American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2019; 20: 1652-1658
DOI: 10.12659/AJCR.916961

Received: 2019.04.13
Accepted: 2019.08.19
Published: 2019.11.10

Secondary Neurolymphomatosis of the Radial Nerve: A Diagnostic Challenge

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Francesca Iacobellis*
ABCDEF 1 Marco Di Serafino*
BEF 2 Roberta Blasio
DEF 1 Luigi Barbuto
DEF 1 Filomena Pezzullo
ABDEFG 1 Luigia Romano

1 Department of General and Emergency Radiology, "A. Cardarelli" Hospital, Naples, Italy
2 Department of Radiology, University of Naples "Federico II", Naples, Italy

* Francesca Iacobellis and Marco Di Serafino contributed equally to this work

Corresponding Author: Francesca Iacobellis, e-mail: iacobellisf@gmail.com
Conflict of interest: None declared

Patient: Male, 55
Final Diagnosis: Neurolymphomatosis of the radial nerve
Symptoms: Pain and soft tissue mass on the right arm
Medication: —
Clinical Procedure: Diagnosis
Specialty: Radiology

Objective: Rare disease

Background: Secondary neurolymphomatosis is a rare clinical condition that may be observed in patients with hematologic malignancies. Clinical findings can overlap with other conditions. Diagnosis can be obtained by magnetic resonance imaging (MRI) and imaging with positron emission tomography (PET) and confirmed by biopsy.

Case Report: A 55-year-old male patient with known previous history of periocular non-Hodgkin's lymphoma mucosa-associated lymphoid tissue (MALT) type presented reporting he had a focal soft-tissue swelling mass on the external side of the right arm, suspected for lipoma. US, MRI, and FDG PET/CT were performed, revealing malignant imaging characteristics of the lesion, suspected to be a neurolymphoma. A biopsy confirmed the nature of the lesion. No further sites of malignancy were detected on whole-body PET/CT.

Conclusions: Lymphomatous involvement of peripheral nerves may clinically overlap with other, more common, benign conditions; therefore, although it is rarer, this diagnosis has to be considered in patients with a clinical history of hematologic malignancies.

MeSH Keywords: Fluorodeoxyglucose F18 • Lymphoma, Non-Hodgkin • Magnetic Resonance Imaging • Ultrasonography, Doppler

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/916961

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Secondary neurolymphomatosis (NL) is a rare clinical condition that may be observed in patients with hematologic malignancies, in which neoplastic cells invade the nerves and the nerve sheath. It can clinically overlap with other conditions such as lipoma or benign or malignant peripheral nerve sheath tumors (PNST). Thus, imaging features are crucial to correctly orient the diagnosis, especially in high-risk patients. The diagnosis can be based on ultrasound (US), further clarified by magnetic resonance imaging (MRI) and nuclear medicine imaging with positron emission tomography/computed tomography (PET/CT), and finally confirmed by biopsy. We describe an unusual case of a secondary NL of the right radial nerve, first diagnosed by US and MRI, further confirmed by nuclear medicine imaging performed with PET/CT, and finally confirmed by biopsy.

Case Report

Case presentation

A 55-year-old male patient presented reporting a soft mass on the external side of the right arm, gradually increasing in size in the last 3 months, and associated with pain radiating to the hand. The lesion was clinically suspected to be a lipoma because of its mobility, stiffness, and absence of abnormalities of the overlying skin. The patient had a past medical history of periocular NHL mucosa-associated lymphoid tissue (MALT) type diagnosed 22 months before (Figure 1), and successfully treated for 3 months with radiotherapy (Figure 2).

