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Editorial

Pediatric and Adult Gliomas: How Different Are They?

Recently, I was discussing the treatment of a pediatric patient who had gliomatosis cerebri. A pediatric neuro-oncologist, one of my respectable friends, insisted on chemotherapy with temozolomide. Because the histologic type was anaplastic astrocytoma (as determined by open biopsy), many would consider radiotherapy the primary option; thus, there was an exciting discussion. On another occasion, the same colleague and I were discussing a pediatric patient with a symptomatic diffuse astrocytoma of the posterior thalamus; this time as well, he insisted on a trial of chemotherapy with carboplatin and vincristine. My colleague's philosophy is that because pediatric gliomas are different from adult gliomas, chemotherapy to defer or avoid radiotherapy is reasonable in cases of low-grade and sometimes even high-grade glioma.

Maybe my colleague is right regarding the difference between pediatric and adult gliomas. There have been numerous reports showing substantial differences in the molecular features underlying pediatric and adult high-grade gliomas. Pediatric and adult glioblastomas were shown to be clearly distinguished by frequent gain of chromosome 1q and lower frequency of chromosome 7 gain and 10q loss in the pediatric form. Platelet-derived growth factor receptor-α (PDGFR-α) was found to be the predominant gene subject to focal amplification in childhood high-grade gliomas.[1,2]

Among the pediatric low-grade gliomas, pilocytic astrocytoma is the predominant histologic type and diffuse astrocytomas are quite rare. In this issue of *Neuro-Oncology*, Stokland et al. from the Children's Brain Tumour Research Centre, University of Nottingham, UK, report on 639 pediatric patients with low-grade gliomas, 63.7% of which were pilocytic astrocytomas and only 5.9% of which were diffuse fibrillary astrocytomas.[3] The predominance of the former type is consistent with other evidence. For instance, in the Brain Tumor Registry of Japan, the incidence of pilocytic astrocytomas peaks in patients between 5 and 9 years old, while that of diffuse astrocytomas peaks in patients between 40 and 44 years old. In the Central Brain Tumor Registry of the United States (CBTRUS), 1,834 pediatric patients (those between 0 and 19 years old) with pilocytic astrocytomas are registered, while only 101 cases of diffuse astrocytoma are found in the pediatric population. Therefore, pediatric low-grade gliomas are mostly pilocytic astrocytomas, and adult low-grade gliomas are mostly diffuse astrocytomas.

Pilocytic astrocytomas and diffuse astrocytomas are classified as WHO grades I and II, respectively. However, pilocytic astrocytoma is not a precursor of diffuse astrocytoma, as there is a distinct difference between the molecular features of the two. There appears to be no role for either *TP53* mutations or aberrant PDGF signaling in the development of pilocytic astrocytomas, in contrast to the role of *TP53* mutations and increased expression of PDGF-A and PDGFR-α as common, early events in the formation of diffuse astrocytomas.[4] Pilocytic astrocytomas also differ from diffuse astrocytomas in their altered and increased expression of immune response genes. Hierarchical clustering analysis using a set of 1,176 genes distinguished pilocytic astrocytomas from diffuse astrocytomas and oligodendrogliomas.[5] Pilocytic astrocytomas are also different from the diffuse astrocytomas clinically, as evidenced by the fact that histology is one prognostic factor in pediatric low-grade gliomas.[3]

Fear of radiation-induced adverse effects has been used to justify the use of chemotherapy for unresectable pilocytic astrocytomas. A number of chemotherapy regimens have been used to delay the need for radiotherapy, including carboplatin and vincristine. A recent randomized trial, Children's Oncology Group A9952, compared the combination of carboplatin and vincristine with the combination of procarbazine, thioguanine, lomustine, and vincristine and reported 5-year event-free survival rates of 40%-50%. More than 400 low-grade gliomas were registered, and 83% of them were pilocytic astrocytomas.[6]

However, although a small study is under way, the role of chemotherapy in the management of pediatric diffuse astrocytomas remains unclear. In adult diffuse astrocytomas, a randomized study comparing radiotherapy and temozolomide is now ongoing in Europe and North America.

Yes, pediatric and adult gliomas are different. Pediatric and adult high-grade gliomas are biologically different. On the other hand, differences between pediatric and adult low-grade gliomas are mainly due to the difference in their histologies.

Whether pediatric diffuse astrocytomas are chemosensitive remains unproven. The UK study reported in this issue also suggests that, because of the small number of diffuse astrocytomas in the pediatric population,

international cooperation will be needed to address the issue of the optimal management of this entity.

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