatives. None of his close relatives had the same signs and symptoms. The masses were stalky in certain places, with a soft consistency and diameters ranging from 1 to 10 cm. The masses were more common along the trunk and the neck, while they were somewhat fewer in the lower extremities and below the knees (Figure 1a, b). On the left forearm, 5 cm distally to the elbow joint, there was a 10×12×7 cm ulcerated, bleeding mass that was fixed at the base for 2 years (Figure 2).



**Figure 1. A, B,** Neurofibromas starting from head and neck to trunk and lower extremities that decreasing partially less below the knees.

In the physical examination, we palpated in his left axilla a hard, irregular mass of approximately 15 × 15 cm fixed at the base. Eye consultation revealed numerous Lisch nodules on the iris bilaterally. Thorax computerized tomography (CT) findings showed an irregular, fixed, nodular mass of 13 × 17 cm localized in the axillar region invading the pleura. In his cranial, abdomen and neck CTs, no other pathology was detected. Neck and abdomen ultrasonography couldn't be performed due to the extensive skin involvement.

The patient was operated on under general anesthesia. The mass on the left forearm was excised along the security border, then the defect was repaired with a split-thickness skin graft taken from the lateral side of the thigh. Left axillary dissection was done and the mass in the axilla was excised after the dissection around the nerve sheath (Figure 3). The affected side of the chest wall and pleura were resected. Then a hemovac drain was placed into the left axillar fossa and sutured primarily.

In the pathologic analysis, we detected a malignant peripheral nerve sheath tumor (MPNST)



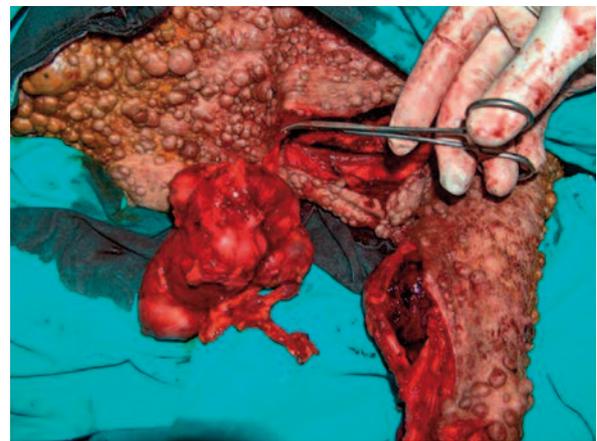
**Figure 2.** Bleeding and ulcerated mass fixed to the base on the left forearm.

in the neighborhood of the neurofibroma by dyeing the tumoral mass on the forearm with hematoxylin-eosin (HE) and examining it under microscopic with a 40 × magnification (Figure 4).

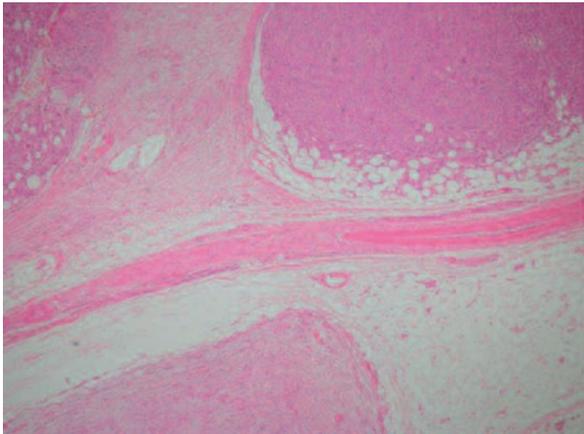
The microscopic investigation with a 400 × magnification of the prepartate of the metastatic axillary mass, dyed with HE, showed presence of mitotic cell dominance, including some pleomorphic malignant spindle cell proliferation (Figure 5). Under microscopic investigation of the same prepartate with the same magnification and dyed with S-100, a scattered positive stain uptake in the cells with S-100 antibody was detected (Figure 6).