Case report

An US examination (Aplio500™ – Canon Medical Systems) of the right arm showed, at the axial and longitudinal B-mode scans, an oval hypoechoic mass developing along the radial nerve course and strictly connected to it, with high vascularity on color Doppler imaging (Figure 3). To better characterize the US features, an MRI examination was performed with a 1.5T scanner (SIGNA™ – GE Healthcare) and optimized protocol including FSE T2W sequences in the 3 planes, SE T1W and STIR sequences in axial and coronal plane, axial DWI with ADC map, and axial GRE 3D T1W Fat-Sat sequence after IV gadolinium administration (1.0 mmol/ml gadobutrol, Gadovist® – Bayer). MRI showed a homogeneous mass arising from the perineurium of the superficial branch of the right radial nerve, hyperintense in T2W sequences (Figure 4A), without fat components (Figure 4B, 4C), isointense to the muscle in T1W sequence (Figure 4D), with restricted diffusion (Figure 5) and high vascularity after intravenous administration of contrast medium (Figure 6). Due to these imaging features and to the patient's history, a secondary NL of the superficial branch of the radial nerve was suspected. Whole-body 18F-fluorodeoxyglucose (18F-FDG) PET/CT was performed, showing pathologically high metabolic activity of the lesion, with a specific uptake value (SUV) of 6.1 (Figure 7). Abnormal uptake was not observed in any other sites of the body. Finally, the biopsy confirmed the diagnosis of secondary NL.

Discussion

Secondary NL consists of the infiltration of the nerve and of the nerve sheath by neurotropic neoplastic cells in non-Hodgkin's lymphoma (NHL) or acute leukemia. It is a rare condition, estimated to occur in only about 0.2% of all NHL cases [1]. The pathophysiology is unclear, and it may present in the context of disease recurrence or as first presentation of a hematologic malignancy. NL can involve peripheral or cranial nerves, nerve roots, or nerve plexuses [2]. NL most commonly presents as progressive painful neuropathy or radiculopathy, but the clinical symptoms depend on the involved sites [3]. Diagnosis requires correlation of clinical and imaging findings, and final confirmation by biopsy of the involved structured [4]. Treatment options include systemic chemotherapy [1] but, currently, there is not a standard treatment for NL involving peripheral nerves, spinal nerve roots, and cranial nerves [5].

When a solitary nerve is involved, NL can clinically overlap benign clinical conditions such as lipoma. When the perineurium is involved, the differential diagnosis should consider benign (e.g., neurofibroma and schwannoma) or malignant (e.g., sarcomas) PNST [6].

US is often the first imaging modality used to evaluate a palpable soft-tissue mass. It allows the evaluation of the internal structure of the lesion and, in most cases, can establish the relationship with the peripheral nerve. The orientation of the lesion along the nerve, the state of nerve fascicles, and the tumor vascularity are features useful for differential diagnosis and treatment planning [7].

In our case, US showed a hypoechoic, highly vascularized mass, developing along the radial nerve course and strictly connected to it. The strict adherence of the lesion to the nerve, associated with neural enlargement and increased blood flow, reflect the infiltration and neovascularization of the nerve and suggestive a diagnosis of NL [8]. These peculiarities are crucial for the differential diagnosis between neurolymphoma and lipoma. Indeed, on US, lipomas appear elliptical or ovoid, well-defined, without signs of invasion of the adjacent structures, avascular, and compressible. The echogenicity may vary from hypoechoic to hyperechoic depending on the number of internal interfaces between fat and other connective elements – pure fat

