Article published online: 2023-12-04

Unusual Extra-Axial and Extracranial Recurrence in an IDH Mutant Astrocytoma: A Case Report

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Indian J Radiol Imaging 2024;34:351–355.

Abstract

Isocitrate dehydrogenase mutant gliomas generally have a better prognosis than their wild-type counterpart. Recurrences are generally within the radiation field in the primary tumoral bed. Remote recurrence is uncommon and is usually intraparenchymal. Transformation to a higher grade has been observed with TP53 mutants. Presentation of glioma as an extra-axial lesion is extremely uncommon. No such cases of remote intracranial extra-axial recurrence have been reported in the literature. We describe the unique imaging findings in this case and attempt to formulate possible diagnoses. Intraoperative and pathological findings confirmed this unusual recurrence pattern.

Keywords
- extra-axial
- extracranial
- recurrence
- IDH mutant
- glioma
- metastases
- astrocytoma

Introduction

Astrocytoma is a diffuse glial tumor with isocitrate dehydrogenase (IDH) mutant status and can be graded between the World Health Organization (WHO) grades 2 and 4.[1,2] The IDH mutant status confers a better prognosis than its wild-type counterpart.[3] Upfront treatment with surgery and radiation is preferred in view of the high risk of recurrence and transformation. Most recurrences are generally within the radiation field, remote recurrence being uncommon.[4,5] Here, we present a case of grade 3 astrocytoma, post-treatment, with simultaneous transformation into higher grade and remote intracranial recurrence as an extra-axial lesion. This has not been reported previously, to the best of our knowledge.

Case Report

A 46-year-old male patient was diagnosed with a left parietal space-occupying lesion extending to the peritrigonal area, splenium of the corpus callosum, and the left occipital lobe. He underwent surgical resection for it, and histopathology revealed an astrocytic IDH and TP53 mutant, the WHO grade 3 tumor with loss of Alpha-thalassemia/mental retardation, X-linked (ATRX) gene. Subsequent postoperative magnetic resonance imaging (MRI) showed the presence of residual disease for which he received radiation therapy (RT) and adjuvant temozolomide (TMZ). After 1 month, post-RT imaging showed some residual disease in the form of T2 intermediate areas. Considering IDH mutant status, it was decided to continue TMZ (►**Fig. 1A** and **B**).

article published online
December 4, 2023

DOI https://doi.org/10.1055/s-0043-1777012.
ISSN 0971-3026.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

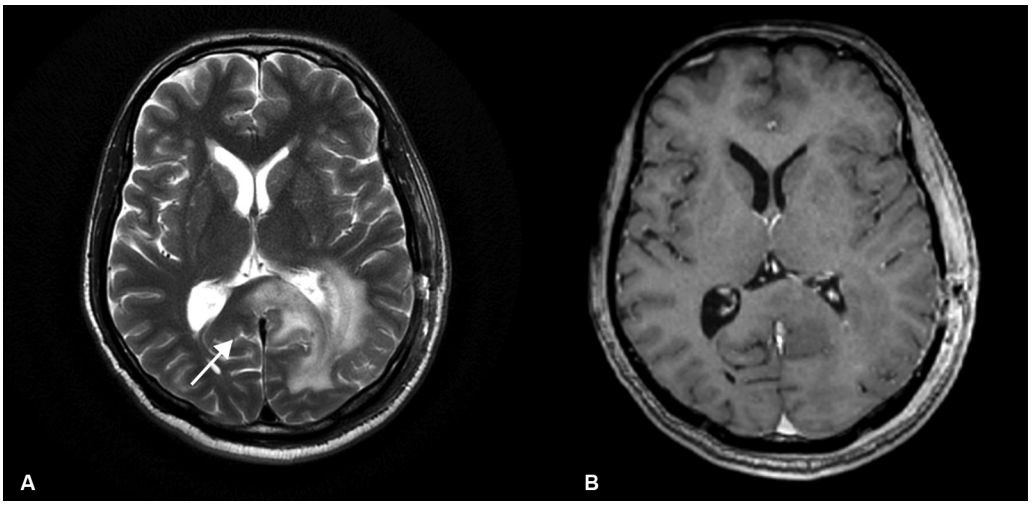

Fig. 1 (**A** and **B**) Axial T2-weighted and post-contrast T1-weighted images showing diffuse infiltrating lesion in the parieto-occipital lobe, extending up to the splenium of the corpus callosum (white arrow) and the trigone of the left lateral ventricle. (index scan). No suspicious enhancement is present.

