KJS
Kosova Journal of Surgery

KOSOVA JOURNAL OF SURGERY

PERSPECTIVE: RIFAT LATIFI: ATLS in Kosova and the "Ghost" Trauma Hospital Building: Is there a hope that trauma care will improve?

MENTOR AHMETI, BATON KELMENDI, MELISSA MISIALEK, DORUNTINA BUNJAKU, FATLUME ARIFAJ, LUAN JAHA, DRITON SADIKU, RIFAT LATIFI: Establishment of Advanced Trauma Life Support (ATLS®) In Kosova through Kosova College of Surgeons and Sanford Health/Sanford Health World Clinics Partnership: The Initial Report

ALAN BILOSLAVO, MANUELA MASTRONARDI, PAOLA GERMANI, NICOLO DE MANZINI: Cutting-Edge Insights: Advancing Laparoscopy in the Management of Diffuse Peritonitis

AJAI K MALHOTRA: Intra-abdominal vascular injuries in severe multiple injured patients: repair, shunt, ligate?

LUMNIJE KQIKU, KURT ALOIS EBELESEDER, RIFAT LATIFI: Treatment and Outcomes of Acute Traumatic Dental Injuries: A Narrative Review

ALBION TOTSI: Management of Esophagogastric Junction Cancer

YEKTA ALTEMUR KARAMUSTAFAOGLU: Innovation in Tracheal Tumors and Stenosis: Recanalization with Endobronchial Shaver

Volume 8
Issue 2
December 2024
ISSN: 3027-5008 (Online)
ISSN: 3027-5016 (Print)

www.kosovajournalofsurgery.net

CASE REPORT

Giant hypothalamic hamartoma: Adult onset of refractory epilepsy with gelastic and generalized tonic-clonic seizures, successfully treated with surgery

Klarisa Prenga*[1], Vojsava Leka[2], Mirel Grada[2], Artemis Ibra[2], Stela Dodaj[2], Florian Dashi[1,2], Mentor Petrela[2]

[1]Department of Neurosurgery, University Hospital Center "Mother Teresa", Tirana, Albania, [2]Department of Neurosurgery and Interventional Neuroradiology, American Hospital 3, Tirana, Albania.

***Corresponding author:**

KLARISA PRENGA

E-mail: *prengaklarisa@yahoo.com*

Abstract

Background: Hypothalamic hamartomas (HH) are uncommon non-neoplastic lesions originating from the floor of the third ventricle. Evidence supports the existence of their intrinsic epileptogenesis activity resulting in gelastic seizures as well as their involvement in secondary epileptogenesis with cortical seizure onset. The initial presentation occurs during the first years of life. Only a few cases of adult-onset are reported in the literature. A refractory epilepsy may develop during the clinical course.

Case Presentation: We report the case of an adult-onset hypothalamic hamartoma that presents with refractory gelastic epilepsy and secondary generalised tonic-clonic seizures. The patient also displayed behavioural disorder, and complained of sexual impotence. MRI findings were consistent with Delalande HH Type IV.

Intervention: Surgery was performed. The patient underwent a left pterional craniotomy. The hamartoma was approached through the left opticocarotid window. A near-total resection as well as a left disconnection were achieved.

Outcome: The immediate postoperative course was notable for transient episodes of short-term memory impairment but was otherwise unremarkable. The patient is seizure-free (Engel class I) at a 1-year follow-up while taking only 500 mg of levetiracetam per day.

Conclusion: In hypothalamic hamartomas presenting with refractory epilepsy, surgical treatment through direct resection and disconnection of the intrinsically epileptogenic tissue provides the best opportunity for achieving seizure freedom. The appropriate surgical corridor is chosen based on radiological findings and the surgeon's experience.

Keywords: Hypothalamic hamartoma, Refractory epilepsy, Adult-onset, Gelastic seizures, Antiepileptic drug.

Introduction

Hypothalamic hamartomas (HH) are non-neoplastic lesions arising from the tuber cinereum and mamillary bodies. Gelastic seizures are the distinctive presentation of HH, with onset in the first years of life. Patients with HH may also present with cognitive impairment, behavioural disorders, and/or central precocious puberty. If not treated, the clinical course is often progressive to a secondary generalised epilepsy.[1] Antiepileptic drugs are known to be poorly effective.

