Acta Biomed 2020; Vol. 91, N. 1: 122-127 DOI: 10.23750/abm.v91i1.8510

Case report

Post-amputation neuroma of radial nerve in a patient with ephitelioid sarcoma: case report and literature review

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Summary. Neuroma, also known as traumatic neuroma or amputation neuroma or stump neuroma, is a focal non neoplastic area of proliferative hyperplastic reaction secondary to peripheral nerve damage that commonly occurs after a focal trauma (acute or chronic) or surgery, such as amputation or partial transection. Neuromas are more commonly located in the lower limbs, followed by head and neck; other extremely rare sites include the ulnar nerve followed by the radial nerve and the brachial plexus. A radiologic plan is necessary to recognize soft tissue lesions with a neural origin and whether they are a true tumor or a pseudotumor such as a neuroma, fibrolipoma, or peripheral nerve sheath ganglion. In oncologic patients the appearance of post-surgical neuromas can produce problems in differential diagnosis with local recurrences. Therefore, with a combination of different imaging techniques, mainly ultrasound (US) and magnetic resonance imaging (MRI), it is possible to characterize neurogenic tumours safely, with a great impact on patient management and to plan an appropriate treatment. Here, we report the first case of post-amputation neuroma of radial nerve in a patient with clinical history of ephitelioid sarcoma with a short literature review. (www.actabiomedica.it)

Key words: neuroma, peripheral nerves, tumors, sarcoma;, ultrasound (US), magnetic resonance imaging (MRI)

Introduction

Neuroma is a rare benign lesion affecting peripheral nerves characterized by nonneoplastic proliferation of the proximal end of a partially or completely transected nerve (1). It can be classified into two categories: terminal neuromas and spindle neuromas (2). The most common presenting symptom is pain, numbness, discomfort or electric shock-like symptoms, but approximately 20% to 30% of all neuromas are painful (3, 4). Neuromas are more commonly located in the lower limbs, followed by head and neck; other extremely rare sites include the ulnar nerve followed by the radial nerve and the brachial plexus (3).

An early accurate diagnosis and appropriate treatment are crucial for a good outcome. A radiologic plan is necessary to recognize soft tissue lesions with a neural origin and whether they are a true tumor or a pseudotumor such as a neuroma, fibrolipoma, or peripheral nerve sheath ganglion (1). Imaging techniques such as ultrasound (US) and magnetic resonance (MRI) imaging are the best modalities to characterize these lesions and have a direct impact on correct management and treatment of patients (1). Here, we report the first case of post-amputation neuroma of radial nerve in a patient with clinical history of ephitelioid sarcoma with a short literature review.

Case report

A 34-years-old man, with a clinical history of excision of a soft tissue mass at the right forearm for epithelioid sarcoma, comes to our department for the appearance of a palpable nodule at the region of the right wrist. The patient reported discomfort at focal pressure at the nodule site. The clinical examination showed a mass of soft tissue with pain on palpation, Tinel's sign positive and there wasn't sign of inflammation.

A search for recurrence of ephitelioid sarcoma was undertaken. Thus, conventional B-mode US, color and power-Doppler (CD and PD) and sonoelastography examination of the right forearm were performed.

