Neurosurg Rev (2019) 42:97–106
DOI 10.1007/s10143-017-0915-z

REVIEW

Hemorrhagic presentation of intracranial pilocytic astrocytomas: literature review

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Received: 5 July 2017 / Revised: 13 September 2017 / Accepted: 26 September 2017 / Published online: 4 October 2017

Abstract Pilocytic astrocytomas (PAs) are seemingly innocuous and benign tumors. However, in recent times, many case series have documented high rates of hemorrhage in these neoplasms. We hereby provide a detailed analysis on hemorrhagic pilocytic astrocytomas (HPA) in adults and report one such case managed at our institute. In addition, salient differences between adult and pediatric hemorrhagic PA have been briefed. Hospital records were retrieved for our case. Literature review was conducted by searching online databases for the following keywords—pilocytic astrocytoma, hemorrhage, cranial, pediatric, and adults. A 22-year-old male with neurofibromatosis-1 presented with sudden onset headache and vomiting of 3-day duration. Imaging revealed a lobulated suprasellar lesion with obstructive hydrocephalus. Pterional transsylvian approach and subtotal resection were performed. Histopathology showed features of PA with bleed. Including current report, a total of 26 cases have been reported. Mean age was 37 years (21–75 years) and they are mostly found in the third decade. The male:female ratio was 2.1:1. Sudden headache with vomiting was the most common symptoms. Tumors were mostly located in cerebral hemispheres (n = 9/34.6%), hypothalamus/suprasellar region (n = 7/27%), and cerebellum (n = 6/23%). Two-thirds underwent gross total excision. There were two deaths and except one case, no recurrences were reported in those with available follow-ups. Hemorrhagic presentation of a PA is rare, although more commonly seen in adults and most commonly located in cerebral hemispheres. Maximal safe resection is the standard treatment and recurrences are rare.

Keywords Pilocytic astrocytoma · Hemorrhage · Hemorrhagic onset · Suprasellar · Chiasmatic hypothalamic · Cerebellum

Introduction

Pilocytic astrocytomas are benign, WHO grade 1 neoplasms constituting 5% of all central nervous system (CNS) tumors [1–3]. They are typically a disease of childhood and adolescence, and cerebellum forms the most common location in them. Adult onset lesions are uncommon and are usually sited in the supratentorial compartment [1–4]. Spontaneous hemorrhage is mostly seen in high-grade gliomas and metastases, and the rates vary from < 1 to 15% [5–8]. Hemorrhagic onset of PA is relatively rare; however, a few recent articles have quoted higher rates in comparison to what has been historically reported [5–7]. Till date, only around 50 cases of hemorrhagic pilocytic astrocytoma (HPA) have been reported in literature, including both adult and pediatric age group. Of these, 26 have been reported in adults [6, 8–41]. Excluding the single case reported by Shibahara et al. of an 8-year-old boy, no case of HPA has been noted in a NF-1 patient [6]. We report a case of a suprasellar-hypothalamic PA with bleed in a 22-year-old NF-1 male patient, managed by surgical resection. This is only the second case of a PA with hemorrhage to be reported in a NF-1 patient, while being the first such case in the adult age group. In addition, we provide a thorough review of all adult cases of HPA reported in English literature till date. Further, a

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comparison between adult and pediatric onset HPA has also been provided.

Materials and methods

Hospital records and operation notes were used for the retrieval of our patient data. Literature review was conducted by searching online databases (Pubmed, Index Scopus, and Google Scholar) for the following keywords—pilocytic astrocytoma, cerebellar astrocytoma, hemorrhagic, cranial, and adults. Only adults (> 18 years) with hemorrhagic presentation of cranial PAs were analyzed in detail. Pediatric cases were analyzed to compare with adult age group. Recurrent tumors, pilomyxoid astrocytomas (PMA), and spinal PAs were excluded in order to have a homogeneous group.

Illustrative case

History A 22-year-old male presented with sudden onset headache and vomiting of 3-day duration. General examination revealed multiple café-au-lait spots over the trunk. His mother had features of neurofibromatosis type 1 (NF-1). Neurological examination was unremarkable except for papilledema.

Imaging An initial non-contrast computed tomography (CT) showed a well-lobulated hyperdense suprasellar lesion with surrounding iso-hypodensity causing obstruction at the foramen of Monro resulting in moderate to severe hydrocephalus, suggestive of a probable vascular lesion (Fig. 1a–c). Magnetic resonance imaging (MRI) showed a heterogeneous suprasellar lesion consisting of a central and peripheral component. The central component appeared isointense on T1WI and hypointense on T2WI and FLAIR showing irregular diffusion restriction. The peripheral component appeared isointense on T1WI, hyperintense on T2WI and FLAIR, and showed thick irregular rim enhancement. There was no evidence of vascular malformations on MR angiography (Fig. 2). With a diagnosis of suprasellar tumor with bleed, patient was operated.