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

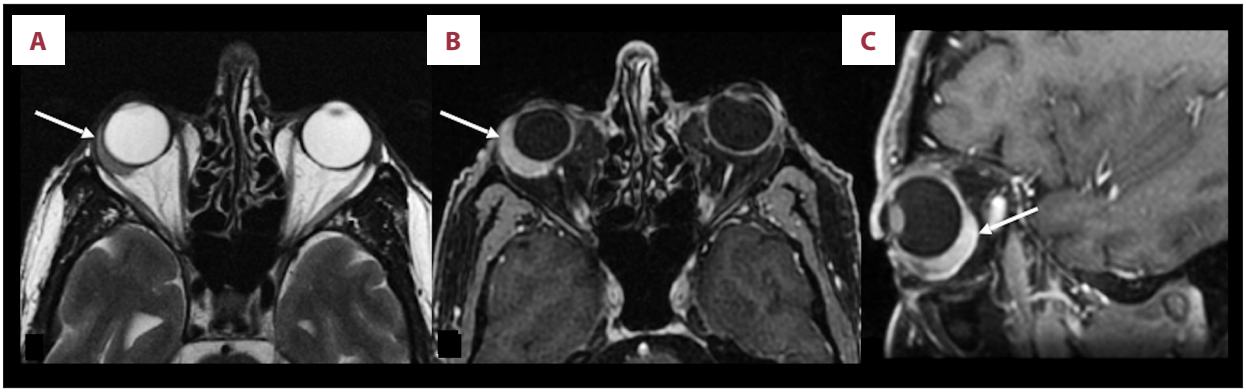

Figure 1. Orbital and ocular MRI: T2W axial (**A**) and T1W axial (**B**) and sagittal (**C**) sequences acquired after intravenous administration of contrast medium after clinical suspicion of intraorbital mass due to exophthalmos. The examination shows a periocular mass, with hypointense signal in T2W sequences, and high vascularity after intravenous administration of contrast medium (**A, B, C** arrows).

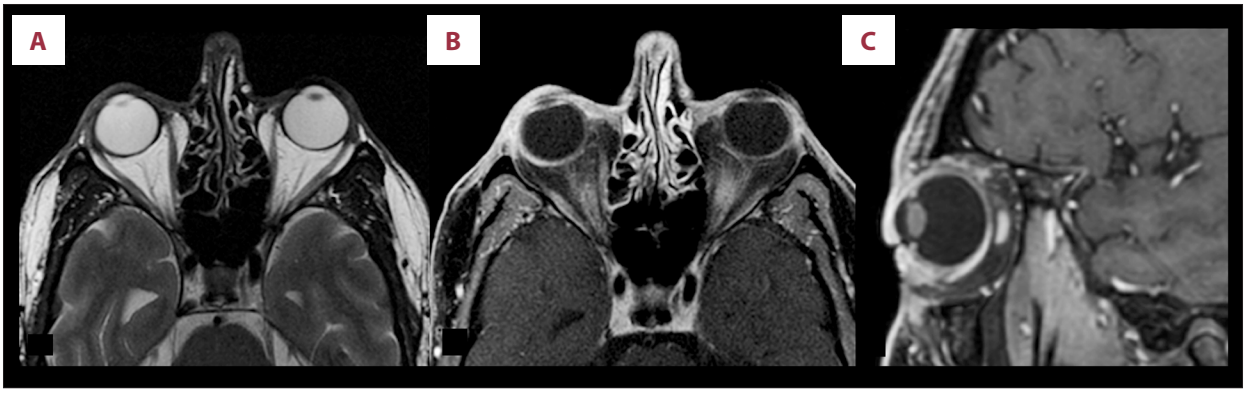

Figure 2. Orbital and ocular MRI: T2W axial (**A**) and T1W axial (**B**) and sagittal (**C**) sequences acquired after intravenous administration of contrast medium, after 3 months of radiotherapy, showing resolution of the mass in comparison with the previous examination (Figure 1).

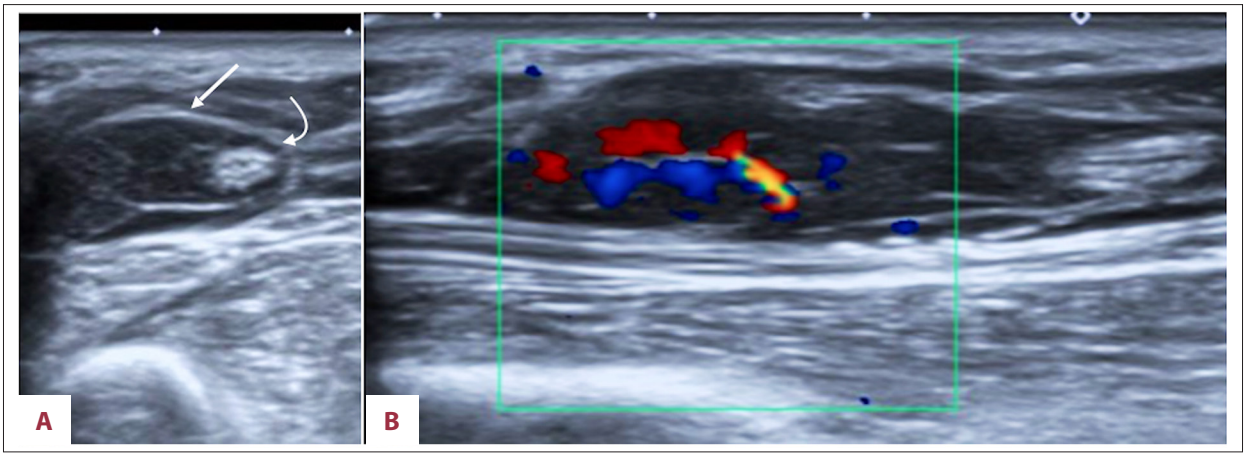

Figure 3. Right arm US shows an oval hypoechoic mass (**A,** straight arrow) surrounding the radial nerve (**A,** curved arrow), with high blood flow on color Doppler (**B**).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

