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Case Report

# A Case of Suspicious Gangliocytoma with Heterogeneously Distributed Lesions in the Thalamus and Basal Ganglia

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We report a case of a 24-year-old woman who presented with an uncomfortable feeling in her right foot with a 6-month history of slight weakness in her right hand. Neuroimaging demonstrated irregular shaped lesions in the left thalamus and basal ganglia in addition to spotty lesions in the contralateral thalamus. The MRI showed high-intensity signals on T2-weighted, fluid-attenuated inversion recovery, and diffusion-weighted images. The lesions demonstrated low-intensity signaling on T1-weighted images and were slightly enhanced with gadolinium. Other examinations including positron emission tomography, MR spectroscopy, and laboratory tests did not reveal any specific information regarding the lesions. The biopsied specimens, from the left basal ganglia, revealed proliferation of dysplastic neuronal cells without any neoplastic glial elements; thus, gangliocytoma (WHO grade I) was the most likely diagnosis. The patient was further observed based on this diagnosis of suspicious gangliocytoma, and the follow-up MRI, performed a year after the biopsy, revealed that the disease was stable. To our knowledge, gangliocytoma in the thalamus and basal ganglia have not been reported. Additionally, the findings of the magnetic resonance imaging (MRI) in this case were unique and different from those previously reported in cases of gangliocytoma. The authors report this unique case and discuss the radiological, pathological, and genetic findings.

**Keywords:** deep brain structure, irregular shaped lesions, gangliocytoma

## Introduction

Gangliocytomas are rare tumors with an incidence ranging from 0.1% to 0.5% of all brain tumors.[1,2] These tumors frequently occur in the cerebral lobe, especially in the temporal lobe.[3] Most gangliocytomas have been reported along with gangliogliomas, and there has been little study of the characteristics of gangliocytomas alone, including radiological data.[3] We report a rare case of suspicious gangliocytoma in the thalamus and basal ganglia with unique radiological findings.

## Case Report

A previously healthy 24-year-old woman presented with an uncomfortable feeling in her right foot, in addition to a 6-month history of slight weakness in her right hand. Head computed tomography (CT) scans demonstrated a low-density area in the left thalamus and basal ganglia. Calcification was not observed. On magnetic resonance imaging (MRI), high-intensity areas were observed in the left thalamus, putamen, and internal capsule through diffusion-weighted images (Fig. 1A), T2-weighted (Figs. 1B and 1C) and fluid-attenuated inversion recovery (Fig. 1D). These hyperintense areas were also found to be spotted in the right thalamus (Figs. 1B–1D). The lesions showed low-intensity signaling on T1-weighted images (Fig. 1E), and demonstrated slight and heterogeneous enhancement with gadolinium (Fig. 1F). The enhancement of contralateral spotty lesions was not obvious. Atrophy of the ipsilateral midbrain was not found. Fluorodeoxyglucose (FDG)-positron emission tomography (PET) showed the lesions had lower uptake than the cerebral cortex, while methionine-PET did not show any uptake areas. Multivoxel MR spectroscopy demonstrated an increased choline/N-acetylaspartate ratio in the T2-hyperintense area. Laboratory tests including labeling with tumor markers, an antinuclear antibody, infectious markers and hormonal basal values were within the normal range. A stereotactic biopsy was performed for diagnosis. We targeted the lateral area of the left caudate head and the anterior limb of the left internal capsule, which were slightly enhanced lesions.

