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Original Research

Diagnostic accuracy of MRI without gadolinium for follow-up of pilocytic astrocytoma in the paediatric population

Adam Ian Macfarlane [a 1], Jewel Hannah Soares [b], Monish Maharaj [b c d]

[a] Department of Neurosurgery, Sydney Children's Hospital, Randwick, NSW, Australia
[b] Faculty of Medicine & Health, The University of New South Wales, Kensington, NSW, Australia
[c] Department of Radiology, Prince of Wales Hospital, Randwick, NSW, Australia
[d] NeuroSpine Clinic, Prince of Wales Private Hospital, Randwick, NSW, Australia

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Highlights

- Pilocytic astrocytoma is a common glial tumour in children and requires long-term MRI follow-up.
- There are concerns about the need for multiple doses of gadolinium in paediatric patients.
- MRI without gadolinium is accurate to detect recurrence or progression of pilocytic astrocytoma in paediatric patients.

- Omission of gadolinium enhanced sequences may lead to reduced cost and resource utilisation.

Abstract

Purpose

Pilocytic astrocytoma is the most common glial tumour in the paediatric population with a long-term life expectancy after surgery. Long-term radiological follow-up with magnetic resonance imaging (MRI) is necessary to detect recurrence of tumour or growth of residual tumour. Established MRI protocols typically dictate post-gadolinium sequences despite concerns around the side-effect and safety concerns of gadolinium-based contrast agents. This study aims to investigate whether omission of gadolinium-enhanced sequences for the long term follow-up MRI for paediatric patients with pilocytic astrocytoma, maintains diagnostic accuracy assessing potential recurrence or growth of residual tumour.

Methods

A retrospective review of follow-up MRI for 47 patients with histopathologically proven pilocytic astrocytoma was performed. Patients with optic pathway or suprasellar glioma were excluded from this study. All patients underwent surgery and had a minimum of 2years of postoperative imaging for review. MRIs were chosen from most recent report of stability or at a time when growth/progression had been diagnosed. Two neuroradiologists and two paediatric neurosurgeons were randomly allocated a series of MRIs with gadolinium enhanced sequences removed, reviewers were blinded to the original report and subsequent treatment decisions. In addition, 30 paired MRI studies were randomly allocated to second review to test interobserver reliability. The reviewer responses were recorded and compared with the original report and analysed with respect to preserved diagnostic accuracy.

Results

170 MRI scans were subject to review across 66 episodes of care for 47 patients. 22.7% of patients experienced growth of residual tumour during the period of follow-up. The sensitivity of non-enhanced MRI for detection of growth was 82% (95%CI 64.40–92.12) with a specificity of 97.10% (95% CI 90.03–99.20). Accuracy was similar for both neuroradiologists and neurosurgeons (91.49% vs. 94%). Interobserver reliability was calculated using Cohen's Kappa co-efficient with a result of 0.792 showing substantial agreement. We also confirmed a statistically significant difference between gross total resection and sub-total resection and correlation with future growth (41% vs. 0%, n=64, p=0.001).

Conclusion

In paediatric patients who have undergone surgery for pilocytic astrocytoma, long term MRI follow-up without gadolinium-enhanced sequences maintains diagnostic accuracy compared

with enhanced sequences. Omission of gadolinium-enhanced sequences may lead to decreased costs, duration of scans and anxiety around follow-up procedures.

Introduction

Pilocytic astrocytoma is a circumscribed astrocytic glioma, and is the most common glial tumour in the paediatric population, accounting for 17.6% of all primary paediatric brain tumours. [1,2]. Most frequently occurring in the posterior fossa, pilocytic astrocytoma can also arise throughout the neuraxis in sites including the hypothalamus, optic chiasm and spinal cord. Pilocytic astrocytoma is classified as a grade 1 tumour in the World Health Organisation 2021 classification with a 10-year survival rate of greater than 95% [2]. Magnetic resonance imaging (MRI) is required in the diagnostic workup for pilocytic astrocytoma as it provides superior tumour characterisation over other imaging modalities. Pilocytic astrocytoma will appear as a cystic lesion with an enhancing mural nodule, although the cystic area is variable and the tumour may be entirely solid [3].

Treatment of pilocytic astrocytoma is largely determined by location, with surgical resection the mainstay of treatment for posterior fossa tumours, importantly the extent of resection (EOR) remains the most reliable predictor of recurrence-free survival [4]. The slow growing and indolent nature of pilocytic astrocytoma mandates maximal safe resection with a focus on preservation of function [5]. This approach may lead to an acceptable rate of second-look surgery when gross total resection is felt to be achievable, albeit with increased risk for neurologic deficit [6]. Rates of gross total resection vary in the literature from 53 to 83%, even when surgical adjuncts such as fluorescence and intraoperative magnetic resonance imaging (MRI) are utilised [7,8]. Progression often presents asymptomatically and prompt management of recurrence, significantly improves outcomes [9,10], therefore postoperative follow-up consists of regular MRI of the brain to detect recurrence of macroscopically resected tumour, or growth of unresected residual tumour [11]. The frequency and duration of this follow-up varies widely and can span over a decade, with truncated strategies considered in the case of complete resection [9,11,12].

