Multinodular and vacuolating neuronal tumor of the cerebrum

Multinodular and vacuolating neuronal tumors of the cerebrum (MVNT) are superficial neuronal tumors in adults that were first documented in 2013 [1].

It is a new pattern of neuronal tumour included in the World Health Organization Classification of Tumors of the Central Nervous System 2016, as a unique cytoarchitectural pattern of gangliocytoma.

There are fifteen reports in the literature to date. They are typically associated with late onset epilepsy.

Clinical, pathological and genetic data could indicate that MVNT aligns more with a malformative lesion than a true neoplasm with origin from a progenitor neuro-glial cell type showing aberrant maturation [2].

Differential diagnosis

Dysembryoplastic neuroepithelial tumor - DNET can appear similar but usually is mostly cortical (rather than subcortical) often has bright FLAIR rim focal cortical dysplasia (Type II) high T2 signal deep to cortex is in the same location but is usually associated with a radial glial band (transmantle sign) and with thickened abnormal overlying cortex perivascular spaces location can be similar usually more elongated along vessel long axis fully attenuating on FLAIR [3].

Treatment

MVNTs appear to be benign tumours with very indolent biological behaviour which can, if asymptomatic, be followed with imaging alone. In symptomatic patients (epileptic) surgical resection often controls seizures, with no tumour regrowth reported [4] [5] [6] [7].

Case series

2017

Thom et al. present a series of ten cases and compare their pathological and genetic features to better characterised epilepsy associated malformations including focal cortical dysplasia type II (FCDII) and low-grade epilepsy associated tumours (LEAT). Clinical and neuroradiology data were reviewed and a broad immunohistochemistry panel was applied to explore neuronal and glial differentiation, interneuronal populations, mTOR pathway activation and neurodegenerative changes. Next generation sequencing was performed for targeted multi-gene analysis to identify mutations common to epilepsy lesions including FCDII and LEAT. All of the surgical cases in this series presented with seizures, and were located in the temporal lobe. There was a lack of any progressive changes on serial pre-operative MRI and a mean age at surgery of 45 years. The vacuolated cells of the lesion expressed mature neuronal markers (neurofilament/SMI32, MAP2, synaptophysin). Prominent labelling

of the lesional cells for developmentally regulated proteins (OTX1, TBR1, SOX2, MAP1b, CD34, GFAPδ) and oligodendroglial lineage markers (OLIG2, SMI94) was observed. No mutations were detected in the mTOR pathway genes, BRAF, FGFR1 or MYB. Clinical, pathological and genetic data could indicate that MVNT aligns more with a malformative lesion than a true neoplasm with origin from a progenitor neuro-glial cell type showing aberrant maturation [8].

Nunes et al. report 33 cases of presumed multinodular and vacuolating neuronal tumor of the cerebrum that exhibit a remarkably similar pattern of imaging findings consisting of a subcortical cluster of nodular lesions located on the inner surface of an otherwise normal-appearing cortex, principally within the deep cortical ribbon and superficial subcortical white matter, which is hyperintense on FLAIR. Only 4 of the cases are biopsy-proven because most were asymptomatic and incidentally discovered. The remaining were followed for a minimum of 24 months (mean, 3 years) without interval change. They demonstrate that these are benign, nonaggressive lesions that do not require biopsy in asymptomatic patients and behave more like a malformative process than a true neoplasm [9].

2013

Huse et al. report 10 cases of a non-neurocytic, purely neuronal tumor affecting adults. Situated in the cerebral hemispheres, with 7 of 10 confined to the temporal lobes, most presented with seizures as their principal clinical manifestations. On magnetic resosnance imaging (MRI), the tumors generally appeared solid and non-contrast enhancing with minimal diffuse infiltration, edema, or mass effect. Six examples demonstrated internal nodularity. Microscopically, the tumor cells were largely distributed into discrete and coalescent nodules exhibiting varying degrees of matrix vacuolization, principally within the deep cortical ribbon and superficial subcortical white matter. Populating elements ranged from morphologically ambiguous to recognizably neuronal, with only two cases manifesting overt ganglion cell cytology. In all cases, tumor cells exhibited widespread nuclear immunolabeling for the HuC/HuD neuronal antigens, although expression of other neuronal markers, including synaptophysin, neurofilament and chromogranin was variable to absent. Tumor cells also failed to express GFAP, p53, IDH1 R132H, or CD34, although CD34-labeling ramified neural elements were present in the adjoining cortex of seven cases. Molecular analysis in a subset of cases failed to reveal DNA copy number abnormalities or BRAF V600E mutation. Follow-up data indicate that this unusual neuronal lesion behaves in benign, World Health Organization (WHO) grade I fashion and is amenable to surgical control [10].

Case reports

2018

A 52-year-old male who presented to the Hospital Universitario Gregorio Marañón with a 2-year-history of absence of seizures. Brain MRI showed a T2-hyperintense lesion with no contrast enhancement affecting his temporal lobe. Temporal craniotomy and microsurgical resection was scheduled. The procedure was uneventful and a grayish, gluey mass was sent for pathologic analysis. The tumor was formed by immature neuronal cells organized in nodules with a vacuolated matrix. A

thorough immunohistochemical analysis showed positivity for: Protein Gene Product 9.5. ATRX. OLIG2. SOX10. p16. Nestin. Synaptophysin. The findings were consistent with multinodular and vacuolating neuronal tumor. The patient has been seizure-free after surgery and with no signs of tumor progression.