Case Report

A 27-year-old man was admitted to our hospital with a two-year history of seizure onset. He first developed dacrystic seizures with fear for no obvious reasons, palpitations, facial flushing, and excessive sweating. For a year now he has also been presenting gelastic seizures that are followed by a fixed stare and, secondarily generalised tonic–clonic convulsions. He complains of sexual impotence. The patient receives treatment with 4.5 g/d levetiracetam, 1.2 g/d phenytoin, and escitalopram 10 mg/d, but the seizures continue with a frequency of 2/d. The patient presents behavioural disorders due to being a former substance abuser, a current heavy self-critic, and a smoker. Neurological examination revealed no abnormalities. Endocrinological evaluation was normal. MRI of the brain demonstrated a non-enhancing lesion, bilaterally attached to the hypothalamus, with a diameter of 27 mm, projecting into the suprasellar cistern [Figure 1]. These findings represent a hypothalamic hamartoma, Delalande type IV. His EEG was of normal background activity. Based on the MRI findings and the classic seizure semiology, refractory to anticonvulsant medications, surgery was indicated.

We performed a left pterional craniotomy. Access to the lesion was achieved through the left opticocarotid triangle [Figure 2]. The capsule was incised, and debulking was performed using ultrasonic aspiration, dissectors, and suction. The contents were removed in a piecemeal fashion. The left oculomotor nerve was found to be adherent to the lesion. Dissection along the right superior margin was difficult, because there was no clear-cut limitation between the right optic tract and the tumor capsule. Near-total resection (NTR) and a left disconnection with the mamillary bodies were achieved.

During the postoperative course, the patient had an isolated episode of crying for no reason. Episodes of short-term memory impairment were also noted. There was no presence of diabetes insipidus. A post-operative MRI of the brain showed minimal residual tissue on the right. The patient was discharged 3 days post-surgery on levetiracetam therapy 500 mg/d. The neuropathological appearance was consistent with hypothalamic hamartoma. After 6 months, a repeat MRI demonstrated the left disconnection with the mamillary bodies as well as a small residual HH tissue remaining under the right optic tract [Figure 3]. At 1-year follow-up the patient is seizure-free with Engel class I outcome. He is presently taking only levetiracetam

