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## Management of paediatric intracranial ependymoma

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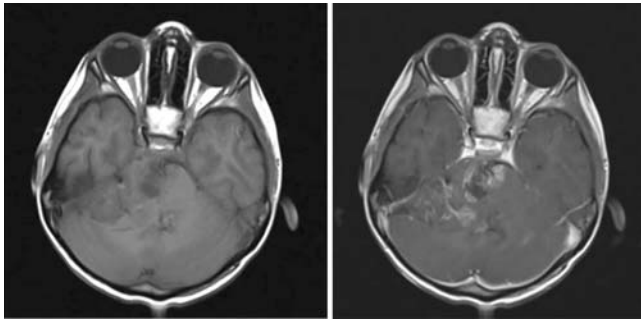
### Abstract

Intracranial ependymoma are relatively common paediatric brain tumours, but their eloquent location and high recurrence rate pose a significant challenge. Gross total resection or maximum safe resection followed by adjuvant radiotherapy are currently the standard recommended treatment, although there is still nearly 50% recurrence risk at 5 years. Chemotherapy has shown some promising results after recent advances in molecular understanding of ependymomas, but needs further evaluation before it could be added to the treatment regime.

**Keywords:** Intracranial Ependymoma, Pediatric, Surgical Management.

### Introduction

Ependymoma are neuroepithelial tumours, and comprise 8-10% of all paediatric tumours.<sup>1</sup> They are predominantly located in the brain in the posterior fossa (70% of the cases), but can be found in the supratentorial region and the spinal cord.<sup>2</sup> Intracranial ependymoma are commonly present in the ventricles, but they can also occur in the cerebral cortex



**Figure-1:** (a,b) MR T1 axial plain and contrast images of a 6 year old boy with a large heterogeneously enhancing ependymoma in the fourth ventricle, extending in to the cerebellopontine angle and brainstem.

in the vicinity of the ependymal lining of the ventricles, and rarely can be purely cortical with no connection to the ventricular wall (Figure-1).<sup>3,4</sup> The WHO classification system classifies ependymomas into 3 grades. Grade I are benign

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(myxopapillary), grade II tumours are also benign and can be divided into 4 sub-types (cellular, papillary, clear-cell and tanycytic), and grade III are malignant tumours (anaplastic). Historically, age at diagnosis, extent of surgical resection and pathological subtypes were considered important prognostic factors. However, there are incongruities in literature regarding relative importance of these clinical parameters. We have reviewed the literature to assess the current recommendations on the management of intracranial ependymomas, and to draw conclusions with regards to the outcomes.

### Review of Evidence

Several factors influence the most appropriate management and outcomes of children with intracranial ependymomas. Surgical resection has been the mainstay of treatment with multiple objectives including tissue diagnosis, removing the mass effect from important neural structures and to open the CSF pathways for relieving hydrocephalus. However, complete excision poses a challenge considering eloquent location of these tumours. Consequently, gross total resection (GTR) is possible in only up to 50% of the cases.<sup>5</sup> Perilongo et al., had reviewed 92 children with ependymomas for extent of resection, and had reported better overall survival after GTR (69.8%) as compared to subtotal resection (STR) (32.5%).<sup>6</sup> They had also reported that GTR group had a better impact on progression free survival (57% vs 11%).<sup>6</sup> Similar conclusions were drawn by Horn et al., in a series of 83 patients.<sup>7</sup> They reported that failure to achieve GTR, histological grade III tumours and less than 3 years age at diagnosis were all factors that resulted in adverse outcomes in childhood intracranial ependymomas.<sup>7</sup>

Cage et al., published a systematic review on outcomes in childhood intracranial ependymomas after combining extent of resection and histological grade.<sup>8</sup> Patients with grade II ependymomas had better survival after GTR alone than with any other treatment modality. In patients with grade III ependymomas, STR with adjuvant radiation was associated with better outcomes than GTR. This was attributed to the fact that grade III tumours were more infiltrative with poorer anatomical boundaries, and thus, aggressive resection to achieve GTR caused more morbidity and resulted in poorer neurological outcomes, as compared to STR.<sup>8</sup>

In a large multi-center retrospective analysis of 463 patients, Amanda et al., reviewed children with grade II and III

intracranial ependymomas with long clinical and radiological follow-ups.<sup>9</sup> Extent of resection, tumour sub-type and type of treatment were significantly associated with better overall survival in their study. GTR was superior to STR for 5-year survival ( $75 \pm 5\%$  vs.  $54 \pm 8\%$ ;  $p = 0.002$ ).<sup>9</sup> However, there was high recurrence rate within 10 years of diagnosis which brought overall survival to  $61 \pm 7\%$  at 10 years; so GTR was not curative for all children.<sup>9</sup> They proposed that GTR alone is not sufficient to treat children with intracranial ependymomas and recommended adjuvant treatments after surgery for better outcomes.<sup>9</sup> Some studies have also proposed 'second-look' surgery for residual ependymomas, however, a large cohort published by Italian investigators found no long-term significant difference in outcomes of children who underwent single surgery with adjuvant therapy, and those who underwent 'second-look' surgery.<sup>10</sup>