In 2020, the Response Assessment in Paediatric Neuro-Oncology (RAPNO) working group published their recommendations for radiologic assessment of paediatric low-grade glioma [13]. The working group state that the use of contrast agents in paediatric low-grade glioma is controversial, and that T2-weighted and T2-weighted-fluid-attenuated inversion recovery (FLAIR) is a superior measure of residual tumour size and of assessing for subsequent changes in the tumour [13], with changes in contrast enhancement not indicative of tumour progression or response [14]. Similarly, the advent of genetically-defined targeted therapeutics in the paediatric low-grade glioma has led to difficulty in defining radiologic progression in patients undergoing these treatments for residual or progressive disease [15]. Banerjee et al found when assessing tumour response in the setting of mitogen-activating protein kinase pathway (MAPK) inhibitors (MEK-inhibitors), increased contrast enhancement was not considered a measure of tumour progression [16]. Despite this, largely based on the lack of literature to the contrary, the RAPNO working group recommend the use of post-contrast sequences remains part of the routine

follow-up for paediatric low-grade glioma, including pilocytic astrocytoma [13].

Gadolinium-based contrast agents (GBCA) are the most commonly used with MRI due to high diagnostic utility and presumed safety [17] accompanied by the fact that there exists no adequate alternate with the same safety and efficacy profile [18]. In recent years number of concerns regarding the use of gadolinium have arisen [19]. Potential unwanted effects of GBCAs include acute allergic reactions, nephrogenic systemic fibrosis and gadolinium deposition [17]. In addition to these concerns, administration of GBCAs requires intravenous cannulation, which can be a painful procedure and adds to paediatric patient stress and anxiety around future MRIs [20]. These protracted MRI surveillance protocols have their own inherent issues, potentially causing continued anxiety for the patient and their family concerning the results, requirement for repeat sedation or GA and their associated risks; being a time intensive process for clinicians and the added cost to the health system [9,20]. Following the discovery of gadolinium deposition in neural tissue, particularly the globus pallidus and dentate nucleus [14] even in patient with normal renal function [20], a number of authors have called for reduction or elimination of gadolinium enhanced sequences for a range of low grade brain tumours in both adult and paediatric patients [9,11,21,22]. A dose-dependent retention has been shown despite the type of GBCA used with the degree depending on the frequency of exposure and the type of chelate [14], with linear ligands having the most culpability [23]. This diverges from the previously held belief that GBCAs only cross the blood–brain-barrier (BBB) at points of disruption due to some pathology, such as infection, tumours or stroke [18]. While no clinical affect has been discovered, given routine use of gadolinium has not even spanned for 50years [20], this is a particular concern in paediatric patients due to their longer life span allowing decades of quiescence and thus increased risk for long term clinical consequences from repeated exposure to their developing tissue [9,14,20,24].

This study aims to investigate whether GBCA-enhanced sequences can be omitted from long term follow-up MRI for patients with pilocytic astrocytoma, whilst maintaining diagnostic accuracy reading potential recurrence or growth of residual tumour. To our knowledge no study has looked to re-review follow-up imaging for pilocytic astrocytoma with gadolinium-enhanced sequences omitted in an effort to determine the diagnostic accuracy of this approach.

Section snippets

Methods

After obtaining approval from the Sydney Children's Hospital Network Human Research Ethics Committee (SCHN-HREC approval number 2022/ETH00166) we conducted a retrospective chart review of all paediatric patients undergoing surgical management of pilocytic astrocytoma between 2012 and 2022. The data was obtained through the electronic health records and central medical records search. Secondary search was conducted through the picture archiving and communication system (PACS). We collected …

Results

170 MRI scans were reviewed and complete data was available for 46 patients across 66 episodes of care as seen in Table 1. All 46 patients had surgery and histopathologic proven pilocytic astrocytoma. The mean age at diagnosis was 6.52±3.93years. After initial surgery, 7 patients were found to have significant residual on post-operative MRI and returned to theatre within a 3-month period. All cases of significant residual were correctly identified on review of unenhanced MRI. In total, 12 …

Discussion

On our review of the MRI imaging, the reviewers came to conflicting conclusion with the original report in 6 instances. In 4 instances the reviewer recorded no growth where there was reported growth on the original report. Two of these instances occurred in one patient, and the opinion of the second reviewer agreed with the first in both instances. This patient had at total of four surgical interventions over a six-year period. The nature of the radiologic progression in this patient was that …

Conclusion

Pilocytic astrocytoma is the most common glial tumour in the paediatric population. Initial surgical management is the mainstay of treatment, and maximal safe resection should be the goal in the posterior fossa location. Post-operative MRI is mandated and long-term imaging follow-up is necessary. This study has shown that gadolinium-enhanced sequences can be omitted without fear of missing true radiologic progression. It is anticipated that removing the need for gadolinium has positive effects …

CRediT authorship contribution statement

Adam Ian Macfarlane: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Jewel Hannah Soares:** Writing – review & editing. **Monish Maharaj:** Data curation. …

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. …

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