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Diagnostic Challenges and Management of a High-Grade Pineal Region Glioma in a 65-Year-Old Adult: A Case Report

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Abstract **Case Report**

Introduction: Pineal region tumors in adults are exceptionally rare and represent a major diagnostic and therapeutic challenge, particularly when they exhibit an ambiguous histological presentation or a high-grade evolutionary profile. ***Case Report:*** We report the case of a 65-year-old patient with no significant medical history, admitted for an increased intracranial pressure syndrome associated with Parinaud's syndrome. Brain magnetic resonance imaging (MRI) revealed a 28x33x39mm pineal region tumor process, causing obstruction of the aqueduct of Sylvius and active triventricular hydrocephalus, which was treated urgently by endoscopic ventriculocisternostomy. The spectroscopic profile was highly suggestive of a high-grade lesion (elevated Choline/NAA ratio). Conversely, stereotactic biopsy revealed an IDH-wildtype astrocytic glial proliferation with a low Ki-67 proliferation index (1% to 3%), contrasting sharply with the radio-clinical aggressiveness. Faced with this anatomo-radiological conflict, the patient was stratified as high-risk according to EORTC/RTOG criteria due to age, critical tumor location, and the partial nature of the resection. Concomitant radio-chemotherapy following an adapted Stupp protocol up to 54 Gy was successfully delivered. ***Conclusion:*** This case illustrates the frequent diagnostic conflict in neuro-oncology between a micro-fragmentary histological profile of indolent appearance and highly aggressive multimodal imaging features. Rapid multidisciplinary management with concomitant radio-chemotherapy remains the therapeutic cornerstone to secure local control against these infiltrating entities of the tectal plate.

Keywords: Pineal region, Astrocytic glioma, Magnetic resonance spectroscopy, Histological diagnosis, Stupp protocol.

1. INTRODUCTION

Pineal region tumors constitute a particularly rare anatomo-clinical entity among central nervous system neoplasms in adults, representing less than 1% of intracranial space-occupying lesions within this population [1]. This highly complex anatomical region is located at the crossroads of ventricular fluid pathways and major deep vascular structures, notably the vein of Galien and the posterior cerebral arteries [2]. The critical proximity to the brainstem and the deep venous network confers a high initial morbidity to these tumor processes [3]. This dangerous nature is mainly linked to the early mechanical obstruction of the aqueduct of Sylvius, responsible for an increased intracranial pressure syndrome due to acute triventricular hydrocephalus.

On the histological level, the pineal region is characterized by great cellular heterogeneity; it can give rise to pinealomas, germ cell tumors, but also to neoplasms of glial origin. In adults, infiltrating gliomas of the tectal plate and the pineal region exhibit a frequently unpredictable evolutionary and aggressive profile [4]. Furthermore, the management of these lesions is sometimes part of a complex syndromic context, such as neurofibromatosis type 1 (NF1), where the fortuitous or synchronous coexistence with other rare entities, like adult optic pathway glioma, poses a major prognostic and therapeutic challenge [5]. Due to the neurosurgical risks of an upfront resection in this highly functional area, stereotactic biopsy stands as the diagnostic standard. Nevertheless, a definitive histopathological diagnosis is frequently defeated by the exiguity of biopsy samples and necrotico-tumor changes, rendering multidisciplinary anatomo-clinical and radiological confrontation indispensable.

According to the consensual recommendations published by the European Reference Network for Rare Adult Solid Cancers (EURACAN), the histological landscape of pineal region tumors in adults is radically

different from that of pediatric cohorts, being characterized by a higher prevalence of primary diffuse midline gliomas that follow an aggressive and malignant biological course [6]. The EURACAN framework emphasizes that establishing an accurate diagnosis in adults is frequently hindered by a profound anatomo-clinical conflict, where advanced neuroimaging features suggest high-grade behavior while stereotactic biopsy specimens, often acquired in an exiguous manner, can paradoxically display indolent, low-grade characteristics [6].

2. CASE PRESENTATION

2.1 History and Clinical Profile

The patient was a 65-year-old male, with no notable medical history, fully autonomous (WHO performance status score = 0), and residing in Souk El Arbaa. The history of the present illness dated back to December 2025, characterized by the progressive onset of disabling holocranial headaches, accompanied by nausea, vomiting, and a progressive decline in visual acuity. These symptoms prompted a specialized consultation at the Department of Neurosurgery of the Hôpital des Spécialités (HSR) in Rabat.

A thorough clinical examination upon admission revealed:

Parinaud's syndrome, characterized by upward vertical gaze paralysis.

Bilateral papilledema on fundoscopy, classified as Grade 2 in the left eye and Grade 3 in the right eye, confirming the direct ophthalmological impact of the increased intracranial pressure.