On microscopic examination, the biopsied specimen revealed scattered proliferation of neuron-like cells (Fig. 2A). The neuron-like cells often had multiple nuclei and contained vacuolation. No neoplastic glial cells were identified in the background. The immunohistochemical staining revealed that the vacuolation of neuron-like cells was positive for synaptophysin (Fig. 2B), and a part of the neuron-like cells were positive for chromogranin A, CD34 and neurofilament protein (NFP) (Figs. 2C–2E). Staining for glial fibrillary acidic protein (GFAP) was positive for reactive astrocytes in the background, but negative for the neuron-like cells (Fig. 2F). NeuN also demonstrated immunonegative staining (Fig. 2G). The Mib-1 labeling index was 0.7% (Fig. 2H). Gangliocytoma (WHO grade I) was the most likely diagnosis based on these pathological findings such as the proliferation of

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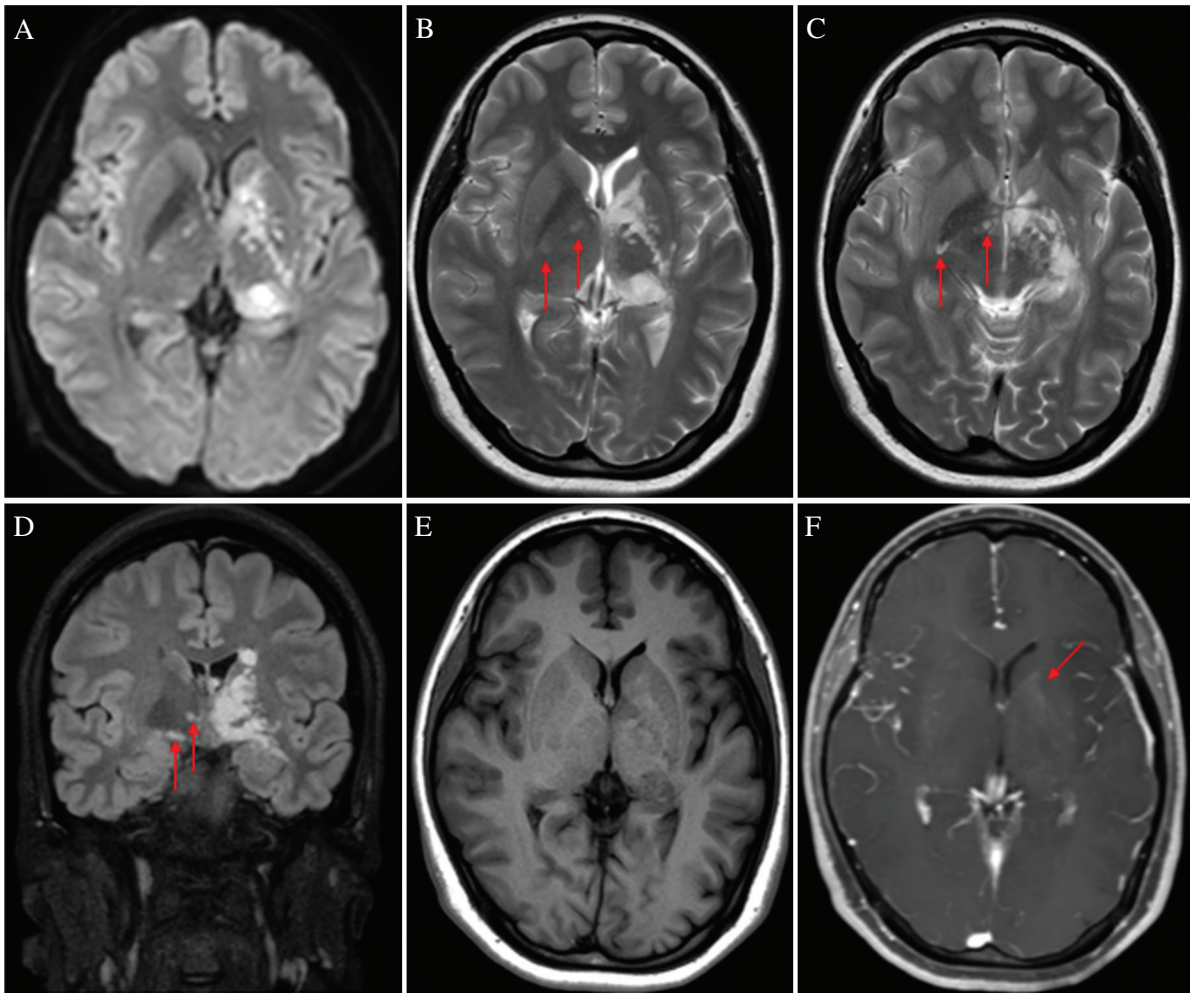


