



## Case Report

# Recurrent adult pilocytic astrocytoma presenting with intraventricular and leptomeningeal spread

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## ABSTRACT

**Background:** Infratentorial pilocytic astrocytomas are uncommon tumors in adulthood but are thought to be prognostically similar to their pediatric counterparts with excellent overall survival following gross total resection. However, given the relative rarity of these tumors, no management guidelines exist for recurrent adult pilocytic astrocytomas (APAs). This lack of consensus is especially problematic for inoperable recurrences or those with aggressive features concerning for malignant transformation.

**Case Description:** In 2017, a 26-year-old female presented with headaches, nausea, vomiting, and blurry vision. A brain magnetic resonance imaging (MRI) demonstrated a large, well-circumscribed mass within the fourth ventricle causing obstructive hydrocephalus. She underwent near-total resection through a midline suboccipital transtonsillar approach. Pathology demonstrated a World Health Organization Grade 1 pilocytic astrocytoma. Despite initial improvement in her symptoms, she developed worsening headaches and lethargy 10 months after surgery and repeat MRI demonstrated recurrent tumor within the entire ventricular system and the subarachnoid spaces of the left cerebellopontine angle suggesting leptomeningeal spread. Due to the unresectable nature of the recurrence, the patient declined any further intervention and succumbed to her disease 6 months later.

**Conclusion:** We present the first case of a recurrent APA presenting with intraventricular and leptomeningeal spread. Although thought to be a benign neoplasm, close interval follow-up with serial imaging is of essential, especially in those patients with known residual tumor, to prevent aggressive recurrences such as this.

**Keywords:** Adult pilocytic astrocytoma, Inoperable recurrence, Leptomeningeal spread, Malignant transformation, Subtotal resection

## INTRODUCTION

Pilocytic astrocytomas are one of the most common benign brain neoplasms of childhood but remain exceedingly rare in adults accounting for only 0.8% of central nervous system tumors in patients >20 years of age.<sup>[30,32]</sup> Although adult pilocytic astrocytomas (APAs) are thought to have an excellent prognosis, especially following complete surgical resection, some have suggested that APAs may exhibit higher recurrence rates with increased incidence of malignant transformation than their pediatric counterparts.<sup>[6,9,12,19,24,30,37,38,40,41]</sup> Given the low incidence of recurrent APAs, no management guidelines exist, however, those presenting

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with local recurrence are typically treated through repeat resection with radiation and chemotherapy reserved for inoperable lesions or as adjuvant therapy for those tumors demonstrating high-grade features.<sup>[3,4,21,22,37,39,40,44]</sup> Leptomeningeal dissemination and spontaneous malignant degeneration are uncommon and present significant surgical and oncologic challenges.<sup>[8,26]</sup> To that end, we present a rare case of a recurrent APA exhibiting intraventricular and leptomeningeal spread <1 year after near-total resection. We also provide a review of the available literature discussing management of recurrent APAs.

