ASK THE EXPERTS

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Ependymoma: current treatment options and a look to the future

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Q What are ependymomas & how frequently do they occur?

Ependymomas are tumors of neuroectodermic origin, arising from the ependymal cells that line the ventricles and the central canal of the spinal cord. Ependymomas are most common in children, and rarely occur in adults. They make up 10–12% of CNS tumors in children, representing the most common brain tumor in children younger than 5 years.

Q What are the common clinical symptoms of ependymoma & how are they diagnosed?

Given the predominant location in the posterior fossa, the most common presenting symptoms and signs are due to raised

supratentorial pressure from obstructive hydrocephalus and cerebellar dysfunction. They include nausea, vomiting, headache, gait disturbances, nystagmus, facial weakness and lethargy in young children. Less common are lower cranial nerve palsies or torticollis, reflecting tonsillar herniation. Infratentorial tumors may manifest as focal neurological deficits or seizures, reflecting the region of the brain that is compressed. Spinal tumors have spinal symptoms that are connected to the anatomical area of origin. The diagnosis is made by gadolinium-enhanced MRI, which demonstrates well-circumscribed lesions with varying degrees of contrast enhancement. The tumors may exhibit cystic components or calcifications.

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Q How do the characteristics of ependymoma differ according to their location & grade?

As for their intracranial location, tumors in the supratentorial compartment (50–60% of adult ependymomas and 30% of pediatric ependymomas) are more often hemispheric or occur in association with the third ventricle, while tumors in the posterior fossa (60% of pediatric ependymomas) are medial (IV ventricle) or lateral (cerebellopontine angle). Spinal ependymomas mainly occur in adults, and are located in the conus medullaris, cauda equina and filum terminale. There are increasing data suggesting that the molecular profile of ependymomas differs according to location. WHO classification recognizes three grades of malignancy that tend to be associated with location [1,2]: grade I tumors (the myxopapillary variant in the conus/cauda and the subependymoma in an intraventricular location), and grade II and III (anaplastic) tumors, which mainly occur in intracranial locations. Grade I tumors are generally indolent tumors, although myxopapillary ependymomas can recur and spread along the cerebrospinal fluid. Conversely, grade III tumors behave aggressively.

Q What are the recommended treatment options for cerebral, infratentorial & spinal cord ependymomas?

Surgery represents the most important treatment modality for all types of ependymomas; the goal is to make a histological diagnosis, remove obstacles to cerebrospinal fluid flow and achieve a complete tumor resection, which is clearly associated with a more favorable outcome. Postoperative limited-field radiotherapy is the standard of care for anaplastic and incompletely resected grade II ependymomas. Craniospinal irradiation is reserved for ependymomas with leptomeningeal spread. The role of chemotherapy is limited; in recurrent tumors after surgery and radiotherapy, temozolomide may have some activity (even if most tumors have unmethylated *MGMT*) and is preferred over platinum

compounds, because they can cause peripheral neurotoxicity.

Q Can you update us on the feasibility of prognostic testing for ependymomas?

The grade of malignancy (grade II vs III), defined by a combination of cell density, proliferative activity, endothelial proliferations and necrosis, is strongly prognostic, while individual histologic factors are not. Molecular alterations differ according to tumor location, but are not as important as tumor grade to predict outcome.

Q How far has research investigating signal transduction pathways as therapeutic targets progressed?

The development of the Collaborative Ependymoma Research Network (CERN) in the USA will facilitate research on new signal transduction pathways to be targeted by specific compounds; the network is led by the MD Anderson Cancer Center (TX, USA), and our institution (University Hospital, Torino, Italy) is part of this group [101]. To date, there are some promising preliminary data on the activity of bevacizumab, a monoclonal antibody against VEGF for recurrent ependymomas. Another potential target is EGFR, which has been found to be amplified in ependymomas; a Phase II study sponsored by CERN is currently investigating the EGFR inhibitor lapatinib in association with dose-dense temozolomide.

Q What do you see as the key goals & challenges for ependymoma treatment in the next 5 years?

The challenge for ependymoma treatment is represented by the identification of different molecular profiles as potential targets of therapy. This is true, for instance, in medulloblastoma, but in ependymoma we are still far away. In this regard, new insights into ependymoma stem cells could lead to advances in management in the next few years.

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References

- 1 Louis DN, Ohgaki H, Wiestler OD *et al.* The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol.* 114, 97–109 (2007).
- 2 Rudà R, Gilbert M, Soffietti R. Ependymomas of the adult: molecular biology and treatment. *Curr. Opin. Neurol.* 21, 754–761 (2008).
- 3 Collaborative Ependymoma Research Network (CERN). www.cern-foundation.org

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