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A case of ganglioneuroma presenting abnormal FDG uptake

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We report a case of ganglioneuroma with abnormal ^{18}F-fluorodeoxyglucose (FDG) uptake. A 26-year-old woman presented to the hospital with a slowly growing abdominal tumor without symptoms. She was diagnosed with neuroblastoma in childhood and treated by surgery and chemotherapy. Computed tomography (CT) revealed huge retroperitoneal tumors and fused ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET)/CT image showed abnormal accumulation of FDG in tumors with maximal standardized uptake value of 2.02. Considering her past history, ganglioneuroma matured from neuroblastoma was considered, the most likely diagnosis. However, a second primary malignant tumor, such as malignant peripheral nerve sheath tumor arising in ganglioneuroma, could not be ruled out. Then, an excisional biopsy was performed and the diagnosis of mature ganglioneuroma was made. Pathological investigation may be needed to differentiate ganglioneuroma from other malignant tumors and, therefore, FDG-PET/CT findings can be helpful for biopsy planning.

Key words: ganglioneuroma, FDG-PET, neuroblastoma, malignant peripheral nerve sheath tumor

INTRODUCTION

GANGLIONEUROMA is a rare, benign and slowly growing tumor, which may mature from neuroblastoma or ganglioneuroblastoma or may arise *de novo*. Although malignant transformation of ganglioneuroma has not been reported previously, the development of a second primary malignancy in patients with neuroblastoma initially treated by chemotherapy and radiotherapy has been known.[1,2]

To the best of our knowledge, the appearance on ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) of ganglioneuroma as the result of the maturation from neuroblastoma has not been previously reported in the English literature. We here report a case of ganglioneuroma with abnormal FDG uptake, presented as multiple and huge tumors extending from the retroperitoneum to the pelvis and considered as the maturation of a neuroblastoma treated by chemotherapy in infancy.

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CASE REPORT

A 26-year-old woman presented with abdominal tumors without symptoms such as pain, hypertension and diarrhea. Laboratory tests showed the following abnormal result: urinary dopamine; 6040 μg/day. Catecholamine metabolites in plasma and urine except urinary dopamine were within the normal ranges. All other relevant laboratory values including plasma and urinary vanillylmandelic acid and homovanillic acid were within the normal ranges.

Her past history revealed that she migrated to a foreign country immediately after birth and was diagnosed with neuroblastoma because of a left adrenal tumor and retroperitoneal tumors at 6 months of age. She underwent resection of the left adrenal tumor and retroperitoneal tumors as far as possible at 6 months of age and chemotherapy for residual retroperitoneal tumors from 6 months

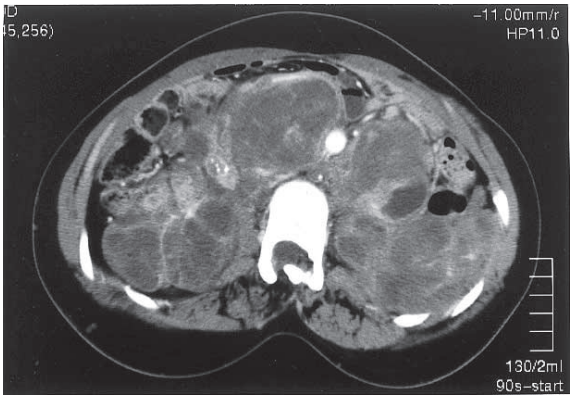


Fig. 1 CT scan of the abdomen shows multiple and huge tumors extending from the retroperitoneum to the pelvis. Contrast-enhanced CT scan shows heterogeneous enhancement of tumors.

to 1 year of age. From 1 to 5 years of age she underwent additional resection for retroperitoneal tumors 5 times, the details of which were unclear.

Computed tomography (CT) revealed multiple and huge tumors extending from the retroperitoneum to pelvis with compression of kidney, aorta, small intestine, colon, and rectum without invasion to them (Fig. 1). Precontrast CT showed punctate or coarse calcification and homogeneously low attenuation. Contrast-enhanced CT showed heterogeneous enhancement. ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy was performed and showed slight accumulation in the early phase in her lower abdomen, suspicious of tumors (Fig. 2).

