Hemorrhagic Presentations of Cerebellar Pilocytic Astrocytomas in Children – a Report of Two Cases and Review of The Literature

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- No conflicts to disclose.

• Spontaneous hemorrhage in Pilocytic Astrocytomas (PAs) are more common that historically reported[9,16,20].

• Hemorrhage in cerebellar PAs represent an important subgroup as:

- Cerebellum accounts for 40% of all PAs in children[2,5]; PAs comprise 15% of primary CNS neoplasms[14].
- Acute tumoral hemorrhage in this location can result in rapid clinical deterioration.

• Two illustrative cases of fatal cerebellar PAs presenting with spontaneous hemorrhage presented.

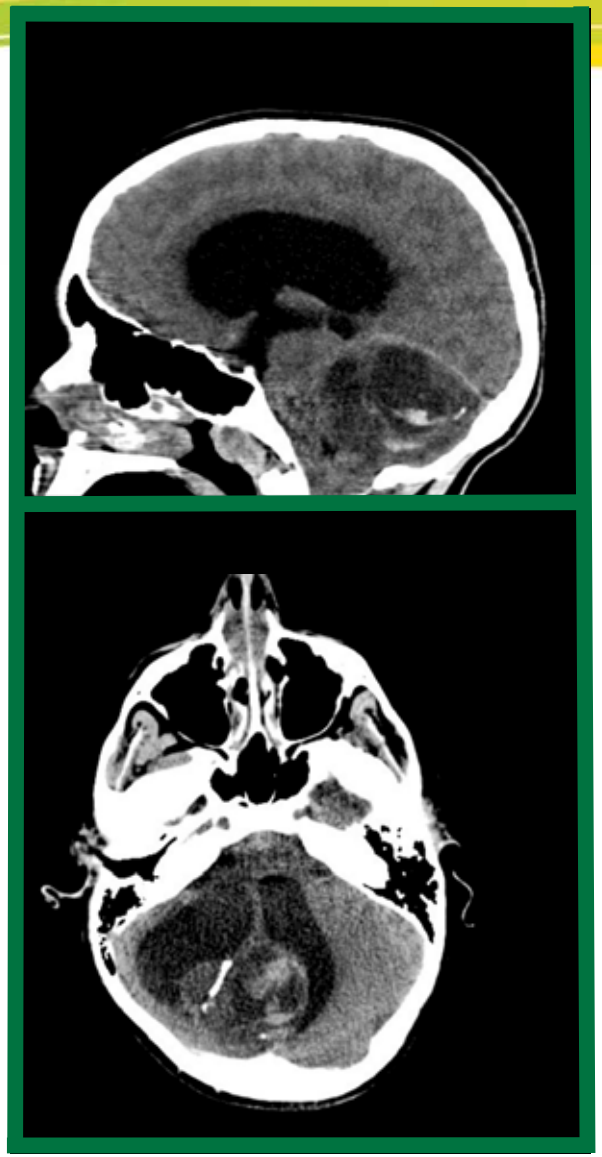
• Literature reviewed for frequency of PAs presenting with spontaneous hemorrhage. Theoretical etiologies discussed.

- 12-year-old boy

- Multiple presentations over preceding year c/o headaches, nausea, and vomiting misattributed to neurodevelopmental, neruopsychiatric, and GI sources.

- Developed progressive ataxia and lethargy before a severe headache and loss of consciousness.

- Non-contrast CT reveals a midline solid and cystic cerebellar mass with a recent intratumoral hemorrhage and obstructive hydrocephalus.



• The patient is intubated and hyperventilated. Mannitol and 3% saline given at a regional hospital.