2.2 Radiological and Spectroscopic Investigations

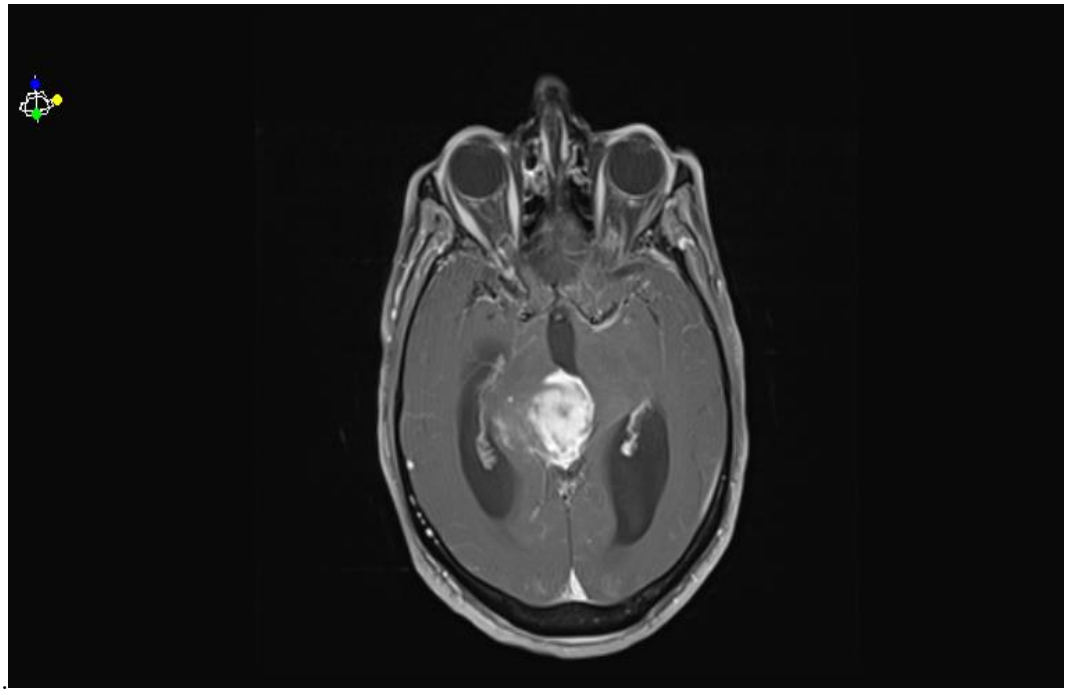
A brain MRI was performed according to a rigorous multimodal protocol (T2, DWI diffusion, SWI, 3D FLAIR, contrast-enhanced T1, perfusion, and magnetic resonance spectroscopy sequences). The results revealed (Figure 1):

Morphology: A midline tumor lesion process centered on the pineal region, with a tissue structure appearing as an isosignal on T2. The mass measured precisely 28x 23 x 39mm. After contrast medium injection, the enhancement was intense and homogeneous.

Infiltration and Mass Effect: The lesion was surrounded by significant peri-lesional edematous infiltration extending toward the right thalamus, the midbrain anteriorly, the pons (the region facing the floor of the fourth ventricle [V4]), and the superior cerebellar peduncles. This immediate proximity to vital brainstem structures constituted a major dosimetric constraint for subsequent radiotherapy planning.

Hydrodynamic Consequences: Complete obstruction of the aqueduct of Sylvius, leading to major and active triventricular hydrocephalus.

Metabolic Profile (Spectroscopy): A marked elevation of the Choline peak associated with a collapsed level of N-acetylaspartate (NAA). The Choline/NAA ratio was measured at 3, which is highly suggestive of a high-grade tumor. An elevation of the lactate peak at long echo time was also documented, indicating anaerobic metabolism and local hypoxic changes.



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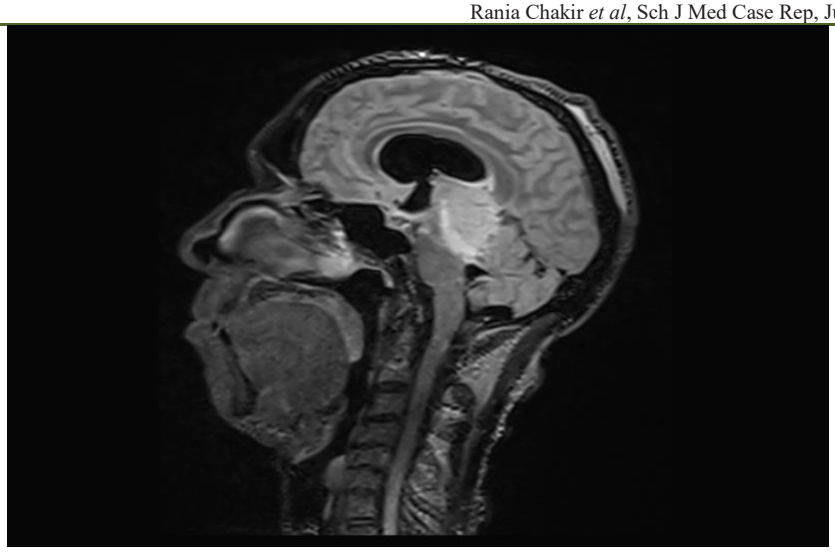

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Figure 1: Initial brain MRI clearly demonstrating a voluminous mass in the pineal region

A: Axial slice in T1 weighted sequence with gadolinium injection

Visualization of a large tumor lesion in the pineal region centered in the midline, showing frank, intense, and relatively homogenous enhancement after contrast medium injection. There is a marked local mass effect with infiltration of adjacent structures and reactive dilatation of the occipital horns of the lateral ventricles, indicating the onset f obstructive ydrocephalus due to compression of the mesencephalic aqueduct (aqueduct of Sylvius.)

