Imaging of the malignant peripheral nerve sheath tumour with emphasis on ultrasonography: correlation with MRI

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Abstract Malignant peripheral nerve sheath tumours affect 0.001 % of the population. The epithelioid subtype accounts for only 5 % of them. We herein present a patient with a palpable mass on the left calf, which was investigated by ultrasonography, ultrasonographically guided fine-needle biopsy and MRI. Ultrasonography estimated the size of the tumour and evaluated its echotexture. Doppler technique detected characteristic corkscrew-type blood vessel entering in the upper pole of the mass. T1-weighted, fat-suppression and gadolinium-enhanced MRI sequences confirmed ultrasonographic findings. In conclusion, although final diagnosis was established by biopsy, ultrasonography and MRI proved complementary in the characterization of the lesion and planning of surgery.

Keywords Nerve · Tumour · MPNST · Ultrasonography · MRI

Riassunto I Tumori Maligni della Guaina del Nervo Periferico (MPNST) colpiscono il 0,001 % della popolazione generale. Il sottotipo epitelioido rappresenta solo il 5 %. Presentiamo qui un paziente con una massa palpabile sul polpaccio sinistro, che è stata studiata con l'ecografia

seguita dalla biopsia con ago sottile ecograficamente guidata ed MRI. Con l'ecografia sono state valutate le dimensioni del tumore e l'eterogeneità della sua consistenza. Con la tecnica Doppler è stato rivelato un vaso sanguigno di tipo caratteristico di “cavatappi” entrare nel polo superiore della massa. MRI sequenze T1 weighted, di soppressione del grasso e dopo somministrazione di mezzo di contrasto paramagnetico hanno confermato i risultati ecografici. In conclusione, anche se la diagnosi finale è stata stabilita tramite biopsia, l'ecografia e la risonanza magnetica hanno fornito dati complementari riguardo alla caratterizzazione della lesione ed alla pianificazione dell'operazione.

Introduction

Malignant peripheral nerve sheath tumours (MPNST) are a group of neurogenic tumours which may be either sporadic or coexist with neurofibromatosis. They constitute an extremely rare entity as they affect only 0.001 % of the general population. The epithelioid subtype of MPNST is even rarer, accounting for only 5 % of these tumours [1–3]. These tumours typically present as palpable soft-tissue masses which can cause pain or even neurologic symptoms [4]. Ultrasonography is the first-line imaging modality for these patients and gives the possibility to initially characterize the mass as it is easy, cost effective and repeatable. However, MRI is superior in tissue characterization and identifies some very important signs which help to establish the right diagnosis [1, 4].

In this case report, we present the ultrasonographic findings of a patient with a palpable mass and we correlate them with MRI findings.

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Fig. 1 Longitudinal extended-field-of-view grey-scale sonogram of the left posterior calf depicts a large fusiform space-occupying lesion situated inside the medial head of the gastrocnemius muscle. The lesion was heterogeneous and mainly hypoechoic. Ultrasonographically calculated dimensions were 23.8×30.8 mm

Fig. 2 A split-screen image was created with the two screens aligned to produce an extended-field-of-view long-axis image (a). This image demonstrates a fusiform solid hypoechogenic mass with heterogeneity. The tumour is seen having hyperechoic tapered proximal and distal ends. An anechoic layer is seen immediately inwards, representing oedema. Bidirectional e-Flow technique reveals the hypervascular pattern of the tumour, consisting of peripheral and central flow signals. There is also displacement of surrounding major blood vessels and a characteristic tortuous, corkscrew feeding blood vessel located at the upper pole of the mass. Contrast-enhanced, FS sequence MR image (b), turned 90° anti-clockwise with a purpose to correlate with the previous ultrasonographic image. We can see a similar imaging of the blood vessel's distribution around the tumour

Case presentation

A 32-year-old male patient presented to the outpatient department with soft-tissue enlargement due to a mass in

Fig. 3 Short-axis colour Doppler (a) and MR image (b) at the level of the intramuscular tumour. The ultrasonographic image (a) demonstrates the vascularity pattern of the tumour. Note a small centrally located anechoic structure measuring 3 mm in diameter which is consistent with a cyst (crosses). T1-weighted image with contrast enhancement (b) shows that MRI findings correlate with the ultrasonographic

the left calf. The mass had gradually increased in size and the patient admitted no history of trauma. The patient initially underwent ultrasonography of the calf with an Aloka Prosound alpha 7 device (Aloka Co. Ltd.) and a 5–13 MHz linear-array transducer. Apart from grey-scale technique, colour, power Doppler and e-Flow technique evaluated the vascularization of the mass. Extended-field-of-view technique illustrated the anatomic relations of the mass with the adjacent structures (Figs. 1, 2, 3). These techniques revealed a partially ill-defined, heterogeneously hypoechogenic space-occupying lesion situated inside the medial head of the left gastrocnemius muscle. An external hyperechoic layer and a hypoechoic layer interior to the previous were detected at the periphery of the lesion. There was also an anechoic, cyst-like structure inside the tumour (Fig. 3a). The lesion was situated far from the local major blood vessels, but showed increased blood flow signals both centrally and peripherally. Namely, tortuous, “corkscrew-type” feeding vessels were observed at the anterior aspect of the mass (Fig. 2a). Further diagnostic work-up included ultrasonographically guided fine-needle biopsy which provided evidence of malignancy without defining the exact type of the tumour. Chest and abdomen CT excluded systematic disease.