**Fig. 1** Diffusion-weighted (A), T2-weighted (B, C) and fluid-attenuated inversion recovery (D) imaging showing high-intensity areas in the thalamus and basal ganglia. These hyperintense areas were also found spotted in the opposite side (B–D, arrows). The lesion shows low-intensity signaling on T1-weighted imaging (E) and slight enhancement on gadolinium-enhanced MR images (F, arrow).

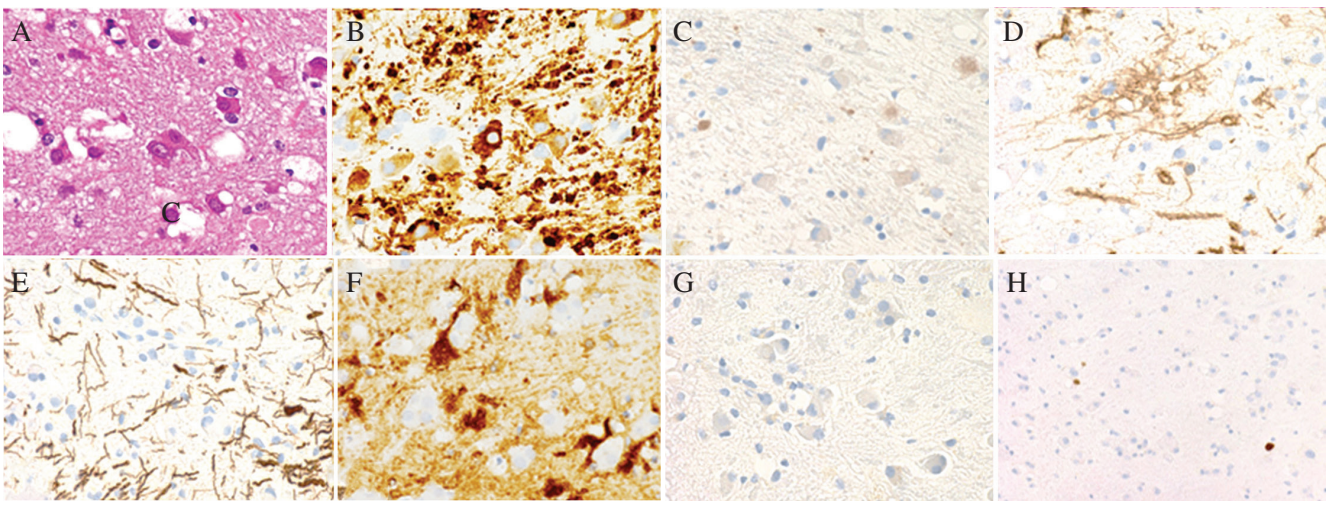


**Fig. 2** Microscopic findings. The tumor reveals scattered proliferation of neuron-like cells, mainly in the gray matter, which has multiple nuclei and contains vacuolation (A). The vacuolation of neuron-like cells are positive for synaptophysin (B), and a part of the neuron-like cells are positive for chromogranin A, CD34, and NFP (C–E). Staining for GFAP is positive for reactive astrocytes in the background, but negative for the neuron-like cells (F). NeuN also demonstrated immunonegative staining (G). The Mib-1 labeling index is 0.7% (H). Original magnification ×60 (A–G), ×0 (H).

dysplastic neuron-like cells without neoplastic glial elements. Genetic analysis demonstrated wild-type status of *IDH-1* (R132H), Histone H3.3, *BRAF* (V600E), and *TERT* promoter, as well as absent *KIAA1549-BRAF* fusion. The patient was observed based on the diagnosis of suspicious gangliocytoma, and the follow-up MRI, performed a year after the biopsy, revealed that the disease was stable.