Surgery A right-sided pterional transsylvian approach was used. Tumor was seen through the optico-carotid corridor occupying the suprasellar cistern. The lesion was encapsulated and had a straw-colored hue. The central part consisted of hemorrhagic component while the peripheral part consisted of a soft-firm, relatively avascular tumor tissue that was fairly suckable in nature (Fig. 3). Subtotal resection was performed leaving a rim of tumor tissue over the hypothalamus.

Hospital course and follow-up Patient had a relatively uneventful post-operative course and was discharged on the seventh postoperative day. Histopathological examination showed areas of glial tissue with increased vascularity and delicate, dilated, and congested vessels. Rest of the tissue showed oval to spindled glial cells of increased density in a fibrillar interstitium exhibiting edema, microcystic change, and Rosenthal fibers—overall features suggestive of a PA with bleed (Fig. 4). At 8 months post-op, MRI showed residual tumor and at the last follow-up of 11 months, patient was doing well with no new neurological deficits and (Fig. 5). In view of a benign histology, it was planned to observe the patient with serial scans and withhold adjuvant therapy.

Results

Including the current report, a total of 26 cases of adult HPA (males—17, females—8, ratio 2.1:1, 1—not available) have been reported. The mean age was 37 years (range, 21–75 years). The age distribution was as follows: third decade (n = 12), fourth decade (n = 6), fifth decade (n = 1), sixth decade (n = 3), seventh decade (n = 2), and eighth decade (n = 1) [1—not available].

Sudden headache and vomiting were the most common symptoms, noted in 9 cases. Vision problems (n = 5), limb paresis (n = 3), and seizures (n = 3) were the next common symptoms. Other presenting features included loss of consciousness (LOC) and obtundation, gait ataxia, aphasia, and transient amnesia. One case had a head injury with no neurological deficits on presentation.

Supratentorial location was common than infratrentorial compartment (ratio 1.8:1). Tumors were mostly located in

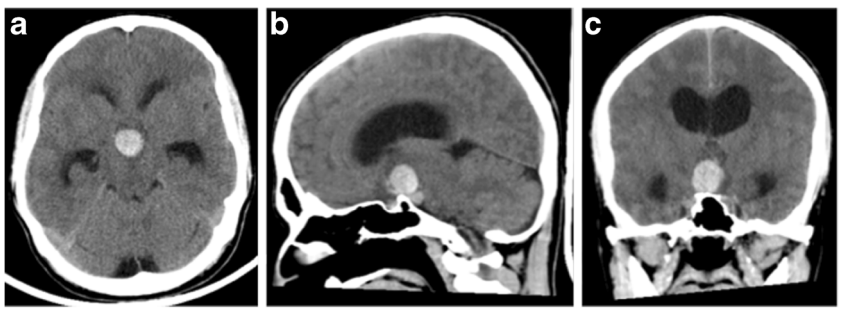

Fig. 1 Non-contrast CT (axial, sagittal and coronal sections) showing a well-lobulated hyperdense suprasellar lesion with surrounding iso-hypodensity causing obstruction at the foramen of Monro resulting in moderate to severe hydrocephalus (**a**–**c**)