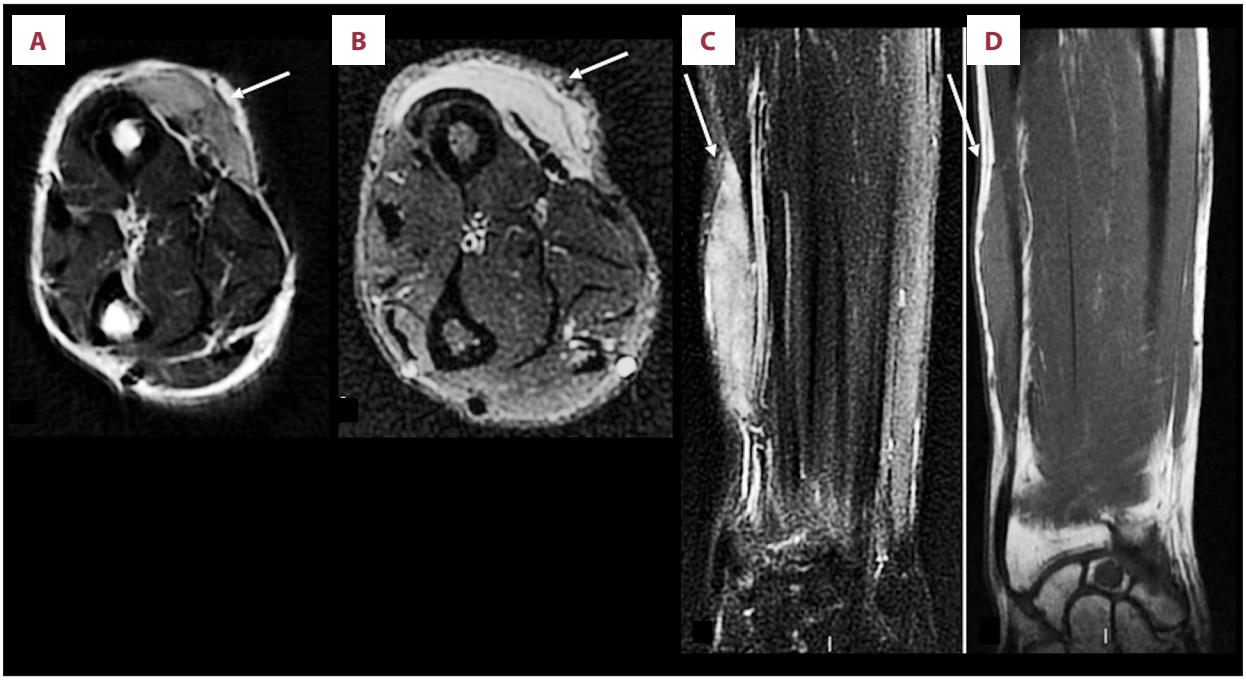

Figure 4. Right arm MRI: T2W axial (**A**), STIR axial (**B**), STIR coronal (**C**), T1W coronal (**D**) sequences show a homogeneous oval mass arising from the perineurium of the radial nerve, hyperintense in T2W and STIR sequences (due to the lack of fat components) and isointense to the muscle in T1W sequences (**A–D,** arrows).

