Case Report

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Transient olfactory hallucinations after insular glioma surgery: a case report

Dilshod Mamadaliev, MD[a], Gayrat Kariev, MD, PhD[a,b], Ulugbek Asadullaev, MD, PhD[a], Jakhongir Yakubov, MD, PhD[a], D.N. Khodjimetov, MD, PhD[a], Bipin Chaurasia, MS[c,*]

Introduction and importance: There are various types of hallucinations reported in the literature (auditory, visual, tactile, gustatory, or olfactory), and most of them are related to psychiatric (schizophrenia) disorders. Olfactory hallucinations related to neurosurgical disorders are uncommon. The authors present a case of a patient with a left insular glioma who developed transient olfactory hallucinations after microsurgical resection of the tumor.

Our Objective is to share a rare case of postoperative complication—olfactory hallucination following insular glioma surgery—which can potentially raise awareness among practicing neurosurgeons.

Case presentation: A 32-year-old male patient underwent left insular glioma resection at our institution in 2024. He developed transient olfactory hallucinations after microsurgical resection of the tumor, which resolved within a month postoperatively.

Clinical discussion: Insular gliomas often grow to a considerable size before becoming symptomatic in many patients. The insular region is regarded as one of the brain's most sophisticated areas, with lesions manifesting in a wide range of symptoms and syndromes including olfactory hallucinations.

Conclusion: Olfactory hallucinations following left insular glioma resection can potentially raise awareness among practicing neurosurgeons regarding this rare postoperative complication. These types of postoperative complications may resolve in a short period if no serious vascular injury has been encountered.

Keywords: glioma, insula, olfactory hallucination

Introduction

Hallucinations are defined as a perception of an external stimulus without the presence of a stimulus. There are various types of hallucinations: auditory, visual, tactile, gustatory, and olfactory, which are usually triggered by psychiatric disorders (e.g., schizophrenia, bipolar disorders, and anxiety disorders) and less commonly by neurological (i.e., cerebrovascular accidents, neoplasia, and infection) diseases.[1]

Olfactory hallucinations have been reported in various other neurological disorders, including Alzheimer's disease, Parkinson's disease, epilepsy, migraine, substance abuse, anorexia, post-traumatic stress disorder, bulimia, and autistic disorders.[2,3] This type of hallucination represents a rare type of hallucination in which the patient reports olfactory perceptions in the absence of any chemical agent. According to the published literature, olfactory hallucinations have been described in only 4.2–14.5% of the general population.[2]. Noteworthy is, that we have not found pertinent data in the literature on a case of olfactory hallucinations followed by insular glioma surgery.

The insular lobe ("Island of Reil") was initially discovered and described by Johann Christian Reil in 1809[4]. The insula is an invisible lobe from the surface, located deep within the lateral sulcus of the brain. Traditionally, the insular cortex has been described as paralimbic or limbic integration of the cortex.[5-11] and one of the regions of predilection for low- and high-grade gliomas (LGGs and HGGs) and due to the deep localization very challenging vascular anatomy.

Insular gliomas account for up to 25% of all LGGs and 10% of all HGGs. They are usually slow-growing tumors of low-grade malignancy and may enlarge in size before a diagnosis is established. The main symptoms of these tumors are complex partial seizures with or without secondary generalization.[3]

It is considered a highly complex surgical procedure to attain gross total resection. There are a number of papers describing surgery-related complications.

In this paper, we report the case of a patient who underwent microsurgical resection of a large left insular lobe tumor and who developed olfactory hallucinations of limited duration in the early postoperative period.

Our work has been reported in line with the Surgical CAse REport 2023 criteria[12].

Case report

A right-handed, 32-year-old man was first evaluated at our institution due to the recent onset of intense headaches and

[a]Department of Skull Base Neurosurgery, Republican Specialized Scientific-Practical Medical Center of Neurosurgery of Uzbekistan, Tashkent, Uzbekistan, [b]Department of Neurosurgery, Tashkent State Pediatric Medical Institute, Tashkent, Uzbekistan and [c]Department of Neurosurgery, Neurosurgery Clinic, Birgunj, Nepal

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*Corresponding author. Address: Department of Neurosurgery, Neurosurgery Clinic, Birgunj, Nepal. E-mail: trozexa@gmail.com (B. Chaurasia).