B: Sagittal slice in FLAIR (or T2) -weighted sequence. Profile of the pineal mass clearly demonstrating its vertical extension and its close anatomical relationship with the structures of the posterior fossa. The tumor exerts direct downward pressure on the tectum (quadrigeminal plate) and infiltrates the upper part of the brainstem (midbrain), while displacing the splenium of the corpus callosum upward. Dilation of the upstream third ventricle is also visible.

Given the urgency of the obstructive hydrocephalus, the patient successfully underwent internal diversion via endoscopic third ventriculocisternostomy (ETV).

2.2 Histopathological and Immunohistochemical Analysis

A stereotactic biopsy of the lesion was performed in this patient. Frozen section control received 6 millimeter-sized fragments showing a material of moderate cellular density composed of glial astrocytic cells with some nuclear atypia on a piloid and myxoid fibrillary background.

The complete immunohistochemical study provided the following results:

Anti-GFAP: Frankly positive
Anti-Olig2: Positive
Anti-ATRX: Negative (positive internal control)
Anti-IDH1: Negative (IDH-wildtype profile)
Anti-P53: Negative
Anti-Ki67: Low, estimated at 1% to 3% depending on the fields.

3.2 Diagnostic Dilemma:

The histopathological conclusion highlighted that the specimen was "hypocellular" and exiguous. The morphological appearance and the very low Ki67 index could mimic a low-grade astrocytoma. However, confrontation with imaging data (intense enhancement, extensive infiltration, and Choline/NAA ratio = 3) raised suspicion of a high-grade glial tumor (such as anaplastic astrocytoma or midline glioma). Precise molecular classification according to the 2021 WHO criteria would have required DNA methylation analysis, which was unavailable at our facility.

2.3 Therapeutic Management

2.3.1 Initial Surgical Treatment

Given the clinical and radiological urgency dictated by the active triventricular hydrocephalus and signs of severe increased intracranial pressure (bilateral papilledema grade 2/3), the patient was managed emergently. An endoscopic third ventriculocisternostomy (ETV) was successfully performed by the neurosurgery team, allowing for immediate internal diversion of the cerebrospinal fluid (CSF). This procedure promptly resolved the increased intracranial pressure syndrome and stabilized the patient's neurological status.

2.3.2 Concomitant Radio-Chemotherapy Protocol (Adapted Stupp)

Following discussion in a Multidisciplinary Oncology Board (tumor board) and anatomo-radiological confrontation, the implementation of the Stupp protocol was selected. Given the aggressiveness profile of the lesion and the infiltration of the midbrain

and pons, a crucial dosimetric adaptation was validated in order to respect the tolerance limits of the brainstem (a critical organ with a "serial" architecture):

External Beam Radiotherapy:

Performed using the volumetric modulated arc therapy (VMAT) technique planned on the Monaco treatment planning system, under immobilization with a 3-point thermoplastic mask.

Dose and Fractionation:

A cautious de-escalation was applied, limiting the total dose to 54 Gy instead of the standard 60 Gy, delivered in 27 fractions of 2 Gy per fraction, at a rate of 5 consecutive weekly sessions.

Concomitant Chemotherapy:

Daily and continuous administration of Temozolomide at a dose of 75mg/m^2, including on radiotherapy rest days. The intake was scheduled in the morning on an empty stomach (or two hours after the last meal), one hour before the irradiation session.

Symptomatic Treatment:

Intensive systemic corticosteroid therapy was rigorously administered in parallel to control the major vasogenic edema documented on MRI and to preserve long-tract neurological functions, followed by a progressive taper after the end of irradiation.

Anti-infective Prophylaxis:

Prevention of opportunistic infection by Pneumocystis jirovecii during chemotherapy through the administration of sulfamethoxazole/trimethoprim (Bactrim Forte).

Clinical and Biological Monitoring:

Faced with the low but real risk of severe or prolonged bone marrow aplasia and Temozolomide-induced thrombocytopenia, weekly biological monitoring was established, including a complete blood count (CBC) with platelet count, as well as a complete liver function test.

2.3.3 Treatment Planning

1. Image Acquisition and Simulation

Positioning and Immobilization:

Treatment planning was conducted under rigorous stereotactic conditions. The patient was placed in a supine position, with the head immobilized using a micro-perforated thermoplastic mask (3- or 5-point) to guarantee daily session reproducibility and to minimize safety margins.

Simulation CT (CT-sim):

A centimetric dosimetric CT scan without contrast medium injection was performed in thin slices (typically < or = to 2 mm) covering the entire brain volume.