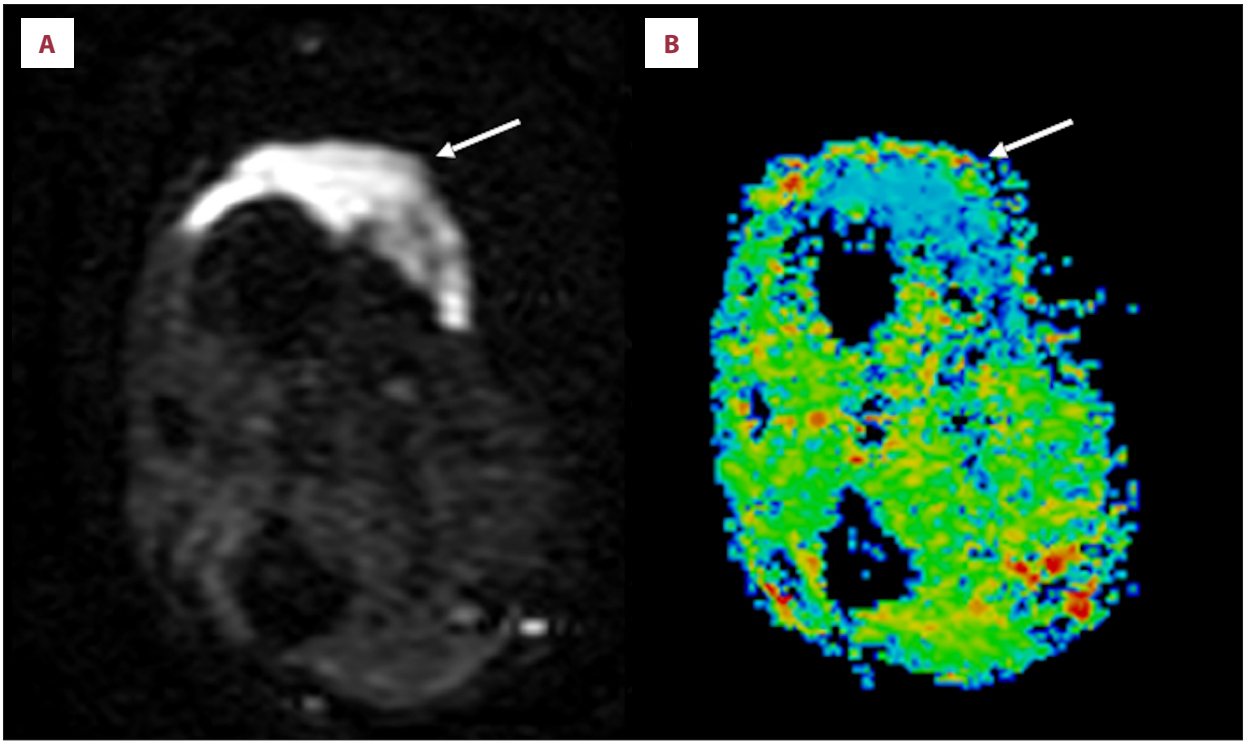

Figure 5. Right arm MRI: DWI axial sequence (**A**) and ADC color map (**B**) show restricted diffusion of the lesion, with hyperintensity in DWI sequence and hypointensity in ADC map, represented in blue in the color map (**A, B,** arrows).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

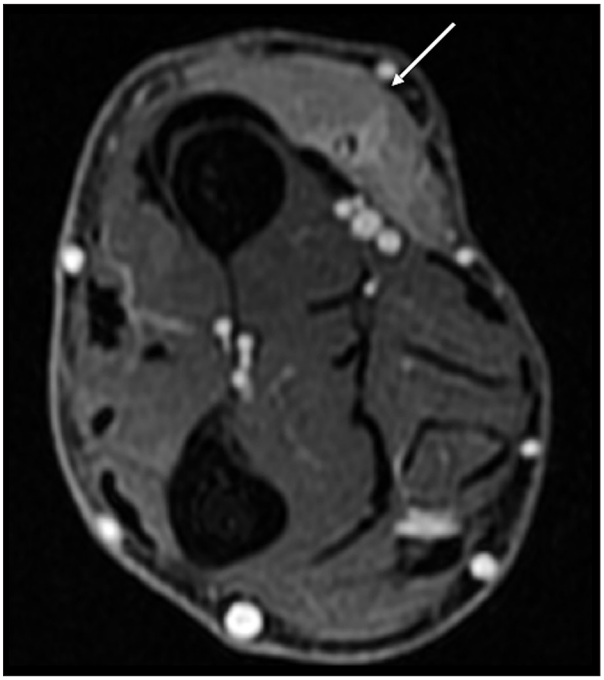

Figure 6. Right arm MRI: T1W GRE axial Fat-Sat sequences acquired after intravenous administration of contrast medium show a hyperintense lesion with high vascularity (arrow).

appears hypoechoic, whereas the presence of interspersed fibrous tissue creates a hyperechoic appearance [9]. Lipomas usually compress or displace adjacent structures, from which they can be easily dissected due to the presence of a good cleavage plane [10].