Although radiation alone does not have a significant role in treatment of ependymomas, it has been shown to improve survival when coupled with surgical resection, particularly in cases where GTR is not possible, as shown in the study by Cage et al.<sup>8</sup> Adjuvant radiotherapy is now part of the standard treatment protocol at most centers for children more than 3 years of age.<sup>11</sup> Historically, prophylactic radiation was also administered to the whole neural axis to prevent recurrence. However, it has not proven to be of any benefit in preventing recurrence and distal metastasis. The St Jude RT-1 trial had recruited 88 children with ependymomas who were administered radiation and followed up for a median of 38.2 months. They concluded that limited volume local irradiation results in good disease control (3-year progression-free survival estimate was  $74.7\% \pm 5.7\%$ ).<sup>12</sup>

Chemotherapy till date, does not have a clearly defined role in management of intracranial ependymoma. Several studies have tried to assess the role of different regimens including vincristine, cyclophosphamide, etoposide, platinum derivatives and methotrexate, with promising results, but none have been able to post outcomes better than adjuvant radiotherapy.<sup>11</sup> Its use is therefore currently limited to recurrent tumours not amenable for surgical resection.

Nearly half the children with intracranial ependymomas will develop recurrence within five years, despite GTR and adjuvant radiation.<sup>13</sup> Most of these recurrences are at the primary tumour site. The recommended treatment protocol for recurrent ependymomas involves surgical resection wherever possible and re-irradiation often using proton-beam therapy, with some centers including chemotherapy as well.<sup>11</sup>

## Conclusion

Extent of resection is the prime prognostic factor followed by age at presentation, both of which have a direct relation to the favourability of outcomes. GTR followed by adjuvant focal radiation remains the optimal choice for paediatric cranial ependymomas and has significantly improved the overall survival and progression-free survival over 5 years follow ups.

## References

1. Amirian ES, Armstrong TS, Aldape KD, Gilbert MR, Scheurer ME. Predictors of survival among pediatric and adult ependymoma cases: a study using Surveillance, Epidemiology, and End Results data from 1973 to 2007. *Neuroepidemiology*. 2012;39:116-24.
2. Nakazato Y. The 4th edition of WHO classification of tumours of the central nervous system published in 2007. *No shinkei geka. J. Neurol Surg*. 2008;36:473-91.
3. Byun J, Kim JH, Kim YH, Cho YH, Hong SH, Kim CJ. Supratentorial extraventricular ependymoma: retrospective analysis of 15 patients at a single institution. *World Neurosurg*. 2018;118:e1-9.
4. Wang M, Zhang R, Liu X, Li D, Qiu C, Zhao P, Zuo Y, Zhang P, Wang J, Sun H. Supratentorial extraventricular ependymomas: a retrospective study focused on long-term outcomes and prognostic factors. *Clin. Neurol. Neurosurg.* 2018;165:1-6.
5. Massimino M, Buttarelli FR, Antonelli M, Gandola L, Modena P, Giangaspero F. Intracranial ependymoma: factors affecting outcome. *Future Oncol* 2009;5:207-216.
6. Perilongo G, Massimino M, Sotti G, Belfontali T, Masiero L, Rigobello L et.al. Analyses of prognostic factors in a retrospective review of 92 children with ependymoma: Italian Pediatric Neuro-Oncology Group. *Med Pediatr Oncol: The Official Journal of SIOP-International Society of Pediatric Oncology*. 1997;29:79-85.
7. Horn B, Heideman R, Geyer R, Pollack I, Packer R, Goldwein J, Tomita T, Schomberg P, Ater J, Luchtman-Jones L, Rivlin K. A multi-institutional retrospective study of intracranial ependymoma in children: identification of risk factors. *J Pediatr Hematol Oncol*. 1999;21:203-11.
8. Cage TA, Clark AJ, Aranda D, Gupta N, Sun PP, Parsa AT, Auguste KI. A systematic review of treatment outcomes in pediatric patients with intracranial ependymomas: A review. *J Neurosurg Pediatr*. 2013;11:673-81.
9. Marinoff AE, Ma C, Guo D, Snuderl M, Wright KD, Manley PE, Al-Sayegh H, Sinai CE, Ullrich NJ, Marcus K, Haas-Kogan D. Rethinking childhood ependymoma: a retrospective, multi-center analysis reveals poor long-term overall survival. *J Neurooncol*. 2017;135:201-11.
10. Massimino M, Solero CL, Garrè ML, Biassoni V, Cama A, Genitori L, Di Rocco C, Sardi I, Viscardi E, Modena P, Potepan P. Second-look surgery for ependymoma: the Italian experience. *J Neurosurg Pediatr*. 2011;8:246-50.
11. Toescu SM, Aquilina K. Current and emerging methods of management of ependymoma. *Curr Oncol Rep*. 2019;21:1-9.
12. Merchant TE, Mulhern RK, Krasin MJ, Kun LE, Williams T, Li C, et.al. Preliminary results from a phase II trial of conformal radiation therapy and evaluation of radiation-related CNS effects for pediatric patients with localized ependymoma. *J Clin Oncol*. 2004;22:3156-62.
13. Antony R, Wong KE, Patel M, Olch AJ, McComb G, Krieger M, et.al. A retrospective analysis of recurrent intracranial ependymoma. *Pediatr Blood Cancer*. 2014;61:1195-201.