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INFANTILE HIGH-GRADE GLIOMA - A LOCAL REVIEW

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Objectives

To review local patients with infantile high-grade glioma and their outcome.

Introduction

Infantile high-grade glioma (IHG) is defined as having an early age of onset at less than 12 months old. Previous analysis showed IHG displays a more stable genome, with most being single mutation driven. The most identifiable mutations for IHG are receptor tyrosine kinase fusions, such as NTRK family, ROS1, ALK and MET.

The current principal treatment for IHG is still surgery, but it is challenging for a complete resection due to hemispheric involvement.

Adjuvant chemotherapeutic drugs are commonly given. In our series, baby POG protocol is used. Unlike other paediatric high-grade gliomas, radiotherapy is less common because of the young age of patients.

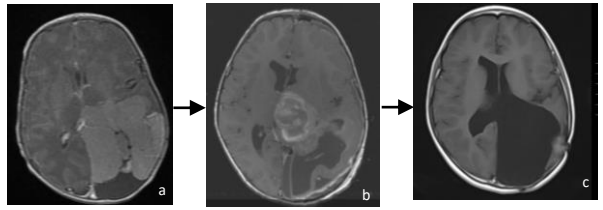
With identifiable somatic mutations, targeted therapy has shown efficacy in IHG. NTRK inhibitors including larotrectinib, selitrectinib and entrectinib display antitumour activity. ALK inhibitors, such as loratinib, also have promising results and claim enhanced blood-brain-barrier penetration.

Despite being a challenging CNS tumour, the prognosis and overall survival of IHG is superior to other high-grade gliomas.

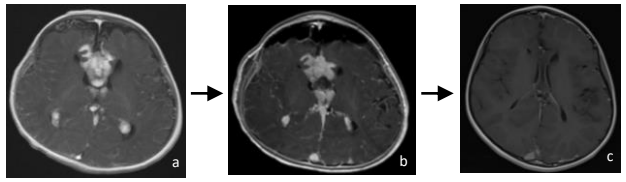
Results

Our series included 8 patients with IHG, mean age of diagnosis was at 3 months old. Seven patients were diagnosed with glioblastoma and one with anaplastic astrocytoma. Four patients were male and four female. Four patients had multi-lobar involvement.

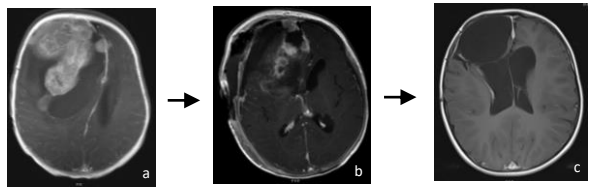
Seven patients had molecular analysis of tumour specimen after primary surgical excision. NTRK fusion was found in 4 patients (ETV6-NTRK3 fusion and TPR-NTRK1 fusion). ALK fusion was found in 1 patient (HMBOX1-ALK). ROS fusion was found in 1 patient (ZCCHC8-ROS1). All patients received chemotherapy with 4 patients switched to NTRK inhibitor afterwards and 1 switched to ROS inhibitor. Two patients passed away.



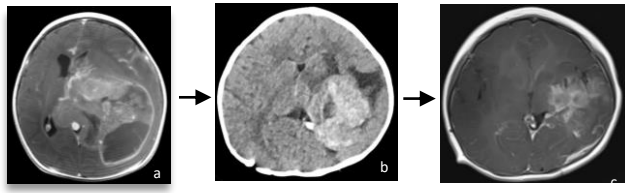
Patient 1. Diagnosis at birth (a): anaplastic astrocytoma.
Could not tolerate chemotherapy, Tumour excised at 3 years old (b). Stable disease at 9 years old (c). The patient was clinically well and able to walk unaided.



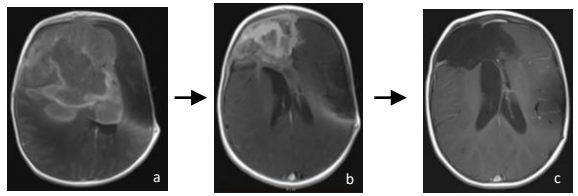
Patient 2. Diagnosis at 7 months old (a): glioblastoma.
Debulking surgery at 2 months (b). Adjuvant chemotherapy was given. Follow up scan (c) at 6 years old shows tumour involution. The patient was diagnosed with global developmental delay, able to walk unaided.