Benign PNSTs usually present on US as a homogeneous hypoechoic mass with posterior acoustic enhancement and peripheral nerve continuity [11]. Schwannomas usually manifest as small, spindle-shaped nodules with proximal and distal tail-like formations, developing eccentrically along the nerve long axis and displacing the fascicles. Neurofibromas present homogeneous, concentric, clearly-bordered, nodular lesions that do not displace the nerve fascicles. Malignant PNSTs grow along the nerve, similarly to benign PNST, and often present as fusiform inhomogeneous masses with areas of internal bleeding, necrosis, and calcifications, with an hypervascularization pattern on color Doppler US. Due to irregular thickening of the outer nerve sheath, some lesions show poorly defined margins or a pseudo-capsule [7].

The described US findings of NL match with those recently reported by Tai et al. [2], demonstrating the diagnostic role of US in this setting; however, even if US detects the lesion and identifies the nervous origin of the mass, US cannot definitively

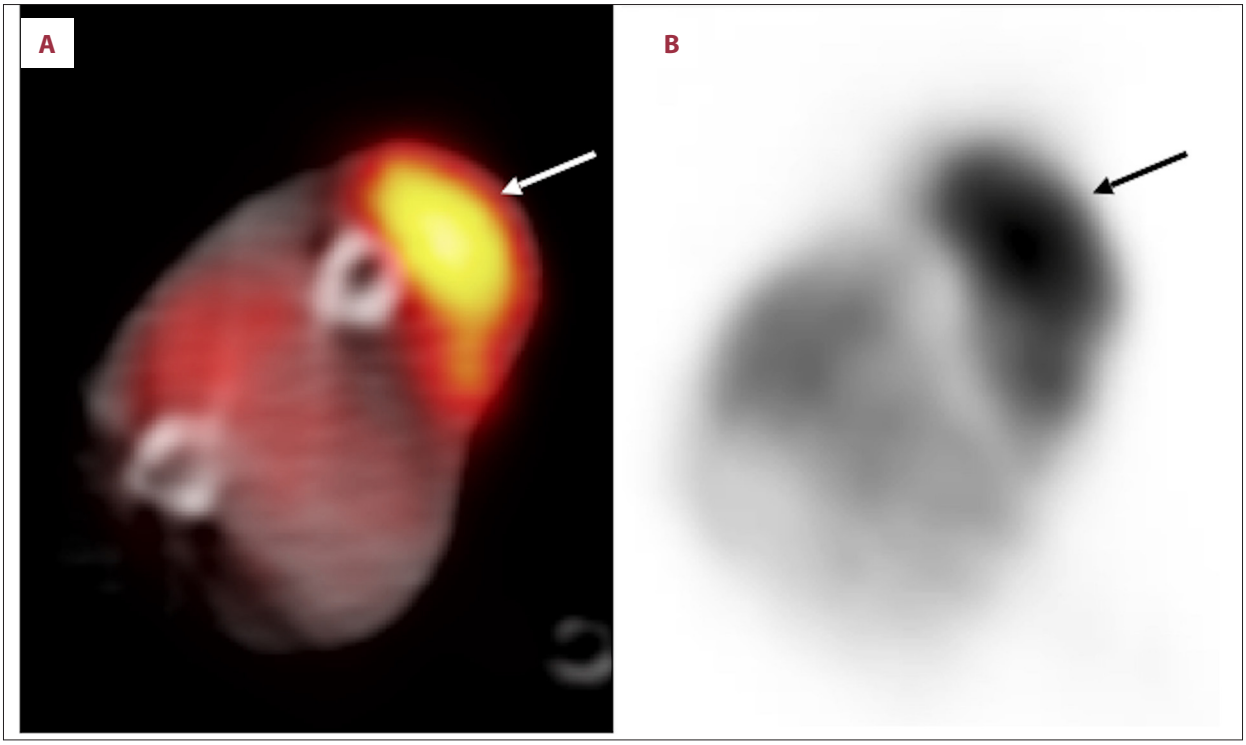

Figure 7. 18F-FDG PET/CT (18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography) – (**A**) CT/PET fused image, (**B**) PET image shows pathological high metabolic activity of the radial nerve lesion with an SUV max (standard uptake value) of 6.1 (**A, B,** arrows).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