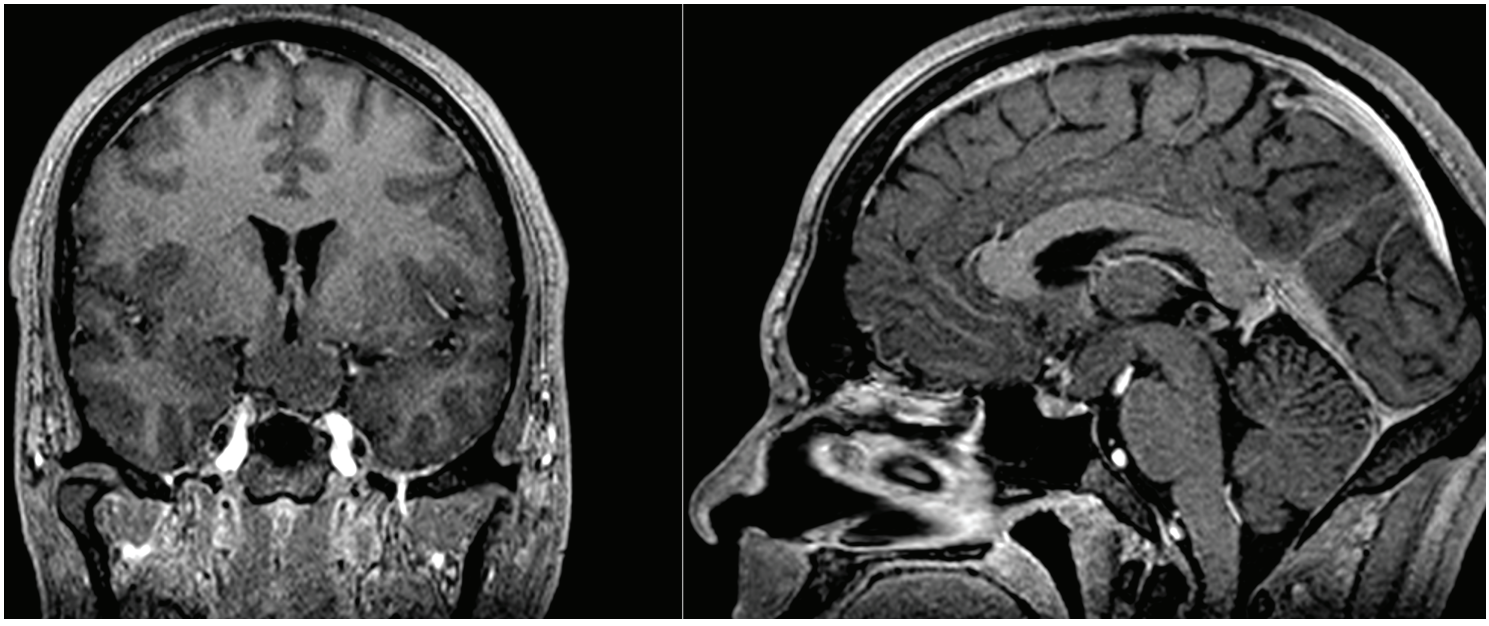


Figure 1 Coronal (left) and sagittal (right) T1- MPRAGE pre-operative gadolinium - MRI showing an isointense lesion arising from the mamillary bodies and tuber cinereum. It has bilateral attachments to the hypothalamus, and it extends into the suprasellar cistern. The floor of the third ventricle is slightly displaced.

500 mg/d. He has not experienced any other episodes of short-term memory impairment. His wife claims that he still has a decreased sexual drive. The endocrinological assessment was performed and revealed normal results. In terms of behavioural disorders, his family members stated that he was doing better.

