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Case Report

Fibular Nerve Neurolymphomatosis as the Initial Presentation of Primary Diffuse Large B-Cell Lymphoma: A Rare Cause of Popliteal Fossa Mass

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Abstract

Neurolymphomatosis is a rare manifestation of lymphoma characterized by the infiltration of lymphocytes into the peripheral nervous system. It can manifest as an initial presentation or a recurrent event. This condition affects various peripheral nervous structures and can imitate unrelated nerve root pathologies or compressive mononeuropathy. Neurolymphomatosis predominantly occurs in malignant B-cell non-Hodgkin lymphomas.

Despite its aggressive and refractory nature, it is crucial to distinguish neurolymphomatosis from other neurological complications associated with lymphoma. Early diagnosis and prompt treatment are imperative for optimizing patient outcomes. In this scientific report, we present a case of primary neurolymphomatosis, where it was identified as the initial presentation of diffuse large B-cell lymphoma affecting the fibular nerve. The patient exhibited a mass in the right popliteal fossa. The diagnosis of neurolymphomatosis involving the right fibular nerve was established based on MRI findings and nerve biopsy results.

Keywords: *Diffuse Large B-Cell Lymphoma; Neurolymphomatosis; MRI; Biopsy; Fibular Nerve*

Introduction

Neurolymphomatosis, a rare manifestation observed in hematologic malignancies, is characterized by the infiltration of lymphocytes into the peripheral nervous system (PNS) [1,2]. It can manifest as an initial presentation or recur during the disease course. Existing literature reports involvement of various PNS components, including peripheral nerves, spinal nerve roots, nerve plexus, and cranial nerves [1,3]. Due to the variability of symptoms depending on the site of involvement, accurate diagnosis can be challenging for physicians. Therefore, it is crucial to distinguish neurolymphomatosis from other neurological complications associated with lymphoma, such as tumor mass-induced compressive neuropathy, paraneoplastic neuropathy, chemotherapy-induced toxic neuropathy, and radiation-induced neuropathy [1,4].

While neurolymphomatosis often results from systemic dissemination of lymphoma or direct extension of a contiguous lesion into the nerve (secondary neurolymphomatosis), it can also present as isolated involvement of the PNS by malignant lymphocytes at the initial presentation (primary neurolymphomatosis) [4,5]. Primary lymphoma of the fibular nerve, an exceedingly rare occurrence, has only been reported in a few cases [6-10]. Herein, we present an exceptional case of primary neurolymphomatosis, representing the initial manifestation of diffuse large B-cell lymphoma involving the fibular nerve, along with a concise review of the relevant literature.

Case Report

A 42-year-old male patient presented with a 12-month history of a gradually enlarging painful mass in the right popliteal area, accompanied by unintended weight loss of 30 pounds. He did not report fever or night sweats, and his past medical history and systematic review were unremarkable. Physical examination revealed two well-defined, firm masses in the popliteal fossa, firmly adhered to the deep plane, with no signs of superficial skin inflammation or lymphadenopathy. Further examination of the lower limb revealed restricted right knee extension with normal strength, weakness in right ankle dorsiflexion, and decreased sensation to light touch in the right lateral leg. Vascular evaluation showed normal pulses throughout both legs.

MRI of the right knee revealed two distinct fusiform masses on the posterior aspect of the knee, measuring 3.7 x 5 x 8.5 cm and 2 x 3.8 x 5 cm, respectively. These masses exhibited a fasciculated appearance and appeared isointense to skeletal muscle on T1-weighted images and hyperintense on T2-weighted images. After the administration of Gadolinium contrast, both masses demonstrated homogeneous enhancement. The first mass extended from the left lateral aspect of the popliteal fossa to the posterolateral part of the leg, while the second mass was located in the inferior-medial region of the lower third of the right thigh, approximately 1 cm from the popliteal fossa. These lesions were found to be contiguous with the fibular nerve. The second mass encased the popliteal artery and vein over a 180° angle, with the preservation of the fatty separation line. Initially, the mass was suspected to be a peripheral nerve sheath tumor, as it exerted a mild mass effect on adjacent muscles but showed no definite intramuscular extension. To obtain a definitive diagnosis, a selective biopsy of the peroneal nerve was performed, which revealed diffuse large B-cell lymphoma involving the peroneal nerve (Neurolymphomatosis) and the surrounding soft tissue. Immunohistochemical analysis showed strong positivity for CD20 markers, confirming the diagnosis of peripheral nerve diffuse large B-cell lymphoma. Subsequently, the patient was referred to the oncology department and underwent treatment with a chemotherapy regimen consisting of rituximab, cytoxan, hydroxydaunorubicin, oncovin, and prednisolone (R-CHOP), in addition to radiotherapy. Unfortunately, despite two months of treatment, the patient succumbed to the disease.