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three episodes of complex generalized seizures, which were followed by a transient speech disorder. Neurological examination was unremarkable, with no signs of olfactory disturbances, motor deficits, or speech impairments. The National Protocolized Uzbek Aphasia Test revealed no evidence of aphasia[13].

Brain magnetic resonance imaging (MRI) (Fig. 1) at 1.5 T (T1-weighted, T2-weighted, Fluid Attenuated Inversion Recovery, perfusion, and tractography) revealed a poorly enhanced intra-axial tumor in the left insula, extending to the anterior surface of the putamen, and lying beneath the fronto-temporal operculum. According to Berger–Sanai classification, it was occupying I + II zones.[8] The tumor also enveloped the planum polare and planum temporale (Fig. 1). Additionally, the inferior fronto-occipital fasciculus (IFOF) and arcuate fasciculus (AF) were displaced and compressed by the tumor tissue.

Surgery

The patient underwent awake surgery using the "asleep-awake-asleep" technique. Our simplified technique of awake craniotomy has been described in a separate article.[6] The patient underwent anesthesia induction, and laryngeal mask airway was used for ventilation. A local anesthetic (bupivacaine) was applied, and a left standard frontotemporal craniotomy was performed. The patient was awakened, and the laryngeal mask was removed to enable full involvement of the patient in functional mapping. After durotomy, sulci, tumor, and gyri limits (Broca's and Wernicke's areas) were delineated with direct electrical stimulation—bipolar electrode tips spaced 5 mm apart. A biphasic current with pulse frequency 60 Hz, single pulse phase duration 1 ms, amplitude 3–4 mA, and stimulation duration 4 s was applied. No more technical facilities were used (no neuronavigation, no functional MRI, and no intraoperative MRI). Language functions were assessed through picture naming tests and counting. Brain mapping was performed via direct electrical stimulation of the cortex in the left fronto-temporo-parietal area (Fig. 2).

Once a safe entry point was defined, the parieto-rolandic operculum was selected for corticotomy. The surface of the insula was reached using the subpial dissection technique, providing better exposure to the lateral part of the Heschl's gyrus. The tumor was resected using tumor forceps and an ultrasonic aspirator-destructor (CUSA Excel), with continuous monitoring of direct electrical stimulation. The portion of the tumor extending to the planum polare and planum temporale was resected via the inferior circular sulcus of the insula. As we went deeper, into the white matter of insula, resecting the deeper parts of the tumor, we noticed that subcortical electrical stimulation caused some phonological disorders in patients such as paraphasia and even speech arrest. Due to multiple intraoperative episodes of speech arrest and paraphasia, during electric subcortical stimulation of AF and IFOF, the extent of resection was cautiously limited to avoid the risk of permanent speech deficits, resulting in partial tumor removal (>60%) (Fig. 3).

As there was a potential involvement of lenticulostriate arteries (LSA) within the medial aspect of the tumor, we have accurately analyzed coronal and axial T2- and T1-weighted MR images in order to exclude whether these perforator vessels were incorporated in tumor or not. In our case, the medial component