For further evaluation, FDG-PET was performed using a dedicated PET scanner (ACCEL, SIEMENS, Erlargen, Germany). Blood glucose level was measured and confirmed to be below 120 mg/d*l*. A whole body acquisition started 60 minutes after the injection of 368.5 MBq of FDG. Contrast-enhanced whole-body CT images were obtained beforehand. Then FDG-PET images and CT images were fused using a commercially available work station (Syngo, SIEMENS, Erlargen, Germany). Coronal FDG-PET image and FDG-PET/CT revealed diffuse and slightly increased accumulation of the tumors extending from the retroperitoneum to pelvis (Fig. 3). The faint accumulation of small bowel around the tumors was considered misregistration. The maximal standardized uptake value (SUV) of the tumors was 2.02. To rule out malignancy, an excisional biopsy of the region showing maximal SUV of 2.02 was performed.

Grossly, the tumor was firm, well circumscribed and surrounded by a fibrous capsule. The cut surface of the tumor displayed a yellow appearance and whorled pattern. There were no cystic, hemorrhagic or necrotic components. Histologic examination revealed clusters of ganglion cells deposited in the neuromatous stroma (Fig. 4), which included mature Schwann cells and fibrovascular

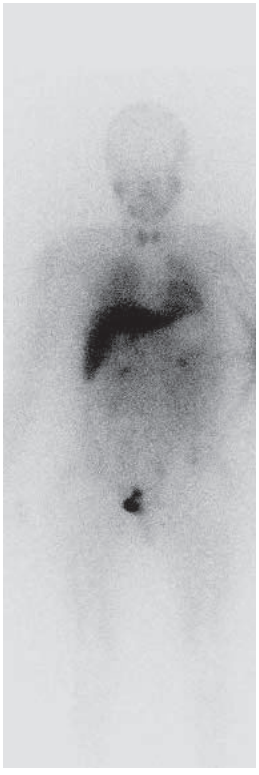


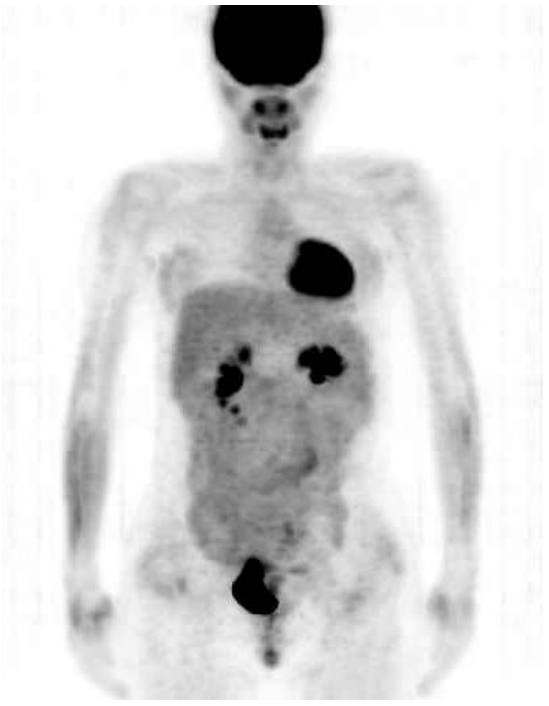
Fig. 2 ^{123}I-MIBG scintigraphy shows slight accumulation in the early phase in her lower abdomen.

septa. Neuroblasts, mitotic figures and amplification of N-myc gene were not seen. Multiple sections revealed no evidence of malignancy.

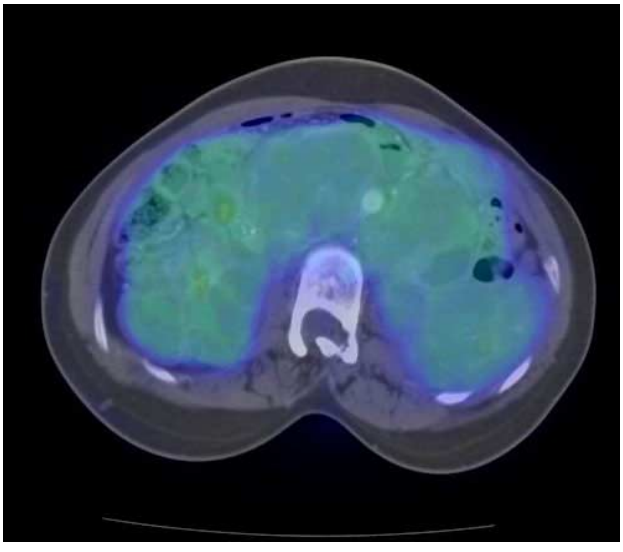
Since the excisional biopsy, she has been observed conservatively and has shown no remarkable change for 1 year.