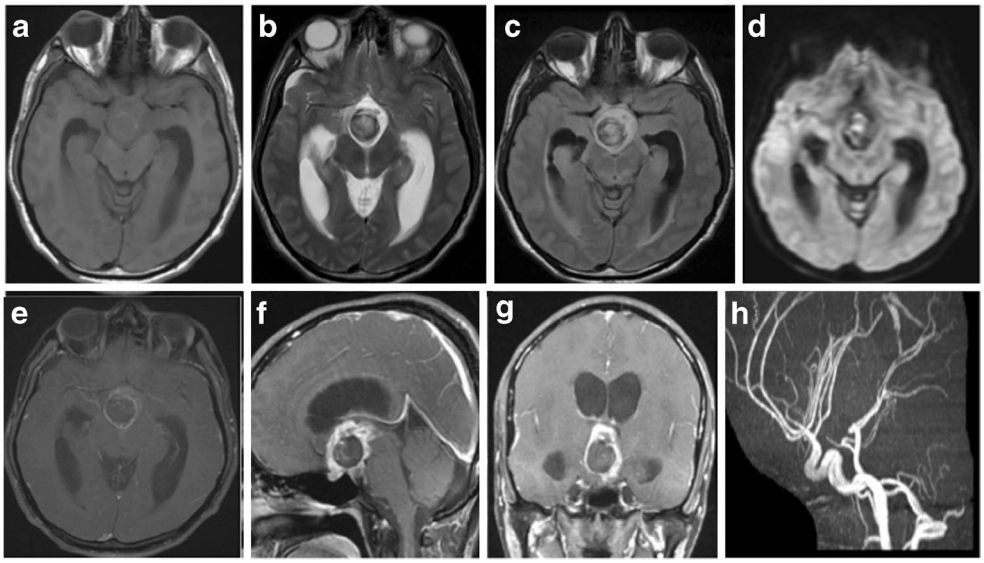

Fig. 2 MRI brain showing a heterogeneous suprasellar lesion consisting of a central and peripheral component. The central component appears isointense on T1WI (**a**), hypointense on T2WI (**b**), and FLAIR (**c**) showing irregular diffusion restriction (**d**). The peripheral component appears isointense on T1WI and hyperintense on T2WI and FLAIR with irregular thick rim enhancement (**e**–**g**). MR angiography showing no evidence of vascular malformations (**h**)

cerebral hemispheres (n = 9/34.6%), hypothalamus/suprasellar region (n = 7.27%) and cerebellum (n = 6.23%). Other locations reported were tectum (n = 2.8%), pons (n = 1.4%), and optic nerve (n = 1.4%). All types of bleeding such as intratumoral, intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), and subdural hemorrhage (SDH) were noted. Intratumoral bleeding was observed in all cases. SAH and IVH were noted in five cases each, in combination with intratumoral bleed. All cases of hemorrhage were spontaneous in origin. None had any underlying predisposition like trauma, thrombocytopenia, DIC, and systemic illness. One case had obstructive hydrocephalus (HCP) without IVH.

External ventricular drain (EVD) was inserted in 3 cases. Gross total excision (GTE) was performed in 17 cases. Near total excision (NTE) (1 case underwent 2 stage surgery) and simple biopsy were performed in two cases each. Subtotal resection (STR) was performed in 3 cases. In one case, diagnosis was confirmed only on autopsy examination. There were 2 deaths (8% mortality). Follow-up was available for 12 cases and except one case, no recurrences were reported. The mean follow-up duration was 20.5 months (range, 3 months-8 years). One case each developed post-operative memory deficits, hemiplegia, and panhypopituitarism, and all of them had tumors in the hypothalamic/suprasellar region. The case with the recurrence was a 35-year-old male who underwent STR for a suprasellar PA. One year later, he developed sacral metastasis was noted for which partial excision was done with adjuvant RT. Eight years later, there was recurrence noted in both the cranial and sacral lesions with diffuse cerebral leptomeningeal dissemination (LMD) for which craniospinal RT was given [36].

Tables 1 and 2 summarize the reported cases of HPA in adults and children, respectively. Although of hemorrhagic onset, 2 reports have been excluded. One was a recurrent case and details were not available for another report [5, 43].

The salient differences between pediatric and adult hemorrhagic PA have been briefed as follows:

(1) A total of 27 pediatric HPA cases have been reported while 26 adult cases have been reported, the ratio being 1.1:1. This is in sharp contrast to the prevalance of non-hemorrhagic PAs in children and adults (being rare in adults).
(2) With respect to the location, in children, cerebellum is the commonest, while supratentorial compartment (cerebral and suprasellar) is the most common in adults.

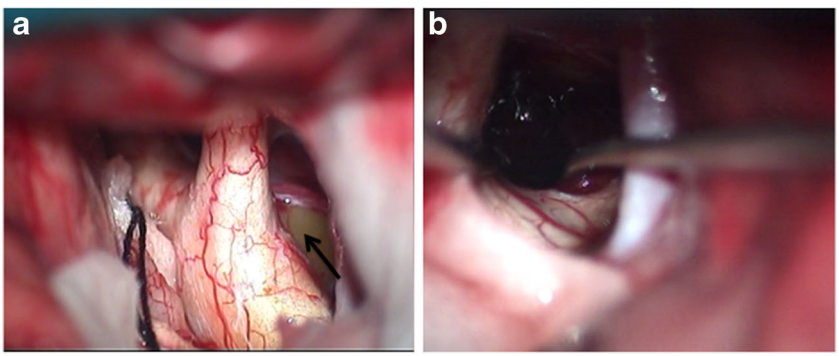

Fig. 3 Intraoperative photographs showing the suprasellar tumor as seen through the right carotico-optic corridor with its straw colored capsule (arrow in **a**) and hemorrhagic contents (**b**)

