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Molecular Pathology of Gliomas

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Section snippets

Key points

- Isocitrate dehydrogenase 1/2 (IDH1/2) mutation status and 1p19q chromosomal arms status are critical for accurate classification of diffuse gliomas in adults....
- IDH1/2-mutated tumors have significantly better outcome than wild-type tumors....
- Diagnosis of glioblastoma can be based on characteristic molecular features alone in the absence of diagnostic histologic features....
- High-grade pediatric gliomas are characterized by histone H3 mutations with K27M or G34 mutations....
- Pediatric low-grade gliomas show...

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Overview

Although primary central nervous system (CNS) tumors account for only 2% of all primary cancers, they cause 7% of deaths from cancer in those younger than 70 years old.[1] Median age of primary brain tumors is approximately 60 years and gliomas represent approximately 26% of all primary CNS tumors. Brain tumors are the second most common cancers in children 0 to 14 years old and a leading cause of cancer-related deaths in pediatric population. Gliomas biologically vary from relatively benign,…

Differential diagnosis

Differential diagnosis of gliomas often can be achieved by combining clinical and imaging features before performing molecular studies. This is because, compared with other cancers, there is a striking correlation between age, location, and the molecular genetics of brain tumor, including gliomas.[5] Diffuse gliomas of small children tend to be located in the midline and carry histone H3 K27M mutation. On the contrary, more benign pediatric gliomas are driven by MAPK pathway alterations, most…

Diffuse Glioma IDH-mutant

The discovery of *IDH1/2* mutations revolutionized understanding of glioma biology and upended a traditional grading system for diffuse gliomas.[9,10] *IDH1/2*-mutant astrocytomas are more likely to occur in younger adults and are associated with a better prognosis matching for grade than their IDH–wild-type counterparts. Studies have shown a significant association between *ATRX* and *TP53* mutations in *IDH1/2*-mutant gliomas. This close association suggests that the *ATRX* alterations are needed with *TP53* …

Pediatric low-grade gliomas

Low-grade gliomas are the most common type of brain tumor in children. Pilocytic astrocytomas, gangliogliomas, and pleomorphic xanthoastrocytomas (PXAs) are noninfiltrating tumors relatively well-demarcated tumors that are common in children and adolescents.37, 38, 39 These tumors follow a benign clinical course and rarely show malignant progression. Pediatric low-grade gliomas do not carry *IDH1/2* or *ATRX* mutations, 1p19q loss, or RTK amplifications characteristic of adult tumors. A large…

Summary

Gliomas represent histologically and molecularly a diverse group of tumors. Although classification still is largely based on histology, molecular features are changing the practice of medicine. The discovery of IDH1/2 mutations and association with ATRX mutations and loss of 1p19q in astrocytoma and oligodendroglioma, respectively, and the definition of molecular IDH–wild-type GBM have dramatically changed the practice of neuropathology and WHO classification and markedly decreased the number…

Clinics care points

- Diffuse gliomas are the most common primary brain tumors with strong correlation between age, tumor location, and molecular biology.…
- In adults, *IDH1/2* mutation status and 1p19q chromosomal arms status are critical for accurate classification.…
- A combination of immunohistochemistry and molecular analysis can classify most adult diffuse

gliomas....

- *IDH1/2*-mutated tumors show significantly better clinical outcomes....
- In pediatric gliomas, aggressive tumors are characterized by histone H3 mutations, whereas...

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First page preview

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KEYWORDS

• IDH1/2 mutation • ATRX mutation • Histone H3 K27M mutation • 1p19q loss
• BRAF fusion • BRAF V600E mutation

KEY POINTS

- Isocitrate dehydrogenase 1/2 (IDH1/2) mutation status and 1p19q chromosomal arms status are critical for accurate classification of diffuse gliomas in adults.
- IDH1/2-mutated tumors have significantly better outcome than wild-type tumors.
- Diagnosis of glioblastoma can be based on characteristic molecular features alone in the absence of diagnostic histologic features.
- High-grade pediatric gliomas are characterized by histone H3 mutations with K27M or G34 mutations.
- Pediatric low-grade gliomas show MAPK pathway alterations most often via BRAF gene fusions or point mutations.

OVERVIEW

Although primary central nervous system (CNS) tumors account for only 2% of all primary cancers, they cause 7% of deaths from cancer in those younger than 70 years old.[1] Median age of primary brain tumors is approximately 60 years and gliomas represent approximately 26% of all primary CNS tumors. Brain tumors are the second most common cancers in children 0 to 14 years old and a leading cause of cancer-related deaths in pediatric population. Gliomas biologically vary from relatively benign, slow growing, and well-demarcated to aggressive rapidly proliferating and diffusely infiltrative tumors. The category of glioma includes tumors originating from the glial cells of the CNS, including astrocytomas, oligodendrogliomas, in both molecular classification has changed the practice of pathology significantly.[2] Until recently, the classification of glioma has been based predominantly on histopathology, based on the resemblance of tumor cells to their presumed normal counterparts. The advance of

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