DISCUSSION

Ganglioneuroma, composed of mature ganglion cells, Schwann cells and nerve fibers, is a rare tumor of neural crest origin in adolescence or young adulthood and can arise from the sympathetic ganglia and the adrenal medulla.[3] The two most common sites for ganglioneuroma are the retroperitoneum and posterior mediastinum (approximately 90%), followed by the cervical region.[3] The most common clinical feature is the palpation of a slowly growing abdominal mass or abdominal pain. Ganglioneuroma can rarely cause symptoms such as hypertension, diarrhea and virilization due to its secretary activity of catecholamines.[4,5] Some ganglioneuromas may arise *de novo* and others may mature from neuroblastoma or ganglioneuroblastoma without reference any previous treatment.[6] Malignant transformation of ganglioneuroma matured from neuroblastoma has not been reported in the English literature. However, some authors have reported a second primary malignant tumor such as malignant



a



b

Fig. 3 a: Coronal PET image shows diffuse increased accumulation of the tumors extending from the retroperitoneum to the pelvis. b: Axial fused FDG-PET/CT image shows abnormal accumulation in tumors.

peripheral nerve sheath tumor (MPNST) arising in ganglioneuroma.[1,2]

Ganglioneuroma manifests as a round or ovoid and well-circumscribed mass. On CT, coarse or punctate calcification like in the present case can be detected in approximately 20% of cases.[7] Precontrast CT reveals either homogeneously or heterogeneously lower attenuation than that of muscle. Contrast-enhanced CT shows

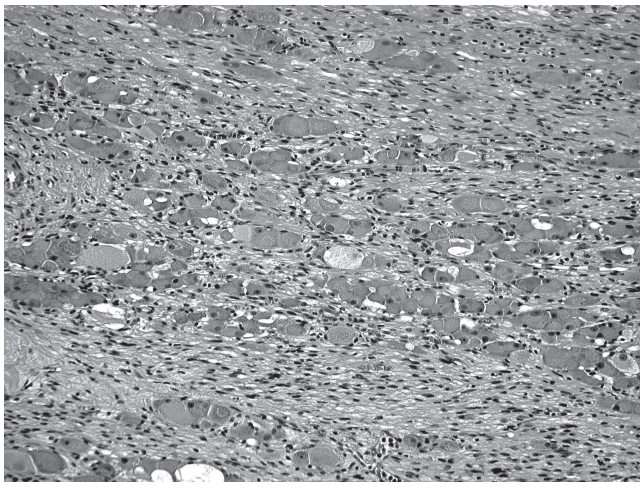


Fig. 4 High power photomicrograph of the tumor shows clusters of ganglion cells deposited in a neuromatous stroma.

from slight to moderate homogeneous or heterogeneous enhancement.[4,5,7,8] MR imaging shows homogeneously low to intermediate signal intensity on T1-weighted images and intermediate to high signal intensity on T2-weighted images. Curvilinear bands of low signal intensity on T1- and T2-weighted images are characteristic of ganglioneuroma.[9]

On ^{123}I-MIBG scintigraphy, slightly increased uptake areas, which reflect production sites of catecholamine in ganglioneuroma, can be seen in approximately 56%, similar to our case. Although the amount of catecholamine secretion correlates with tumor size, the degree of accumulation of ^{123}I-MIBG does not correlate with it.[10] Indeed, in the current huge tumors, faint ^{123}I-MIBG uptake was seen.

The utility of FDG-PET is well established and plays an important role in detecting, characterizing and monitoring various tumors. Although the degree of FDG uptake generally correlates with histological grading, with greater FDG uptake in high grade soft tissue tumors, some benign tumors can show high FDG uptake.[11] FDG-PET findings of ganglioneuroma have not been previously reported. However, Cardona et al. reported that quantitative evaluation, using the maximal SUV with cut-off 1.8, is useful in distinguishing benign neurogenic tumors from malignant ones such as MPNST.[11] Although, considering the current patient's past history, ganglioneuroma matured from neuroblastoma was considered strongly and most probably, malignant tumors like MPNST arising in ganglioneuroma could not be ruled out either because the tumor showed a maximal SUV of 2.02. Thus an excisional biopsy was performed, and the diagnosis of ganglioneuroma was confirmed histologically.

In conclusion, we here demonstrated a case of ganglioneuroma matured from neuroblastoma, showing abnormal FDG accumulation. Pathological examination may

be needed to differentiate ganglioneuroma from other malignant tumors and, therefore, FDG-PET/CT findings can be helpful for biopsy planning.

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