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Case Report

Multinodular and vacuolating neuronal tumor: A case report and literature review

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Abstract

Background: Multinodular and vacuolated neuronal tumor (MVNT) is a benign neuronal tumor that is newly recognized as architectural appearance that may be related to ganglion cell tumors in 2016 World Health Organization Classification of Tumors of the Central Nervous System. Herein, we report a case of MVNT in a 60-year-old man with a thorough literature review.

Case Description: A 60-year-old male was pointed out the presence of intracerebral neoplasm located in left frontal lobe by a comprehensive medical examination. We suspected dysembryoplastic neuroepithelial tumors and proposed him to wait and see, but he wished to undergo surgery for diagnosis. We performed en bloc resection and pathological findings were consistent with MVNT. He was discharged on the 8th day after the operation without any complications. He remained stable without recurrence at the 16-month postoperative follow-up.

Conclusions: Further studies may be helpful to fully understand the radiological and histological findings of MVNT development. As a result, we will be able to prevent the aggressive treatment if we established their major features.

Key Words: Brain tumor, multinodular and vacuolated pattern, radiographic characteristics

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INTRODUCTION

Multinodular and vacuolated pattern is newly recognized as architectural appearance that may be related to ganglion cell tumors in 2016 World Health Organization Classification of Tumors of the Central Nervous System.[6] Multinodular and vacuolating neuronal tumors (MVNT) of the cerebrum were first documented in 2013.[5] They are characterized by multiple tumor nodules, vacuolar alteration, and widespread immunolabeling for human neuronal protein HuC/HuD. A PubMed search using the keywords "multinodular," "vacuolating," "neuronal," and "tumor" identified only 16 cases. Herein, we present the 17th MVNT case in a 60-year-old man who had no complaint. We revealed the radiographic characteristics of this entity with a thorough literature review.

CASE REPORT

A 60-year-old Japanese man underwent a comprehensive medical examination with brain magnetic resonance imaging (MRI). The neurological examination indicated no significant findings. However, MRI revealed a

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25 mm × 17 mm, nonenhanced lesion with gadolinium in the left superior frontal gyrus as a hypointense mass in T1-weighted imaging (T1WI) and hyperintense in T2-weighted imaging (T2WI) and fluid attenuated inversion recovery (FLAIR) without any mass effect or edema [Figure 1a-d]. He was referred to our hospital for further evaluation. Since he did not show any neurological symptoms and the images suspect a benign lesion, we proposed him and his family to wait and see. However, they proposed us to remove the lesion and make a confirmed diagnosis.

The tumor was exposed via a transcortical approach and we could not identify the obvious boundary between tumor and normal brain. Total en bloc resection was performed with intraoperative navigation. The postoperative course was uneventful and he was discharged on the 8th day after the operation without any complications. He remained stable without recurrence of the lesion on MRI at the 16-month postoperative follow-up [Figure 1e-g].

Histopathological findings

We could resect the tumor en bloc and performed total resection of tumor [Figure 2a]. The lesion had a multinodular appearance laying on the gray-white matter junction under low-power magnification microscopic examination [Figure 2b-d]. We could see alpha-internexin expression in tumor stroma [Figure 2c] and the proliferation of cells resembling ganglion cells, with eccentric

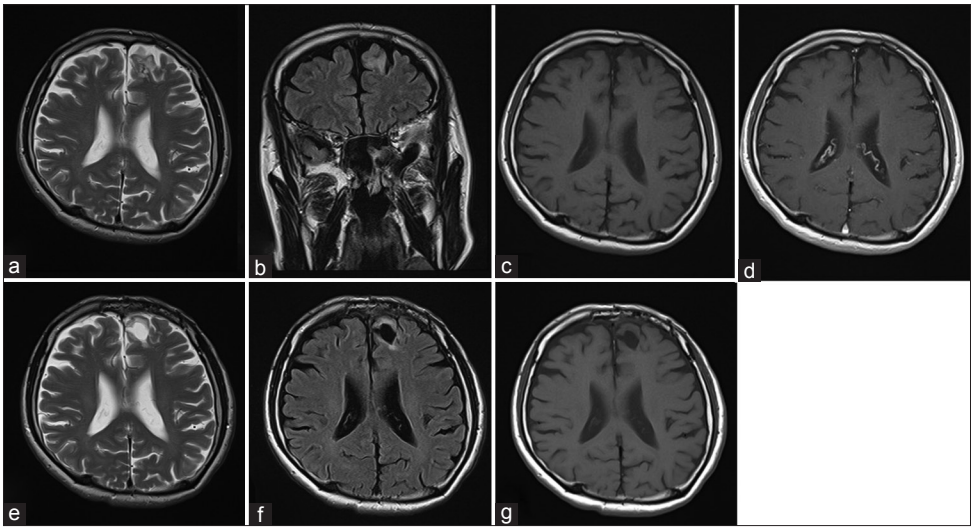

Figure 1: Preoperative MRI revealed the lesion identified in the left superior frontal gyrus (a-d). The lesion showed hyperintensity on T2WI (a) and FLAIR (b). The lesion demonstrated slight hypointensity on T1WI (c) and does not exhibit mass effect, contrast enhancement (d), or associated edema. Postoperative MRI (16 months after operation) showed total resection and the removed cavity with no evidence of tumor recurrence by T2WI (e), FLAIR (f), and T1WI (g)