## CLINICAL PRESENTATION

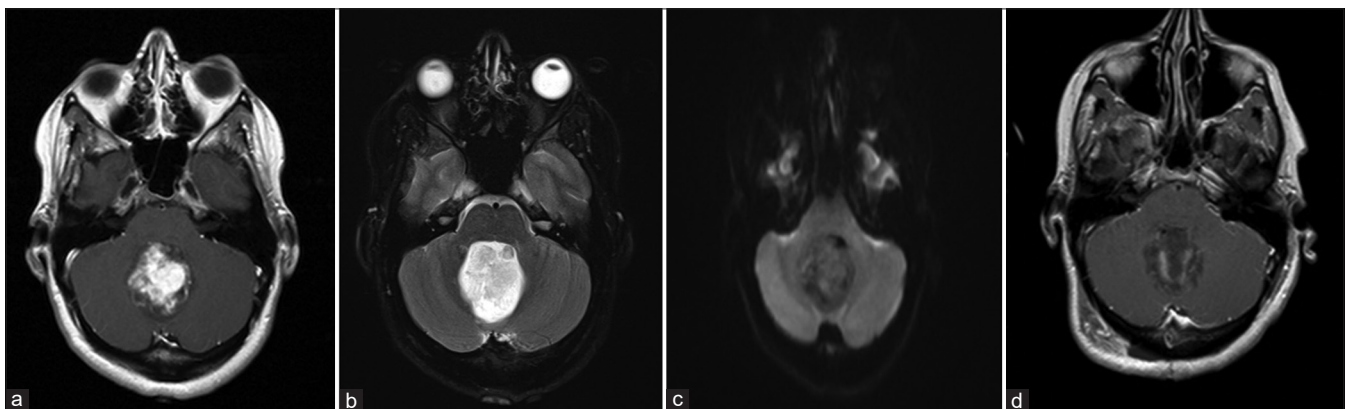
An otherwise healthy 26-year-old female presented in 2017 with severe headaches, nausea, vomiting, and visual changes. After fundoscopic examination demonstrated Grade 5 papilledema, contrast-enhanced brain magnetic resonance imaging (MRI) was performed revealing a 4.8 × 4.4 × 4.1-cm mass centered in the fourth ventricle resulting in obstructive hydrocephalus [Figure 1]. She subsequently underwent near-total resection with only a small portion of the tumor intentionally left on the floor of the fourth ventricle in an effort to prevent damage to the brainstem. Postoperatively, her hydrocephalus did not resolve and required ventriculoperitoneal shunting. Following this second procedure, she progressed well and was discharged home with no postoperative complications. The final pathology demonstrated presence of eosinophilic granular bodies and Rosenthal fibers with immunohistochemistry showing focal Olig-2 staining as well as GFAP and vimentin positivity confirming that the tumor was a World Health Organization Grade 1 pilocytic astrocytoma [Figure 2]. IDH-1, p53, neurofilament, and BRAF gene rearrangement testing were negative. Despite initial improvement in her symptoms, at 10 months

postsurgery, she developed new-onset headaches, confusion, and lethargy. Repeat MRI demonstrated widespread tumor recurrence throughout the entire ventricular system and the subarachnoid spaces of the left cerebellopontine angle (CPA) suggesting leptomeningeal spread [Figure 3]. Due to the unresectable nature of the recurrence, the patient declined any further intervention and succumbed to her disease 6 months later.

## DISCUSSION

Pilocytic astrocytomas are one of the most common gliomas of childhood. However, in adults, they are much less frequent with an incidence of 3.4/1 million.<sup>[32]</sup> In children, they usually occur in the cerebellum, whereas in adults, they are equally likely to be supratentorial.<sup>[7]</sup> Due to their frequently benign nature, these tumors typically only present after they have grown large enough to produce symptoms of increased intracranial pressure or obstructive hydrocephalus.<sup>[3,37]</sup> Given the rarity of APAs, most neurosurgeons manage them based on the extrapolation of data from pediatric cases. However, recent studies have suggested that APAs may behave more aggressively with higher rates of recurrence and malignant transformation than their pediatric counterparts.<sup>[12,24,37,40]</sup> Yet, no consensus on the management and treatment of recurrent APAs exists. Here, we discuss the current understanding of APA behavior and the possible therapeutic avenues that have been explored thus far.

Several studies have shown that increasing patient age is correlated with lower rates of overall survival in pilocytic astrocytomas with 5-year survival dropping from 96.5% in pediatric patients to approximately 53% in patients older than 60.<sup>[7,22]</sup> Furthermore, APAs appear to have increased recurrence rates and higher potential to undergo



**Figure 1:** Imaging performed in April 2017. (a) Preoperative T1 contrast enhancing MRI demonstrating a well-circumscribed lesion within the fourth ventricle. (b) Preoperative T2 MRI demonstrating no significant surrounding edema or infiltration of the normal brain parenchyma. (c) Preoperative DWI demonstrating no diffusion restriction. (d) Postoperative T1 contrast enhancing MRI demonstrating no obvious residual tumor.