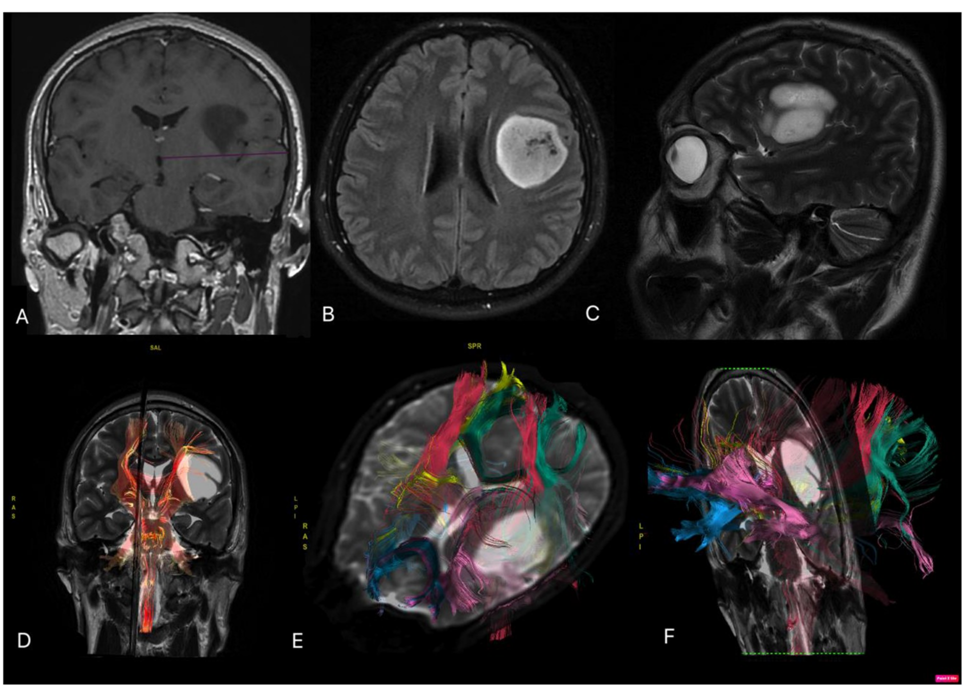

Figure 1. Preoperative contrast-enhanced MRI of the patient. Tumor tissue has poor contrast enhancement. (A–C) Insular lesion lying above the sylvian fissure (Zone I + II according to Berger–Sanai) depicts hyperintense on axial T2 Fluid Attenuated Inversion Recovery WI and coronal planes. (D–F) DTI tractography illustrating on T2 (D) and on DWI semi oblique axial images (E), Corticospinal tract fibers are being compressed and IFOF (green) is mostly displaced and some fibers are incorporated in tumor mass (E,F). MR tractography (E,F) demonstrates displacement of the IFOF (green) and superior longitudinal fasciculus (yellow) fibers.

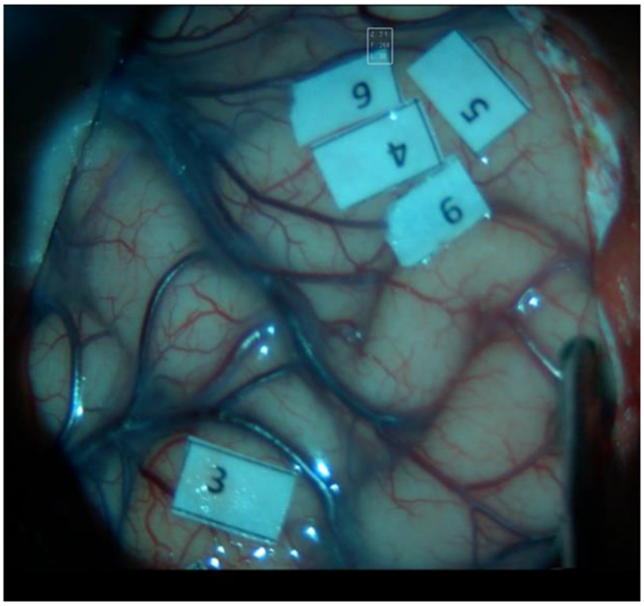

Figure 2. Intraoperative photo of cortical mapping, labeling the frontotemporal cortex: “3”—posterior end of superior temporal gyrus—receptive speech (Wernicke’s area). Labels 4, 5, 6, and 9 are on the motor speech cortex (Broca’s area).

of the tumor was the direct intraoperative visualization of the LSA. At the time of visualization of the LSA within the tumor, resection was stopped. Deep resection adjacent to the internal capsule was halted when alterations in the intraoperative motor evoked potentials were detected. Pathological examination of the tumor specimen confirmed a WHO Grade II diffuse astrocytoma (Fig. 4).

