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References

1. Theodoridis A, Makrantonaki E, Zouboulis CC. Malignant atrophic papulosis (Köhlmeier-Degos disease)-A review. Orphanet J Rare Dis 2013;8:10.
2. Amato C, Ferri R, Elia M, Cosentino F, Schepis C, Siragusa M, *et al*. Nervous system involvement in Degos disease. AJNR Am J Neuroradiol 2005;26:646-9.
3. Subbiah P, Wijdicks E, Muenter M, Carter J, Connolly S. Skin lesion with a fatal neurologic outcome (Degos' disease). Neurology 1996;46:636-40.
4. Ye L, Lekgabe E, Tsui A, Gaillard F. The evolution of cerebrovascular changes in Köhlmeier-Degos disease: An 11-year follow-up case report. J Clin Neurosci 2018;48:114-7.
5. Dastur DK, Singhal BS, Shroff HJ. CNS involvement in malignant atrophic papulosis (Kohlmeier-Degos disease): Vasculopathy and coagulopathy. J Neurol Neurosurg Psychiatry 1981;44:156-60.
6. Caviness Jr VS, Sagar P, Israel EJ, Mackool BT, Grabowski EF, Frosch MP. Case 38-2006: A 5-year-old boy with headache and abdominal pain. N Engl J Med 2006;355:2575-84.
7. Moss C, Wassmer E, Debelle G, Hackett S, Goodyear H, Malcomson R, *et al*. Degos disease: A new simulator of non-accidental injury. Dev Med Child Neurol 2009;51:647-50.
8. Yeo TH, Vassallo G, Judge M, Laycock N, Kelsey A, Crow YJ. Infantile neurological Degos disease. Eur J Paediatr Neurol 2011;15:167-70.
9. Matsuura F, Makino K, Fukushima T, Matsubara N, Shibuya M, Higuchi T, *et al*. Optic nerve and spinal cord manifestations of malignant atrophic papulosis (Degos disease). J Neurol Neurosurg Psychiatry 2006;77:260-2.
10. Sharma S, Brennan B, Naden R, Whelan P. A case of Degos disease in pregnancy. Obstet Med 2016;9:167-8.

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Post-Operative Seizure Freedom Need not be Elusive in Mild Oligodendroglial Hyperplasia and Epilepsy (MOGHE)

Sir,

The histopathologic spectrum of cortical lesions causing epilepsy is ever expanding. Mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE) is a clinicopathologic entity that has been described fairly recently.[1] The first description was in a series of frontal lobe epilepsy patients, which had been initially classified as non-lesional on histopathology.

MOGHE is characterized by clusters of hyperplastic oligodendroglial cells exhibiting increased proliferation near cortico-medullary junctions, with subcortical white matter T2/FLAIR hyperintensity suggestive of focal cortical dysplasia (FCD). The previous descriptions have been restricted to frontal and rare temporal lobe epilepsies, and with poor post-surgical outcomes.[1-3]

Below we present a patient with medically refractory epilepsy and histology-proven MOGHE with an excellent postoperative outcome, and discuss possible strategies by which the same may be ensured in patients with suspected MOGHE.

A 28-year-old agriculturist with an uneventful past history, presented with daily nocturnal seizures since 12 years of age, despite being on 4 anti-seizure medications (ASMs). These events were all brief, hypermotor, associated with fear, irrelevant verbalization, and left upper limb dystonic posturing. Examination was unremarkable.

Video EEG showed interictal spikes over the right fronto-central regions (F4, C4). Multiple habitual events were captured of the semiology described above, electrographically characterized by pre-ictal spiking over the right frontal region with spread to the midline parasagittal (F4, Fz) regions [Figure 1a].

A 3-Tesla epilepsy protocol MR brain showed ill-defined T2/FLAIR hyperintensity in the posterior part of the right middle frontal gyrus, with poor gray-white junction differentiation. Neuropsychological assessment was suggestive of pre-frontal dysfunction. PET-MRI showed hypometabolism extending beyond the lesional zone in the right frontal region. Magnetoencephalogram (MEG) showed bilateral posterior frontal (right > left) dipoles. Functional MRI obtained to localize the left hand motor function, showed activation away from the lesional zone on MRI [Figure 1b-f].

After discussion in pre-surgical meet, patient underwent surgical resection under electrocorticography and neuronavigation