Image Fusion:

To optimize the targeting of this complex anatomical region, the simulation CT was fused with the structural brain MRI sequences (contrast-enhanced T1, FLAIR) and...

2. Target Volume Delineation

Target volume delineation was performed in accordance with international EORTC recommendations:

GTV (Gross Tumor Volume): This encompassed the macroscopic tumor mass visible on imaging, measuring $28 \times 23 \times 39\text{ mm}$ and centered on the pineal region/tectal plate, as well as the surrounding infiltration visible on the imaging sequences.

CTV T (Clinical Target Volume): Although EORTC guidelines initially advocated for a 20 to 30 mm microscopic expansion margin around the GTV for high-grade gliomas, this was cautiously reduced. Due to the deep location of the lesion and its immediate contiguity with critical neurological structures, a 15 mm margin was applied around the GTV. This volume was rigorously cropped at the level of healthy anatomical barriers (tentorium cerebelli and bony structures of the skull base) to avoid unnecessary irradiation of healthy brain tissue.

PTV (Planning Target Volume): A geometric safety margin of 3 mm was added around the CTV to account for setup uncertainties and daily mechanical variations of the linear accelerator.

Organs at Risk (OARs) Delineation: Brainstem, spinal cord, optic chiasm, right and left optic nerves, right and left lenses, right and left temporal lobes, whole brain, pituitary gland, healthy brain (whole brain minus CTV T).

3. Dose Calculation and Optimization (On the Monaco TPS)

VMAT Technique:

Planning utilized image-guided radiotherapy delivered via programmed volumetric modulated arc therapy (VMAT) with coplanar arcs. This technique allows sculpting the dose around the tectal lesion while creating a steep dose gradient anteriorly.

Optimization Trade-off:

This is where the dosimetric compromise was determined. The planners (physicists and dosimetrists) configured highly restrictive cost functions for the brainstem to prevent the dose from exceeding the toxic threshold of 55 Gy. This calculation achieved the prescription isodose (95%, i.e., 51.3 Gy) perfectly encompassing the PTV, while drastically lowering the exposure of adjacent healthy structures (optic nerves, temporal lobes, chiasm).

Analysis and Dosimetric Results (DVH)
Results: Quantitative Evaluation of the Dosimetric Treatment Plan

Quantitative evaluation of the validated treatment plan, extracted from the dosimetric statistics table, objective an excellent balance between tumor coverage and radioprotection of organs at risk (OARs):

1. Target Volume Coverage and Homogeneity (PTV T 54Gy)

For a volume of 146.913cm 3, the mean dose delivered to the PTV was 54.11 Gy, which demonstrates excellent adequacy with the nominal prescription dose. The maximum dose (D max) was very well controlled and contained at 57.2 Gy, representing 106% of the prescribed dose, thereby avoiding the appearance of clinically unfavorable hot spots within or near the lesion (Figures 2, 3).

The planning target volume coverage (PTV T) strictly meets international ICRU standards:
Coverage Isodose: The volume was encompassed between the 95% - 107% isodoses of the prescribed dose.

Coverage Index (V 95%): 95% of the prescription dose (i.e., a dose level of 51.3 Gy) was received by 99.21% of the target volume, guaranteeing near-total coverage and high protection against the risk of marginal recurrence (Figure 3).

Homogeneity (D 2%): The dose received by the most irradiated 2% of the volume (D2 %) remained strictly below 107% of the nominal dose, confirming the optimal homogeneity profile of the IMRT/VMAT plan generated on the Monaco console.

Regarding Critical OARs:
Brainstem: For a volume of 30.042cm^3, the mean dose was restricted to 48.24 Gy. Only 2.00% of its volume received a dose of 54.11 Gy, and the absolute maximum dose was safely capped at 54.94 Gy, thereby avoiding the risk of radiation-induced encephalopathy or long-tract necrosis.

Optic Pathways: The chiasm and optic nerves were ideally spared. The recorded (D max) was 24.23 Gy for the right optic nerve and 22.55 Gy for the left optic nerve, representing values well below the functional toxicity thresholds.

Other Structures: The lenses (LENS+3mm were preserved with a Dmax = 7.62Gy and a Dmean = 5.73 Gy.

Healthy Brain: The mean dose received by the healthy brain (healthy brain - CTV T) was maintained at a low level of 22.84 Gy.