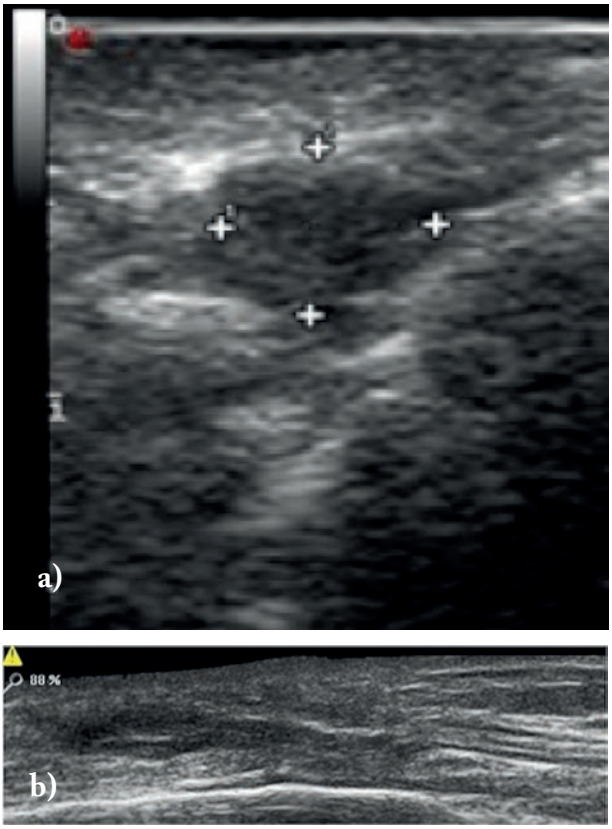

Figure 1. US B-Mode axial view (**a**), longitudinal view (**b**): marginated homogeneously hypoechoic fusiform mass with echogenic strands inside and a "bulbous end" morphology appearing to be in continuity with a normal nerve proximally. In longitudinal US B-mode scan we evaluated clearly the hypoechoic nerve entering in the ovalar mass, which didn't infiltrate the muscular fascia. We studied also the radial nerve along its whole course where the nerve echostructure was normal and with stable size

B-mode US showed a marginated homogeneously hypoechoic fusiform mass with echogenic strands inside and "bulbous end" morphology appearing to be in continuity with a normal nerve proximally (Fig 1). In longitudinal B-mode scan we evaluated clearly the hypoechoic nerve entering in the ovalar mass, which didn't infiltrate the muscular fascia. We studied also the radial nerve along its whole course where the nerve echostructure was normal and with stable size. On CD examination, few vascular signals inside and around the radial nerve were detected (Fig 2a).

US Strain Elastography (USSE) was performed with the patient lying in the some position as for B-mode scanning by applying a light compressione with the US probe. The US elastogram was displayed over the B-mode image in a color scale depending on the magnitude of strain: red (soft tissue), green (intermediate degree of stiffness), and blue (hard, anelastic

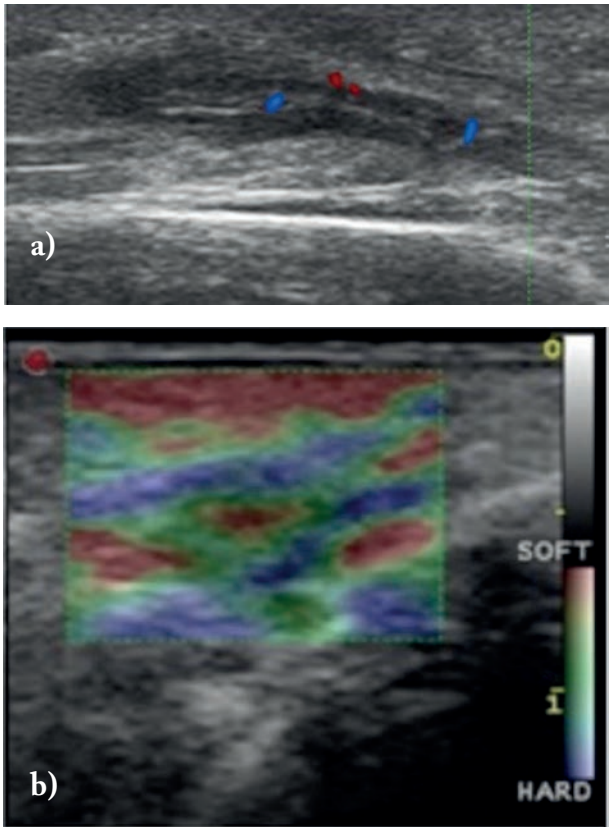

Figure 2. (**a**) Color-Doppler US (longitudinal view): few vascular signals inside and around the radial nerve. (**b**) US-elastography (axial view): the soft tissue nodule showed elasticity in the whole area with a contextual small mixed red area inside

tissue). The soft tissue nodule showed elasticity in the whole area with a contextual small mixed red area inside (Fig 2b).