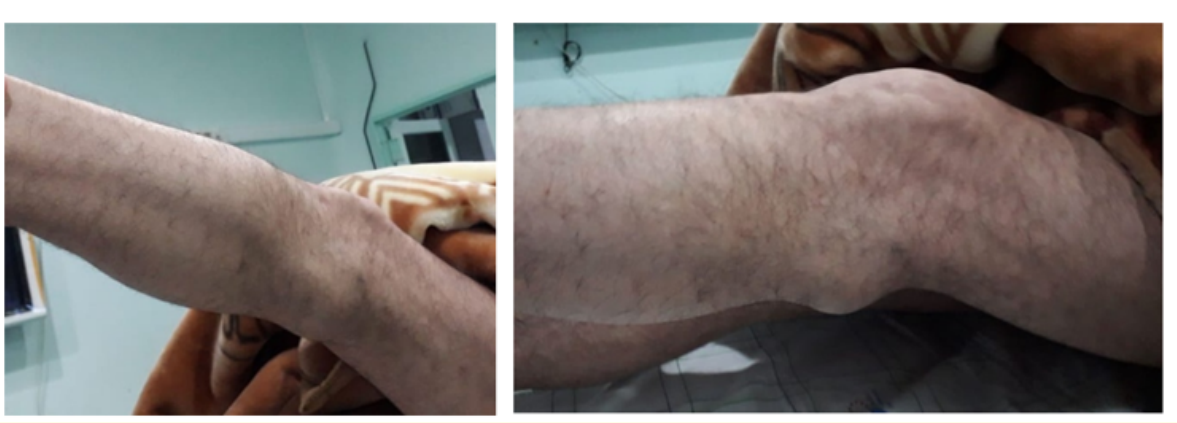

Figure 1: *Clinical findings: Two masses of right popliteal fossa.*

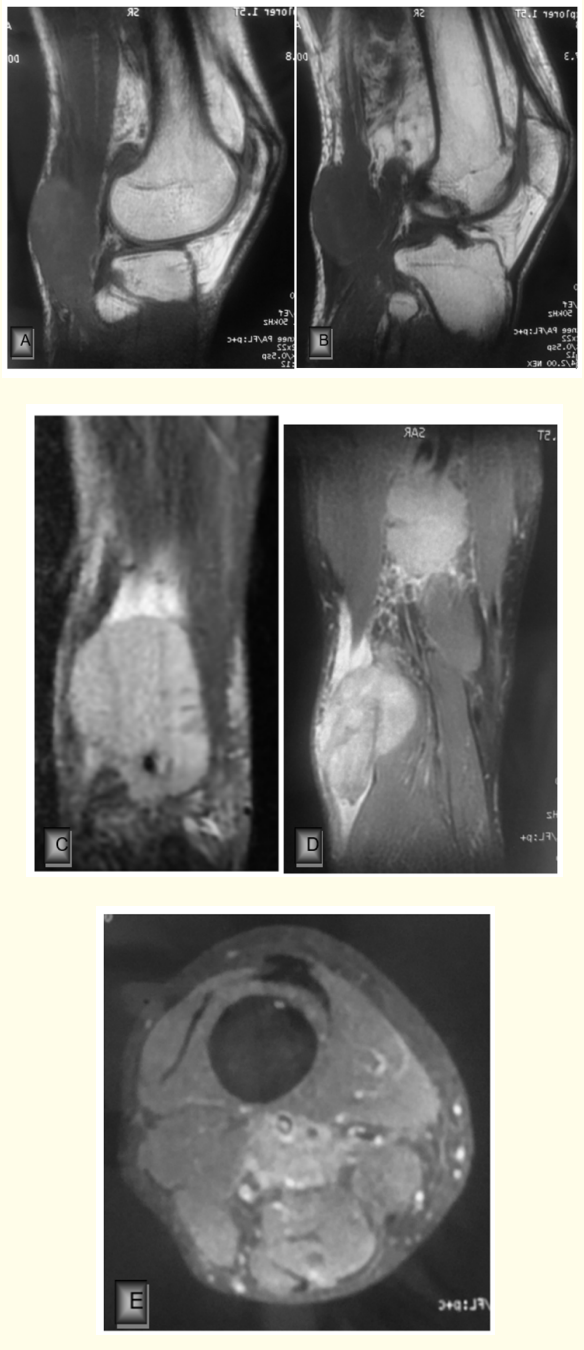

Figure 2: *MRI of the right knee (A, B: Sagittal T1 weighted images, C: Coronal T2 STIR image, D: Coronal T1 FAT SAT after injection of Gadolinium image, E: Axial T1 FAT SAT after injection of Gadolinium image), demonstrated two well defined fusiform masses on the posterior face of the right knee (the first at the left lateral extremity of the popliteal fossa extended to the posterolateral part of the leg: Figure A, and the second mass is located at the inferior-medial extremity of the lower third of the right thigh almost at 1 cm of the popliteal fossa : Figure B), with a fasciculated appearance, which were isointense to the skeletal muscle on T1 (Figure A and B), hyper-intense T2 STIR, homogeneously enhancing after injection of Gadolinium (Figure C and D).*

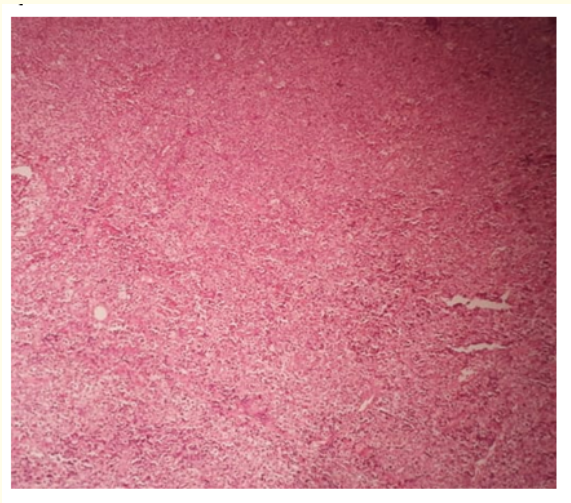

Figure 3: *Histopathologic findings of the Biopsied specimens showed Large, irregularly-shaped lymphoid cell proliferation with a diffuse pattern. These atypical lymphoid cells have a large nucleus with clear perinuclear space due to shrunken cytoplasm (hematoxylin and eosin stain, ×400).*

Figure 4: *Immunohistochemical stain shows large lymphoid cells that are positive for CD20.*

Discussion

Neurolymphomatosis is an infrequent and poorly understood entity that can manifest as an initial presentation or recurrence of lymphoma [1,4]. Initially described by Lhermitte and Trelles [1,11] in 1934, it involves the invasion of malignant lymphoid cells into peripheral nerves, roots, and cranial nerves. Peripheral nerves are affected in approximately 60% of cases, followed by spinal nerve roots (48%),

nerve plexus (40%), cranial nerves (46%), and various other locations (58%) [1,12]. The precise frequency of neurolymphomatosis remains unclear due to its rarity [12]. Studies conducted by the International Primary Central Nervous System Lymphoma Collaborative Group have reported that 26% to 29.5% of cases represent an initial presentation of systemic lymphoma, with variable peripheral nerve involvement ranging from 20% to 66% [1,12]. Peripheral nerve involvement in neurolymphomatosis can occur through either systemic dissemination of lymphoma or direct extension from a contiguous lesion [1,4]. Primary neurolymphomatosis with isolated peripheral nerve involvement at initial presentation is even rarer [1].