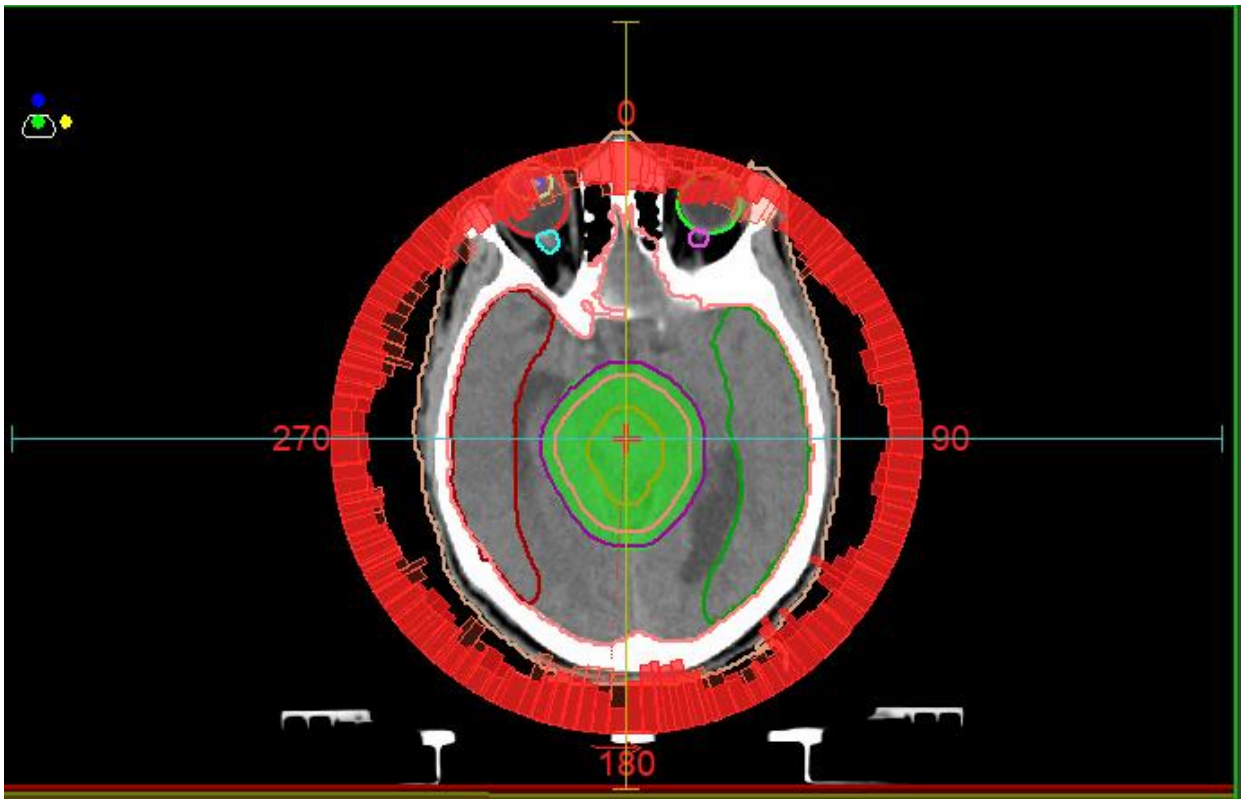

Figure 2: Dosimetric planning of an infiltrating glioma of the pineal region (Monaco Console). Axial CT slice illustrating the 54 Gy isodose distribution for a treatment using volumetric modulated arc therapy (VMAT)

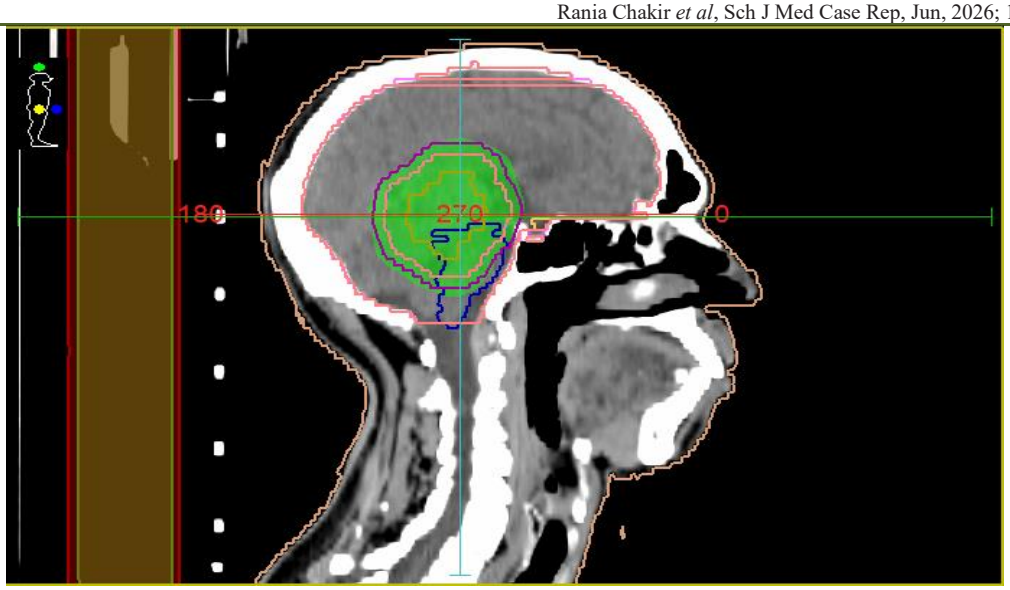

Figure 3: Dosimetric planning in sagittal view (Monaco Console) – Dose distribution at the midline. Sagittal centering CT slice illustrating the dose distribution profile (VMAT) and the close anatomical relationships between the target volume and the brainstem

