Malignant transformation to schwannoma in a patient affected by type 1 neurofibromatosis as demonstrated by F-18-FDG-PET/CT

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Abstract

Neurofibromatosis type I (NF1) is an autosomal dominant multisystem disorder. Patients with NF1 are at increased risk for developing both benign and malignant tumours. We report the case of a patient with histologically documented NF1, who underwent F18-FDG-PET/CT for staging purposes. The study revealed intense uptake at multiple masses located at the thighs (the largest presented SUV max of 6.8), popliteal regions, legs, left foot, left supraclavicular region, and at the thoracic wall between the 11th and 12th right ribs. The surgical biopsy of the largest popliteal lesion with higher uptake at F18-FDG-PET/CT documented the presence of a malignant schwannoma at histological examination. In conclusion, F18-FDG-PET/CT was probably able to help the discrimination between benign lesions related to known NF1 and the malignant transformed ones, and to assist clinical decision making.

Key words: PET, neurofibromatosis, malignant degeneration

Introduction

Neurofibromatosis type I (NF1) is a common autosomal dominant multisystem disorder, and its classical features are "café au lait" spots, iris Lisch nodules, neurofibromas, and skin fold freckling. Neurofibromas are the most common tumour associated with NF1, and among the three subtypes (cutaneous, subcutaneous, and plexiform) plexiform neurofibroma (PN) represents a major cause of morbidity [1, 2]. Neurofibromas can potentially occur at any site arising from peripheral nerve branches or sheaths of peripheral nerve fibres and are derived from Schwann cells or multi-potential cells of neural crest origin [3]. Patients with NF1 are at increased risk of developing both benign and malignant tumours. Benign plexiform neurofibromas have an increased risk of malignant degeneration into malignant peripheral nerve sheath tumours (MPNSTs), which are neurofibrosarcomas that tend to metastasize widely. Patients with NF1 have a decreased overall survival rate due to the possible development of MPNSTs, which are the main cause of mortality in patients with NF1 [4].

Case report

We report the case of a 76-year-old male patient with histologically documented NF1 (genetically inherited Von Recklinghausen disease). The patient underwent F18-FDG-PET/CT for staging purposes after magnetic resonance (MR), computed-tomography (CT), and ultrasonography (US). F18-FDG-PET/CT was performed with fasting state for at least 6 hours and glucose

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level lower than 150mg/dl. An FDG dose of 5.5MBq/Kg was administered intravenously and a 2D mode ordered-subset-expectation-maximization (OS-EM) imaging (with septa) was acquired 60 minutes after injection on a Discovery ST PET/CT tomograph (General Electric Company — GE® — Milwaukee, WI, USA) with standard CT parameters (80 mA, 120 Kv without contrast; 4 minutes per bed-PET-step of 15 cm). The reconstruction was performed in a 128 × 128 matrix and 60 cm field of view. The PET images were analyzed visually and semi-quantitatively by measuring the maximum standardized uptake value (SUVmax). SUV was expressed as SUVbody weight (SUVbw — g/ml) and automatically calculated by the software (Volumetrix for PET/CT; Xeleris™ Functional imaging workstation; General Electric) on the basis of the following parameters: weight of the patient expressed in kilograms; height expressed in centimetres; tracer volume expressed in ml; radioactivity at injection time expressed in MBq; post injection activity in the vial expressed in MBq; injection time; starting time acquisition; and decay half-time of the radioisotope (standard 109.8 minutes for F18-FDG). A written consensus was obtained before the study.

The study revealed intense uptake at multiple masses located at the thighs (the largest presented SUV max of 6.8), popliteal regions, legs, left foot, left sovraclavear region, and at the thoracic wall between the 11th and 12th right ribs (Figure 1).