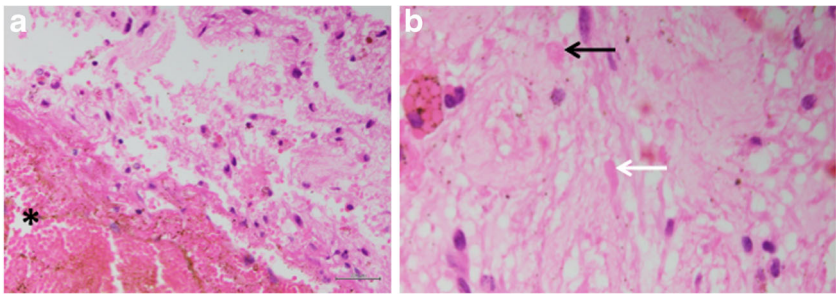

Fig. 4 **a** Microphotographs (H&E) showing the prominent hemorrhage in the neoplasm (asterisk) and the microcystic change (× 200). **b** Note the microcystic changes along with eosinophilic granular body (black arrow) and Rosenthal fiber (yellow arrow) (× 400)

(3) The male: female ratio is 1.1:1 in pediatric, while being more common in males (1.8:1) in adults.
(4) With regard to outcome, all 3 cases with morbidity had tumors in suprasellar location.
(5) There were five deaths (18.5%) reported in pediatric population, while two deaths (8%) were noted in adult age group.

Furthermore, the comparative features between adult onset non-hemorrhagic (NH) versus hemorrhagic PAs are as follows:

(1) In NHPA, no gender predilection is reported but there is clear male predominance in HPA.
(2) In both of them, supratentorial compartment is the commonest location. However, hypothalamus is also a common locus in HPAs as opposed to NHPAs.
(3) The mortality rates are similar in both types.

Discussion

Hemorrhagic onset in brain tumors is mostly noted with high-grade gliomas and metastases, ranging from 0.6 to 14.6% [5, 8, 44]. Although often being highly vascular tumors, clinical presentation of a PA with hemorrhage is rare. However, few recent articles have quoted hemorrhage rates in PA that are comparable/higher than with other glial tumors [5, 6, 8, 34, 45]. Recently, Lieu et al. observed that PAs had the highest rate of hemorrhage (1 out of 5, 20%) for the primary brain tumor group as compared to GBM (7.8%), in their retrospective study of 761 consecutive cases of brain neoplasms [5]. Shihabara et al. performed a retrospective analysis of 445 consecutive neuroepithelial tumors to estimate the rate of hemorrhage in various tumor types and observed that PAs/PMAs had a higher hemorrhagic rate than glioblastoma multiforme (GBM), anaplastic oligodendroglioma, or anaplastic ependymoma [6]. With the exception of 2 articles, all reports have been in the form of isolated case reports, hence the exact rate of bleed in a PA is still unclear [6, 8]. Till date, only 53 cases of HPA have been reported in literature, of which 27 are in pediatric age group and the remaining 26 in adults, although there is a possibility of under reporting and reporting bias, given the high percentage of hemorrhage observed in PAs in recent studies [6, 8–41]. Although PAs are relatively common in NF-I patients than non NF-1 patients, with the exception of a single case reported by Shibahara et al. (of their four cases), none of the HPAs have been reported in NF-1. This was an 8-year-old boy with NF-1 features who presented with intratumoral hemorrhage in a cerebellar PA that was surgically resected [6]. We report only the second case of HPA in a NF-1 case and the first such case in an adult.

Till date, many authors have provided short and concise reviews on HPA with varying inclusion criteria [16, 21, 23, 25]. Of all these, the most comprehensive analysis was provided by Shibao et al., wherein they reviewed a total of 43 cases of PA presenting with hemorrhage (including 1 case of theirs) including both adults and children, with respect to the age, gender and locations of the tumors [35]. However, since that paper highlighted on the pathological basis of bleeding in PAs, descriptions of the presenting features, type of treatment

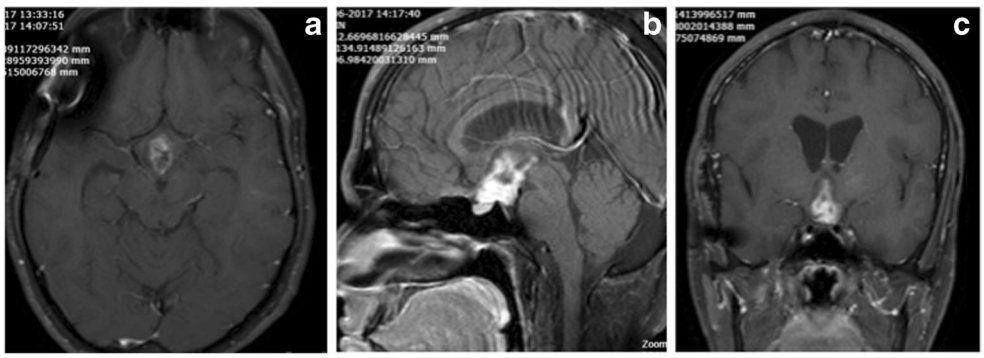

Fig. 5 Post-operative MRI at 8 months showing residual tumor in the suprasellar cistern