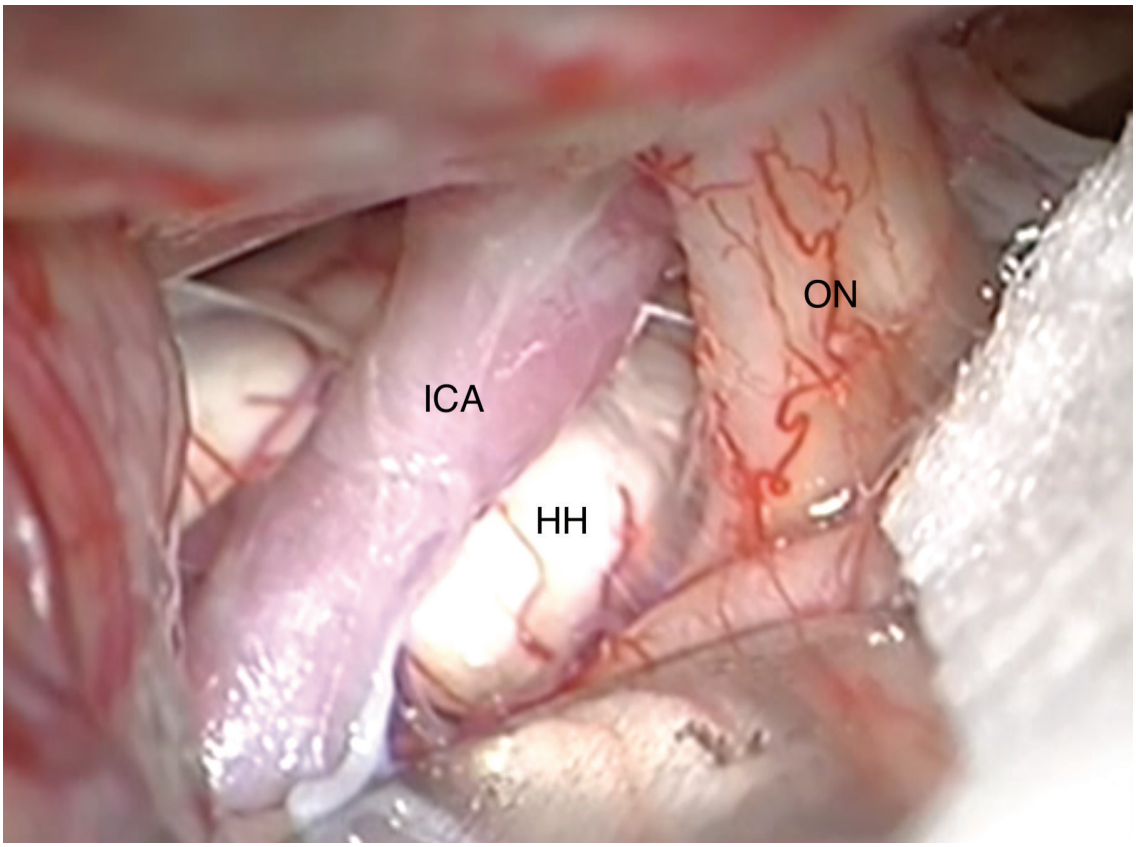


Figure 2 Intraoperative moment showing the hypothalamic hamartoma (HH) that resembles the normal brain tissue. Left internal carotid artery (ICA) and left optic nerve (ON).