Structure	Volume (cm³)	Min. Dose (Gy)	Max. Dose (Gy)	Mean Dose (Gy)	Ref. Vol. (cm³)	Ref. Vol. (%)	Ref. Dose (Gy)	Dosimetric Criterion	% in Volume	Is in SS	Heterogeneity Index	
PTV T 54 Gy	146,913	49,278	57,279	54,110	145,760	99,21	51,300	100,00	yes	1,06	0,36	0,56
Brainstem	30,042	2,792	54,944	48,243	0,601	2,00	54,111	100,00	yes	7,21	0,10	0,10
Right optic nerve	0,834	8,751	24,233	13,736	0,000	0,00	54,000	100,00	yes	2,16	0,10	
Left Optic nerve	0,969	8,068	22,558	12,738	0,000	0,00	52,535	100,00	yes	2,39	0,10	
LENS+3mm	2,571	3,916	7,628	5,735				100,00	yes	1,58	0,00	
Healthy Brain- CTV T	1316,536	0,830	57,279	22,848	431,157	33,00	27,339	100,00	yes	30,72	0,40	
Pituitary Gland	0,147	29,119	42,018	35,093				100,00	yes	1,36	0,00	
Right temporal lobe	92,544	15,828	52,940	27,135	1,851	2,00	39,492	100,00	yes	1,71	0,00	
Left Temporal Lobe	78,525	15,659	41,568	25,264	0,000	0,00	52,410	100,00	yes	1,68	0,00	
Patient	4906,926	0,020	51,257	3,432				97,83	no	301,22		
Total brain	1405,920	0,830	57,279	24,586	84,856	6,04	54,000	100,00	yes	32,82		

Figure 4: Table of cumulative dosimetric statistics of the treatment plan

Comprehensive quantitative summary for the planning target volume (PTV T 54Gy) and all organs at risk (brainstem, optic nerves, lenses, temporal lobes, pituitary gland). This table rigorously demonstrates compliance with dose constraints, as well as the heterogeneity (1.06) and conformity (0.56) indices of the validated plan for this clinical case.

The treatment was completed without any major therapeutic interruption, paving the way for the adjuvant chemotherapy phase with sequential Temozolomide.

4. DISCUSSION

Gliomas of the pineal region and the tectal plate are rare clinical entities, representing less than 1% of all adult intracranial tumors. Unlike low-grade tectal gliomas frequently observed in the pediatric population, which often follow an indolent course, gliomas of the pineal region in older adults often present with aggressive clinical characteristics and high-grade imaging criteria. This case highlights the profound diagnostic dilemma encountered when low-grade histological results from a small stereotactic biopsy sharply contrast with advanced neurospecific imaging and spectroscopy characteristics strongly suggestive of a high-grade histological tumor, ultimately requiring an aggressive multidisciplinary therapeutic strategy.

Clinical presentation and urgency

The anatomical location of the pineal gland, bordered by the third ventricle, the vein of Galen, and the quadrigeminal cistern, explains why small lesions cause early and severe neurological symptoms. Our 65-year-old patient presented with classic characteristics of pineal region tumors: a subacute intracranial hypertension syndrome (IHS) due to obstructive hydrocephalus and Parinaud's syndrome.

Parinaud's oculomotor syndrome, characterized by paralysis of upward vertical gaze, light-near dissociation, and convergence nystagmus, is caused by direct mechanical compression of the superior colliculi of the tectal plate.

In patients presenting with symptomatic hydrocephalus, restoration of cerebrospinal fluid (CSF) flow is an immediate priority that takes precedence over

definitive tissue diagnosis. While ventriculoperitoneal shunting (VPS) has historically been used in the initial management of these masses, endoscopic ventriculocisternostomy (EVC) performed on our patient is currently considered the gold standard. EVC effectively bypasses the aqueductal obstruction, avoids complications of dependence related to shunt hardware, significantly reduces the risk of peritoneal metastasis, and can sometimes be combined with a simultaneous endoscopic tumor biopsy.

Diagnostic discrepancy: Histology vs. Advanced neuroimaging

The primary clinical challenge lies in the sampling bias inherent in stereotactic biopsy. Due to the anatomical complexity of the pineal region and the proximity of highly critical deep vascular structures, biopsy samples are, by technical necessity, small in size [2]. This limitation frequently leads to histological undergrading of the lesion [7, 8]. In our case, the evidence of a low Ki-67 proliferation index (1 to 3%) sharply contrasted with the clinical presentation of intracranial hypertension, the significant tumor volume (28 x 23 x 39 mm) [6], and the highly suspicious spectroscopic profile. It is therefore highly probable that key areas of high malignancy, such as foci of hypercellularity, endothelial-capillary proliferation, or focal necrosis characteristic of high-grade gliomas, were missed during stereotactic targeting [8].