MRI examination was further performed with a 1.5 tesla resonance magnetic imager (Symphony – Siemens. Erlangen), which showed a well-definited ovoid subcutaneous lesion with an intermediate signal intensity (similar to that of muscle) on T1-weighted images and an intermediate-high signal intensity with a typical fascicular pattern on FSE T2-weighted images (with and without fat-saturation) (Fig 3). Histopathological examination, after excision, showed the definite diagnosis of amputation neuroma of radial nerve.

Discussion

Epithelioid sarcoma (ES) is a rare, high-grade malignancy that represents the most common primary soft tissue sarcoma of the hand (5, 6). ES predominantly affects young adults in their second or third decade of life, but may occur at any age; males are disproportionately affected with a ratio approaching 2:1 (5, 6).

Local recurrence often occurs within 1 to 2 years of treatment, and these patients often proceed to develop distant metastasis (5, 6). Radical tumor excision is the primary treatment for patients with ES (5). Therefore, differentiating between benign and malignant masses is important to prevent delays in the treat-

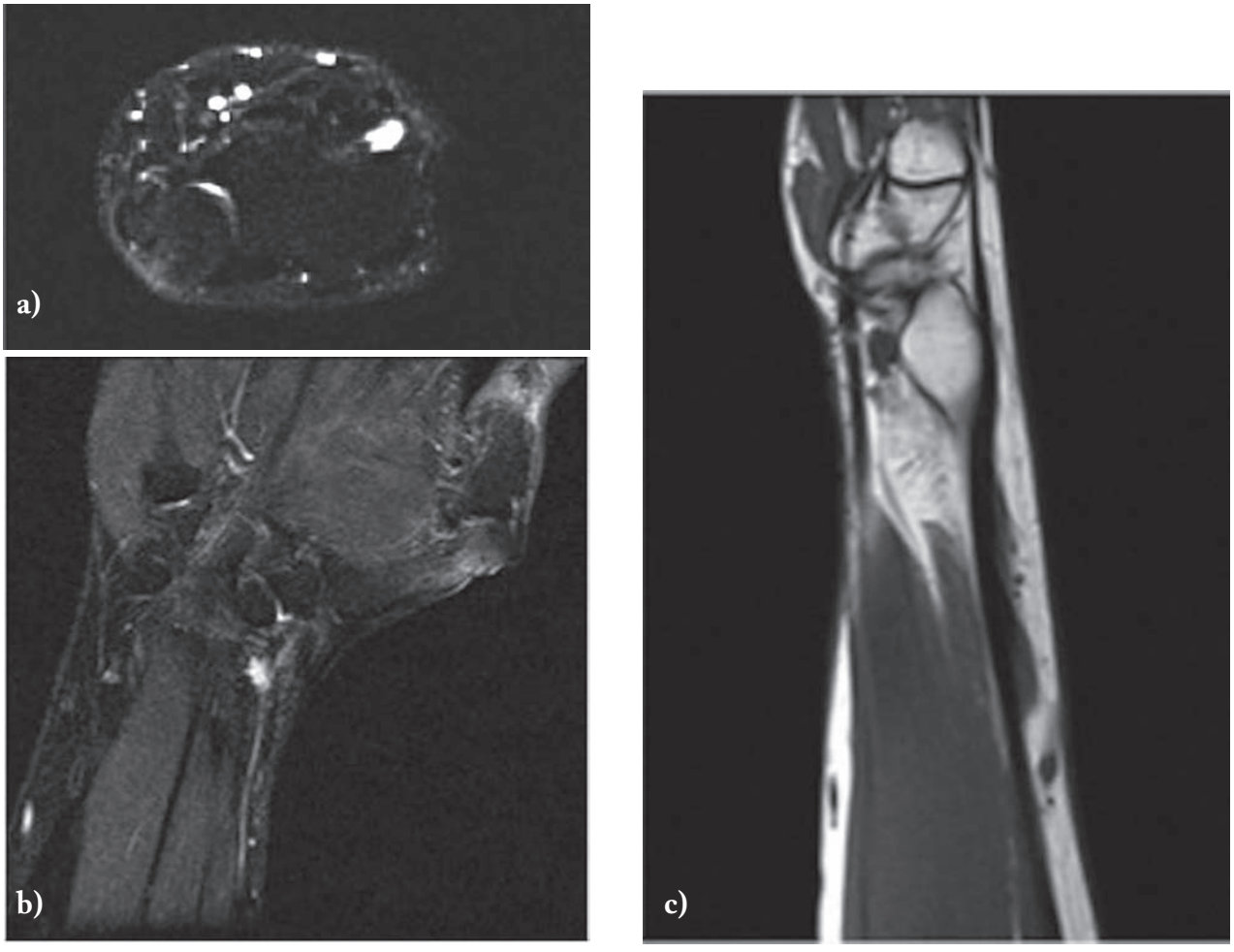

Figure 3. (**a**) FSE T2-w Fat-Sat axial (**a**) and coronal (**b**), T1-weighted sagittal sagittal (**c**): well-definited ovoid subcutaneous mass with an intermediate signal intensity (similar to that of muscle) on T1-weighted images and an intermediate-high signal intensity with a typical fascicular pattern on FSE T2-weighted images

ment of the malignant masses and avoid unnecessary surgical treatments for the benign masses.

Neuroma, also known as traumatic neuroma or amputation neuroma or stump neuroma, is a rare benign lesion affecting peripheral nerves and classified in the sub-category of pseudotumors from the World Health Organization classification of main peripheral nerve sheath tumors and considered in the scientific literature as purely benign lesions (7). Neuroma is a focal non neoplastic area of proliferative hyperplastic reaction secondary to peripheral nerve damage that commonly occurs after a focal trauma (acute or chronic) or surgery, such as amputation or partial transection (3). It is usually seen between 1 month and 12 months after injury but in literature cases have been reported as 8 days, or as late as 40 years (8). Neuromas are more commonly located in the lower limbs, followed by head and neck; other extremely rare sites include the ulnar nerve followed by the radial nerve and the brachial plexus (3).