Table 1 Summary of adult HPA cases reported in the literature

Author/year	Age/sex	Clinical features (duration)	Location-type of bleed	Management	FU duration, recurrence, outcome
Glew [17]	30/M	HA, seizure, rapid vision loss	Hypo-intratumoral, SAH	Biopsy	Dead
Charles et al. [11]	26/F	Rapid proptosis, vision loss	Optic nerve-intratumoral, SAH	GTR	NA
Lones and Verity [27]	69/F	Hemiparesis	BG-intratumoral, IVH	None	Autopsy
Sorenson et al. [37]	58/F	Transient amnesia	Hypo-intratumoral	Biopsy	12 months—mild improvement, memory deficits
Matsumoto et al. [29]	45/M	Sudden HA, bitemporal hemianopia	Hypo-intratumoral, SAH, IVH	2 stages-STR f/b NTR	6 months—no recurrence, L hemiplegia persisted
Hwang et al. [20]	34/M	Sudden HA, vomiting, LOC	Hypo-intratumoral, SAH, IVH	GTR	11 months—no recurrence
Bell et al. [9]	NA	HA-exact details NA	Cerebral (frontal)-intratumoral	GTR	Alive and independent, no mention of recurrence, mean FU 33 m for the entire cohort
Taraszewska et al. [38]	38/M	Head injury	R cerebellum-intratumoral	GTR (3 weeks later)	3 years—no recurrence
Oka et al. [32]	21/M	Sudden HA, vomiting, vertigo	Tectum-intratumoral, IVH	GTR	23 months—no recurrence
Lyons [28]	75/M	Aphasia	Cerebral (temporal)-intratumoral (2 episodes)	GTR	NA
Sekula et al. [34]	65/M	HA and vision changes (1 week), obtundation	Suprasellar, HCP-intratumoral	STR	FU NA, Panhypopituitarism,
Li et al. [26]	32/M	HA, neck stiffness (3 weeks)	Cerebral (R TP)-intratumoral	GTR	6 months—no recurrence
	34/M	HA, diplopia (2 weeks)	Cerebral (L PO)-intratumoral	GTR	6 months—no recurrence
White et al. [8]	22/F	Seizures	Cerebral (temporal)-intratumoral	GTR	NA
	25/M	L hemiparesis, R VF defect	BG-intratumoral	GTR	
	25/M	Seizures	Cerebral (occipital)-intratumoral	GTR	
	58/F	HA, ataxia	Pons-intratumoral	GTR	
Shibahara et al. [6]	21/M	Sudden HA, vomiting	Tectum- intratumoral, IVH	EVD f/b GTR	NA
	22/M	Sudden HA, vomiting, ataxia, monoparesis	Cerebellum, medulla-intratumoral	Resection	
Kato et al. [22]	20/F	Sudden HA	Cerebral (L frontal)-intratumoral + SAH	GTR	NA
Kim et al. [23]	37/F	Sudden HA, vomiting	R Cerebellum-intratumoral	GTR	3 months—no recurrence
	53/M	HA (3 weeks)	L cerebellum-intratumoral	GTR	3 months—no recurrence
Shibao et al. [35]	29/M	HA, nausea, gait ataxia	Cerebellum-intratumoral	GTR+ EVD	NA
Simonova et al. [42]	35/M	Raised ICP	Suprasellar-intratumoral	STR	1 year—sacral mets-PE and local RT 8 years—recurrence of cranial + sacral and diffuse brain LMD-cranio-spinal RT; 1 year later—good regression
Galgano et al. [15]	30/F	Sudden HA, obtundation	R cerebellum-intratumoral, SDH	NTR + EVD	3 years—no recurrence
Present report (2017)	22/M	Sudden HA, vomiting-NF1	Hypo-intratumoral	STR	9 months, good, stable residual tumor present

Excluded: Shingu et al. [43]—recurrent PA with bleed and Lieu et al. [5]—details NA

Abbreviations: *HPA* hemorrhagic pilocytic astrocytoma, *HA* headache, *Hypo* hypothalamic, *SAH* subarachnoid hemorrhage, *GTR* gross total resection, *NA* not available, *BG* basal ganglia, *IVH* intraventricular hemorrhage, *STR* subtotal resection, *NTR* near total resection, *LOC* loss of consciousness, *HCP* hydrocephalus, *R* right, *TP* temporo-parietal, *L* left, *PO* parieto-occipital, *VF* visual field, *f/b* followed by, *EVD* external ventricular drain, *mets* metastasis, *PE* partial resection, *LMD* leptomeningeal dissemination, *RT* radiotherapy, *SDH* subdural hematoma, *NF-1* neurofibromatosis type 1