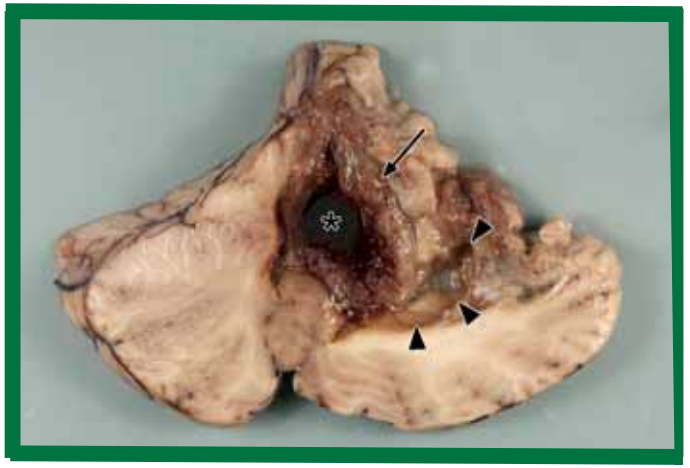
• Transferred to our tertiary treatment center.

• Urgent EVD placed, 200cc of CSF drained. Initial ICP of 70mmHg relieved.

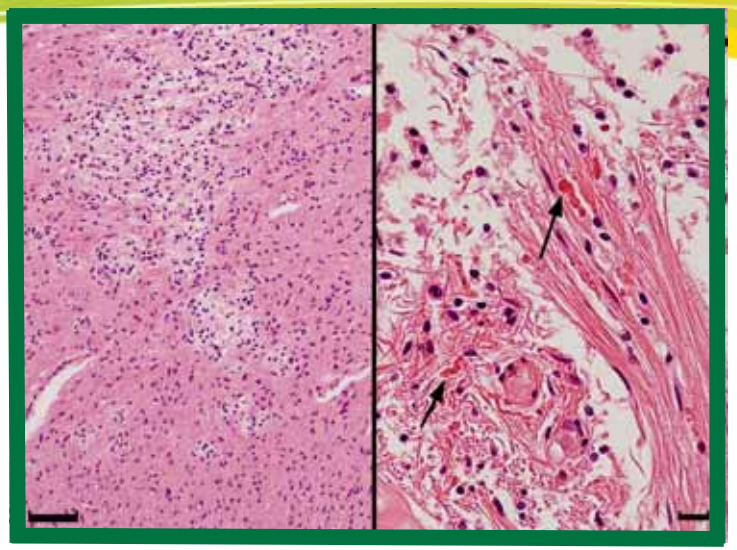
• Remained GCS 3/15 with absent brainstem reflexes.

• Declared clinically brain dead the following day.

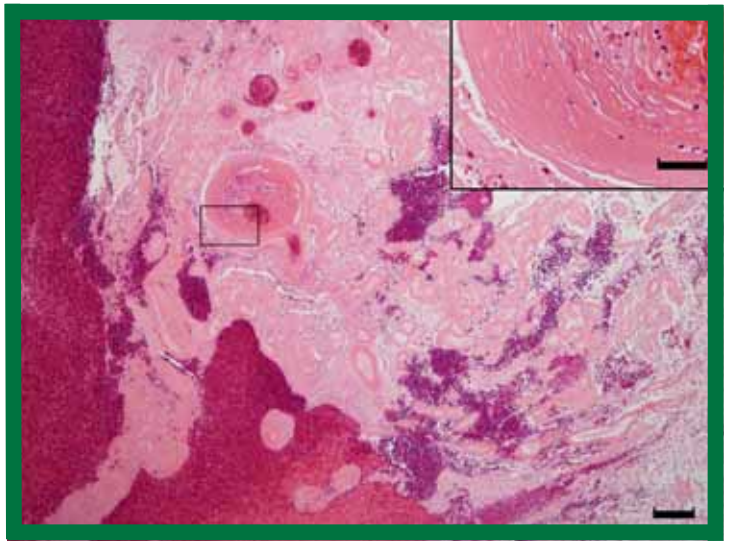
• Autopsy disclosed a nodular PA within posterior vermis and right paramedian region, an associated cyst, and a fresh 3cm hematoma. Mass effect caused supratentorial displacement of the anterior vermis and compression of the medulla by adjacent tonsils. Moderate hydrocephalus confirmed.



•Tumor shows (left) pathognomonic dimorphic differentiation of a PA with compact fibrillary regions merging into central microcystic fields (H&E, bar – 100um), and (right) bundles of neoplastic piloid astroglia in looser microcystic regions grouped around vascular pedicles with frequent Rosenthal fibers (arrows) (H&E, bar – 20um).