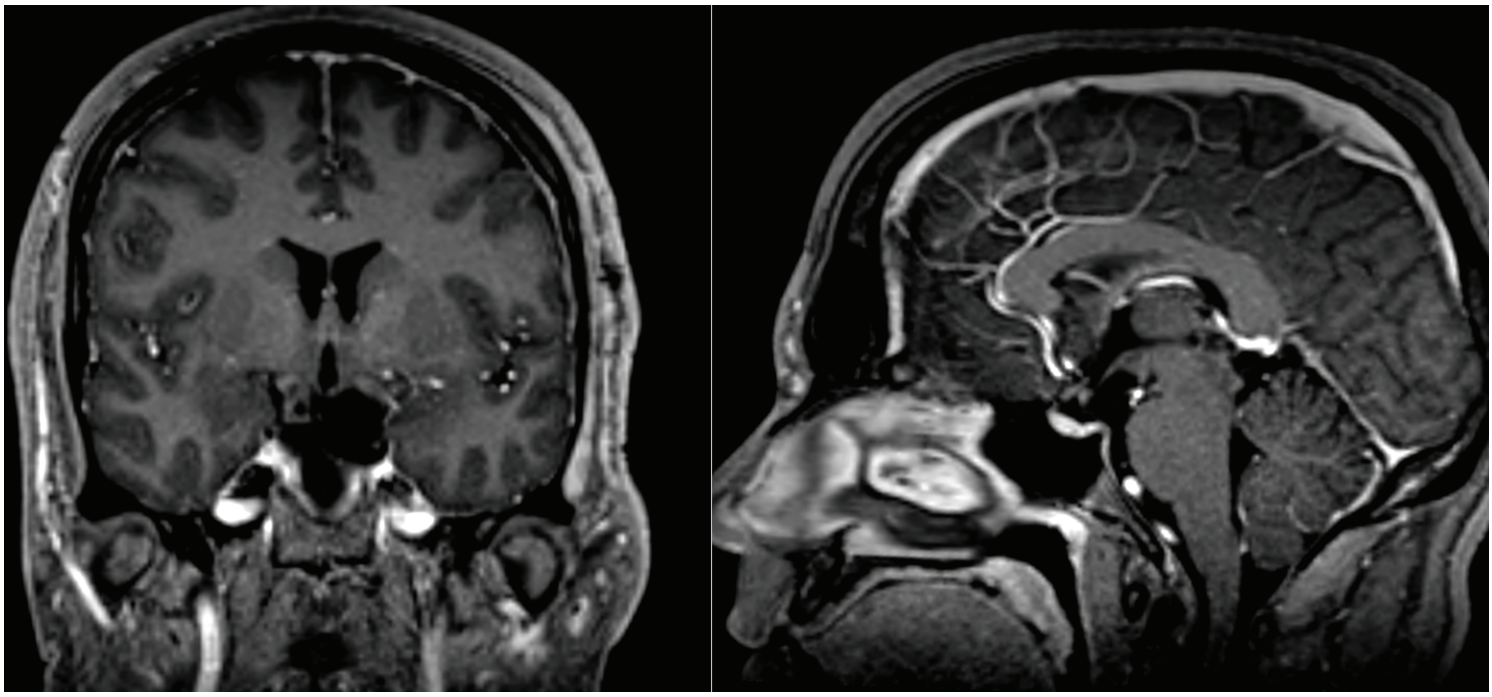


Figure 3 Coronal (left) and sagittal (right) T1-MPRAGE MRI at 6-months post-surgery showing right residual HH tissue.

Discussion

We report a hypothalamic hamartoma Delalande type IV with onset of gelastic epilepsy and tonic-clonic generalisation at adult age. The patient also presents behavioural disorders. Only a few cases of adult-onset are reported in the literature, manifesting with partial or generalised seizures, but no gelastic epilepsy.[2-4] In favour of these reports, Mullatti *et al*. state that when the epilepsy begins later in life, gelastic seizures are not prominent, and these adults do not develop cognitive impairment or behavioural disturbances as in our case.[2]

The seizure semiology of our patient and the classical radiological findings are diagnostic of hypothalamic hamartoma. EEG assessment did not reveal HH as the source of seizure activity, but this is a common finding in the case of deep-seated lesions.[5] The patient's gelastic epilepsy is resistant to multiple drugs, and has evolved to secondary generalisation, indicative of the surgical treatment. The lesion is inferiorly attached to the hypothalamus, and it has a cisternal component. A pterional approach provides the shortest route to the supracellar cistern, but it has some limitations regarding the narrow surgical corridor, carrying the risk of injury to surrounding critical structures.[6,7] Despite its broad attachment to the hypothalamus, we achieved a near-total resection as well as a left disconnection with the mamillary bodies. The patient is seizure-free at 1-year follow-up, with Engel class I outcome. The post-operative short-term memory impairment was transient, and it may have been caused by working in close vicinity with mammillary bodies. However, it is found to be a common complication with both "from below" and "from above-transventricular" approaches to this region, with transventricular approaches having the highest risk due to the possibility of fornices damage.[13] The concept of disconnective surgery was proposed by Delalande and Fohlen to be sufficient to treat seizure activity, and the extent of the resection is reported in literature to have a direct correlation with seizure reduction.[6,8,9]

The most frequently used minimally invasive techniques in the treatment of HHs include stereotactic radiofrequency thermocoagulation (SRT) and gamma knife radiosurgery (GKS).

The effectiveness of SRT in comparison with resective surgery (RS) was studied by Wang *et al.* in 2021.[10] They found that 7 patients out of 13 in the SRT group achieved seizure freedom. Meanwhile, among the 13 patients treated with RS, 9 patients were seizure-free at last follow-up [Table 1]. A possible limitation of this study may be the fact that patients who underwent microsurgery had larger HHs at baseline. Authors advocate that SRT can offer similar results to resective surgery for the treatment of small HH.[10] Furthermore, the group from Japan conducted a study to confirm the efficacy of SRT in treating giant HHs.[14] Nine of their sixteen patients continued to experience gelastic, tonic, and generalised tonic-clonic seizures, while 1 patient showed prolonged disturbance of consciousness, making a full recovery only after 3 months [Table 1]. A robotic-guided radiofrequency ablative disconnection in Delalande type III hamartoma is described in the literature, resulting in a seizure-free patient at 1-year follow-up.[11]

A multi-institutional retrospective research study on GKS for HH is reported in 2024 by Tripathi *et al*.[12] They conclude that primary GKS is an effective treatment for Regis I-III HH, and in cases of giant hamartomas, a combined surgical resection with adjuvant GKS is a preferred option. Additional studies also support these findings.[16,17] Results from some of the largest published series on HH treatment are included in Table 1, comparing data between RS, SRT, and stereotactic radiosurgery (SRS). Permanent complications, including hemiparesis, short-term memory impairment, visual field defects, and hormonal deficiency, are documented in the literature and are mostly linked to surgical resection. In terms of controlling HH's associated seizures, surgical management by direct resection and disconnection of the intrinsically epileptogenic tissue provides the best opportunity for achieving seizure freedom.[6,9]

Conclusion

Our results with this case indicate the validity of the pterional approach in giant hypothalamic hamartomas with a cisternal component, even in HH with bilateral extent. When discussing surgical strategy, radiographic and anatomic features should come into consideration. A meticulous surgical technique is important to achieve good results and avoid complications.