Histologically, neuromas are composed of multiple and non-encapsulated axons, Schwann cells, endoneurial cells, and perineurial cells, surrounded by prominent scar tissue with dense collagen; dystrophic calcifications are rarely seen in the lesional area (3, 4). Disorganization of the neurogenic tissue (caused by multidirectional proliferation of cells in an abortive attempt to repair the injured nerve) allows traumatic neuromas to be distinguished from neurofibroma (9).

Two types of traumatic neuromas have been described, spindle neuromas and terminal (also called lateral) neuromas (3, 10).

Terminal neuroma originates at the end of the severed nerve and it is usually due to the proliferation of axons in any direction without the support of the Schwann cells in an abortive attempt to repair the nerve (3, 10). Terminal neuroma represents a normal pattern of healing of the nerve and is often asymptomatic (3). Spindle neuroma currently is considered as resulting from chronic stimulation and friction and it is localized in the nerve away from the severed nerve ending and represents the response of a peripheral nerve subjected to microtrauma due to stretching or compression by the localized scar tissue (3, 10).

An early accurate diagnosis and appropriate treatment are crucial for a good outcome (1). A radiologic plan is necessary to recognize soft tissue lesions with a neural origin, their association with a peripheral nerve, and whether they are a true tumor or a pseudotumor such as a neuroma, fibrolipoma, or peripheral nerve sheath ganglion (1, 11).

Imaging techniques such as ultrasound (US) and magnetic resonance (MRI) imaging are the best modalities to characterize these lesions and have a direct impact on correct management and treatment of patients (1, 11). In addition, US can be used to guide biopsy in difficult and uncertain cases when the lesion is either indeterminate or there is concern that the lesion is malignant (12).

Following the guidelines regarding soft tissue tumors in adults approved by the European Society of Musculoskeletal Radiology (ESSR) for peripheral nerve tumors, biopsy could be avoided in cases of purely benign lesions (1, 12).

US is the primary examination method for superficial soft tissue masses to confirm their size, location, the borders of the tissue masses, internal echo characteristics, internal blood low signal and association between the masses and the surrounding structures (13, 14). US offering high-resolution imaging, is quick and easy to perform and can assess vascularity that eliminates having to administer MRI contrast, saving costs and avoiding potential complications (14).