This sampling error constitutes a classic and well-documented pitfall in the literature on deep brain tumors [7, 8]. The micro-fragments collected may indeed target areas of low cellularity or reactive gliosis at the periphery of the mass, thus missing the core of the high-grade tumor component. Faced with this dilemma, the diagnostic paradigms formalized by the 2021 WHO classification of tumors of the central nervous system prove indispensable [9]. This major update, supported by EANO 2021 recommendations [10], has redefined the criteria for aggressiveness in adult gliomas by placing molecular profiling and the integration of advanced neuroimaging data on the same level, or even above, simple morphological analysis or mitotic counts on small samples [9, 10].

By way of example, entities such as Diffuse midline glioma, H3 K27-altered (WHO Grade 4), can present deceptively reassuring histological characteristics on small samples while maintaining a daunting clinical prognosis [9]. Although the H3 K27 status and DNA methylation studies could not be performed in our institution, the overall radio-spectroscopic behavior mandated aggressive management. In our observation, the IDH-wildtype molecular character, combined with the aggressiveness evidenced by MRI and spectroscopy, formed the cornerstone of the therapeutic decision [9, 10], fully justifying the immediate recourse to combined radio-chemotherapy.

However, conventional MRI and magnetic resonance spectroscopy (MRS) strongly refuted this indolent nature:

Conventional MRI: The tumor exhibited intense and homogeneous contrast enhancement, as well as major perilesional vasogenic edema (33 x 45 x 37 mm), extending to the thalamus, midbrain, and pons. True low-grade tectal gliomas are conversely characterized by an absence or minimum of enhancement and are not accompanied by significant peripheral edema [7].

MR Spectroscopy: MRS serves as a non-invasive surrogate for evaluating tumor biology. In this patient, the Choline/NAA ratio was markedly elevated at 3, accompanied by a lactate peak. Choline is a marker of cell membrane turnover, while NAA represents neuronal integrity. A ratio of this magnitude is a classic signature of high-grade malignancy, reflecting intense cellular proliferation and metabolic stress that contradict the low Ki67 count obtained on the micro-fragments [7, 9].

Applicability and relevance of prognostic stratification criteria (EORTC and RTOG) in the molecular era

A recurring debate in neuro-oncology surrounds the use of historical prognostic classification systems, such as the EORTC criteria (Pignatti score) and the RTOG Recursive Partitioning Analysis (RPA) [12, 13]. These models are sometimes perceived, incorrectly, as being exclusively reserved for patients who have undergone maximal surgical resection. However, analysis of contemporary literature and European guidelines demonstrates that their application is not only legitimate but crucial for patients who have undergone biopsy alone [10, 13]. This is particularly true when the tumor is located within an inoperable and highly critical anatomical region such as the pineal region. In these stratification models, the absence of surgical resection is not an evaluation bias, but is explicitly coded as a major and independent adverse prognostic factor, justifying immediate therapeutic intensification [12, 13].

The EORTC prognostic score (Pignatti score) in the face of midline tumors

The score by Pignatti *et al.,* (EORTC 22844/22845) historically identified five risk factors predictive of unfavorable overall survival for adult gliomas: age over 40 years, astrocytic histology, large tumor size, pre-existing neurological deficit, and a lesion crossing the midline. The presence of at least three of these criteria places the patient in the so-called "high risk" group [12].

In our observation, the patient undeniably accumulated three of these major factors: an age of 65 years, an astrocytic nature, and midline involvement (pineal region infiltrating the brainstem). Comparison with large EORTC cohorts confirms that these high-risk patients exhibit significantly unfavorable survival curves

[12], legitimizing the immediate implementation of a more aggressive therapeutic protocol.

The RTOG RPA classification and the integration of modern molecular status

In parallel, the RPA classification system developed by the RTOG (notably the work of Curran et al.) remains one of the most robust clinical tools for stratifying patients with malignant gliomas [12, 13].

The impact of age and type of surgery: In the classic RTOG model, advanced age (critical threshold at 50 years, accentuating after 65 years) combined with the impossibility of performing surgical resection (stereotactic biopsy only) mechanically classifies the patient into an unfavorable prognostic group (Classes V or VI) [13]. International literature highlights that the simple impossibility of surgical cytoreduction doubles the risk of local progression, independent of adjuvant treatments.

The convergence with modern WHO classification: Although the RTOG RPA relies on traditional clinico-histological criteria, its confrontation with contemporary molecular data reinforces its relevance [9, 10, 13]. The integration of the molecular status in our 65-year-old patient highlighted an IDH-wildtype profile. According to the modern WHO classification [9] and EANO recommendations [10], an adult IDH-wildtype astrocytic glioma, even in the presence of deceptively reassuring or low-grade micro-fragment histological criteria due to a biopsy pitfall, behaves biologically like a glioblastoma (WHO Grade 4) [9].

Conclusion on the overall therapeutic strategy

The combined and cross-referenced application of the EORTC criteria and the RTOG RPA made it possible to definitively resolve the diagnostic and prognostic uncertainty inherently linked to the small size of the biopsy sample [12, 13]. By confronting these clinical scores with the molecular realities of the 2021 WHO [9] and EANO [10] classifications, our approach aligns with literature data that formally refute a passive observation (watch-and-wait) attitude in older adults for these midline locations. It provides the essential scientific and ethical justification for the immediate initiation of maximal active therapy combining focal radiotherapy and chemotherapy with Temozolomide.