• A hematoma is identified bordered by a collapsed telangiectatic array of empty sclerotic hyalinized blood vessels, and a large channel showing micro-aneurysmal dilatation and mural fibrinoid necrosis (insert) (H&E, bar – 200um, bar insert – 50um).

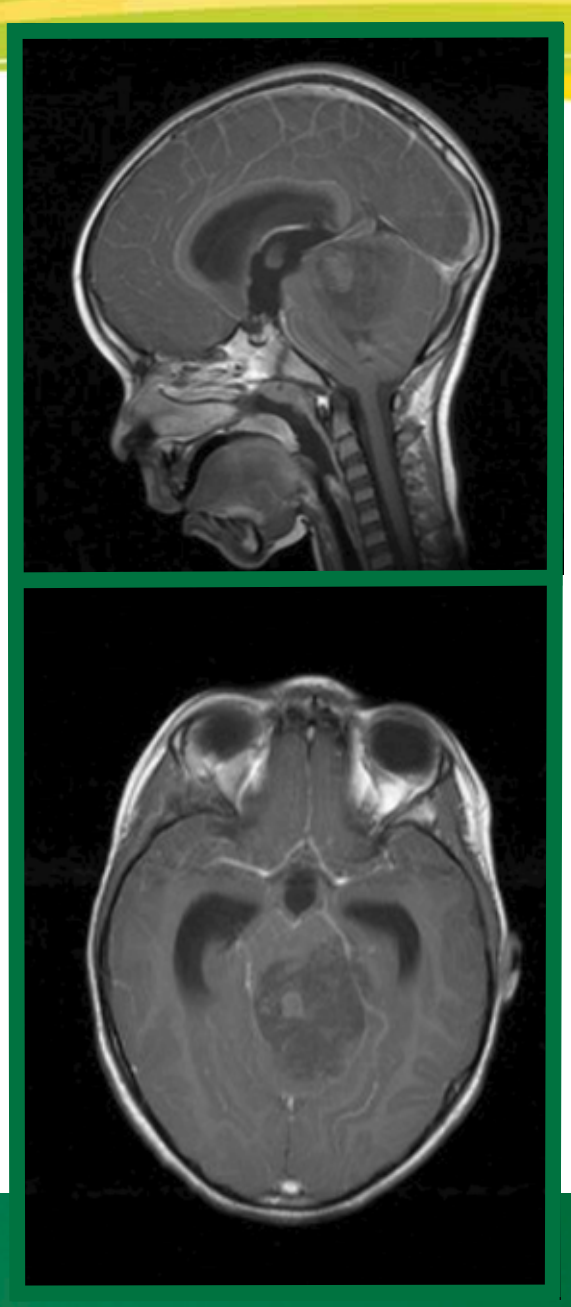


- Healthy 5-year-old girl

- Single episode of severe headache two weeks prior to abrupt lost of consciousness after toileting.

- Regained consciousness, though became increasingly obtunded before presenting to the emergency room with a GCS of 10/15.

- Initial CT reveals a posterior fossa mass. Mannitol is given prior to a pre-operative MR scan disclosing a large non-enhancing cerebellar mass within the vermis and left hemisphere. Recent patchy intra-tumoral hemorrhage, associated brainstem compression, and obstructive hydrocephalus are present.



• A seizure occurred immediately following the MR scan, requiring intubation with ventilator support.

• Thereafter, her pupils became bilaterally dilated and non-reactive.

• An emergent EVD was inserted, followed by subtotal resection of the mass, limited by vascularity of tumor capsule.

• Post-operatively, brainstem reflexes were absent, and follow-up imaging confirmed a diffuse ischemic injury involving the brainstem, deep nuclear gray matter, and cortex of both parieto-occipital regions.

