The impact of technical adjuncts in the surgical management of cerebral hemispheric low-grade gliomas of childhood

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Abstract

Pediatric brain tumors occur with a frequency of 24 to 27 cases/year within a cohort of 1 million children. Nearly 25% of these lesions will involve the cerebral hemisphere, with the low-grade glioma representing the most common group of tumors in this location. Pilocytic and fibrillary astrocytomas are the most frequently encountered glioma, although other variants, such as the ganglioglioma, pleomorphic xanthoastrocytoma, astroblastoma, ependymoma, and oligodendroglioma, must also be considered in the differential diagnosis. The etiology of these tumors remains obscure, although may be linked to therapeutic radiotherapy, previous history of hematopoietic malignancy, and maternal exposure to nitrosamine-laden foods. An associated link to a phakomatosis, e.g., neurofibromatosis, tuberous sclerosis, has also been documented to exist with astrocytomas, in particular. The goals of surgery include a complete removal, in most circumstances, with an attempt to alleviate an associated seizure disorder when intractable. This is possible in nearly every type of hemispheric glioma with the aid of intraoperative navigational systems, i.e., frameless stereotaxy, neurophysiological based stimulation mapping, and electrocorticography. In the setting where a complete removal is possible, no further therapy is warranted. For those lesions that are incompletely resected, conservative management with routine diagnostic imaging follow-up is appropriate. Reoperation is necessary if recurrence is documented and radiotherapy is utilized for those lesions that are incompletely resected following recurrence.

Incidence and etiology

Approximately 24 to 27 cases of pediatric brain tumors will develop yearly in a population base of one million children up to the age of 15 years [1–3]. In most of these series of patients, between 15% and 25% of tumors occupy the cerebral hemispheres [4]. Thus, the likelihood of this location being primarily involved with a low-grade or malignant tumor varies between 5 and 8 cases per million children each year. In particular, infants have a nearly twofold higher likelihood of developing a cerebral hemispheric tumor when compared to other children [2, 4, 5], although this gap decreases after the first decade [6, 7].

The most common tumor involving the cerebral hemispheres is the low-grade astrocytic glioma [4, 8–10]. In an updated series of over 150 hemispheric tumors in children under the age of 15 years, low-grade astrocytomas occupied nearly 50% of all histologic categories [11]. By adding the higher grade gliomas, the incidence increases to 65% [12]. This is in distinction to an overall incidence of 35% for pediatric low-grade astrocytomas regardless of location [13]. Low-grade cerebral astrocytomas most commonly affect children in the latter few years of
the first decade and the first half of the second decade [14, 15]. Low-grade astrocytomas of the hypothalamus, thalamus, and optic pathways usually present in children within the first five years of life [16].

The etiology of the majority of childhood brain tumors remains elusive. However, children with phakomatoses such as neurofibromatosis and tuberous sclerosis are at higher risk of subsequently developing a tumor within the central nervous system [17]. Neurofibromatosis type I carries with it an increased likelihood of developing an astrocytoma, particularly of the optic pathways. As many as 35% of all children with optic pathway gliomas are known to have neurofibromatosis [18, 19] and as many as 70% of patients with an intraorbital glioma will have this particular phakomatosis [20]. Tuberous sclerosis usually is associated with cortical tubers, i.e., hamartomas. However, these patients may also develop subependymal giant cell astrocytomas within the ventricular system near the foramen of Monro.

It has been observed in a recent case control study that relatives of children who have central nervous system tumors are more likely to develop malignancies of the brain or the hematopoietic-lymphocytic systems when compared to the general population [21]. In addition to this inherited predisposition, other factors that increase the astrocytoma development risk include maternal exposure to foods and products rich in nitrosamines, and drugs. An apparent protective effect against the development of an astrocytoma was found with a maternal history of miscarriage and stillbirth [22].

A previous history of radiotherapy predisposes a child to developing a brain or skull base tumor later in life. Perhaps the classic example of this may be found in those children who received scalp irradiation for tinea capitis [23], usually at a low cumulative dose (< 1 Gy). The secondary tumors were typically meningiomas, although gliomas were also reported to occur. After prophylactic radiotherapy to the central nervous system in children with acute lymphocytic leukemia, malignant gliomas and meningiomas developed with a two to three-fold higher incidence than in age-matched children from the same time period [24, 25]. In these cases the radiation dose did not exceed 2.4 Gy, and the latency period was as long as ten years. Subsequently, numerous examples of radiation-induced astrocytomas, as well as sarcomas and meningiomas, have been reported. Thus, a second, histologically different tumor developing several years later in a previously radiated field supports the concept of a radiation-induced tumor [25–27].

**Classification**

Despite the molecular markers now available, the pathological classification of gliomas still relies significantly on the histopathology as determined with hematoxylin-eosin staining. The histology also appears to best predict prognosis, although this is now supplemented with cell kinetic data, molecular genetics, and cytogenetics. Notwithstanding, the heterogeneity demonstrated to occur in astrocytomas, along with the sometimes small sample size provided to the pathologist, makes it likely that errors in diagnosis will occur. This, combined with the fact that low-grade gliomas have a tendency to change phenotype, necessitates a thorough initial approach to the histological classification including several opinions from neuropathologists who specialize in neuro-oncology.

The simplest and most widely referred to classification scheme in use today is based on the original work published by Kernohan nearly 50 years ago [28]. All astrocytic gliomas are categorized into four grades depending on degrees of anaplasia, nuclear pleomorphism, cell density, endothelial proliferation, and necrosis. This system often results in difficulty distinguishing between grade I and II tumors, although this is less of a problem with the grade III and IV tumors [29]. This controversy has been somewhat simplified by the recent World Health Organization’s (WHO) three-tiered classification [28, 30]. Astrocytomas are comprised of a monotonous, moderately cellular background of astrocytes with very little pleomorphism. Anaplastic astrocytomas demonstrate a more dramatic pleomorphism and a higher cell density. The gemistocytic variant is comprised of 50% or more plump astrocytes and behave clinically as an anaplastic tumor. The find-