Post 11 cycles of chemotherapy, he presented to the emergency services with vomiting, altered sensorium, and right-sided hemiparesis. MRI at the time showed a new onset large extra-axial predominantly cystic lesion with a peripheral papillary solid component in the left high frontal region (►**Fig. 2A–C**). The index tumor bed was stable. The cystic component was T1 hyperintense, and T2 hypointense (features of subacute blood on MRI), which made us consider the possibility of a subpial hematoma. Adjacent sulcal hyperintensity on T1-weighted images was seen, raising suspicion of cerebral venous thrombosis (CVT). The other differentials proposed were intracranial recurrence of the primary tumor, extra-axial recurrence, and a remote possibility of a collision tumor with associated tumor bleed.

The patient improved on conservative management with antiedema measures. Post a multidisciplinary tumor board discussion, it was planned to observe the patient and continue TMZ. However, a follow-up MRI after 4 weeks showed an increase in the lesion size (►**Fig. 3A–C**). Hence, surgical resection of the lesion was done. Intraoperatively, an extra-axial lesion was noted (►**Fig. 4A, B**). The histopathology revealed a high-grade infiltrating (IDH-mutant) astrocytic tumor, central nervous system WHO grade 4, with loss of ATRX (►**Fig. 5A, B**). This suggests the same histomorphological features as the primary tumor with progression to a higher grade.

Postoperative scan 1 month later showed resection cavity with no other suspicious enhancement or lesion (►**Fig. 6A, B**). Adjuvant RT was also given to the postoperative bed. Five months post-surgery, the patient developed back pain, for which MRI of the spine with screening of the brain was done. This revealed nodular pachymeningeal enhancement along the right temporal lobe and the periorbital dura along the left temporal convexity (►**Fig. 7A, B**). Also noted were altered signal intensity lesions in the dorsolumbar vertebral bodies (►**Fig. 8A–C**). These findings in the given setting were suspicious for metastases, and a biopsy from the vertebral body lesions was planned. However, the patient worsened clinically and eventually succumbed to the disease. Hence, a pathological confirmation was not possible.

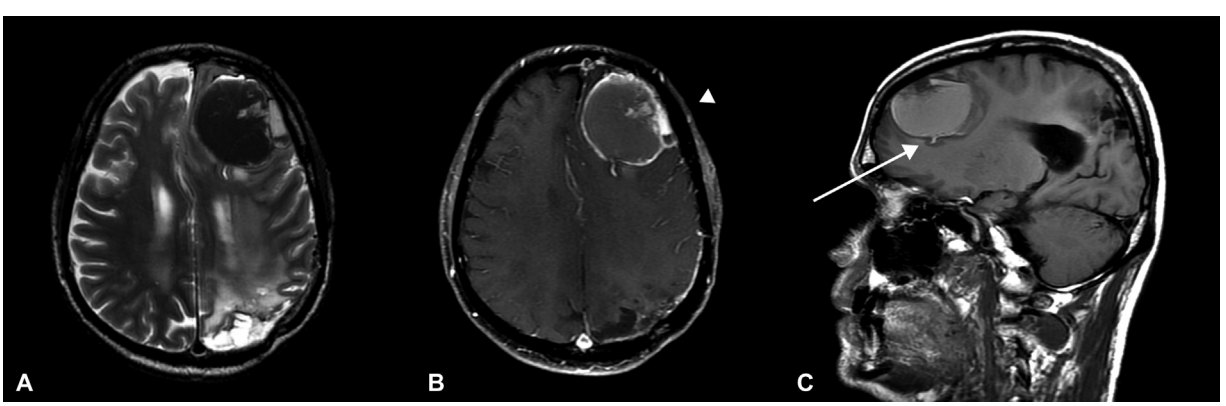

Fig. 2 (**A–C**) Axial T2-weighted, post-contrast T1-weighted, and sagittal T1-weighted images post-radiation therapy and 11 cycles adjuvant chemotherapy showing new onset large extra-axial predominantly cystic lesion with a peripheral enhancing papillary solid component in the left high frontoparietal region (arrowhead). The index tumor bed showing no new lesion. The cystic component is T1 hyperintense and T2 hypointense. Adjacent sulcal hyperintensity is noted on the T1 weighted image.