## Discussion

Neurofibromatosis (NF) is a well-documented hereditary disease characterized by multiple

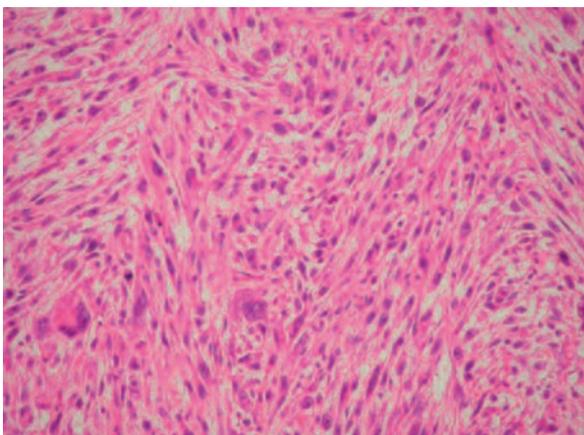


**Figure 3.** Left axillary metastatic mass was dissected from the brachial plexus.

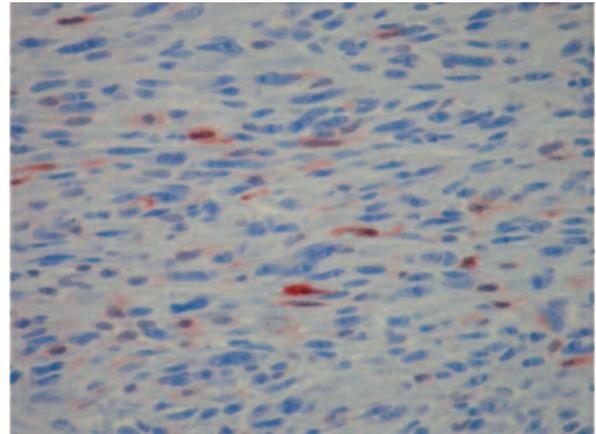


**Figure 4.** HE  $\times$  40. MPNST at the neighborhood of neurofibrom.

café-au-lait macules, multiple peripheral neurofibromas, axillary or inguinal freckling, optic gliomas, Lisch nodules and a first-degree relative with NF1<sup>1,7</sup>. Cardinal diagnostic criteria of NF1, both specific and sensitive, in adults were established in 1987 by National Institutes of Health Consensus<sup>3</sup>. Since some of these criteria could be unclear in childhood, especially under eight years of age, delayed diagnosis may manifest later in life<sup>1,3,5</sup>. Skin pigmentation (café-au-lait spots) may have been present since birth or early childhood<sup>8</sup>. In this case, the patient was diagnosed at approximately 10 years of age. Initial symptoms were cutaneous neurofibroma, starting from the head and spreading to the whole body, and continuing to increase in size and number throughout adulthood.



**Figure 5.** (Axillary metastatic mass) Mitotic cell dominance including some pleomorphic malignant spindle cell proliferation. HE  $\times$  400.



**Figure 6.** A scattered positive stain uptake in the cells with S-100 antibody was detected.

Lammert et al<sup>9</sup> found a statistically significant inverse relationship between the number of neurofibromas and serum 25-OH vitamin D concentration. In our patient, nearly the whole body was covered with neurofibromas, but the serum level of vitamin D was normal.

The NF1 gene provides instructions for making a protein called neurofibromin on the 17<sup>th</sup> chromosome<sup>3,9</sup>. This protein is a tumor suppressor in keratinocytes and melanocytes<sup>10</sup>. We didn't investigate neurofibromin level in this patient. NF1 is occasionally associated with mental retardation. Patients with NF1 may have growth anomalous or neurologic development disorders. Also, there's a significant tendency to development of tumor formation in this population that should be monitored carefully. Mental retardation and motor deficiency which may be a geriatric symptom were detected in his examination.

Malignant peripheral nerve sheath tumor (MPNST, malignant schwannoma, neurogenic sarcoma, neurofibrosarcoma) derives from the Schwann cells of peripheral nerves, and can spread by perineural invasion or hematogenously. Radiation therapy could delay recurrence of MPNST, but long-term survival results are not greatly improved<sup>11</sup>.

In our patient, as a complication of NF1, there was an axillary lymph node metastasis invading the brachial plexus and pleura. Patients with neurofibromatosis need careful follow up because of the possibility of hidden carcinomas underneath the neurofibromas. Moreover, the most important factor in preventing serious complications of NF1 is early diagnosis in childhood.

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