The patient then underwent MRI using a 1.0 T magnet. This examination confirmed the presence of a heterogeneous, ovoid space-occupying lesion, which showed high-signal intensity on T1-weighted images, but no suppression of the signal intensity on fat-suppression (FS) images. Intravenous administration of paramagnetic contrast agent revealed peripheral enhancement pattern and heterogeneous enhancement of the centre of the mass. There was surrounding muscle and fascia oedema, but no bone involvement (Figs. 2b, 3b).

Fig. 4 Histologic examination showed the polygonal shape of cells and the prominent nucleoli within them. These pathologic findings were consistent with epithelioid MPNST

Based on these findings, surgery was decided to achieve complete surgical excision of the tumour with negative wide margins. On gross examination, the tumour was greyish, elastic, with ill-defined margins and its size was $2.9 \times 2.3 \times 2.4$ cm. There was also a centrally located necrotic area which was 1.4 cm in diameter.

Pathological microscopic examination demonstrated middle-sized, spheroid, spindle or polygonal neoplastic cells with eosinophilic cytoplasm and large nuclei containing prominent nucleoli. On immunochemistry, the neoplastic cells were diffusely positive in vimentin and S-100 protein. Numerous neoplastic cells were positive in GFAP. The whole population of neoplastic cells was negatively evaluated for SMA, melan A, desmin, synaptophysin, CD 34, CD 57 and CD 99. Based on histology and immunochemistry, the tumour was characterized as an epithelioid MPNST (Fig. 4).

Twenty days after the surgery, the patient was diagnosed with a metastatic lesion in the cervical spine. After evaluation by an oncologist, the patient started chemotherapy.

Discussion

The term peripheral nerve sheath tumours (PNST) describe a group of both benign and malignant tumours. Benign tumours include schwannomas and neurofibromas, whereas malignant tumours (MPNST) include malignant schwannoma and neurofibrosarcoma [1]. MPNST may be either combined with underlying neurofibromatosis I or occur sporadically. The former case accounts for two-thirds of MPNST, whereas the latter may be encountered after radiation therapy. MPNST as a whole, represent 5–10 % of

all malignant soft-tissue tumours and have a reported incidence of 2–5 % in patients with NF-1, but are extremely rare in the general population with an incidence of only 0.001 % [2, 3].

Malignant peripheral nerve sheath tumours affect both male and female patients without significant sex predilection and usually occur in patients 20–50 years of age. These patients usually present with a soft-tissue mass involving major nerves and causing pain or other neurologic symptoms like muscle weakness and sensory deficits. Symptoms are associated with malignancy [1, 4]. MPNST typically affect major nerve trunks like the sciatic nerve, the brachial plexus and the sacral plexus, whereas they rarely affect cranial nerves [3, 4]. Other locations include the chest wall, the posterior mediastinum and the lumbar spine. MPNST may also be multifocal [5, 6]. In extremely rare cases, they can be primary intraosseous [7].

Plain radiographies of MPNST are generally unremarkable or demonstrate soft-tissue masses without specific characteristics apart from the fusiform shape of the tumour, rarely with a surrounding rim of fat. Osteoid, chondroid or amorphous calcification is unusual [1, 4]. Displacement of major blood vessels constitutes an important angiographic finding of a deep PNST. Even more typical of a neurogenic tumour is the angiographic finding of “corkscrew-type” vessels at both poles of the mass. These vessels are considered to be caused by the hypertrophy of vasa nervorum. In our case, we observed the “corkscrew-type vessels” sign using the Power Doppler and the e-Flow technique. In general, angiographically or ultrasonographically detected increased vascularity of a PNST is suggestive of malignancy [4].

Imaging findings of both ultrasonography and MRI which classify a mass as neurogenic include its fusiform shape with evidence of entering and exiting nerve along with its location in a typical nerve distribution. It is also noted that the muscle innervated by a nerve affected by a PNST may appear atrophic; a sign not seen in other types of soft-tissue masses. When a tumour is characterized by rapid growth and central necrosis, malignancy should be excluded. However, central necrosis can be found inside benign ancient schwannomas as well [4, 8].