No significant uptake was seen at the many other lesions detected by CT and MR at the right proximal arm along the route of the brachial nervous plexus, the thighs, legs, and lumbar nerve roots, probably because of their benign nature. The patient underwent surgical biopsy of the largest popliteal lesion with highest uptake at F18-FDG-PET/CT, documenting the presence of a malignant schwannoma at histological examination (Figure 2). In particular, fine needle biopsy results constituted compact spindle cells arranged in short bundles or interlacing fascicles showing malignant changes with atypical pleomorphic elements and diffuse nuclear reactivity for S100 protein underlining pleomorphic morphology of the atypical elements.

Discussion

PN are benign tumours formed along branches of nerves, nerve plexus, or spinal nerve roots, composed of axons, Schwann cells, fibroblasts, perineural cells, mast cells, collagen fibrils, and extracellular matrix, and are a possible complication of NF1 [2]. They represent a major cause of serious morbidity in NF1, resulting in pain, impaired function, and disfigurement and are at risk of malignant degeneration [2]. The majority of PN lesions have low FDG–PET SUV values, consistent with the benign nature of these lesions [1].

Malignant sarcomatous transformation of neurofibromas (usually the plexiform subtype) to a neurofibrosarcoma (MPNST) are a major cause of mortality in patients with NF1, and optimal management and final prognosis depend on early and accurate detection of malignant transformation [1]. Clinical indicators of malignant degeneration include persistent or increasing pain, increasing tumour size, and neurologic deficits, but these findings may be seen in both benign and malignant lesions, so surgical biopsy is often necessary to exclude malignancy [5]. Magnetic resonance imaging (MRI) and CT have been shown to be excellent tools for the non-invasive evaluation of tumour extent, but they are often not reliable in
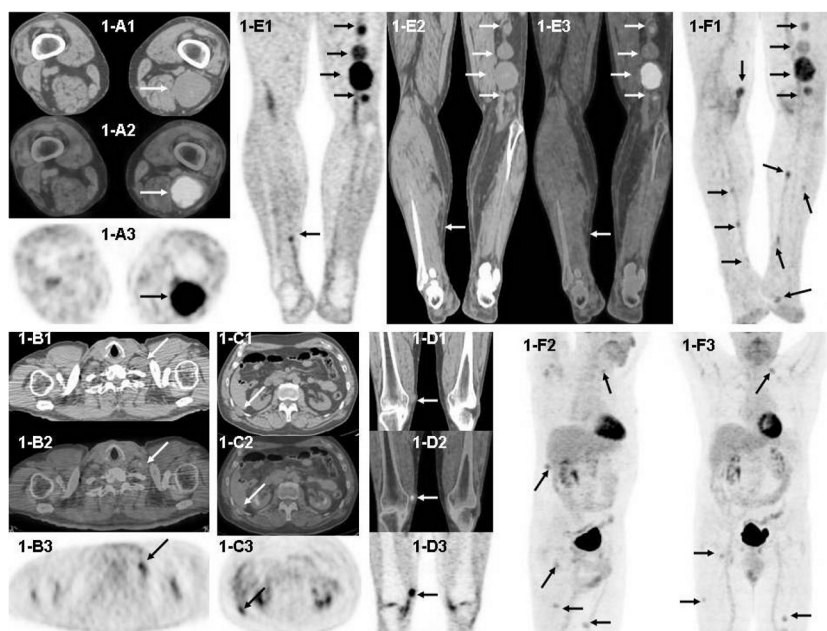

