Anaplastic ependymoma

Anaplastic ependymomas (WHO grade III ependymoma) are characterised by a higher proliferative rate and a greater tendency to infiltrate surrounding brain or disseminate into cerebrospinal fluid causing drop metastases.

Epidemiology

About 25% of ependymomas exhibit features of anaplasia with a high mitotic rate, cellular pleomorphism, and intratumoral necrosis; these are considered WHO grade III.

Anaplastic ependymomas, are far more common in the pediatric age group, frequently arising as supratentorial ependymoma.

see also Spinal anaplastic ependymoma.

Pathology

These tumours have a greater propensity to infiltrate surrounding brain or spinal cord parenchyma and have a higher proliferative rate.

Radiographic features

An anaplastic ependymoma typically presents as a calcified cystic tumour in the supratentorial parenchyma or transependyma

Treatment

see Anaplastic ependymoma treatment.

Outcome

Complete surgical removal resulting in cure is unlikely for anaplastic ependymoma.

Even if post-operative imaging demonstrates no residual tumour, the median time to first recurrence is approximately 18 months and to second recurrence is an additional 12 months.

Case series

15 pediatric patients with ependymomas carrying YAP1-MAMLD1 fusions, with their characteristic

histopathology, immunophenotype and molecular/cytogenetic, radiological and clinical features. The YAP1-MAMLD1 fusion was documented by RT-PCR/Sanger sequencing, and tumor genomes were studied by molecular inversion probe (MIP) analysis. Significant copy number alterations were identified by GISTIC (Genomic Identification of Significant Targets in Cancer) analysis. All cases showed similar histopathological features including areas of high cellularity, presence of perivascular pseudo-rosettes, small to medium-sized nuclei with characteristic granular chromatin and strikingly abundant cells with dot-like cytoplasmic expression of epithelial membrane antigen. Eleven cases presented features of anaplasia, corresponding to WHO grade III. MRI showed large supratentorial multinodular tumors with cystic components, heterogeneous contrast enhancement, located in the ventricular or periventricular region. One of two variants of YAP1-MAMLD1 fusions was detected in all cases. The MIP genome profiles showed balanced profiles, with focal alterations of the YAP1 locus at 11q22.1-11q21.2 (7/14), MAMLD1 locus (Xp28) (10/14) and losses of chromosome arm 22q (5/14). Most patients were female (13/15) and younger than 3 years at diagnosis (12/15; median age, 8.2 months). Apart from one patient who died during surgery, all patients are alive without evidence of disease progression after receiving different treatment protocols, three without postoperative further treatment (median follow-up, 4.84 years). In this to date, largest series of ependymomas with YAP1-MAMLD1 fusions we show that they harbor characteristic histopathological, cytogenetic and imaging features, occur mostly in young girls under 3 years and are associated with good outcome. Therefore, this genetically defined neoplasm should be considered a distinct disease entity. The diagnosis should be confirmed by demonstration of the specific fusion. Further studies on large collaborative series are warranted to confirm this findings [1)].

Fourteen patients with anaplastic ependymomas were enrolled from 2006 to 2014. Six cycles of induction chemotherapy were administered to all patients before they underwent tandem HDCT/auto-SCT. Patients who were older than 3 years of age were administered RT after two cycles of induction chemotherapy. In patients under 3 years of age, RT was either omitted or delayed until they reached 3 years of age, if the patients experienced CR after tandem HDCT/auto-SCT. All patients, including two who experienced disease progression during induction treatment, underwent the first HDCT/auto-SCT, and 13 subsequently underwent the second HDCT/auto-SCT. One patient died from hepatic VOD during the second HDCT/auto-SCT; other toxicities occurring during tandem HDCT/auto-SCT were manageable. Relapses or progression occurred in seven patients, and five of seven of them remain alive till date after salvage treatment, including surgery and RT. The 5-year overall and event-free survival rates were 85.1% ± 9.7% and 50.0% ± 13.4%, respectively. These findings suggest that multimodal treatment including tandem HDCT/auto-SCT could be a feasible option for improving survival in children with anaplastic ependymomas [2)].

Case report

A 38-yr-old woman with a 1-mo history of vertigo and slow left sided gaze drift. She underwent microsurgical gross total resection of the CPA ependymoma via retrosigmoid approach. The histopathology was grade III anaplastic ependymoma. She tolerated the surgery well and her postoperative course was uneventful. She received radiation therapy and there was no recurrent disease in follow-up studies. Important steps of the surgical approach and microsurgical techniques in resection of these challenging tumors are demonstrated in this 3-dimensional surgical video [3)].

A 7-year-old boy experiencing a convulsive attack underwent surgical tumor resection, and magnetic resonance imaging of the head revealed a tumor-like lesion in the right parietal lobe. Although adjuvant radiotherapy was performed after total tumor resection, a focal recurrent lesion appeared soon afterward. They initiated chemotherapy with bevacizumab after resection of the recurrent lesion, but bevacizumab was unable to control tumor progression. At this writing, he remains bedridden and requires tube feeding and artificial ventilation.

Since Li-Fraumeni syndrome is a genetic disease that is caused by mutation of the tumor suppression gene TP53, patients should generally not be treated with radiotherapy or alkylating agents that induce DNA damage. However, if the prognostic benefit of postoperative adjuvant therapies is thought to surpass the risk of long-term secondary cancer, it is appropriate to consider these therapies after consultation with the patient and family. Postoperative treatment protocols are controversial, and their role should be further explored in cases of Li-Fraumeni syndrome complicated with malignant gliomas [4].

2015

A 12-year-old girl with an anaplastic ependymoma of the left temporal lobe. She underwent initial image-guided resection following biopsy. A postoperative MRI showed a macroscopic resection. She subsequently relapsed and indeed had 11 local and distant relapses managed by 12 separate craniotomies and tumour resection, 4 courses of radiotherapy and chemotherapy.

For patients with multiple relapses, surgery should be considered primarily to re-resect any symptomatic lesion. This case demonstrates that multiple tumour resections can be undertaken with limited morbidity for the patient and with maintenance of quality of life [5].

2014

A young child presented to the emergency department of a tertiary care hospital with on and off headache, focal seizures involving the left side of the body, weakness of left upper and lower limbs and vomiting for 2 weeks. Examination showed an alert child with grade 4/5 powers in left upper and lower limbs. Blood investigations were normal. An urgent CT of the brain showed intra-axial mass in the right frontal cerebral cortex, superolateral to the right lateral ventricle. MRI of the brain showed supratentorial extraventricular mass of 5.20×3.70×3.80 cm, in the right frontal cortex, emitting heterogeneous signals on T1, T2 and fluid-attenuated inversion recovery sequences and impression of astrocytoma, ependymoma or choroid plexus papilloma was made. Complete surgical resection of mass was performed. Histopathology of the mass proved it as WHO grade III anaplastic ependymoma. The child made an uneventful postoperative recovery and radiotherapy was followed [6].

1)
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6)

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