distinguish among schwannoma, neurofibroma, malignant PNST [11], and neurolymphoma, so further imaging modalities are required.

MRI has a reported sensitivity in NL of 77% [3]. It plays an important role due to its panoramicity, multiplanarity, and high resolution for soft tissue, allowing identifying and differentiating between benign and malignant masses. MRI can depict the location and distribution of the lesion and the relationships with surrounding organs, and can characterize the tissue components and identify signs suggesting a specific etiology [12–15]. In the described case, MRI examination showed an oval mass arising from the perineurium of the involved nerve, hyperintense in T2W and STIR sequences, and lacking fat components, with restricted diffusion and high vascularity. The lymphomatous involvement of the nerve sheath typically appears as an infiltrative fusiform lobulated mass enveloping the nerve fascicles, characterized by increased signal on fluid-sensitive sequences, restricted diffusion, and high vascularity. It is associated with slight thickening and hyperemia of the nerve [3]. Although these MRI features suggest the differential diagnosis with more common lipomatous lesions (well circumscribed non-enhancing mass with fat-signal intensity on all sequences), the diagnosis with may be more complex, especially without anamnestic support [6,16].

MRI signs suggestive of benign peripheral neurogenic neoplasms are the “target sign” (a central area of hypointensity with a peripheral hyperintensity seen in T2W and DWI sequences), the “fascicular sign” (hypointense foci within the hyperintense area on T2W sequences), the “split fat sign” (presence of fat at the upper and lower poles of a lesion on T1W images, suggestive of intermuscular location), or the presence of a hyperintense peripheral rim on T2W sequences [6]. None of these MRI signs was presented by the lesion described in our case. Malignant PNST instead tends to be more heterogeneous on T1W and T2W images (due to the necrotic and hemorrhagic areas within) and often shows perilesional edema on T2W images (suggestive of perilesional infiltration), solid or peripheral enhancement, or bony involvement [6]. DWI sequences may be helpful in differentiating between benign and malignant soft-tissue tumors, as malignant tumors usually show restricted diffusivity with lower ADC values, whereas benign tumors usually have higher ADC values. However, there are some exceptions and overlap [13,17,18].

18F-FDG PET/CT can show avid uptake along the affected nerves, with a reported sensitivity of 88% in NL. In our case, PET/CT demonstrated a focal increased pathological FDG uptake of the lesion detected by MRI examination, without any further areas of abnormal uptake in other body sites. 18F-FDG PET/CT is helpful in differentiating benign from malignant lesions, as benign neoplasms usually show low-intermediate SUVs [3]. 18F-FDG PET/CT is an effective imaging modality for evaluating treatment response in patients with lymphoma and NL, in association with MRI [19]. Limitations of 18F-FDG PET/CT include lack of specificity because infection or inflammation can produce false-positive results [20].

Mass biopsy with histopathological confirmation is the criterion standard diagnostic method, allowing visualization and characterization of malignant cells [20]; however, especially in small lesions, it can be associated with permanent neurological deficit. Therefore, in typical cases, when the primary tumor is already known and characterized, biopsy can be avoided by starting with therapy [3].

Conclusions

Lymphomatous involvement of peripheral nerves can simulate common benign conditions and, although rare, it should be considered in the differential diagnoses of masses in patients with a history of hematologic malignancies.

Ultrasound is recommended as first-line investigation, as it can demonstrate the strict connection of the lesion with the peripheral nerves and the increased blood flow, suggestive of NL.

MRI and 18F-FDG PET/CT have a crucial role in further characterization of suspected lesions, helping to distinguish between benign and malignant masses.