Funding: No funding was received for this manuscript.

Conflicts of interest: There are no conflicts of interest.

Data availability: Data can be made available on request, with patient anonymity.

Author Contributions:

[KP] served as the corresponding author. Responsible for the conception, design and writing of the manuscript.

Provided data collection, interpretation and analysis. Drafted the manuscript.

[VL] and [SD] were responsible for clinical management of the patient and neurologic evaluation. Data collection and analysis.

[MG] was involved in the clinical and operative management of the patient. Data collection_and analysis. Provided help during the overall process.

[AI] was responsible for clinical management of the patient in the floor. Data collection.

[FD] neurologic and neurophysiologic management of the patient. Provided data collection and interpretation focusing in electroencephalography and epileptic activity.

[MP] was the attending surgeon responsible for the patient's care. Concepted the idea. Supervised the overall project. Contributed to data collection and interpretation. Played a significant role by providing valuable critical insights. Editing the manuscript. Writing of the revised manuscript.

Table 1. Comparative outcomes between large published series of RS, SRT, and SRS for HH treatment.

Series	Technique	Nr. of cases	Early post-procedure outcome	Permanent complications	Seizure outcome >12months follow-up
Wang *et al.*[10] 2021	SRT	n=13	n=3 hypothyroidism n=1 weight gain n=1 short-term memory impairment	n=2 hypothyroidism	n=7 ILAE 1 n=2 ILAE 2 n=4 ILAE 4
Shirozu *et al.*[14] 2016	SRT	n=16	n=5 high fever n=1cyst enlargement n=3 hyperphagia n=6 hyponatreamia n=10 Horner's syndrome n=1 consciousness disturbance n=1 epidural hematoma		n=13 free from GS n=4 tonic seizures n=2 generalised tonic-clonic seizures n=3 GS
Doddamani *et al.*[11] 2024	robotic guided radiofrequency ablation	n=1			n=1 ILAE 1
Regis J *et al.*[15] 2004	SRS	n=30	n=1 hyperthermia		n=7 cessation of partial complex seizures n=18 improvement in their seizure rate. n=3 increase of GS
Regis J *et al.*[16] 2017	SRS	n=57	n=3 poikilothermia n=8 seizure increase n=2 requiring additional RS to achieve Engel I-II		n=15 Engel I n=15 Engel II n=12 Engel III n=6 Engel IV
Hamdi H *et al.*[17] 2021	SRS	n=48	n=8 seizure increase		n=19 Engel I n=14 Engel II n=8 Engel III n=7 Engel IV
Wei et al.[18] 2022	SRS	n=7	n=1 seizure increase n=2 HH enlargement requiring additional RS		n=1 Engel I n=4 Engel II n=1 Engel III n=1 Engel IV
Tripathi *et al.*[12] 2024	SRS	n=39	n=8 seizure increase n=2 hormonal deficiency n=1 poikilothermia n=4 requiring additional RS	n=2 hormonal deficiency	n=18 Engel I & II n=9 Engel III n=10 Engel IV n=1 no change
Wang *et al.*[10] 2021	Transcallosal	n=13	n=3 hypothyroidism n=4 diabetes insipidus n=2 short-term memory impairment	n=3 hypothyroidism n=1 diabetes insipidus	n=9 ILAE 1 n=1 ILAE 2 n=2 ILAE 4 n= 1 ILAE 5
NgYT *et al.*[19] 2006	Transcallosal interforniceal	n=26	n=1 homonymous hemianopsia n=1 mild left hemiparesis n=1 meningitis n=1 hydrocephalus n=15 short-term memory impairment n=4 diabetes insipidus n=5 weight gain n=2 hypothyroidism	n=1 homonymous hemianopsia n=1 hydrocephalus requiring lumboperitoneal shunt n=2 short-term memory impairment n=1 hypothyroidism	n=14 seizure-free n=9 >90% reduction of seizure frequency n=1 reduction 50-90% of seizure frequency n=2 no change