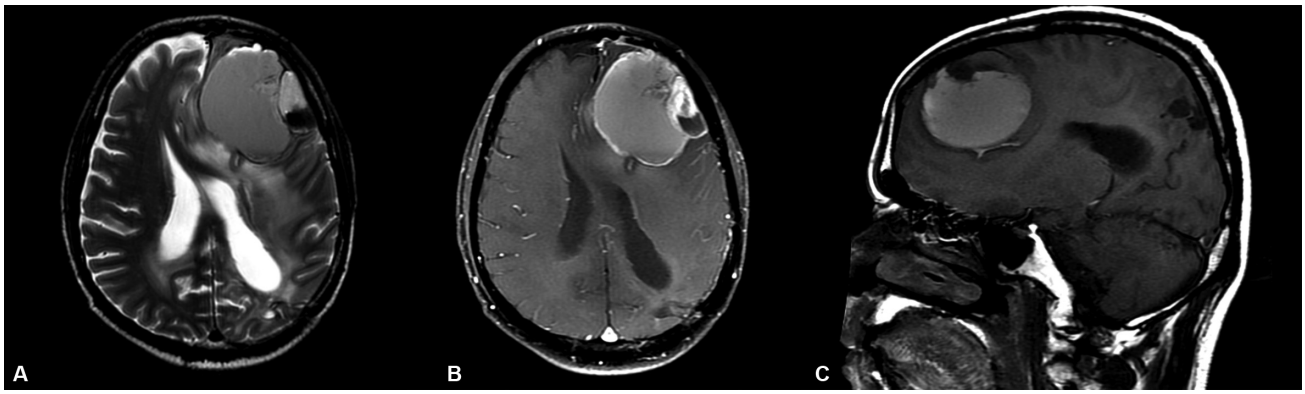

Fig. 3 (**A–C**) Axial T2-weighted, post-contrast T1-weighted, and sagittal T1-weighted images post 4 weeks (on observation) showing an increase in the size of lesion and mass effect with cystic component now being T1 hyperintense and T2 intermediate.

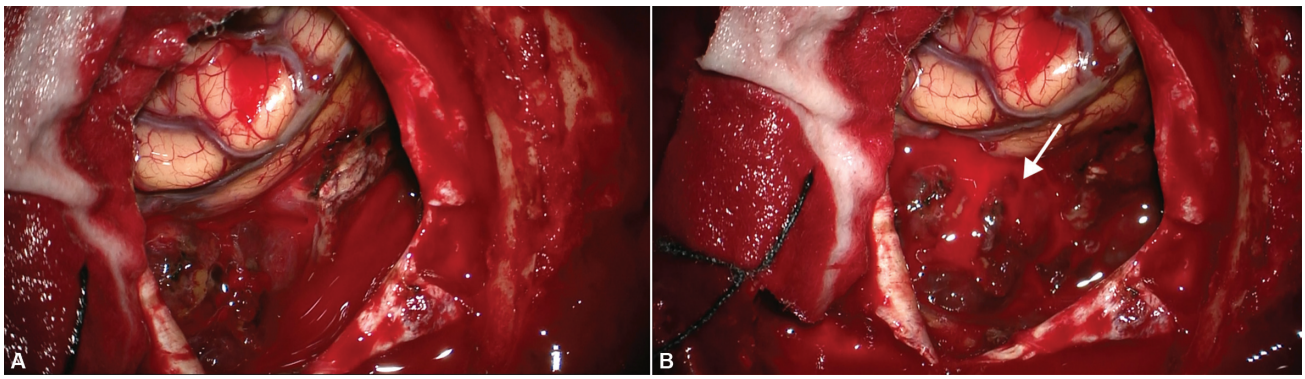

Fig. 4 (**A**) Intraoperative photograph of the tumor membrane (capsule) stuck to the normal brain. (**B**) Solid component of the tumor along with the capsule stuck to the normal brain (white arrow).

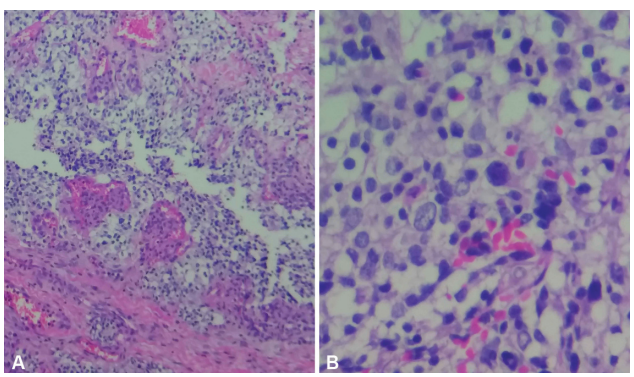

Fig. 5 (**A, B**) Hematoxylin and eosin stain low power (10x) and high power (40x) images of the resected lesion showing tumor cells.