Department and Institution where work was done

Department of General and Emergency Radiology, “A. Cardarelli” Hospital, Naples, Italy

Conflict of interest

None.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

References:

1. Choi YJ, Shin JA, Kim YH et al: Neurolymphomatosis of brachial plexus in patients with non-Hodgkin's lymphoma. Case Rep Oncol Med, 2013; 2013: 492329
2. Tai R, Maingard J, Nambiar M, Lim K: High-grade B-cell lymphoma relapse presenting as neurolymphomatosis of the median nerve. BMJ Case Rep, 2019; 12(3): pii: e228742
3. Lim AT, Clucas D, Khoo C et al: Neurolymphomatosis: MRI and (18) FDG-PET features. J Med Imaging Radiat Oncol, 2016; 60(1): 92–95
4. Arrigoni F, Bruno F, Zugaro L et al: Role of interventional radiology in the management of musculoskeletal soft-tissue lesions. Radiol Med, 2019; 124(4): 253–58
5. Sato H, Hiroshima S, Anei R, Kamada K: Primary neurolymphomatosis of the trigeminal nerve. Br J Neurosurg, 2019 [Epub ahead of print]
6. Kakkar C, Shetty CM, Koteshwara P, Bajpai S: Telltale signs of peripheral neurogenic tumors on magnetic resonance imaging. Indian J Radiol Imaging, 2015; 25(4): 453–58
7. Gruber H, Glodny B, Bendix N et al: High-resolution ultrasound of peripheral neurogenic tumors. Eur Radiol, 2007; 17(11): 2880–88
8. Vijayan J, Chan YC, Therimadasamy A, Wilder-Smith EP: Role of combined B-mode and Doppler sonography in evaluating neurolymphomatosis. Neurology, 2015; 85(9): 752–55
9. Lee JY, Kim SM, Fessell DP, Jacobson JA: Sonography of benign palpable masses of the elbow. J Ultrasound Med, 2011; 30(8): 1113–19
10. Gennaro S, Merciadri P, Secci F: Intraneural lipoma of the median nerve mimicking carpal tunnel syndrome. Acta Neurochir (Wien), 2012; 154(7): 1299–301
11. Reynolds DL Jr., Jacobson JA, Inampudi P et al: Sonographic characteristics of peripheral nerve sheath tumors. Am J Roentgenol, 2004; 182(3): 741–44
12. Bellelli A, Silvestri E, Barile A et al: Position paper on magnetic resonance imaging protocols in the musculoskeletal system (excluding the spine) by the Italian College of Musculoskeletal Radiology. Radiol Med, 2019; 124(6): 522–38
13. Bruno F, Arrigoni F, Mariani S et al: Advanced magnetic resonance imaging (MRI) of soft tissue tumors: techniques and applications. Radiol Med, 2019; 124(4): 243–52
14. Petralia G, Padhani AR, Pricolo P et al., Italian Working Group on Magnetic Resonance: Whole-body magnetic resonance imaging (WB-MRI) in oncology: Recommendations and key uses. Radiol Med, 2019; 124(3): 218–33
15. Balbo-Mussetto A, Saviolo C, Fornari A et al: Whole-body MRI with qualitative and quantitative analysis of DWI for assessment of bone marrow involvement in lymphoma. Radiol Med, 2017; 122(8): 623–32
16. Burt AM, Huang BK: Imaging review of lipomatous musculoskeletal lesions. SICOT J, 2017; 3: 34
17. Pekcevik Y, Kahya MO, Kaya A: Characterization of soft tissue tumors by diffusion weighted imaging. Iran J Radiol, 2015; 12(3): e15478
18. Robba T, Chianca V, Albano D et al: Diffusion-weighted imaging for the cellularity assessment and matrix characterization of soft tissue tumour. Radiol Med, 2017; 122(11): 871–79
19. de Vaugelade C, de Clermont-Gallerande H, Meyer M et al: FDG PET/CT in pediatric neurolymphomatosis. Clin Nucl Med, 2017; 42(5): 255–57
20. Briani C, Visentin A, Campagnolo M et al: Peripheral nervous system involvement in lymphomas. J Peripher Nerv Syst, 2019; 24(1): 5–18

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]