Figure 1. F18-FDG-PET/CT images and highlighted sites of pathologic uptake at lesions (arrows): multiple masses at thighs, popliteal regions, legs, left foot, left sovraclavear region, and at thoracic wall between 11th and 12th right ribs. In particular, the anterior view (1-F3) and 45° lateral view (1-F2) of whole body maximum intensity projection (MIP), anterior view of legs MIP (1-F1), axial view of CT (1-A1), fused (1-A2) and PET (1-A3) images of largest popliteal lesion, coronal PET (1-E1), CT (1-E2) and fused (1-E3) images of some legs lesions, axial CT (1-B1), fused (1-B2) and PET (1-B3) images of left sovraclavear lesion, axial CT (1-C1), fused (1-C2) and PET (1-C3) images of thoracic wall lesion (between 11th and 12th right ribs), coronal CT (1-D1),fused (1-D2), and PET (1-D3) images of a right leg lesion (arrows) are shown.
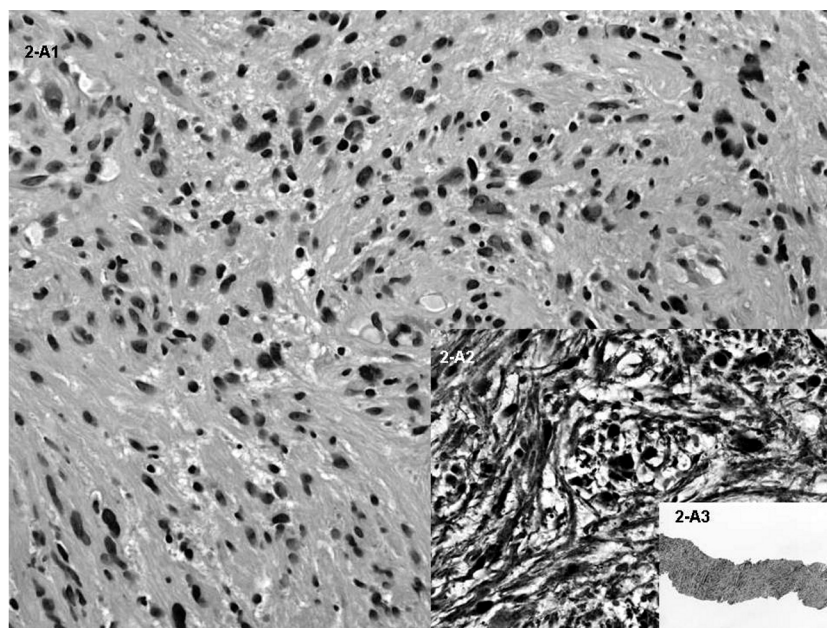
Figure 2. Histological images of fine needle biopsy constituting compact spindle cells arranged in short bundles or interlacing fascicles (2-A3 magnified at 40X); the lesion shows malignant changes with atypical pleomorphic elements (2-A1 magnified at 200X); moreover, diffuse nuclear reactivity for S100 protein underlines the pleomorphic morphology of the atypical elements (2-A2 magnified at 200X).

accurately characterizing a lesion as benign or malignant [6]. As surgical resection of the entire tumour is often not feasible because of the associated morbidity, and biopsies may yield false-negative results due to sampling error, metabolic imaging techniques such as FDG PET has been found to be helpful in detecting tumour recurrence and in differentiating benign from malignant lesions [7–9]. Cardona et al. examined 25 neurogenic soft tissue tumours in 13 patients (5 with NF1) and found that FDG–PET distinguished between malignant peripheral nerve sheath tumours and benign neurogenic tumours with 100% sensitivity and 83% specificity [10].

Differentiating between benign and malignant tumours is very important as MPNSTs and malignant schwannoma are aggressive and frequently have poor prognosis, but this can be difficult in presence of multiple benign tumours. In our case, the histological examination performed at the popliteal lesion with the highest uptake confirmed this hypothesis suggesting diagnostic criteria to possibly distinguish malignant from benign lesions; even if biopsy and histological examination were performed in one lesion only it could be assumed that all lesions characterised by significant uptake are similar. Basu et al. published the case of a patient with histopathologic diagnosis of malignant schwannoma in the background of NF1-von Recklinghausen's disease, very similar to ours [1].

Conclusions

In conclusion, in this clinical case, F18-FDG-PET/CT was probably able to help discriminate between benign lesions related to the known NF1 and the malignant transformed ones, and to assist clinical decision making.

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