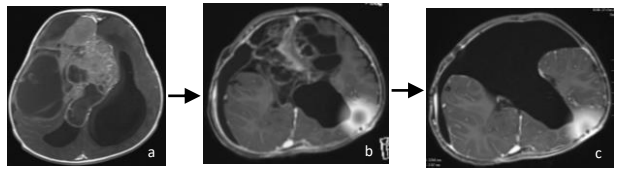
Patient 3. Diagnosis at 5 months old (a): glioblastoma (NTRK3 fusion+).
Tumour was excised twice one month later. Patient completed 8 cycles of chemotherapy, followed by NTRK inhibitor and surgical excision at 2 years old (b). Scan c at 3.5 years old shows no recurrence. The patient was clinically well and able to walk unaided.



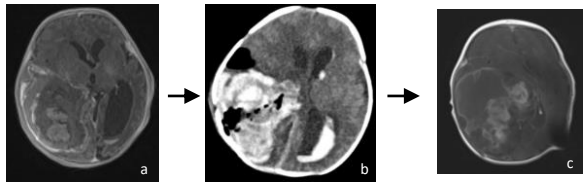
Patient 4. Diagnosis at 2 months old (a): glioblastoma (ETV6-NTRK3 fusion+).
NTRK inhibitor started at 6 months old after 3 doses chemotherapy.
Tumour haemorrhage at 1 year old (b) with operations performed.
Second generation NTRK inhibitor started subsequently. Disease progression (c).
The patient passed away at 22 months old.



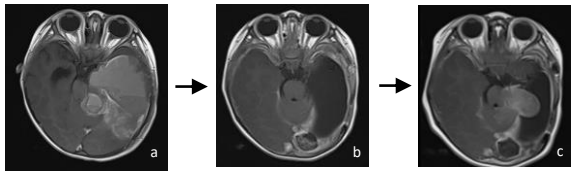
Patient 5. Diagnosis at 1 month old (a): glioblastoma (ALK fusion+).
Tumour excised and VP shunt inserted (b). Eight cycles of chemotherapy completed. Second surgery performed at 4 months old. Follow up scan at 16 months old (c) shows stable disease with no recurrence. Patient was able to walk with assistance.



Patient 6. Diagnosis at 3 months old (a): glioblastoma (NTRK1 fusion+).
Eight cycles of chemotherapy completed, followed by NTRK inhibitor at 7 months old (b). Surgical excision performed at 1 year old.
Follow up scan at 2 years old (c) shows no recurrence.
Patient was diagnosed with global developmental delay.



Patient 7. Diagnosis at birth (a): glioblastoma (NTRK fusion+).
Biopsy done with intraoperative haemorrhage (b). Seven cycles of chemotherapy completed. Last dose chemotherapy withheld due to low blood counts.
Tumour rapidly progressed with multi-lobar involvement requiring emergency VP shunt at 6 months (c). Patient switched to NTRK inhibitor. Critical condition at publication of this poster.



Patient 8. Diagnosis at 4 months old (a): glioblastoma (ROS1 fusion+).
Partial tumour excision and 11 months of chemotherapy was given, followed by ROS1 inhibitor (b). Disease progression (c) after 11 months of ROS1 inhibitor.
The patient passed away at 35 months old.

Discussion and Conclusion

The documented overall survival of IHG is less dismal (20% at 5 years) compared to other high-grade gliomas. Our series currently reports 75% (6/8) survival at 1.5 years. Post chemotherapy tumour behaviour showed the potential of NTRK/ALK positive IHG to differentiate into low grade gliomas. The use of targeted therapy during rapid phase of tumour growth may therefore improve long term outcome. Nonetheless the opportune time for surgical intervention for this group of young patients remains elusive.

In our opinion, infantile high-grade glioma should be regarded as a unique tumour entity and a multidisciplinary approach is paramount in improving survival for this group of patients.

References:
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Gilani, Ahmed, et al. "Genomic and Epigenomic Re-Categorization of Congenital Glioblastoma and Desmoplastic Infantile Ganglioglioma." Child's Nervous System, 2023.