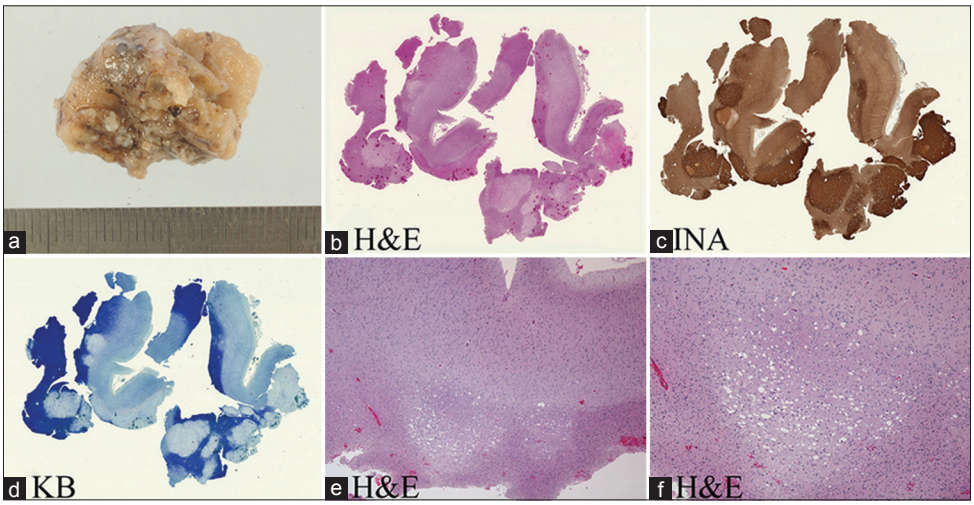

Figure 2: The lesion was resected in an en bloc fashion (a). Microscopy with low power magnification demonstrating a well-demarcated subcortical lesion abutting gray and white matter (b, hematoxylin and eosin stain (H and E)). Alpha-internexin (INA) expression is detected in tumor stroma (c) and Kluber-Barrera (KB) staining confirms the absence of myelin in the tumor lesion (d). The lesion demonstrates clear delineation from the surrounding brain without evidence of infiltration (e-f, H and E)

round nuclei, foamy, and relatively ample eosinophilic cytoplasm [Figure 2e and f]. Mitotic figures or vascular proliferation were absent. On immunohistochemical analysis with neuronal antigens, the tumor cells showed positive staining for HuC/HuD [Figure 3a]. The neuronal tumor cells demonstrated weak to moderate cytoplasmic immunoreactivity to neuronal nuclear antigen (NeuN), synaptophysin, and nuclear oligodendrocyte transcription factor (Olig2) [Figure 3b-d]. The ganglioid cells showed negative staining for glial fibrillary acidic protein [Figure 3e]. Immunostaining for p53, CD34, and mutant IDH1R132H was negative. The MIB-1 staining index was <1%. These findings led us to diagnose the lesion as MVNT.

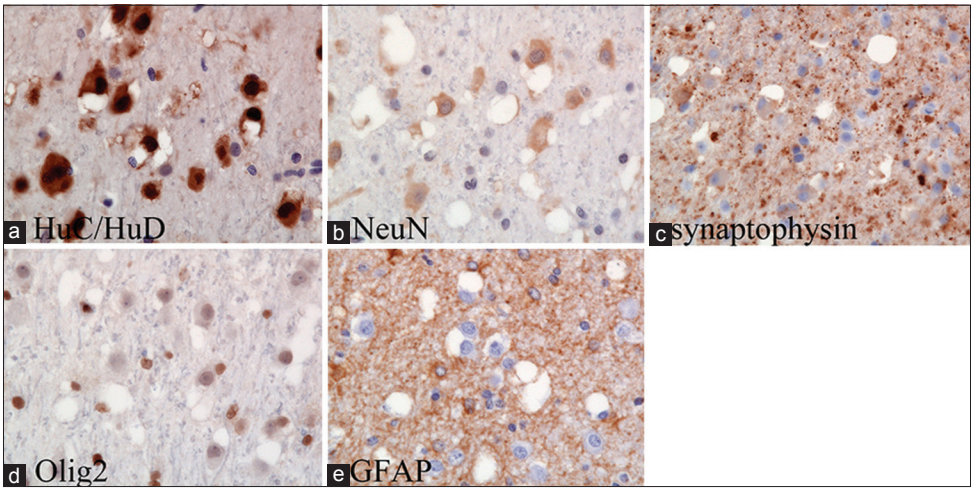

Figure 3: The neuronal tumor cells are intensely stained by HuC/HuD (a), but negatively or weakly stained for neuronal nuclear antigen (NeuN) (b), synaptophysin (c) and nuclear oligodendrocyte transcription factor (Olig2) (d). The ganglioid cells are unreactive for glial fibrillary acidic protein (GFAP) (e)