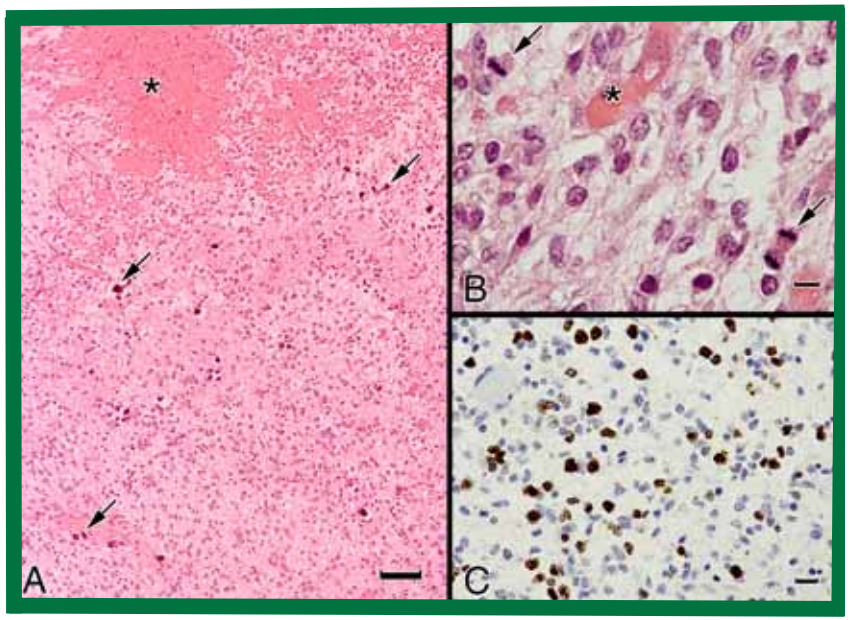
• Following consultation with the family, the patients' medical management was discontinued and she died shortly thereafter.

• Surgical biopsies displayed:

A) Sheets of fresh hemorrhage (asterisk), bordering dimorphic pattern of spongiotic and fibrillary regions with several calcospherites (H&E,bar – 100um). No rosenthal fibers or eosinophilic granular bodies present. Limited angiocentric growth identified.

B) High magnification shows bipolar tumor cells with moderate nuclear pleopmorphism, mitotic figures (max 6-8/10 high power microscopic fields) (arrows), and congested capillaries (asterisk, H&E, bar – 10um). No IDH-1 or IDH-2 mutations detected, and p53 immunoexpression <10%.

C) MIB-1 labeling index ranges 10-20% (MIB-1 immunohistochemistry, bar – 20um), warranting an anaplastic designation.



• Findings consistent with anaplastic variant of a PA.

• Once considered an infrequent occurrence[7,18,19], spontaneous hemorrhage in PAs now well recognized in literature[1,8-10,13,16,20], present in 8-11% of PAs[16,20].

• Nine known cases published describe hemorrhagic presentations of cerebellar PAs[7-10,13,16,18,19] with presentations occurring in two forms:

- 3/9[9,13,16] patients had complaints over 10 day to 4 week period prior to hemorrhagic presentations due to cerebellar dysfunction, or features suggestive of increased ICP. This scenario mirrors our first case.
- 6/9[7-8,10,16,18-19] patients presented with acute onset of symptoms and/or signs of elevated ICP, similar to our second case. Only one was reported as fatal and occurred in a patient also suffering a transient episode of symptoms two weeks prior to presentation. Suggests that minor transient signs can deceptively precede a catastrophic acute ictus.

•Factors considered in etiology for hemorrhage in PAs:

- 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
- Presence of vascular proliferation
- Mechanical support of the vascular bed by surrounding tumor parenchyma

•Theorized mechanisms in our cases:

- Case one is a conventional PA with cyst and mural nodule; the hemorrhage is believed to be caused by micro-aneurysms formed as a result of abnormal flow dynamics through sclerosed and hyalinzed vasculature.
- Case two is an anaplastic variant; bleed likely related to rapid tumor growth, predominance of background myxoid matrix, and thin walled vasculature.

1. Regardless of etiology, PAs presenting with spontaneous hemorrhage occur in approximately 10% of cases.

2. With 40% of PAs arising in the cerebellum, these presentations pose a precarious scenario which can quickly result in rapid clinical decline.

3. Multidisciplinary collaboration is useful to ensure steps of acute management are performed efficiently with imaging obtained in a timely manner to compliment Neurosurgical management for potentially life endangering presentations of otherwise indolent tumors in children.

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