Journal of Integrative Oncology
ISSN: 2329-6771

Elm'hadi et al., J Integr Oncol 2016, 5:2
DOI: 10.4172/2329-6771.1000170

Case Report Open Access

A Huge Malignant Peripheral Nerve Sheath Tumor Revealing Von Recklinghausen's Disease

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Abstract

Only a few cases of malignant peripheral nerve sheath tumor (MPNST) associated with Von Recklinghausen's disease or type I neurofibromatosis (NF-1) have so far been reported worldwide. We present a case of a 27 year old man with MPNST of the left thigh associated with NF-1. The diagnosis was based on clinical, radiological and histopathological evidence. He presented a large mass of thigh, deeply adhering, with the presence of collateral venous circulation. He also presented multiple café-au-lait spots, with a many neurofibromas. MRI of the hip and left thigh showed the presence of a bulky tissue process, badly limited, measuring 24,6×11×12 cm occupying the anterolateral and posterolateral lodge with an intermediate signal in T1, discreetly more intense in T2. The microscopic and immunohistochemical findings supported the final diagnosis of MPNST with mesenchymal differentiation. The staging was negative. Also, the diagnosis of NF-1 is held according to the presence of two NIH criteria. The decision of the multidisciplinary meeting was to make a neoadjuvant chemotherapy to surgery with a doublet of adriamycin and ifosfamide with surveillance for other tumor development or multisystem complications. The presence of a large mass on the path of a peripheral nerve requires a careful examination of the skin for signs evoking a von Recklinghausen disease.

Keywords: Malignant peripheral nerve sheath tumor; Neurofibromatosis; Von Recklinghausen's disease

Abbreviations: NF1: Neurofibromatosis 1; MPNST: Malignant Peripheral Nerve Sheath Tumor; NIH: National Institutes of Health; EMA: Epithelial Membrane Antigen; MRI: Magnetic Resonance Imaging; CT: Computer Tomography; Who: World Health Organization

Introduction

Neurofibromatosis 1 (NF1) or von Recklinghausen's disease is a genetic disease characterized by a high variability of clinical expression. Diagnosis is usually clinical. Malignant transformation is rare and dreadful. We present a case revealed by a huge malignant peripheral nerve heath tumor revealing von Recklinghausen's disease.

Case Report

We present a case of a Moroccan 27 year old men, with no particular history which reports the appearance a mass of the upper and outer of the left thigh gradually increasing volume. No family or personal histories of neurological, musculoskeletal, dermatological or visual disease were noted. On medical examination, the patient has café au lait spots in different sizes and shapes on all over the body accentuated in the trunk (Figure 1) with the presence of many neurofibromas in the dorsal trunk and roots of members. The mass of thigh was large, hard, deeply adhering, with the presence of collateral venous circulation (Figure 2). Blood pressure was 110/70 mmhg. The patient does not present cognitive impairment, focal neurological deficits or skeletal anomalies and visual acuity and fundus were normal. A biopsy of the mass of thigh was performed, histological examination has shown a very dense population of atypical spindle cells with wavy, hyperchromatic nuclei and high mitotic activity with Alternating hypercellular/ hypocellular region. The results of immunohistochemical staining showed positivity for S-100 protein, CD-34, EMA, actine muscle lisse ,neutofilament, desmine, myogene and Ki-67 for 30%. The microscopic and immunohistochemical findings supported the final diagnosis of MPNST with mesenchyme differentiation. Meanwhile, The diagnosis of neurofibromatosis type I is held according to the presence of two of National institutes of health (NIH) Consensus Development Conference criteria:1) Six or more café au lait macules larger than 1.5 cm in post pubertal individuals 2)Two or more neurofibromas of any type . MRI of the hip and left thigh showed the presence of a bulky tissue process, badly limited, measuring 24,6×11×12 cm occupying the anterolateral and poster lateral lodge with an intermediate signal in T1, discreetly more intense in T2, encompassing deep vascular pedicle with multiple hypo intense areas in enhancement after gadolinium injection

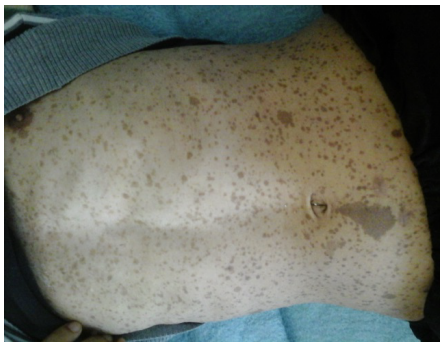

Figure 1: Café au lait spots in different sizes and shapes in the trunk.

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Received April 02, 2016; **Accepted** May 18, 2016; **Published** May 27, 2016

Citation: Elm'hadi C, Khmamouche MR, Toreis M, Tanz R, Mahfoud T, et al. (2016) A Huge Malignant Peripheral Nerve Sheath Tumor Revealing Von Recklinghausen's Disease. J Integr Oncol 5: 170. doi:10.4172/2329-6771.1000170

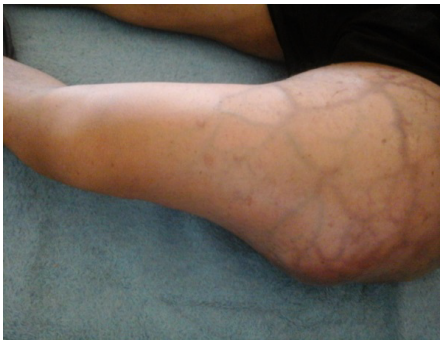

Figure 2: Large mass of thigh with the presence of collateral venous circulation.

showing a necrosis. The brain CT and thoraco-abdominal-pelvic showed no secondary location and not any deep neurofibroma. Bone scan showed fixing heterogeneous left femoral shaft. The decision of the multidisciplinary meeting was to make a neoadjuvant chemotherapy to surgery with a doublet of Adriamycin and ifosfamide with surveillance for other tumor development or multisystem complications.