Table 2 Summarizing the cases of cranial hemorrhagic pilocytic astrocytomas reported in children

Author/year	Age/sex	Clinical features	Location-type of bleed	Management	Follow-up, recurrence, outcome
Mauersberger and Cuevas-Solorzano [31]	10/M	NA	Cerebellum (vermis)-NA	NA	Recovered
	10/F	NA	Cerebellum (vermis)-NA	NA	Dead
Fogelson et al. [13]	9/M	HA, vomiting, ataxia	Cerebellum-intratumoral	GTE	Improved
Vincent et al. [40]	14/F	Lethargy, vomiting, ataxia	Cerebellum-intratumoral	Excision	Good functional recovery
Byard et al. [10]	5/F	Sudden LOC and sudden death	Chiasm-NA	None	Autopsy confirmation
Golash et al. [18]	13/F	Sudden retro-orbital pain, vomiting, vision blurring, diplopia, papilledema, HCP	Hypo-intratumoral + ICH	VPS f/b biopsy	6 months—no rec
van Ouwerkerk and Dirven [39]	8/M	Acute severe HA, LCN palsy, quadriparesis	Medulla-intratumoral	Hematoma evacuation, biopsy f/b NTE (after 5 moths)	4 months—rapid progression -2nd surgery; RT given; 5 years—no rec
Devi et al. [12]	4/M	Sudden LOC and collapse	Suprasellar-intratumoral + IVH	EVD	Autopsy confirmation
Mesiwala et al. [30]	13/M	Acute HA, lethargy, ataxia (10d)	Cerebellum-intratumoral	GTE	Good recovery
Garg et al. [16]	13/M	HA, vomiting, LOC	Hypo-intratumoral, SAH	NTE	7 months—minimal residual
White et al. [8]	12/M	HA	Tectum-intratumoral	GTE	NA
	18/M	HA, vomiting	Cerebral (parietal)-intratumoral	GTE	
	11/M	HA, vomiting	Pineal-intratumoral	GTE	
	5/M	HA, R hemiparesis, HCP	Thalamus-intratumoral	GTE	
	17/F	HA, seizures	Cerebral (occipital)-intratumoral	GTE	
	10/F	HA, vomiting	BG-intratumoral	GTE	
	12/F	HA	Hypo-intratumoral	Biopsy	
Lee et al. [25]	15 m/M	Lethargy, vomiting	Cerebellum-intratumoral, SAH, SDH	NTE	30 months—no rec
Frassanito et al. [14]	7/F	Sudden severe HA, vomiting, LOC and later mutism (regained consciousness after 8 days)	Tectal plate—intratumoral + superior vermis	GTE (8 weeks later)	Good recovery
Shibahara et al. [6]	8/M	NF-1	Cerebellum-intratumoral	NA	NA
Kumar et al. [24]	16/F	HA, ataxia, vision blurring (2 weeks), papilledema	R cerebellum-intratumoral	GTE	3 months—no rec
Kapoor et al. [21]	9/M	Sudden HA, LOC (1 day), papilledema	Cerebral (corpus callosum) -intratumoral, IVH	NTE	12 months—no rec
	8/F	Poor feeding, HA, vomiting (1 month), papilledema, 6th n palsy	Suprasellar-intratumoral, IVH	VPS, STR	4 months—no rec
Wilson et al. [41]	12/M	Rec HA, vomiting (1 year), f/b ataxia, sudden HA, LOC	Cerebellum-intratumoral	EVD	Autopsy confirmation
	5/F	Sudden HA, LOC	Cerebellum-intratumoral	EVD, STR	Died
Ramdurg and Maitra [33]	9 m/NA	Drowsiness	R cerebellum-intratumoral	GTE	NA

Abbreviations: *HA* headache, *Hypo* hypothalamic, *SAH* subarachnoid hemorrhage, *GTE* gross total excision, *NA* not available, *BG* basal ganglia, *IVH* intraventricular hemorrhage, *STR* subtotal resection, *NTE* near total excision, *rec* recurrence, *LOC* loss of consciousness, *HCP* hydrocephalus, *R* right; *TP* temporo-parietal, *L* left, *PO* parieto-occipital, *VF* visual field, *f/b* followed by, *EVD* external ventricular drain, *LMD* leptomeningeal dissemination, *RT* radiotherapy, *SDH* subdural hematoma, *NF-1* neurofibromatosis type 1

received, recurrence rates and outcomes (including mortality) were not evaluated by the authors. Ours is the first detailed review of hemorrhagic PAs in adults in the literature attending to all the above factors. Further, a comparison between adult and pediatric onset HPA has also been provided (in the Results and table section).