Postoperative course

The patient developed a mild speech disorder (disarticulation and paraphasia) and acute olfactory hallucinations, characterized by the perception of nonexistent odors, within 1–4 days postoperatively. The hallucinations involved odors that the patient previously found pleasant (e.g., soup and juice) suddenly becoming unpleasant. These unpleasant smells persisted even in the absence of any odor stimuli. The hallucinations occurred several times a day, lasted for several hours, and were not associated with alterations in consciousness.

Disarticulatory deficit resolved within 1 month postoperatively with the assistance of neuropsychological and speech therapy. As anticonvulsant therapy, a dual regimen of Carbamazepine (400 mg per day) and Valproic Acid (1000 mg per day) was prescribed during the early postoperative period. A week later, the olfactory hallucinations resolved. No seizures were recorded postoperatively. Follow-up MRI of the patient at 28 days postoperatively depicted a partial resected apical area of the insular region, and no significant growth of the astrocytoma in comparison with previous immediate postoperative brain computed tomography (Fig. 5).

Discussion

The insular cortex acts as a transitional zone between the allocortex and neocortex and is a vital part of the paralimbic system, involved in various functions such as motor control, sensory perception, language, olfaction, auditory-vestibular integration, and cognitive processing[9]. Translational research on animals and humans has been demonstrated a link between the insula and a number of structures, including the neocortex and limbic cortex (i.e., olfactory bulb, anterior cingulum, amygdala,

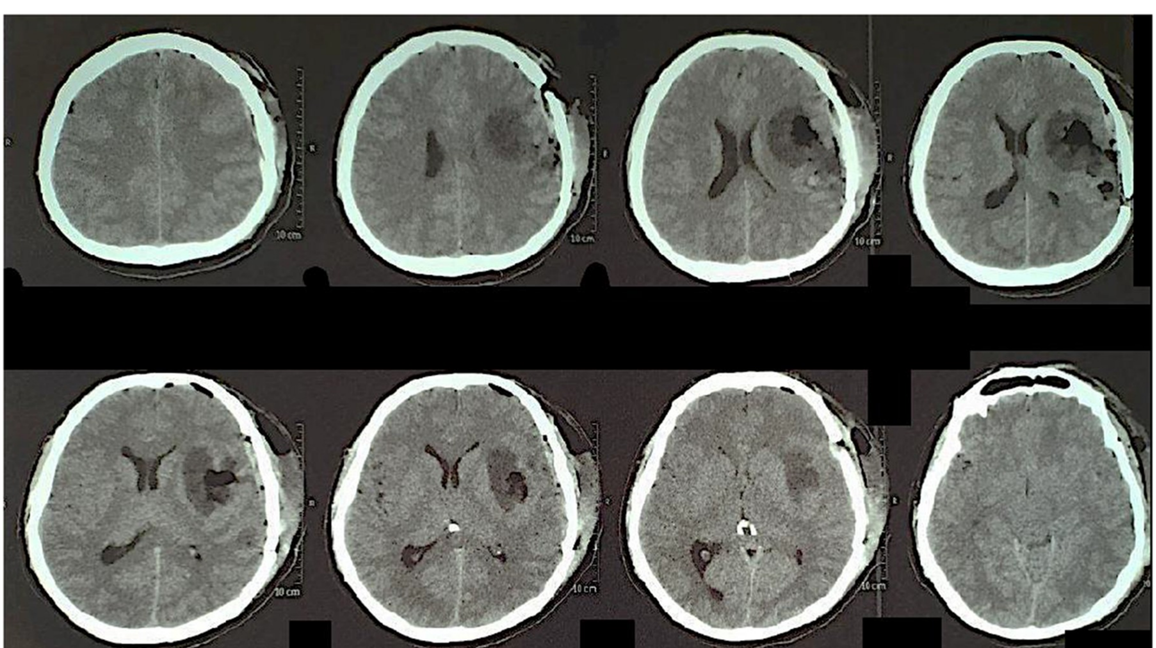

Figure 3. Immediate postoperative computed tomography depicting left insular tumor partial resection and slight peri-insular ischemia and local edema.