Table 1: Clinical and demographic characteristics

Age (year)/Sex	Location	Clinical manifestation (duration)	Surgery	Follow-up (month)
Huse *et al*. [2013][5]				
38M	R temporal	Dizziness, loss of attention (2 years)	SR	8
54F	L temporal	Dizziness, dysarthria, blurred vision, R numbness (one episode)	TR	67
38F	R parietal	Grand mal seizure (one episode)	SR	16
35M	R temporal	Episodic confusion (14 months)	SR	6
54M	R temporal	Partial complex and grand mal seizure (>40 years)	TR	11
31F	L temporal	Simple complex, and grand mal seizure (2 years)	SR	12
41M	R temporal	Confusion after motor vehicle accident (one episode)	TR	60
63F	R temporal	L numbness and tingling (1 year)	TR	36
64M	L temporal	Staring and mumbling (1 episode)	Biopsy	N/F
52F	L frontal	Episodic vertigo (2 years)	TR	N/F
Bodi *et al*. [2014][1]				
34F	L frontal	Intractable epilepsy (24 years)	TR	27
71F	L temporal	None (MND: dysarthria and increased difficulty with swallowing)	(-)	22
Fukushima *et al*. [2015][4]				
37M	L parietal	Epileptic seizure with speech arrest	TR	18
Nagaishi *et al*. [2015][7]				
22F	L frontal	Continuous headache (2 weeks)	SR	6
Yamaguchi *et al*. [2016][8]				
41F	R temporal	Complex partial seizure after motor vehicle accident (22 years)	SR	N/A
Cathcart *et al*. [2017][3]				
29M	R temporal	Complex partial seizure, headache	Biopsy	N/A
Present case				
60M	L frontal	No complaint	TR	16

F: Female, L: Light, M: Male, MND: Motor neuron disease, N/A: Not available, N/F: No follow-up, R: Right, SR: Subtotal resection, TR: Total resection

DISCUSSION

MVNTs tend to be recognized by the presence of seizure or seizure equivalents, but our case is incidentally found by a comprehensive medical examination. The lesions had potentially suspect of gliomas or the patients suffered from some neurologic complaints, then surgical extirpations were made to remove the lesions and to determine the definite diagnosis in almost all cases except one case.[1,3-5,7,8] The exact incidence of MVNTs is unknown and only 17 cases including ours are reported up to now [Table 1].[1,3-5,7,8] The median age of diagnosis was 44.9 years (range 22–71 years). Eight out of 17 cases were male patients and all of the cases except our case showed some neurological symptoms and the most common location was the temporal lobe (11 cases, 64.7%). Follow-up intervals are available from 12 cases and the average was 23.1 months. In addition, none of the patients demonstrated disease progression. The lowest patient's age is 22-year-old case, and probably MVNTs are acquired lesion as a previous report mentioned.[4] Huse *et al*. mentioned that MVNTs might indicate a neoplastic genetic background in a subset of their cases, and the cases should be continuously followed by images to know better what MVNTs are.[5]

The differential diagnosis from radiological findings included dysembryoplastic neuroepithelial tumor (DNT), low-grade glioma, cortical dysplasia, hamartoma, and so on. The lesions show small bubbly appearing indolent subcortical tumor and usually have difficulty to be identified in computed tomography. On MRI, the lesions show iso- or hypointense on T1WI, hyperintense on T2WI, and increased signal in FLAIR sequences as we can identify this appearance in case of DNTs.[2] In addition, there are no evidence of edema or mass effect in all cases.[1,3-5,7,8] However, the lesions appear as a cluster of well-circumscribed hyperintense T2WI signal bubbles located predominantly in the subcortical white matter and exhibit a small cystic component where we cannot see this characteristics in DNTs.[2] In particular, the entities were diagnosed as DNT in some previous cases.[1,5] This difference can distinguish these two entities. The radiographic characteristics are shown, resulting in uniform appearances, in Table 2. The data allow us to diagnose a subcortical white matter lesion with or without some multiple satellite nodules around the main multinodular lesion as MVNT.