Pathogenesis of hemorrhage in PA

Multiple theories have been proposed by different authors, for the occurrence of such hemorrhages in PA. White et al. reported that the frequently observed abnormal vasculature in PAs such as thin-walled ectatic blood vessels, degenerative mural hyalinization of vessels, and glomeruloid endothelial hyperplasia contribute to the hemorrhage in these tumors [8]. Further, presence of calcospherites was noted to be a probable predisposing factor for hemorrhage [41]. Similarly, White et al. concluded that local metabolic factors may play a role in the development of hemorrhage as microcalcifications were observed in 25% of their cases [8]. In one of the reports, Shibao et al. noted that patients with HPA tend to be older as compared to non-hemorrhagic PAs. Hence, degenerative vascular changes may be responsible for the bleed as concluded by the authors of the study [35]. It was observed by Kapoor et al. that the perihemorrhagic calcifications and the presence of disproportionate mass effect might indicate the presence of a benign neoplasm that may have bled [21]. However, Shibahara et al. noted no correlation between onset of hemorrhage in PA and PMAs and clinic-pathological features like age of the patient, tumor location, tumor mitotic activity, or microvascular proliferation [6].

In their case report of medullary astrocytoma (with oligodendroglial component) in a child, van Quwerkerk and Dirven suggested that the hemorrhage might have been because of the abnormal fragile vasculatures in the oligodendrogliotic component or in occult coexisting vascular malformations [39]. Rarely, neoplastic aneurysms or peripheral arterial aneurysms may result in tumoral hemorrhage but have not been reported as an etiological factor in HPA [46, 47]. In one report of an elderly male with HPA, amyloid angiopathy was noted in the surrounding region [28].

Wilson and colleagues attributed the interaction of a variety of factors such as rate of tumor growth, tumor invasion of blood vessels, necrosis of blood vessels and/or tumor, blood coagulability and local fibrinolysis, intrinsic structural features of the tumor vasculature, and the presence of vascular proliferation. These factors were thought to predispose, initiate, and propagate bleeding [41]. One key mechanism that has often been correlated to the hemorrhagic episode is the upregulated expression of vascular endothelial growth factor (VEGF). Sie et al. noted higher VEGF expression in both GBM and PA [48]. Further, they noted that vascular integrity in cerebellar PAs was as unstable as that of GBM, hence making these blood vessels more prone to breakdown. An earlier report by Leung et al. had also observed elevated VEGF expression in PAs [49].

Association of NF-1 with cerebrovascular diseases, including narrowed or ectatic vessels, vascular stenosis, aneurysm, and moyamoya disease is known, and hence, the mechanism and incidence of intratumoral hemorrhage in NF1-PA might differ from that of sporadic PA [6]. In our case (including MR angiography), we did not find any such findings, and hence, the definite cause of hemorrhage remains unclear.

Clinical features and imaging

Since the hemorrhagic event is often acute and apoplectic in onset, the duration of symptoms is usually short, ranging from few days to few weeks [8]. Sudden headache and vomiting are the most common symptoms of such hemorrhagic tumors. In a few cases, the symptoms may have a more gradual development before deteriorating abruptly [6, 41]. Also, at the episode of hemorrhage, majority of the patients are known to experience new symptoms [8]. Seizures are also a common feature in lobar tumors, as was noted in two out of six cases in this present report. Further, depending on the location, focal deficits can be noted, such as gait ataxia, limb paresis, aphasia, and others. Surprisingly, one case presented with head injury and no neurological deficits.

Imaging findings are non-specific and are dependent on the type and severity of bleeding. In cases of severe intratumoral bleed filling the entire lesion, the findings would be similar to any spontaneous cerebral hemorrhage and identification of the presence of a tumor would be difficult in such situations [21, 26]. Although edema is usually not seen in PAs, it may be prominent in HPA due to the hemorrhage [23]. In milder cases of hemorrhage filling only a part of the lesion, findings such as a heterogeneous mass lesion with/without a mural nodule, with/without enhancement, may be observed [21, 23, 26, 41]. Li et al. reported the use of perfusion imaging in such tumors that depict low rCBV (relative cerebral blood volume) values in relation to brain parenchyma compared to other tumors such as hemangioblastomas [26]. However, due to higher incidences reported by many recent studies, many authors have concluded that PA needs to be considered in the differential diagnosis of neoplasms with a sudden neurological ictus and raised ICP, at least in common locations such as the cerebellum [6, 8, 41].