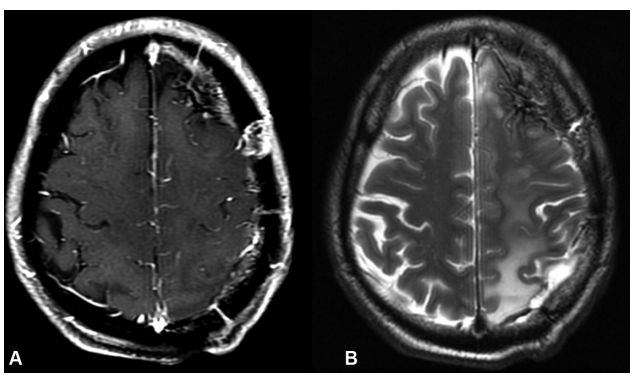

Fig. 6 (**A, B**) Postoperative (1 month) axial T2-weighted and post-contrast T1-weighted image showing surgical bed with gross total resection of the lesion. No suspicious lesion is noted.

Given the clinical features and imaging findings, we conclude this to be likely due to disseminated disease. Thus, the case demonstrated both extra-axial and extracranial recurrence.

Discussion

IDH mutant astrocytomas generally show increased progression-free survival compared with de novo glioblastoma (IDH wild type). The standard of care currently is maximal safe surgical resection and concurrent chemoradiation. Most of the patterns of failure and recurrence post-therapy are within the gross tumor volume.[6] Malignant degeneration of IDH mutant tumors has been observed with acquisition of additional genetic mutation and transformation into higher grade.[7]

TP53 mutant IDH mutant gliomas can show recurrence in remote intracranial regions.[8] The underlying pathogenetic mechanisms are not well understood. Nakae et al[4] have proposed the role of 8q gains and ability for interlobar metastases. Also hypothesized is tumor migration through the tracks of major fiber bundles.[4]

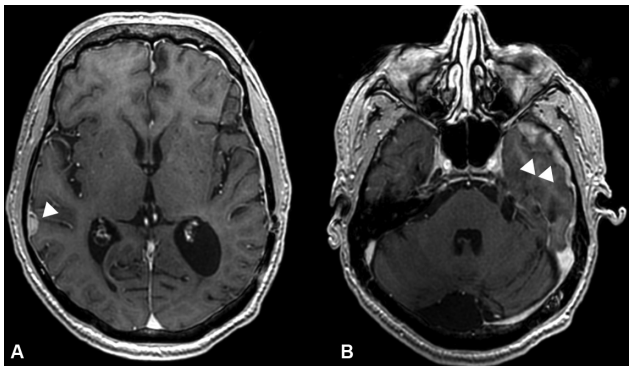

Fig. 7 (**A, B**) Post-contrast T1-weighted images (5 months post-surgery) showing nodular pachymeningeal enhancement along the right temporal lobe, the left frontotemporal lobe, and the periorbital dura along the left temporal convexity (arrowheads).

Extra-axial tumors include a spectrum of tumors involving the extra-parenchymal tissue, the majority of which have meningeal origin. The most common are meningiomas, which demonstrate broad-based dural contact and the "dural tail sign."[9] In contrast, gliomas are generally intra-axial. When they extend to involve the dura, they may show features similar to meningiomas, including the dural tail sign.[10] This is common in peripheral glioblastomas.[11] The "cerebrospinal fluid (CSF) cleft sign" may help differentiate intra-axial and extra-axial tumors, being positive in extra-axial tumors.[12] However, utility is limited in malignant meningiomas where it becomes difficult to distinguish the location.

There have been case reports of primary extra-axial gliomas.[10,11,13,14] However, an extra-axial, remote intra-cranial recurrence of an IDH mutant glioma has yet to be reported in our search of existing literature. In the present case, due to the unlikely possibility of such a recurrence, we had considered other diagnoses in keeping with the imaging findings.

The large extra-axial lesion with T2 hypointense and T1 hyperintense signal was suggestive of signal characteristics of early subacute blood on MRI. The pattern of change of T2 intensity into a more hyperintense signal was also similar to progression into late subacute and chronic blood.[15] The surrounding sulcal T1 hyperintensity was assumed to be the hyperintense vein sign seen in isolated cortical vein CVT.[16] Thrombosis of isolated cortical veins has been speculated to be a mechanism for subpial hemorrhages.[17] In view of the imaging findings, we contemplated the possibility of a large subpial hematoma with CVT. Subpial hematomas typically show blood deposition along the cortical surface and are more common along the frontal lobe.[17,18] This was similar to our case, although subpial hematomas are rare in adults.[18]