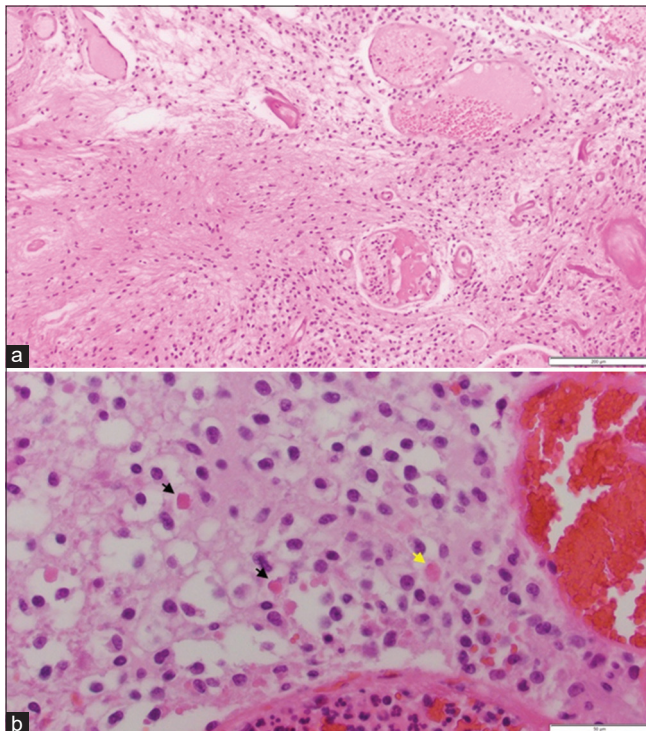
malignant transformation. Maximal safe resection should be the goal whenever feasible as studies have shown that extent of resection correlates directly with increased survival.<sup>[12,37]</sup> However, postsurgical management of APAs, including adjuvant treatments for subtotal resections and surveillance imaging to identify tumor progression/recurrence, remains controversial.

In the pediatric population, several retrospective series examined the benefit of surveillance imaging for pilocytic astrocytomas and concluded that patients with a gross

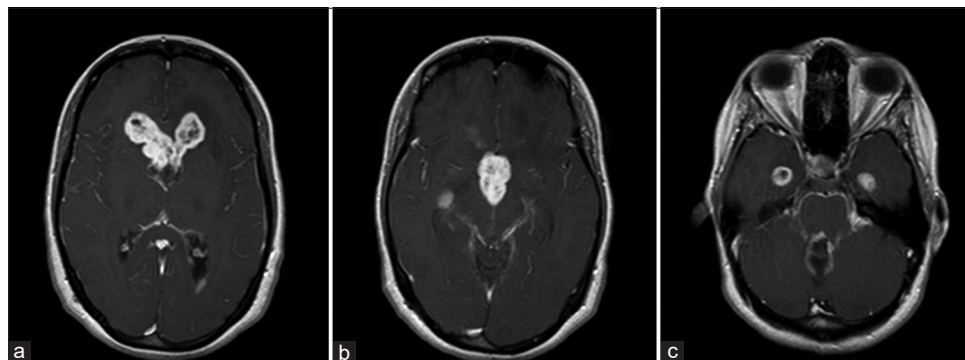
total resection have a very low likelihood of recurrence and may not benefit from long-term surveillance.<sup>[1,10,27]</sup> They found that most recurrences happened within 3 years of resection and thus advocated for more intensive screening during the 1<sup>st</sup> year followed by incrementally larger observation periods over a total of 3–5 years. However, other series identified recurrences at even later time points and thus argued for more long-term follow-up.<sup>[11]</sup> If we adapt these findings to APAs, which are known to have higher recurrence rates and less favorable prognoses than their pediatric counterparts, then it may be beneficial to obtain more frequent interval imaging within the first few years after resection and continue to follow these patients long-term, especially in those with known subtotal resections.<sup>[6,24]</sup>