Although ultrasonography is highly sensitive in demonstrating soft-tissue tumours, its ability to detect malignancy is low [2]. High-resolution ultrasound depicts MPNST as inhomogeneous, hypoechoic, fusiform masses connected with a peripheral nerve and having a partly and irregularly thickened hyperechoic outer nerve sheath, representing a pseudocapsule. Sometimes, MPNST may have a poor outer margin [8]. Other important findings that should raise suspicion of a MPNST include diameter larger than 5 cm, ill-defined margins, central necrosis or haemorrhage, oedema and calcification. However, the aforementioned findings are

not highly specific and further diagnostic work-up is needed. Colour, power and spectral Doppler technique are of considerable assistance in detecting malignancy as they easily demonstrate vascular changes suggestive of malignancy like occlusions, stenosis, shunts, trifurcations and loops [2]. Spectral Doppler of MPNST reveals that the newly formatted vessels show a duplex spectrum which is characterized by high velocity. The duplex spectrum of these vessels may differ in velocity and wave form in different parts of the tumour. The resistance index can be low when there are arteriovenous communications [8]. Doppler technique constitutes an advantage of ultrasonography as it permits evaluation of the vascular morphology and flow dynamics. Moreover, recent technological advances like the use of linear-array transducers of up to 17 MHz, artefact reduction software or image compounding technology have upgraded ultrasonography in soft-tissue imaging. Thus, ultrasonography and MRI should be complementary in the evaluation of soft-tissue tumours [2, 8].

CT has a small contribution to the diagnostic approach of soft-tissue masses. A heterogeneous mass or a mass with high attenuation values in unenhanced CT is more likely malignant [2].

MRI is useful when approaching soft-tissue masses as it reveals their anatomical relationships with the surrounding structures and characterizes their components [2]. MRI findings characterizing benign neurogenic tumours include their fusiform shape, the tapered ends, the “split-fat” and the “fascicular” sign, the low-to-intermediate T1-weighted and the high T2-weighted signal intensity. The signal intensity of a neurogenic tumour on T2-weighted images may be homogeneously high or create a “target sign” [1]. MRI findings of MPNST include a mass larger than 5 cm with ill-defined margins and surrounding oedema due to infiltration of surrounding tissues. Other findings include heterogeneity, central necrosis and increased heterogeneous enhancement with peripheral nodular enhancement. However, benign lesions with degeneration may also appear heterogeneous. Similarly, calcification is common in malignant tumours, but can also be found in benign schwannomas. Thus, it should be remembered that imaging findings of benign and malignant PNST overlap [1, 4, 7]. Studies on the diagnosis of MPNST concluded that MRI is 61 % sensitive and 90 % specific in diagnosing malignancy when it shows at least two of the following criteria: large diameter of the mass, peripheral enhancement, perilesional oedema and intratumoural cysts [9]. Clinical factors associated with MPNST include location on the limbs, pain and short-time interval between onset of symptoms and surgery. Multimodality imaging was reported to be 83 % sensitive and 85 % specific in diagnosing MPNST [10].

Positron emission tomography (PET) has been recently used to examine the ^{18}F -fluorodeoxyglucose uptake of MPNST [11]. Bone scintigraphy can show mild uptake of radionuclide within the tumour. However, it was shown that Ga-67 citrate uptake was significantly higher in malignant than in benign PNST [4].

MPNST are histologically characterized as spindle-cell sarcomas with subtypes like malignant schwannomas, glandular malignant schwannomas, malignant epithelioid schwannomas and malignant Triton tumours. Fine-needle aspiration biopsy may suggest the diagnosis, but biopsy after surgical excision and immunohistochemistry establishes the definitive diagnosis [3]. Central necrosis and haemorrhage characterize MPNST's histology [7, 12].

As MPNST are high-grade sarcomas, treatment includes a combination of surgical resection with wide resection margins, adjuvant chemotherapy and radiation therapy. Local recurrence and metastases occur in 40 and 60 % of cases, respectively. Metastases usually affect the lung, bone, pleura and retroperitoneal space. Lymph nodes are affected in 9 % of patients. The MPNST's reported 5-year survival rate is 43.7 % [4, 7]. Negative prognostic factors of MPNST include diameter larger than 5 cm with underlying neurofibromatosis and the location of the tumour in the head or neck [13]. Recent research has brought to light potential molecular drivers and targets for treatment, which could create new therapeutic options in the future [14].

Conclusion

Although MRI is considered superior to ultrasonography in characterizing soft-tissue masses and detects a number of signs which lead to the diagnosis of a MPNST, ultrasonography is usually the first-line imaging modality when dealing with a palpable mass, as it is cost effective, easy to perform and reproducible. As a consequence, radiologists should be aware of the ultrasonographic appearance of a neurogenic tumour in general and especially of the MPNST. Proper and complete diagnostic imaging work-up should identify malignancy of a PNST and lead to earlier diagnosis and treatment.

Conflict of interest Vasileios Rafailidis, Theodora Kaziani, Costas Theocharides, Athanasios Papanikolaou, Dimitrios Rafailidis, declare that they have no conflict of interest.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). All patients provided written informed consent to enrolment in the study and to the inclusion in this article of information that could potentially lead to their identification.

Human and animal studies The study was conducted in accordance with all institutional and national guidelines for the care and use of laboratory animals.

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