Another unlikely differential considered was a collision tumor. These most commonly involve a meningioma in collision with a glioma.[19] Here the meningioma component may be dural-based, which can give rise to an appearance similar to the present case.[19] However, the rest of the imaging findings precluded the possibility. Also, we note that in post-RT patients, radiation-induced meningiomas generally present after a mean interval of around 10 years.[20]

Meningeal dissemination of gliomas is rare and is usually observed in the late stages of the disease. Potential factors include the anatomical location (tumors near the subventricular zone), ventricular entry during surgery, repeated resections, and depressed immune function post-chemo and radiotherapy.[21]

Extracranial metastases of grade 4 astrocytomas have been reported in less than 0.5% of cases. Common sites include the lymph nodes, bone, soft tissue, skin, and liver.[22,23] In skeletal metastases, vertebral bodies are most commonly involved,[24] likely through seeding from the Bateson plexus.[24] Spread via breakdown of the blood–brain barrier via tumoral vessels or invasion of dural veins, lymphogenous, and hematogenous spread by direct extracranial bone and soft tissue infiltration, through the CSF, by ventricular shunting are proposed mechanisms.[24,25]

In the present case, nodular pachymeningeal enhancement and vertebral body lesions were observed. The possible factors in the case include a history of multiple neurosurgical procedures,

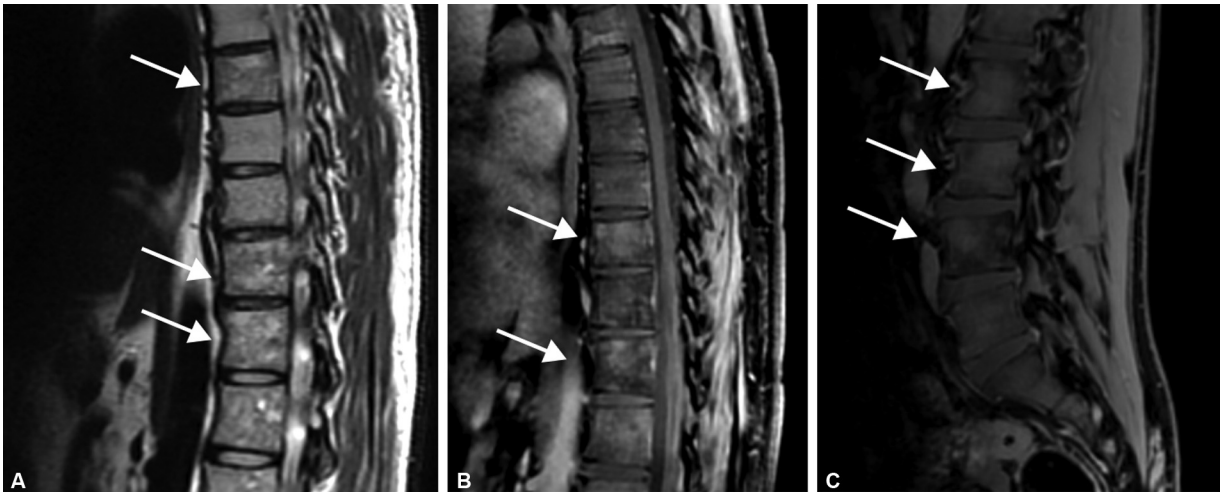

Fig. 8 (**A–C**) Sagittal T2-weighted and post-contrast sagittal T1-weighted images (5 months post-surgery) showing altered signal intensity enhancing lesions in multiple vertebral bodies (arrows).

which may have predisposed to CSF dissemination. Postoperative meningeal enhancement is another differential; however, it usually shows smooth meningeal enhancement, unlike the nodular enhancement noted in the present case. Also, the lack of such changes in the post-surgical imaging and worsening clinical symptoms preclude this.

The unique features in our case include (1) site distant (frontal region) to primary tumoral bed (parieto-occipital lobe), thus excluding the possibility of tumoral seedling along the postoperative track; (2) extra-axial lesion with signal characteristics of subacute blood, and possible pachymeningeal and extracranial spread in the form of skeletal metastases. The progression of the lesion prompted intervention and pathological confirmation.

Conclusion

We reported a rare presentation of recurrence in an IDH mutant astrocytoma as an extra-axial lesion remote to the primary site and possible pachymeningeal, extracranial (vertebral body lesions). A high index of suspicion and close clinicoradiological follow-up is required to monitor the course of recurrence in post-treatment gliomas and guide appropriate management strategies.

Informed Consent
Informed consent has been obtained from the patient for using clinical details and imaging.

Funding
None.

Conflict of Interest
None declared.

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