## Discussion

There have been a small number of reports that have addressed gangliocytoma alone.[1,2,4–18] Gangliocytomas are mostly reported along with gangliogliomas. Previously reported locations of gangliocyotmas include the cerebral lobe,[4–12] the spine,[1,2,12,13], the medulla,[14,15] the hypothalamus,[16] the third ventricle,[17] and the pineal gland.[18] Ganglicytoma of the pituitary and dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) are separately reviewed in the WHO classification of *Tumours of the endocrine organs*[19] and *Tumours of the central nervous system*.[3] To our knowledge, gangliocytoma in the thalamus and basal ganglia have not been reported.

The MRI findings in this case, demonstrated irregular shaped lesions in the deep brain with spotted lesions in the contralateral thalamus, were unique and different from previous reports. It was difficult to consider diagnosing a gangliocytoma from the preoperative MRI alone. A germ cell tumor of the basal ganglia was radiologically suspected at first. However, low-density CT findings, absence of midbrain atrophy, lack of gadolinium enhancement along with lack of uptake on the Methionine-PET were not compatible a diagnosis of germ cell tumors. The majority of reported gangliocytomas reveal masses of iso- to low-intensity signal on T1-weighted images and high-intensity signal on T2-weighted images.[1,4,6,8,10,12–14] In these cases, calcification and cyst formation are frequently observed.[1,5,8,11,12] Some of these cases demonstrate gadolinium enhancement,[5,6,10,11–15,17] however some cases do not.[2,4,12] Dural tail sign was reported in two cases.[6] Heterogeneously distributed lesions observed in this case have not been previously reported.

Additionally, the spotted lesions observed in the contralateral thalamus were an unprecedented finding of gangliocytoma. A tumor that spread to the opposite side along nerve fibers, such as the anterior commissure and the optic radiation has been reported in cases of glioblastoma.[3] However, it might be reasonable in the case of gangliocytoma to consider that the spotty lesions occurred as multifocal lesions rather than invasive lesions. Dysplastic neuronal cells can originate from the periventricular area, as in normal neurogenesis, and some may stay ectopically in the white matter.[20] The bilateral deep brain lesions in our case might have resulted from ectopic proliferation of dysplastic neurons generated from the periventricular area.

A limitation of this case is that the biopsied specimens comprised just a small portion of the tumor but was used to explain the whole aspect. A tumor is categorized as a ganglioglioma if it has neoplastic ganglion cells in combination with neoplastic glial cells.[3] The spectrum of gangliogliomas varies between tumors ranging from a predominantly neuronal phenotype to a dominant glial population.[3] Therefore, the lack of neoplastic glial cells in the biopsied specimens did not rule out ganglioglioma. The final diagnosis was thus suspicious gangliocytoma.

Genetic profiles specially addressing gangliocytomas have not been reported, but a close genetic relationship to gangliogliomas seems to be possible.[3] *IDH1/2* is often wild type in ganglion cell tumors and a mutation status strongly supports the diagnosis of diffuse astrocytoma.[3] *BRAF* V600E mutation is the most common genetic alternation in gangliogliomas, occurring in 20–60%. Histon H3.3 mutation was reported as absent in gangliogliomas, but present in some cases of anaplastic ganglioglioma located in midline area.[21] *hTERT* mutation was reported mainly in adult anaplastic gangliogliomas.[22] The genetic profiles of our case were not specific but compatible with ganglion cell tumor. In addition, they did not support malignant tumors including diffuse astrocytoma or anaplastic ganglioglioma, and these data helped us to select observation.

In conclusion, we reported a rare case of suspicious gangliocytoma located in the thalamus and basal ganglia, which were previously unreported sites. The MRI results demonstrated heterogeneously distributed lesions in the deep brain, with spotted lesions in the contralateral thalamus. The present case is unique and demonstrates different MRI findings from previous reports.

## Conflicts of Interest Disclosure

The authors declare that there is no conflict of interest. All authors who are members of the Japan Neurosurgical Society (JNS) have registered online self-reported COI disclosure statement forms through the website for JNS members.

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