Central nervous system primitive neuroectodermal tumors: still a useful classification?

Corey Raffel, M.D., Ph.D., 1 and James T. Rutka, M.D., Ph.D., F.R.C.S.C. 2

1Section of Pediatric Neurosurgery, Nationwide Children’s Hospital, Department of Neurological Surgery, The Ohio State University College of Medicine, Columbus, Ohio; and 2Division of Neurosurgery, The Hospital for Sick Children, Toronto, Ontario, Canada

The terminology for small, round, blue cell tumors of the CNS has been confusing from the beginning. The initial description of medulloblastoma by Bailey and Cushing 1 in 1925 suggested that the cell of origin was the medulloblast, a cell type now considered not to exist. Because of phenotypic similarities, Hart and Earle 2 in 1973, lumped a group of pediatric brain tumors previously known as medulloblastoma, pineoblastoma, cerebral neuroblastoma, and so on into a group of tumors they called primitive neuroectodermal tumors (PNETs). Since this time, much has been written about PNETs, their cell of origin, molecular biology, clinical behavior, and prognosis. Of note, these CNS PNETs are entirely different from the peripheral nervous system PNETs characterized by a translocation between chromosomes 11 and 22.

With the advent of molecular biology techniques including transcriptional profiling, exon-array, and single-nucleotide polymorphism–array technologies, the distinctions between cerebellar medulloblastoma and supratentorial PNETs have become better defined. In 2002, Pomeroy and colleagues 5 used transcriptional profiling to show that supratentorial PNETs and atypical teratoid tumors were distinct from each other and quite distinct from medulloblastomas. In addition, they showed that these 3 groups of tumors had distinctly different prognoses. Prior to this work, 2 different, mutually exclusive genetic alterations had been described in medulloblastoma by Raffel and coworkers. 6,9 One group had mutations in the sonic hedgehog pathway, the other in the Wnt pathway. The work of Pomeroy and colleagues also suggested that medulloblastoma may encompass more than a single tumor type, as the tumors with sonic hedgehog pathway alterations were distinguishable from other medulloblastomas by their gene expression pattern. 5 Building on this work, Dr. Michael Taylor and his group have shown that medulloblastomas can be divided into at least 4 subtypes based on their gene expression profiles. The age at presentation and prognosis are distinct for each subtype, suggesting that these are really different tumors. 4 These authors suggest that the differences may result from differing cells of origin giving rise to each tumor type, a hypothesis supported by the others. 7,8 Interestingly, the Group C subtype seems to carry an especially grim prognosis, being responsible for most cases of CSF dissemination and death in the medulloblastomas as a whole. Information about nonmedulloblastoma PNETs has been more scarce. For example, Li et al. 3 have recently reported on the use of advanced genetic strategies to identify frequent amplification of a microRNA polycistron on chromosome 19 in aggressive PNETs. Overall, the work on the subclassification of these tumors suggests that the term PNET may have outlived its usefulness for CNS tumors and that each different tumor previously included in the classification should be identified by its unique name.

In this issue of Neurosurgical Focus, 3 papers on PNETs are published. In the first paper, the authors present 2 cases of intraspinal tumors. One tumor is intramedullary, and the other, occurring in the region of the conus medullaris, appears to be intradural, extramedullary in location. Of note, both patients underwent appropriate workup to ensure that the spinal tumors did not represent drop metastases from a medulloblastoma. Although drop metastases into the CSF have been well reported, intramedullary metastases, usually in the cervical spinal cord, have been reported and hypothesized to be caused by cells falling into the central canal of the cord. This article provides a comprehensive review of the topic, including a discussion of the molecular changes seen in PNETs, along with the incidence and special features of intraspinal tumors.

In the second paper in the issue, the authors present 2 cases of the recently described “embryonal tumor with
abundant neuropil and true rosettes” (ETANTR). These tumors, classified within the PNETs, are clearly a distinct tumor type. An ETANTR is a malignant tumor presenting in young children, and the authors describe the case of a patient who survived for 7 years, the longest period yet reported for this rare tumor. The authors provide an excellent review of this rare, recently described tumor type, with careful presentation of the ETANTR's clinical outcomes, cytogenetic changes, and relationships with medulloblastoma and ependymoblastoma.

The third paper in this issue of Neurosurgical Focus focuses on a case of supratentorial PNET appearing in a patient after radiotherapy was performed for a craniopharyngioma. As mentioned in the paper, 4 criteria are needed to identify a tumor as being likely induced by radiotherapy: 1) the tumor in question must arise in the irradiated field, 2) sufficient time must have elapsed between the irradiation and the appearance of the tumor in question, 3) the patient cannot have a syndrome that predisposed him/her to the tumor in question, and 4) the tumor in question must be easily differentiated from the initial tumor for which the irradiation was delivered. The case presented in this paper seems to meet these criteria because the PNET arose in the field of irradiation delivered to treat the initial craniopharyngioma, the PNET presented 8 years after radiotherapy, the patient was not known to have any of the syndromes associated with the development of PNETs, and the 2 tumors were distinctly different. Although other reports of radiation-induced PNETs exist and are referenced in this paper, the current case is of interest because the patient was treated with radiation therapy without adjuvant chemotherapy, a common combination in other reports of radiation-induced PNETs, indicating that irradiation alone may in rare cases cause the PNET. (DOI: 10.3171/2011.1.FOCUSIntro)

References


Neurosurg Focus / Volume 30 / January 2011