Therapeutic strategy and justification for dosimetric de-escalation

Beyond emergency cerebrospinal fluid (CSF) diversion, optimal definitive surgical management of pineal masses in adults remains highly complex. As detailed at length by Ruelle et al., direct aggressive surgical resection in this anatomical territory is profoundly limited by its midline location and the surrounding critical neurovascular structures [2]. Although traditional open surgical approaches—such as infratentorial supracerebellar or transtentorial occipital approaches—have historically been used to achieve maximal and safe tumor reduction, they entail great procedural complexity [2, 3]. In cases of primary infiltrating adult gliomas involving the tectal plate or the pineal stroma, radical cytoreductive surgery poses an unacceptable risk of major and irreversible postoperative neurological morbidity, notably permanent oculomotor paralysis, vigilance disorders, and catastrophic deep venous infarction due to the proximity of the vein of Galen [2, 6]. Consequently, modern neuro-oncology strategies are moving away from radical surgical resections of infiltrating tumors [2, 6]. Instead, a minimally invasive surgical paradigm combining endoscopic ventriculocisternostomy (EVC) with a simultaneous stereotactic or endoscopic biopsy, as performed in our patient, represents the safest and most effective initial strategy [2, 3, 6]. This allows for effective control of hydrocephalus while ensuring the retrieval of tissue fragments required for molecular and histopathological diagnosis, setting aside attempts at cytoreduction in favor of early adjuvant therapies [2, 6].

The therapeutic choice validated by our multidisciplinary oncology committee (RCP), based on an adapted Stupp protocol, is fully in line with current management recommendations for high-grade midline gliomas, while pragmatically responding to the patient's anatomical constraints. Historically, the major clinical benefit of adding adjuvant chemotherapy to exclusive radiotherapy in infiltrating adult gliomas was formalized by the randomized RTOG 9802 trial, particularly for high-risk entities [13]. Nevertheless, the critical midline infiltration, the IDH-wildtype molecular character, and the radio-spectroscopic aggressiveness of the lesion led us to favor the contemporary approach of the Stupp protocol (concomitant and adjuvant Temozolomide) [11, 12].

Our patient's management thus aligns perfectly with the international clinical recommendations described in the EURACAN synthesis by Lombardi et al., which advocates a paradigm shift away from direct and aggressive surgical resections for infiltrating tumors of the adult pineal region [6]. Given the prohibitive risk of catastrophic deep venous complications and neurological morbidity associated with open surgery in this eloquent midline territory, contemporary recommendations establish minimally invasive management, comprising CSF diversion associated with stereotactic needle biopsy as the gold standard approach [6].

5. CONCLUSION

Gliomas of the pineal region in older adults constitute a rare and highly complex clinical entity, at the crossroads of real diagnostic, prognostic, and therapeutic challenges. Due to the inherent smallness of samples in this deep and eloquent anatomical territory, the medical-surgical management of these tumors can no longer rely

exclusively on conventional micro-fragment histological analysis. As our case illustrates, the latter is frequently faulted by a major sampling bias, exposing the patient to the critical risk of tumor underestimation (undergrading) and delaying the initiation of adapted treatment.

This clinical case thus highlights the capital importance of multimodal imaging, and more particularly magnetic resonance spectroscopy (MRS), which asserts itself as an indispensable non-invasive tool to correct an initial erroneous or underestimated histological diagnosis. By objectifying metabolic profiles formally suggestive of high malignancy characterized by a sharp elevation of the Choline/Creatine ratio, a lactate peak, and a collapse of N-acetylaspartate (NAA), MRS transcends purely morphological analysis. It allows the multidisciplinary team to be guided toward an aggressive therapeutic strategy, in perfect adequacy with the biological reality and kinetics of the tumor. In the era of the 2021 WHO classification, the demonstration of a highly suspicious radio-spectroscopic profile combined with an unfavorable molecular status (such as IDH-wildtype character) must prevail over reassuring histology resulting from a small biopsy.

Faced with these high-grade tumors of the pineal region, the rapid implementation of sequential and standardized medical-surgical treatment is imperative. Initial management must imperatively secure the CSF pathways, almost systematically compromised by critical obstructive hydrocephalus, by favoring endoscopic ventriculocisternostomy (EVC), which offers the major advantage of coupling the resolution of the hypertensive emergency in a single step with simultaneous biopsy. Subsequently, the early initiation of the Stupp protocol, associating normofractionated focal radiotherapy and concomitant then adjuvant chemotherapy with Temozolomide, remains the indispensable therapeutic standard to hope for achieving durable local control and slowing tumor progression. The major challenge of this combined approach, however, lies in maintaining a delicate balance between necessary oncological aggressiveness and maximum preservation of neurological functions. In these older, frail patients exposed to cumulative neurocognitive morbidity, the personalization of management and supportive therapeutic care constitute the sine qua non condition for maintaining an optimal quality of life.

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