Discussion

Malign Peripheral Nerve Sheath Tumors (or MPNST) are defined by the WHO classification in 2013 as developed malignancies [1] from a peripheral nerve; or a benign tumor of the nerve sheaths; or in a patient with neurofibromatosis type 1. These are a very rare tumor with approximately 5-10% of all soft tissue sarcomas [2]. The incidence in the general population is 0.001% and 5-10% of NF1 patients [3] often in a sporadic fashion and rarely radiation-induced. They usually appear between the third and fourth decade but earlier disclosure is particularly possible in NF1 patients [4]. The sex ratio is close to 1 with a slight female predominance [4].

Most MPNSTs develop mainly with peripheral nerves such as the sciatic nerve, the brachial plexus and the sacral plexus. They are usually deep-seated and often involving the proximal upper and lower extremities as well as the trunk [3]. The clinical expression is variable including radicular pain, parenthesis, motor weakness or enlarging palpable mass whose Rapid increasing should raise malignant degeneration of a neurofibroma often in the setting of NF1 [5].

Imaging studies have a dual purpose: to distinguish between benign tumors and MPNST and specify the local and general extension of these tumors. MRI is the imaging modality of choice for characterizing MPNST. These tumors share basic imaging characteristics with their benign counterparts such as neurofibromas and schwannomas they are distinguished by four 4 features: a size ≥ 5 cm; peripheral enhancement; edematous areas périlésionnelles; and cystic areas intratumoral (hemorrhages or necrosis) [6]. For patients with NF1: heterogeneity in T1 is also in favor of a malignant lesion.

MPNSTs are most likely to metastasize to the lungs, bone and the pleura. For this reason, a chest computed tomography scan is the preferred imaging study to screen for distant disease. A bone scan should also be obtained to help identify metastatic bone disease

The diagnosis of MPNST is provided by histology with very heterogeneous appearance because the cells have varying degrees of differentiation Schwann; fibroblast or périneuriale. Malignancy is suggested by features such as invasion of surrounding tissues, invasion of vascular structures, nuclear pleomorphism, necrosis, and mitotic activity [4]. Immunohistochemically, there are no specific markers MPNST. However more markers are often used to differentiate these tumors other differential diagnoses (melanoma, fibrosarcoma, synovial sarcoma monophasic, leiomyosarcoma or more rarely neurofibroma and schwannoma cell). The most frequently used markers are S-100 protein, Leu-7 and myelin basic protein. S-100 protein is the most widely used antigen for neural differentiation and can be identified in 50%. Leu-7 and myelin basic protein are found in about 50% and 40% of MPNSTs respectively [7]. Ki-67 greater than 20 has identified as being an independent prognostic factor [8].

NF-1 is one of the most fascinating and common autosomal dominant disorders, affecting one in 3,000 individuals. It is a multisystem complex disease, with patients having myriad of manifestations, including an increased prevalence of both benign and malignant neoplasms throughout the body [9].

Neurofibromatosis type 1 (NF-1) is diagnosed clinically based on the presence of two of the following seven criteria developed by a panel of experts in 1987 refined by a second conference in 1997 : at least five café-au-lait spots greater than 5 mm (six greater than 15 mm if prepubertal); two or more neurofibromas of any type or one plexiform; freckling in the axillary or inguinal regions; optic glioma; distinctive bony lesion such as sphenoid dysplasia, or thinning of the long bone cortex with or without pseudoarthrosis; Two or more iris hamartoma (Lisch nodules); A first-degree relative with NF 1 based on the above criteria [10].

Common genetic support involved in the genesis of these two diseases is the NF1 gene (located on the long arm of chromosome 17) encoding the "Neurofibromin" protein [11].

Other malignancies may be associated with NF 1 with a frequency of 3.6% to 4.6%. Apart from neurofibromas, other tumors such as pheochromocytoma, duodenal and ampullary carcinoid tumors, pancreatic adenocarcinoma, malignant schwannoma, gastrointestinal stromal tumors and sarcomas occur more commonly in NF-1 patients [12].

The therapeutic standard of locally advanced MPNST is the induction chemotherapy followed by eventually local therapy by surgery and /or radiotherapy if the response.

In all cases, the prognosis is poor with an overall 5-year survival of 25% in case of NF1 and 50% in case of isolated tumor [11]. Local recurrence is frequent and metastases (lung, liver, skin, bone) that appear within an average of 2 years. Patients with NF1 were previously thought to have a worse prognosis than did patients with sporadic MPNSTs [13].

Conclusion

The presence of a large mass on the path of a peripheral nerve requires a careful examination of the skin for signs evoking a von Recklinghausen disease.

Competing Interests

The authors declare that they have no competing interests.

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