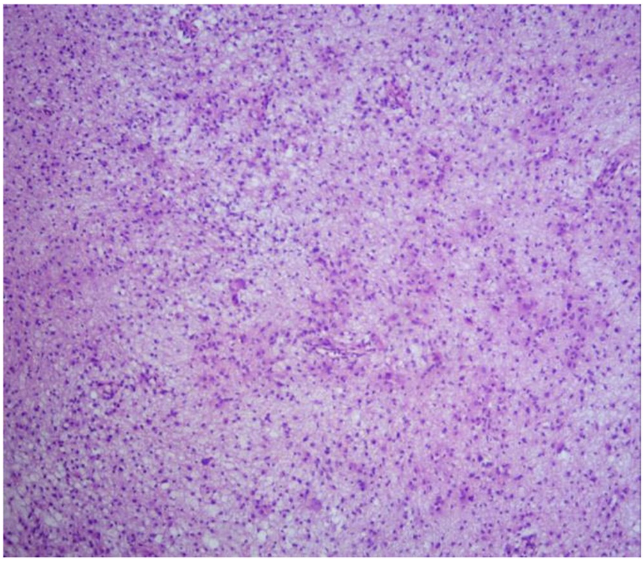

Figure 4. Pathological examination of the tumor specimen showing the features of a WHO Grade II diffuse astrocytic glioma. H&E. Magnification ×100.

hippocampus, and thalamus), which may explain the origination of olfactory hallucinations.[14]

There have been described different types of dysfunctions and deficits of the aforementioned neurological functions, including even musical hallucinations[1]. The mechanisms responsible for phantosmia according to Henkin *et al*. may be related to decreased gamma-aminobutyric acid activity in specific areas of the insula, which are responsible for odor perception. Nevertheless, mechanisms causing phantosmia effect are complex, and currently, no clear data have been found explaining definitive reasons[15].

Insular gliomas often grow to a considerable size before becoming symptomatic. Occasionally, these tumors are incidentally discovered during MRI scans.

Surgical intervention for these tumors is particularly challenging due to their proximity to the internal capsule and the complex anatomical relationship with the segments and branches of the middle cerebral artery (MCA). The lateral LSAs, which supply the internal capsule, often run along the inner side of insular tumors. Although the number of lateral LSAs can range from 1 to 21, the occlusion of even a single branch may lead to significant infarction of the subcortical ganglia and internal capsule, resulting in motor and language deficits[7,16].

There is a documented role of intraoperative MRI in achieving gross total resection or even supratotal resection of gliomas, especially LGG. The meta-analysis by Li *et al*. clearly describes the benefit of utilization of intraoperative MRI on the extent of resection and survival rate, concluding that the progression-free period was longer in the groups that underwent intraoperative magnetic resonance imaging compared to conventional neuronavigation ($p = 0.012$)[17]. However, in our case due to lack of resources, we could not use this facility.

When surgery is performed on the dominant hemisphere, better outcomes can be achieved through awake surgery with