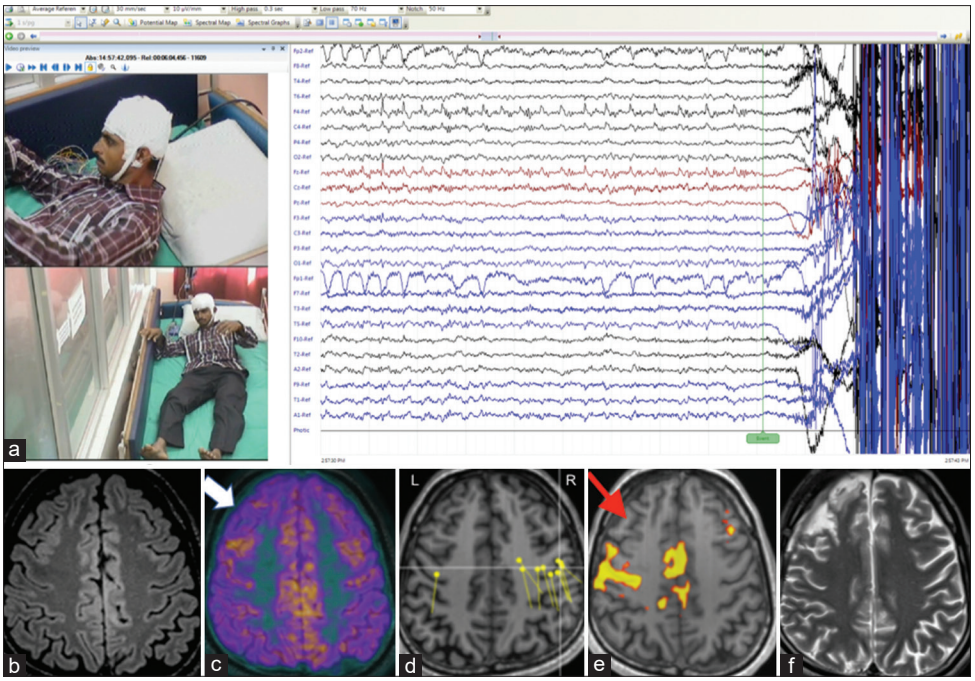

Figure 1: (a) Pre-ictal spiking seen over right frontal and midline anterior parasagittal leads (F4, Fz) prior to obscuration by myogenic artifacts. (b) Axial 3D FLAIR images showing ill-defined area of blurred gray-white junction in the posterior aspect of the right middle frontal gyrus (c) PET-MR showing hypometabolism in the same region. (d) Magnetoencephalogram (MEG) shows right >> left posterior frontal dipole clusters. (e) Functional MRI showing activation away from the lesional zone (red arrow) during left hand motor task. (f) T2/FLAIR post-operative MRI showing excision cavity in the right middle frontal gyrus corresponding to the PET hypometabolism

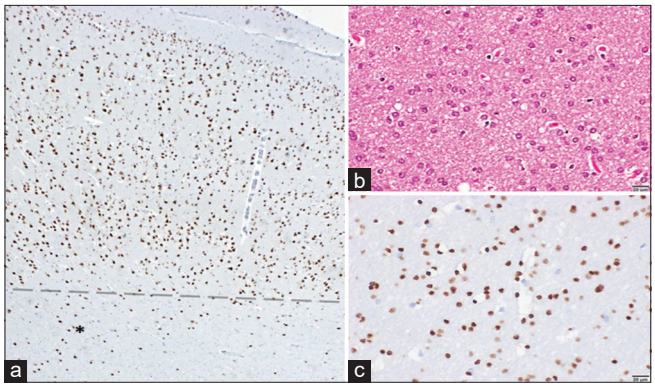

Figure 2: Histopathology of the biopsy specimen: (a) NeuN immunohistochemistry showing preserved cortical hexalaminar architecture, with heterotopic neurons (*) in the subjacent white matter (dotted line represents the gray white junction. (b) White matter shows increased cellularity with oligodendroglial hyperplasia, as evident on Olig2 stain (c)

guidance. On the basis of the non-invasive investigations that indicated that the epileptogenic zone possibly extended beyond the MR-lesional zone, and ECoG showing spiking till the right pre-motor strip, an extended resection was preferred over standard lesionectomy. Histopathology of the biopsy specimen showed preserved cortical lamination with hexalaminar architecture, with no evidence of dysmorphic neurons or balloon cells. The white matter showed increased nuclear density due to oligodendroglial hyperplasia with prominent perineuronal and perivascular satelittosis. On immunohistochemistry, Olig-2, which specifically labels oligodendroglial cells, highlighted their increased density. No MIB-1 labeled cells were seen [Figure 2]. Based on the clinical, radiological, and biopsy findings, a diagnosis of MOGHE was made.

Patient continues to be seizure-free 3 years post-surgery, and is currently on three ASMs. EEG performed one year post-operatively showed no epileptiform discharges.

The range of epilepsy surgery specimens that are classified as non-lesional range from 2 to 26% in various series.[4-6] In a series of 1381 resected epilepsy surgery brain specimens, Schurr *et al*.[1] found that 52 (3.7%) cases could not be classified histopathologically and were labeled non-lesional. However, on re-evaluation, in a subset (42%) of these patients, an increase of Olig2-, and PDGFR-alpha-immunoreactive oligodendroglia in white matter and deep cortical layers was noted, with heterotopic neurons in white matter and increased subcortical oligodendroglial cells. They coined the term "Mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE)" to describe this new entity. The heterotopic neurons were found subjacent to corticomedullary junction, and not in the deep (>500 μm from cortical layer) white matter, which differentiates these from Palmini Type II mild malformations of cortical development (MCD).[7] Dysmorphic neurons, balloon cells, and dyslamination are absent, unlike in focal cortical dysplasias (FCDs).[8] Absence of inflammation and neuroepithelial tumor infiltration are the other criteria for MOGHE. All the patients in this cohort had drug-resistant

frontal lobe epilepsy with median age of onset at 3 years, T2/FLAIR hyperintensities at the gray-white junction, and multifocality. Post-operatively, only 33% of the patients were free from disabling seizures. Duration of epilepsy correlated with the degree of oligodendroglial hyperplasia; with younger patients have higher proliferation rates.