They present a thorough review addressing this uncommon tumor along with a description of the 17th reported case of MVNT, a tumor that was described for the first time in 2013. Further studies and case studies are necessary to establish a well-defined morphological and immunohistochemical profile along with knowledge about its natural history [11].

2015

Fukushima et al. report a case of MNVT involving a 37-year-old man who presented with an epileptogenic, superficial solid lesion in the left parietal lobe. Histomorphology of the resected specimen was characterized by nodular lesions with vacuolation. Nodules comprised irregular proliferation of neuronal cells, which ranged from ganglion-like forms to those with indistinct lineage. Immunohistochemical analysis showed that the lesional cells stained positively for HuC/HuD, synaptophysin, and Olig2, and negatively for NeuN, neurofilament, chromogranin A, GFAP, CD34, IDH1(R132H), and BRAF(V600E). Eighteen months following surgery, the patient is well and without neurological deficits. MVNTs are distinctive tumors that should be differentiated from ganglion cell tumors, dysembryoplastic neuroepithelial tumors, and malformation of cortical development [12].

2014

Bodi et al. report the findings in two cases with similar features, a surgical resection and the other an autopsy specimen.Case 1, a 34-year-old female, underwent surgical resection for a multinodular non-enhancing frontal white matter lesion causing intractable epilepsy. Case 2, presented with motor neurone disease (MND) at the age of 71 and MRI scanning revealed extensive multinodular non-enhancing white matter lesions in the temporal lobe. There was no history of epilepsy and post mortem histology confirmed MND.Macroscopically multiple small grey well-formed, discrete and coalescent nodules were seen in the deep cortex and subcortical white matter. On histology, mature-looking neurons with large cytoplasmic vacuoles were distributed in a fibrillary background, where vacuoles were also noted. In the resected tumour scattered oligodendroglia-like cells were present. No ganglion cells were seen. The vacuolated cells exhibited immunopositivity for synaptophysin, HuC/HuD and p62 but were negative for NeuN, neurofilament, GFAP, IDH1, nestin and CD34. Electron microscopy showed non-membrane bound cytoplasmic vacuoles in the neurons and in some neuronal processes. The seizures recurred in Case 1.Some clinicopathological features of this lesion suggest a possible relationship with dysembryoplastic neuroepithelial tumour (DNT) although the morphological features are not typical of DNT. Case 2 demonstrates that MVNT may remain asymptomatic [13].

References

[1], [6], [10]
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 Sep;23(5):515-24. doi: 10.1111/bpa.12035. Epub 2013 Feb 1. PubMed PMID: 23324039.

[2], [8]
Thom M, Liu J, Bongaarts A, Reinten RJ, Paradiso B, Jäger HR, Reeves C, Somani A, An S, Marsdon D,

McEvoy A, Miserocchi A, Thorne L, Newman F, Bucur S, Honavar M, Jacques T, Aronica E. MULTINODULAR AND VACUOLATING NEURONAL TUMOURS IN EPILEPSY: DYSPLASIA OR NEOPLASIA? Brain Pathol. 2017 Aug 19. doi: 10.1111/bpa.12555. [Epub ahead of print] PubMed PMID: 28833756.

3) https://radiopaedia.org/articles/multinodular-and-vacuolating-neuronal-tumours

4) , 13) Bodi I, Curran O, Selway R, Elwes R, Burrone J, Laxton R, Al-Sarraj S, Honavar M. Two cases of multinodular and vacuolating neuronal tumour. Acta Neuropathol Commun. 2014 Jan 20;2:7. doi: 10.1186/2051-5960-2-7. PubMed PMID: 24444358; PubMed Central PMCID: PMC3899932.

5) , 12) Fukushima S, Yoshida A, Narita Y, Arita H, Ohno M, Miyakita Y, Ichimura K, Shibui S. Multinodular and vacuolating neuronal tumor of the cerebrum. Brain Tumor Pathol. 2015 Apr;32(2):131-6. doi: 10.1007/s10014-014-0198-9. Epub 2014 Aug 22. PubMed PMID: 25146549.

7) , 9) Nunes RH, Hsu CC, da Rocha AJ, do Amaral LLF, Godoy LFS, Watkins TW, Marussi VH, Warmuth-Metz M, Alves HC, Goncalves FG, Kleinschmidt-DeMasters BK, Osborn AG. Multinodular and Vacuolating Neuronal Tumor of the Cerebrum: A New “Leave Me Alone” Lesion with a Characteristic Imaging Pattern. AJNR Am J Neuroradiol. 2017 Jul 13. doi: 10.3174/ajnr.A5281. [Epub ahead of print] PubMed PMID: 28705817.

11) Gonzalez-Quarante LH, Ruiz-Juretschke F, Sola Vendrell E, Gil de Sagredo Del Corral OL, Agarwal V, Garcia-Leal R. Multinodular and vacuolating neuronal tumor of the cerebrum. A rare entity. New case and review of the literature. Neurocirugia (Astur). 2018 Jan - Feb;29(1):44-55. doi: 10.1016/j.neucir.2017.08.003. Epub 2017 Oct 28. PubMed PMID: 29111096.