CD and PD techniques are a simple, non-invasive method able to increase the specificity of US by providing a real-time evaluation of vascularity, which is an important clue in distinguishing benign from malignant lesions; malignant tumors show an increased number of vessels, which generally appear distorted and deformed, and multiple peripheral poles (15).

According to the literature, US features such as well marginated hypoechoic ovalar masses with echogenic strands (fascicular pattern) in direct continuity with the radial nerve allowed to establish the possible neural origin of these soft tissue masses, specifically the neuromas (16). Other tumours of neural origin have been reported to be hypoechoic, e.g. neurofibromas and schwannomas, but these frequently were also associated with acoustic enhancement simulating cysts, which was not present in our case (16).

More recently, US contrast agents and US-elastography have been proposed as additional diagnostic

tools for the evaluation of various organs including soft tissue masses (17).

Stiffness of the tissue structures may be accessed using ultrasound strain elastography (USSE) (18). By applying pressure to the inspection sites, USE acquires response information resulting from the pressure and determines the tissue stiffness (18). The two most frequently used USSE methods are SE and shear wave elastography (SWE). SE acquires the deformation information of the tissues under pressure, with greater deformations indicating lower tissue stiffness and less deformations representing greater tissue stiffness and presents the results in different colors or differing degrees of brightness (18). SWE obtains the shear wave information from the tissues under pressure, with faster propagation velocities of shear wave indicating greater tissue stiffness, and also presents the results in different colors or differing degrees of brightness (18). In addition, SWE also measures and quantifies the shear wave propagation velocities at the regions of interest, and therefore provides more information compared with SE (18). Stiffness of a malignant tumor is typically higher compared with a benign tumor (17).

USSE has been widely accepted as an effective method for differentiating between malignant and benign tumors. Although differentiation of malignant and benign soft tissue masses using USE has rarely been investigated, some current studies aimed to assess the importance of strain elastography (SE) for the differentiation of malignant and benign soft tissue masses (18). However, to date, no case of neuroma studied with USSE is reported in the literature.

Contrast-enhanced ultrasound (CEUS) using second-generation contrast agents is a "new" simple, immediate, and effective diagnostic tool: microbubbles circulate freely inside the body and constitute an intravascular contrast agent; therefore, they permit analysis of both macro- and microvascular blood flow (19-22). To date, the value of CEUS for the examination of superficial lesions has not been studied in detail. CEUS previous studies of soft-tissue tumors demonstrated that microbubble-enhanced US can improve the detection of perfusion if compared with CPD (15, 23): in a substantial number of tumors that appear only sparsely vascularized with CPD, CEUS gives a completely different impression by depicting more vessels and more intense perfusion (15). Therefore, with these results, our group is planning to evaluate tumor neovasculature with CEUS.

MRI is the gold standard for superficial and deep lesions. Utilizing MRI it is possible to characterize the lesions: size, intratumoral lobulations, morphology, margins (well or ill defined) and detect perilesional edema, cystic changes (necrosis), interval change in size, vascularity, and effects on sur- rounding structures (1). The benefits of MR imaging are: less operator dependent, can assess deep structures more confidently, can cover a larger body part (whole-body MRI), can assess for skip lesions that often occur a long the nerve (14). However, the potential downside of MRI is that is relatively more time consuming and less available than US (1).

US and MRI are commonly used alone or in combination to study peripheral nerves (1). Overall, US is well suited for very small and superficial structures, whereas MRI is good for deeper lesion such as those located deep in the brachial plexus, lumbar plexus, and in patients with a high body mass index (1, 11). US is often the imaging modality initially used to study peripheral nerves in centers where both US and MRI are available (1, 11).

Conclusion

To conclude, we can assert that in oncologic patients treated for soft tissue sarcomas, the appearance of post-surgical neuromas can produce problems in differential diagnosis with local recurrences. Therefore, with a combination of different imaging techniques, mainly US and MRI, it is possible to characterize neurogenic tumours safely, with a great impact on patient management and to plan an appropriate treatment.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 21 May 2019
Accepted: 13 July 2019
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