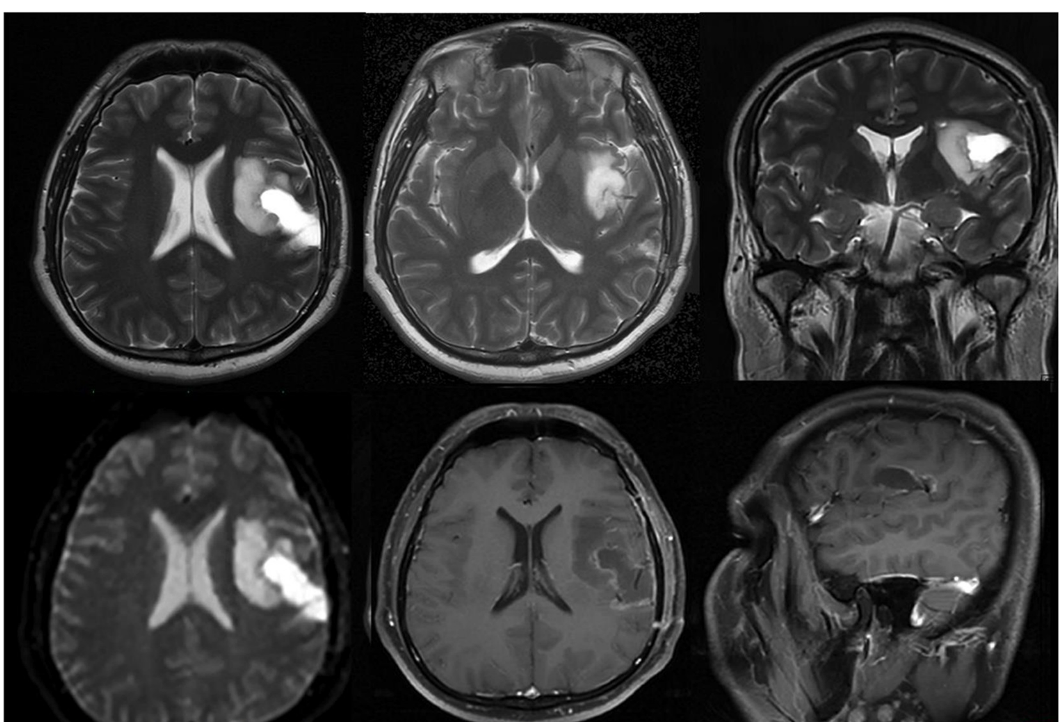

Figure 5. Postoperative MRI of the patient in 28 days follow-up period, depicting the partially resected apical area of the insular region, with no significant growth of the astrocytoma compared to the previous immediate postoperative brain computed tomography.

intraoperative electrical mapping and a transopercular approach. This technique provides broader surgical exposure of the insula and reduces the risk of vascular injuries at the level of the Sylvian arteries[5].

Some studies also suggest a hemisphere-specific role in odor processing, with hemispheric differences associated with valence processing. The right hemisphere may be more specialized for pleasant stimuli, while the left hemisphere may be more sensitive to unpleasant stimuli[10,18,19]. This is also confirmed in the case of our right-handed patient who reported experiencing unpleasant odors as phantosmia.

However, it is difficult to predict which specific area of the insular cortex is responsible for odor perception; therefore, it is crucial to preserve arterial supply (which is basically provided by the superior trunk of the M1 bifurcation of the MCA). Studies indicate that there is a certain correlation between the thickness of the insular cortex in healthy participants with a better olfactory performance[20].

Conclusions

The insular lobe is brain's one of the most intricate and functionally sophisticated areas, with lesions giving rise to an array of symptoms, including olfactory disturbances, language deficits, and psychological impairments. A particularly uncommon but notable postoperative complication of insular gliomas can be olfactory hallucination, or phantosmia that may last for a short period of time. However, meticulous microsurgical techniques aimed at preserving critical blood supply and venous drainage are key factors for successful outcome. Nonetheless, while we have described a single case of olfactory hallucination in the postoperative period, further research is essential to advance diagnostic methods and conduct detailed anatomical and physiological studies to pinpoint the specific site within the insular cortex responsible for olfaction.

Take home message

Olfactory hallucinations following a left insular glioma resection can potentially raise awareness among practicing neurosurgeons regarding this rare postoperative complication, thus enabling them

a. to include it in the corresponding informed consent form *a priori*,
b. to recognize it when it occurs after surgery.
c. to reassure their patients about its subsidence.

Ethical approval

Ethical approval is not required for case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

All authors have contributed equally to the formation of the manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

None.

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