Garganis *et al*.[2] described two patients with "temporal-plus" epilepsy and biopsy-proven MOGHE, demonstrating that MOGHE need not be limited only to the frontal lobe. They suggested that when "temporal-plus" epilepsies present with normal hippocampi or subtle T2/FLAIR abnormalities only on MR, and refractory epilepsy, MOGHE should also be considered.

The good postoperative outcome in our patient could be attributed to the comprehensive mutltimodality evaluation and intra-operative corticography that ensured the complete excision of the epileptogenic zone. Due to the additional information available, a more extensive resection was undertaken rather than the standard lesionectomy. This demonstrates that good surgical outcomes are not unachievable in MOGHE, provided the workup and the resection is complete.

Hatlieb *et al*.[9] demonstrated two distinct MR imaging subtypes in 25 MOGHE patients; subtype I was characterized by increased laminar T2/FLAIR signal at the corticomedullary junction, whereas subtype II showed reduced corticomedullary differentiation due to increased signal of the adjacent white matter. They hypothesized that MR changes in MOGHE are age-related and the first subtype is seen in younger patients (median age of 2.6 years), and the second subtype is seen in older children (median age of 14.1 years). The laminar hyperintensities seen in type I are presumably due to delayed myelination, whereas heterotopic neurons and immature oligodendroglial precursor cells (OPCs) are responsible for the hyperintensities in type II.[10] Imaging subtypes in MOGHE are dynamic and possibly evolve from subtype I to II as the brain matures. At some point, OPCs overcome the maturational arrest and differentiate to a limited extent into mature myelinating oligodendrocytes.[9]

The role of aberrant glial cells in epileptogenesis is ambiguous; though some reports of oligodendroglial lesions being associated with epilepsy are available. Subgranular cortical layers may be compromised by oligodendroglial hyperplasia, leading to aberrant network activity. Also, recurrent seizures may themselves trigger oligodendrogliogenesis. Further research into mechanisms by which oligodendroglia contribute to epileptogenesis is needed.

MOGHE is an emerging cause of refractory epilepsy; awareness of this entity might impact the pre-operative evaluation and surgical planning and hence postoperative outcomes. Seizure freedom can be achieved with multimodality evaluation and extended resections.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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References

1. Schurr J, Coras R, Rössler K, Pieper T, Kudernatsch M, Holthausen H, *et al*. Mild malformation of cortical development with oligodendroglial hyperplasia in frontal lobe epilepsy: A new clinico-pathological entity. Brain Pathol 2017;27:26-35.
2. Garganis K, Kokkinos V, Zountsas B, Dinopoulos A, Coras R, Blümcke I. Temporal lobe "plus" epilepsy associated with oligodendroglial hyperplasia (MOGHE). Acta Neurol Scand 2019;140:296-300.
3. Hamilton BE, Nesbit GM. MR imaging identification of oligodendroglial hyperplasia. AJNR Am J Neuroradiol 2009;30:1412-3.
4. Plate KH, Wieser HG, Yasargil MG, Wiestler OD. Neuropathological findings in 224 patients with temporal lobe epilepsy. Acta Neuropathol 1993;86:433-8.
5. Mathieson G. Pathologic aspects of epilepsy with special reference to the surgical pathology of focal cerebral seizures. Adv Neurol 1975;8:107-38.
6. Wolf HK, Wiestler OD. Surgical pathology of chronic epileptic seizure disorders. Brain Pathol 1993;3:371-80.
7. Palmini A, Najm I, Avanzini G, Babb T, Guerrini R, Foldvary-Schaefer N, *et al*. Terminology and classification of the cortical dysplasias. Neurology 2004;62:S2-8.
8. Blümcke I, Mühlebner A. Neuropathological work-up of focal cortical dysplasias using the new ILAE consensus classification system-practical guideline article invited by the Euro-CNS Research Committee. Clin Neuropathol 2011;30:164-77.
9. Hartlieb T, Winkler P, Coras R, Pieper T, Holthausen H, Blümcke I, *et al*. Age-related MR characteristics in mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE). Epilepsy Behav 2019;91:68-74.
10. Krsek P, Maton B, Korman B, Pacheco-Jacome E, Jayakar P, Dunoyer C, *et al*. Different features of histopathological subtypes of pediatric focal cortical dysplasia. Ann Neurol 2008;63:758-69.

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