Pathology

Grossly, PAs are relatively soft, gray textured, well-defined lesions. Cysts both peripheral and central can be seen. On microscopic examination, the following features are noted-low to moderate cellularity, biphasic pattern consisting of densely fibrillated areas rich in Rosenthal fibers and loose

cellular areas containing microcysts, and eosinophilic granular bodies [3, 9, 45]. It is however to be noted that Rosenthal fibers and eosinophilic granular bodies are not consistent findings in all PAs [8]. Calcification is uncommon feature, but can sometimes be extensive [3]. Mitoses are rare and Ki67/MIB labeling indices usually vary < 1%, but values up to 4 % can be seen [50]. However, Shibao et al. noted a high intratumoral variation of MIB-LI, ranging from 0.5 to 13% in their single case of HPA. This focally high MIB-LI, according to the authors, might indicate reaction to tumor destruction as a result of hemorrhage [35]. Often, microvascular proliferation resulting in thick-walled hyalinized and glomeruloid vessels and necrosis may be noted on microscopy [6, 51]. On examining the relationship between proliferative activities, microvascular proliferation, and hemorrhagic events, Shibahara et al. observed that neither Ki-67 labeling index nor microvascular proliferation was different in hemorrhagic PA as opposed to non-hemorrhagic PA. Therefore, they concluded that hemorrhage may not be suggestive of either malignancy or aggressiveness pathologically [6]. On immunohistochemistry, PAs show diffuse positivity for GFAP and S-100 protein while being sparsely positive/negative for p53 antigen [2, 34]. Differential diagnoses include ganglioglioma, dysembryoplastic neuroepithelial tumor (DNET), low-grade diffuse astrocytomas, oligodendrogliomas, pleomorphic xanthoastrocytoma, and others [2]. The biological and molecular markers of these tumors are still not clearly understood. Further research will be required to elucidate the genetic disposition and natural history of these histologically benign lesions.

Treatment and outcome

Surgical resection remains the treatment of choice for PAs and complete macroscopic resection provides excellent results. However, in strategic locations such as optic pathway or hypothalamus, subtotal resection might suffice due to the fear of causing new neurological deficits. Surgery remains the standard of care even in recurrent tumors, if located in feasible and operable locations [3, 52, 53]. However, for small residual or recurrent PAs, radiosurgery represents an alternative treatment modality providing long-term local control [42]. Role of radiotherapy (RT) is controversial as spontaneous tumor regression and arrested growth of the residual tumor is a known phenomenon in PAs as reported by many authors [52, 54]. While some authors have documented improved progression-free survival for those who received upfront RT compared with observation, few others have noted negative impact of radiation [4, 55]. Usually, RT is reserved for salvage, unresectable disease, relapse, or progression [56, 57]. Pilocytic astrocytomas are benign neoplasms and the 10-year survival is excellent, approaching 95–100% in some series [1, 9, 50, 52]. However, few authors have reported aggressive clinical course and poorer outcome for adult PAs [4, 51]. In the present review, one recurrence was observed. With regard to mortality in adults, a mortality of 8% was noted that is comparable with the non-hemorrhagic PAs [55, 57]. However, in pediatric age group, 18.5% mortality was noted that was higher than the non-hemorrhagic PAs [52, 53]. Although, the two adult mortalities were reported in 1977 and 1991 and none in the recent past, Wilson et al., in 2016, reported two fatal cases of cerebellar PA in children [17, 27, 41]. Hence, it can be well presumed that HPA might portend a slightly worse prognosis than non-hemorrhagic PAs, although pathological reports suggest that hemorrhage might not reflect either malignancy or aggressiveness [6]. Nevertheless, due to the variable distribution (orbit, optic nerve, hypothalamus, lobar, cerebellum, brainstem etc..) and the small number of cases, the exact significance of hemorrhage in these tumors cannot be elucidated.

Limitations of the study

Firstly, few of the reported cases date back to pre-1990s. Treatment and surgical techniques have changed greatly since then and these may have contributed to different outcomes.

Secondly, with such limited number of cases, detailed statistical analysis was not feasible.

Thirdly, the mean FU was 20.5 months (range, 3 months–8 years) which is quite short for a benign lesion like PA. Hence, it is difficult to comment on the long-term prognosis of such cases.

Conclusions

Hemorrhagic presentation of a pilocytic astrocytoma is rare, however more common in adults. Cerebral hemispheres and cerebellum are common locations in adults and children respectively. Hemorrhagic presentation might portend a slightly poor prognosis, although difficult to comment because of variable factors. Maximal safe resection is the standard treatment and recurrences are rare. Role of radiotherapy is controversial in subtotal resections. Due to limited number of reported cases, it remains difficult to comment on the long-term prognosis of such cases.

Funding No funding was obtained for this study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Ethical approval was felt not necessary as it was a single case operated in standard manner and a review of existing world literature was done.

Informed consent Informed consent was taken from the patient.

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