Neurolymphomatosis predominantly affects non-Hodgkin's lymphoma, with diffuse large B-cell lymphoma being the most common subtype, followed by follicular lymphoma [13]. The sciatic nerve is the most frequently involved site in primary neurolymphomatosis [1,6,13], although the underlying reasons for this predilection remain unknown [14]. Some hypotheses suggest that B-cells may either persist or originate within the sciatic nerve, potentially facilitated by specific cell adhesion molecules that have yet to be identified [15]. Additionally, rare cases have been reported involving the brachial plexus, ulnar, median, and radial nerves, as well as the sympathetic chain [13,14].

Clinical diagnosis of neurolymphomatosis can be challenging due to its varied symptoms, which depend on the specific sites involved. These symptoms encompass painful or painless mononeuropathy, painful radioculopathy, cranial neuropathy, and polyneuropathy [13]. However, some cases may present without symptoms. In our case, the patient presented with an unusual manifestation characterized by a painful mass in the popliteal fossa. Given the unclear clinical manifestations and the rarity of neurolymphomatosis, radiologic evaluation and histologic examination are crucial for accurate diagnosis and appropriate management, aiming to prevent complications and potential morbidity. Magnetic resonance imaging (MRI) is particularly valuable for differential diagnosis from other masses and for assessing the extent of the lesion. However, surgical biopsy of the affected structure remains the gold standard [13]. MRI typically reveals diffuse enlargement of the peripheral nerve with mass formation along its course, which may or may not exhibit contrast enhancement [13,16,17]. Dark spots interspersed within the mass on T2-weighted images have also been observed, although their underlying cause remains uncertain [16]. These imaging findings may be attributed to the characteristics of lymphoma, which tend to surround adjacent tissues and preserve the shape or contour of the involved structure, rather than infiltrating or destroying the tissue. Therefore, the presence of diffuse nerve enlargement, mass formation, relatively preserved nerve fascicles, and vascular structures are important imaging signs for distinguishing lymphoma from other conditions such as malignant peripheral nerve sheath tumors, which typically exhibit characteristic nerve architecture destruction and heterogeneous features [13,18].

Doppler ultrasound can serve as an initial diagnostic tool for neurolymphomatosis due to its non-invasiveness, ready availability, and absence of radiation exposure. Ultrasound examination reveals nerve thickening and increased vascularity on color Doppler images in cases of neurolymphomatosis [19-21]. In addition to providing prognostic information, ultrasound may aid in identifying an appropriate biopsy target [21].

Fluorodeoxyglucose-18 positron emission tomography/computed tomography (^{18}FDG-PET/CT) is a highly sensitive method for detecting neurolymphomatosis and evaluating the extent of the disease throughout the body. Approximately 91% to 100% of cases exhibit ^{18}FDG uptake within the peripheral nervous system [21]. On ^{18}FDG-PET, neurolymphomatosis typically presents as patchy linear intense ^{18}FDG uptake along the affected nerve, with the presence of nerve thickening and skip lesions [21]. MRI and PET/CT play pivotal roles in the diagnosis of neurolymphomatosis, with sensitivity rates of 87.5% and 100%, respectively [20,22].

Currently, there is no consensus on the imaging diagnosis of neurolymphomatosis. A nerve biopsy with histological confirmation is required for a definitive diagnosis. However, due to the risk of permanent neurological deficits, this procedure is not routinely performed on all patients with neurolymphomatosis [23]. Imaging, in conjunction with clinical, biochemical, and electrophysiological studies, plays a significant role in the evaluation of these patients [21,24].

Treatment approaches for neurolymphomatosis encompass systemic chemotherapy, intrathecal chemotherapy, and radiotherapy. Despite receiving treatment, the prognosis remains poor, likely due to the absence of a standardized treatment strategy [13,22].

Conclusion

Neurolymphomatosis should be in the differential diagnosis of any neuropathy, especially one that is painful and rapidly evolving in appropriate clinical settings. Radiological investigation plays a vital role, especially in cases where biopsy is difficult to perform or to avoid painful procedure.

Conflict of Interest

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Author's Contributions

All authors contributed to this work. All authors have read and approved the final version of the manuscript.

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