Fohlen *et al.*[20] 2003	Pterional and/ or endoscopic disconnection	n=18	n=2 hemiplegia n=1 paresis CN III n=2 diabetes insipidus n=4 hormonal disturbance	n=1 hemiplegia n=1 paresis CN III n=3 hormonal disturbance	n=9 Engel I n=1 Engel II n=8 Engel III
Drees *et al.*[21] 2012	Transcallosal interforniceal/ pterional / orbitozygomatic and/or endoscopic disconnection	n=40	n=1 death due to multiple venous strokes n=1 death after discharge during a seeizure n=11 hormonal disturbance n=4 asymptomatic intracranial hemorrhage/ischemia n=1 hemiparesis due to intracranial hemorrhage n=1 hemianopsia due to intracranial hemorrhage n=2 post-operative infection	n=1 hemianopsia n=11 hormonal disturbance	n=10 Engel I n=17 Engel III n=8 Engel IV
Palmini *et al.*[22] 2002	RS	n=13	n=3 asymptomatic thalamic infarct n=1 capsular infarct causing mild deficit	n=1 capsular infarct causing mild deficit	n=2 Engel I n=11 Engel I & II
Abla *et al.*[23] 2011	Orbitozygomatic / orbitozygomatic and transventricular	n=10		n=1 poikilothermia n=1 diabetes insipidus n=1 visual field deficit n=1hemiparesis	n=4 seizure-free n=4 >50% reduction of seizure frequency n=1 no change

References:

1. Striano S, Striano P. Clinical features and evolution of the gelastic seizures-hypothalamic hamartoma syndrome. Epilepsia. 2017;58 Suppl 2:12-15. doi:10.1111/epi.13753.

2. Mullatti N, Selway R, Nashef L, et al. The clinical spectrum of epilepsy in children and adults with hypothalamic hamartoma. Epilepsia. 2003;44(10):1310-1319. doi:10.1046/j.1528-1157.2003.04103.x.

3. Sone D, Kaido T, Watanabe M, Murata Y, Taniguchi G, Otsuki T. Adult-onset refractory epilepsy with hypothalamic hamartoma and no gelastic seizures successfully treated by stereotactic thermocoagulation: A case report. Seizure. 2016;37:32-34. doi:10.1016/j.seizure.2016.02.013.

4. Liu C, Hu W, Zhang C, et al. Anatomical features decide the atypical seizure manifestation of parahypothalamic hamartomas. Front Neurol. 2022;13:981488. Published 2022 Sep 12. doi:10.3389/fneur.2022.981488.

5. Mittal S, Mittal M, Montes JL, Farmer JP, Andermann F. Hypothalamic hamartomas. Part 1. Clinical, neuroimaging, and neurophysiological characteristics. Neurosurg Focus. 2013;34(6):E6. doi:10.3171/2013.3.FOCUS1355.

6. Mittal S, Mittal M, Montes JL, Farmer JP, Andermann F. Hypothalamic hamartomas. Part 2. Surgical considerations and outcome. Neurosurg Focus. 2013;34(6):E7. doi:10.3171/2013.3.FOCUS1356.

7. Abla AA, Rekate HL, Wilson DA, et al. Orbitozygomatic resection for hypothalamic hamartoma and epilepsy: patient selection and outcome. Childs Nerv Syst. 2011;27(2):265-277. doi:10.1007/s00381-010-1250-7.

8. Delalande O, Fohlen M. Disconnecting surgical treatment of hypothalamic hamartoma in children and adults with refractory epilepsy and proposal of a new classification. Neurol Med Chir (Tokyo). 2003;43(2):61-68. doi:10.2176/nmc.43.61.

9. Feiz-Erfan I, Horn EM, Rekate HL, et al. Surgical strategies for approaching hypothalamic hamartomas causing gelastic seizures in the pediatric population: transventricular compared with skull base approaches. J Neurosurg. 2005;103(4 Suppl):325-332. doi:10.3171/ped.2005.103.4.0325.

