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 than 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, neuropsychiatric, 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 microaneurysmal 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.

Case Two
• 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 calciospherites (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 pleomorphism, 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\textsuperscript{7,18,19}, spontaneous hemorrhage in PAs now well recognized in literature\textsuperscript{1,8-10,13,16,20}, present in 8-11\% of PAs\textsuperscript{16,20}.

Nine known cases published describe hemorrhagic presentations of cerebellar PAs\textsuperscript{7-10,13,16,18,19} with presentations occurring in two forms:

- 3/9\textsuperscript{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\textsuperscript{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.

Discussion
• 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 hyalinized 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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