As the pathological diagnosis accompanies with some difficulties as previous authors discussed, the

Table 2: Radiographic characteristics of patient cohort

T1WI	T2WI	FLAIR	Gd enhancement	Edema or mass effect	Satellite nodule	Size (mm)	Other findings
Huse *et al*. (2013)[5]							
N/M	hyper	hyper	(-)	(-)	(+)	41 × 22	
N/M	hyper	hyper	(-)	(-)	(+)	17 × 18	
iso	hyper	hyper	Faint (+)	(-)	(+)	30 × 24	
N/M	hyper	hyper	(-)	(-)	(-)	36 × 26 × 19	
iso	hyper	hyper	(-)	(-)	(+)	17 × 26 × 14	
iso	hyper	hyper	Faint (+)	(-)	(+)	31 × 25 × 31	
N/M	hyper	N/M	(-)	(-)	(-)	20	
hypo	hyper	hyper	(-)	(-)	(+)	22	MRS: choline/NAA ratio elevated
iso	hyper	hyper	(-)	(-)	(-)	N/M	
N/M	hyper	hyper	(-)	(-)	(+)	25 × 14 × 20	
Bodi *et al*. (2014)[1]							
N/M	hyper	N/M	N/M	(-)	(+)	N/M	
N/M	hyper	N/M	N/M	(-)	(+)	N/M	
Fukushima *et al*. (2015)[4]							
iso	hyper	hyper	(-)	(-)	(-)	26 × 17 × 14	MRS: choline/NAA ratio elevated
Nagaishi *et al*. (2015)[7]							
N/M	hyper	hyper	(-)	(-)	(+)	37 × 27	MRS: choline/NAA ratio elevated
Yamaguchi *et al*. (2016)[8]							
iso	hyper	hyper	(-)	(-)	(-)	N/M	CT: no calcification
Cathcart *et al*. (2017)[3]							
mild hyper	hyper	hyper	(-)	(-)	(-)	27 × 26 × 21	
Present case							
Hypo	hyper	hyper	(-)	(-)	(-)	25 × 17	

FLAIR: Fluid-attenuated inversion recovery, Gd: gadolinium, MRS: magnetic resonance spectroscopy, N/M: not mentioned, T1WI: T1-weighted imaging, T2WI: T2-weighted imaging

establishment of definite imaging characterization may help to avoid invasive surgical interventions.[1,3-5,7,8] Unless the clinical conditions are severe or uncontrollable by some medications, it is a better attitude to this rare entity that clinicians propose a patient wait and see. The actual background, including pathogenesis of MVNTs, remains unknown, and further studies on larger series might be necessary to better understand the behavior of MVNTs development.

CONCLUSION

Although extremely rare and usually nonfatal, MVNT should be considered in the differential diagnosis of multinodular lesion with no edema in the subcortical white matter. The clinician can suggest the best way to manage the rare entity by well-understanding of the neuro-radiologic behavior of MVNTs.

Declaration of patient consent

The patient and his family have given the necessary consent for the case report to be published.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bodi I, Curran O, Selway R, Elwes R, Burrone J, Laxton R, *et al*. Two cases of multinodular and vacuolating neuronal tumour. Acta Neuropathol Commun 2014;20:2-7.
2. Bulakbasi N, Kocaoglu M, Sanal TH, Tayfun C. Dysembryoplastic neuroepithelial tumors: Proton MR spectroscopy, diffusion and perfusion characteristics. Neuroradiology 2007;49:805.
3. Cathcart SJ, Klug JR, Helvey JT, L White M, Gard AP, McComb RD. Multionodular and vacuolating neuronal tumor: A rare seizure-associated entity. Am J Surg Pathol 2017;41:1005-10.
4. Fukushima S, Yoshida A, Narita Y, Arita H, Ohno M, Miyakita Y, *et al*. Multinodular and vacuolating neuronal tumor of the cerebrum. Brain Tumor Pathol 2015;32:131-6.
5. Huse JT, Edgar M, Halliday J, Mikolaenko I, Lavi E, Rosenblum MK. Multinodular and vacuolating neuronal tumors of the cerebrum: 10 cases of a distinctive seizure-associated lesion. Brain Pathol 2013;23:515-24.
6. Louis DN, Perry A, Reifenberger G, von Deimling, Figarella-Branger D, Cavenee WK, *et al*. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: A summary. Acta Neuropathol 2016;131:803-20.
7. Nagaishi M, Yokoo H, Nobusawa S, Fujii Y, Sugiura Y, Suzuki R, *et al*. Localized overexpression of alpha-internexin within nodules in multinodular and vacuolating neuronal tumors. Neuropathology 2015;35:561-8.
8. Yamaguchi M, Komori T, Nakata Y, Yagishita A, Morino M, Isozaki E. Multinodular and vacuolating neuronal tumor affecting amygdala and hippocampus: A quasi-tumor? Pathol Int 2016;66:34-41.