INTRODUCTION

Pediatric brain tumor

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PEDIATRIC patients with primary brain tumors present some of the most challenging cases encountered by neurosurgeons. Brain tumors are the second most common neoplasms in children and the most common solid neoplasms. Furthermore, brain tumors have overtaken leukemia as the leading cause of childhood cancer death.¹ Surgical and adjuvant therapies result in reasonably good survival rates in many pediatric brain tumor types. For instance, standard treatment (maximal safe resection, craniospinal irradiation, and myeloablative chemotherapy) results in long-term survival of greater than 90% in low-risk patients with the Wnt molecular subtype of medulloblastoma.³ However, the intensive therapies necessary to achieve these outcomes often result in permanent cognitive, neurological, and end-organ damage, as well as secondary malignancies later in life. Pediatric high-grade gliomas such as noninfantile glioblastoma, high-grade midline gliomas, and diffuse intrinsic pontine gliomas (DIPGs) have dismal outcomes similar to those seen in their adult counterparts. Even low-grade/benign tumors in children present with significant difficulties given their greater propensity to arise from eloquent structures such as the optic apparatus, hypothalamus, and brainstem, necessitating surgeries associated with increased morbidity and a lifetime of dealing with the direct and indirect effects of the tumor. This issue of *Neurosurgical Focus* presents key pediatric brain tumor topics of interest with the goal of providing our readers insights into the latest advancements in the field.

Arguably, the most difficult to treat of all pediatric brain tumors are DIPGs. These inoperable tumors are resistant to irradiation and chemotherapy, and most affected patients die within a year of diagnosis. Until recently, pathologic confirmation was not necessary to initiate treatment for DIPG; however, in this new age of precision medicine where next-generation sequencing can be leveraged to choose therapies specific for each tumor, biopsy

of DIPGs can be critical in directing patients to the appropriate clinical trials offering targeted molecular and immune therapies, as reported by Williams et al. DIPG treatment failures are in large part due to the inaccessible nature of the brainstem to chemotherapies, molecular targeting agents, and immune therapeutics. To overcome this barrier, agents can be delivered directly to the brainstem parenchyma. Rechberger et al. compare the infusate parameters of direct drug delivery to the brainstem via convection-enhanced delivery and osmotic pump delivery in rodent models. Bander et al. describe the conformation changes within the brainstem of patients undergoing convection-enhanced delivery. Beccaria et al. demonstrate how low-intensity pulsed ultrasound can be used to disrupt the blood-brain barrier, which has implications in treating DIPGs, as well as other pediatric brain tumors where the blood-brain barrier significantly limits the delivery of therapeutic agents.

Craniopharyngiomas are also difficult-to-treat tumors that often result in profound disturbances of the pituitary–hypothalamic axis and require surgery to resect the tumor and associated cysts as well as irradiation of adjacent normal tissues. Targeted therapies directed against *BRAF* mutations have been successful in treating papillary craniopharyngioma in adults, but few agents have been tested against adamantinomatous craniopharyngioma, which is more common in children than in adults.² Hengartner et al. offer an excellent review of the molecular biology of adamantinomatous craniopharyngiomas and present information about a number of molecular agents that can potentially target the pathways altered in these tumors. These agents targeting adamantinomatous craniopharyngioma could improve outcomes by both reducing the need for surgery/irradiation and decreasing the size of the tumor before surgery/irradiation.

Next-generation sequencing technology has revolution-

ized our approach to the diagnosis of tumors, monitoring of treatment responses, and surveillance of disease recurrence. Changes (mutations, translocations, epigenetic marks) in the nucleic acid sequences that are only present within tumors can be detected in a cell-free state from small quantities of fluid (blood, CSF) among “a sea” of normal nucleic acid sequences.⁴ In this issue, Bounajem et al. and Azad et al. describe how this “liquid biopsy” technology is being applied to the pediatric population with brain tumors.

Some of the most important scientific advancements in tumor biology have been led by neurosurgeon scientists studying pediatric brain tumors. These advancements include the molecular subtyping of tumors into distinct subgroups containing specific prognostic and treatment implications, ascertaining of tumor cells of origins, and precision medicine–guided therapies specific for each patient’s tumor. We are pleased that the contributors to this issue used this wealth of knowledge to provide an update in pediatric brain tumors.

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Disclosures

The authors report no conflict of interest.

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