10. Wang S, Zhao M, Li T, et al. Stereotactic radiofrequency thermocoagulation and resective surgery for patients with hypothalamic hamartoma. J Neurosurg. 2020;134(3):1019-1026. Published 2020 Apr 17. doi:10.3171/2020.2.JNS193423.

11. Doddamani RS, Chandra PS, Kota R, Ahemad N, Tripathi M. Robotic-guided radiofrequency ablative disconnection of hypothalamic hamartoma. Neurosurg Focus Video. 2024;11(1):V19. Published 2024 Jul 1. doi:10.3171/2024.4.FOCVID2450.

12. Tripathi M, Sheehan JP, Niranjan A, et al. Gamma Knife Radiosurgery for Hypothalamic Hamartoma: A Multi-Institutional Retrospective Study on Safety, Efficacy, and Complication Profile. Neurosurgery. Published online July 11, 2024. doi:10.1227/neu.0000000000003110.

13. Feiz-Erfan I, Horn EM, Rekate HL, et al. Surgical strategies for approaching hypothalamic hamartomas causing gelastic seizures in the pediatric population: transventricular compared with skull base approaches. J Neurosurg. 2005;103(4 Suppl):325-332. doi:10.3171/ped.2005.103.4.0325.

14. Shirozu H, Masuda H, Kameyama S. A proposed new classification system of hypothalamic hamartomas in the era of stereotactic

ablation surgery. J Neurosurg. Published online December 13, 2024. doi:10.3171/2024.7.JNS24560.

15. Régis J, Hayashi M, Eupierre LP, et al. Gamma knife surgery for epilepsy related to hypothalamic hamartomas. Acta Neurochir Suppl. 2004;91:33-50. doi:10.1007/978-3-7091-0583-2_4.

16. Régis J, Lagmari M, Carron R, et al. Safety and efficacy of Gamma Knife radiosurgery in hypothalamic hamartomas with severe epilepsies: A prospective trial in 48 patients and review of the literature. Epilepsia. 2017;58 Suppl 2:60-71. doi:10.1111/epi.13754.

17. Hamdi H, Ferrante P, Spatola G, et al. Epileptic hypothalamic hamartomas impact of topography on clinical presentation and radiosurgical outcome. Epilepsy Res. 2021;173:106624. doi:10.1016/j.eplepsyres.2021.10662.

18. Wei Z, Vodovotz L, Luy DD, Deng H, Niranjan A, Lunsford LD. Stereotactic radiosurgery as the initial management option for small-volume hypothalamic hamartomas with intractable epilepsy: a 35-year institutional experience and systematic review. J Neurosurg Pediatr. 2022;31(1):52-60. Published 2022 Oct 21. doi:10.3171/2022.9.PEDS22200.

19. Ng YT, Rekate HL, Prenger EC, et al. Transcallosal resection of hypothalamic hamartoma for intractable epilepsy. Epilepsia. 2006;47(7):1192-1202. doi:10.1111/j.1528-1167.2006.00516.x

20. Fohlen M, Lellouch A, Delalande O. Hypothalamic hamartoma with refractory epilepsy: surgical procedures and results in 18 patients. Epileptic Disord. 2003;5(4):267-273.

21. Drees C, Chapman K, Prenger E, et al. Seizure outcome and complications following hypothalamic hamartoma treatment in adults: endoscopic, open, and Gamma Knife procedures. J Neurosurg. 2012;117(2):255-261. doi:10.3171/2012.5.JNS112256.

22. Palmini A, Chandler C, Andermann F, et al. Resection of the lesion in patients with hypothalamic hamartomas and catastrophic epilepsy. Neurology. 2002;58(9):1338-1347. doi:10.1212/wnl.58.9.1338.

23. Abla AA, Rekate HL, Wilson DA, et al. Orbitozygomatic resection for hypothalamic hamartoma and epilepsy: patient selection and outcome. Childs Nerv Syst. 2011;27(2):265-277. doi:10.1007/s00381-010-1250-7.