Little data exist to help guide postsurgical adjuvant therapy for subtotally resected APAs. Radiation therapy (XRT) has been evaluated in several studies with mixed findings. A recent study evaluating overall survival following subtotal resection of APAs found that those patients who received postoperative XRT had significantly higher mortality rates compared to those that received surveillance alone.<sup>[20]</sup> Other retrospective studies have found good local control in subtotally resected or recurrent APAs that underwent XRT but found no difference overall survival.<sup>[14,15,18,23,42,43]</sup> Although these studies are susceptible to selection bias, as older patients, and lesions with evidence of increased aggressiveness or eloquent location tend to more frequently receive postoperative XRT, their results emphasize the need for future prospective studies evaluating the role of XRT in APAs.<sup>[16,24,37,40]</sup>

Although no standard chemotherapeutic regimen exists for APAs, various drug combinations, with or without XRT, have been used in recurrent/inoperable pilocytic astrocytomas with varying degrees of effectiveness.<sup>[2,5,17,29,39]</sup> Since pilocytic astrocytomas are known to



**Figure 2:** (a) Low-power view demonstrating typical oval nuclei, low mitotic activity, and Rosenthal fibers. (b) High-power view demonstrating eosinophilic granular bodies.



**Figure 3:** Imaging performed in March 2018. (a) T1 contrast-enhanced MRI demonstrating tumor recurrence within the frontal horns of the lateral ventricle. (b) T1 MRI demonstrating recurrent tumor within the third ventricle. (c) T1 MRI demonstrating leptomeningeal enhancement in the left cerebellopontine angle and temporal horns.

express higher levels of VEGF-A, immunotherapy agents such as bevacizumab have also been utilized in inoperable cases and have demonstrated promising results in the adult population.<sup>[13,35,44]</sup> Unfortunately, BRAF V600E mutations are very rare in APAs, thus limiting the use of inhibitors such as dabrafenib. However, upregulated mTOR signaling appears to be present in a majority of cases providing another potential avenue for therapeutic targeting.<sup>[33,40]</sup>

Leptomeningeal disease in recurrent APAs remains significantly difficult to manage because, by definition, it is unresectable. Biopsy may be warranted to determine if the lesion has malignantly transformed. In addition, molecular testing may also increase diagnostic and prognostic accuracy as DNA methylation has been shown to help determine tumor grade when histologic features alone remain ambiguous.<sup>[24,31]</sup> Although it is still unclear what factors influence the development of leptomeningeal spread, it has been suggested that subtotal resections of periventricular APAs may increase the risk of recurrence in the leptomeninges.<sup>[25,34,36]</sup>

In our patient, the tumor involved the fourth ventricle and resection may have led to leptomeningeal spread within the CPA. However, this does not fully explain how the tumor casted the entire ventricular system. Given that the patient was shunted for hydrocephalus, this may have led to ventricular seeding yet this would likely have tracked along the catheter rather than involving even the contralateral lateral ventricle.<sup>[28]</sup> Furthermore, even in those patients who develop leptomeningeal recurrence, casting of all the ventricles has never been reported. This suggests the presence of a much more insidious process. Unfortunately, in our patient, the recurrence was inoperable, and the lesions were too diffuse to perform stereotactic radiosurgery so whole-brain XRT and chemotherapy were her only options. As a result, the patient declined a biopsy to evaluate for malignant transformation and did not pursue any further treatment.

## CONCLUSION

We report a rare case of a recurrent APA presenting with diffuse intraventricular and leptomeningeal spread. This atypical and fatal case highlights the need for improved management guidelines and better diagnostic criteria for these tumors in the adult population. Novel molecular profiling may help detect subtle differences in tumor grade and, in turn, better direct adjuvant therapy in patients with known residual or recurrent disease. Although thought to be a benign neoplasm, close interval follow-up with serial imaging may be useful in those patients with known residual tumor.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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