Astrocytoma IDH-mutant

- Tumor-associated long non-coding RNAs show variable expression across diffuse gliomas and effect on cell growth upon silencing in glioblastoma
- Peripheral biomarkers predict survival in patients with glioblastoma treated with temozolomide
- Cerebrospinal fluid D-2-hydroxyglutarate for IDH-mutant glioma: utility for detection versus monitoring
- Impact of Infection on Survival Outcomes in High-Grade Gliomas: A Retrospective Analysis of 26 Cases in Our Fifteen-Year Experience-Janus Faced Phenomenon
- Do the benefits of IDH mutations in high-grade glioma persist beyond the first recurrence? A multi-institutional retrospective analysis
- Surgical outcomes in high-grade adult type diffuse gliomas (ATDG) with a previous diagnosis of anaplastic astrocytoma without adjuvant therapy
- MTAP immunohistochemistry as a surrogate marker of CDKN2A loss in brain tumors: A meta-analysis and literature review
- A series of 309 awake surgeries with transcortical approach for IDH-mutant low-grade glioma involving the insula: long-term onco-functional outcomes in 253 consecutive patients

Astrocytoma, IDH-mutant tumors are World Health Organization grade 2, World Health Organization grade 3, and World Health Organization grade 4 brain tumors found in adults. They are diffuse infiltrating astrocytic tumors where there is no identifiable border between the tumor and normal brain tissue, even though the borders may appear relatively well-marginated on imaging.

General information

A diffuse astrocytoma with a mutation in either the IDH1 or IDH2 gene. Use of the former term “low-grade glioma” is discouraged.

Since most diffuse astrocytomas carry the IDH mutation, historical data (pre-IDH era) regarding what was formerly called low-grade astrocytomas (WHO grade II) is reflective of the current category to a limited extent.

These tumors tend to occur in children and young adults. They are relatively rare, comprising only ≈ 5% of primary brain tumors, and 15% of all gliomas. Pediatric (age < 20 years) diffuse astrocytomas (IDH mutation status not determined) occur at a rate of 0.26 per 100,000, about half that for adult (0.48).

There is a predilection for temporal, posterior frontal and anterior parietal lobes. In the pediatric population, a significant number occur in the thalamus, which is unusual in adults.

Characterized by slow growth. Most present with seizures.

Classification

● Astrocytoma IDH-mutant Grade 2

- Astrocytoma IDH-mutant Grade 3
- Astrocytoma IDH-mutant Grade 4

Subtypes of IDH-mutant diffuse astrocytoma.

DNA methylation patterns of metabolic genes successfully distinguished the molecular subtypes of IDHmut and IDHwt gliomas. Promoter methylation of lactate dehydrogenase A negatively correlated with protein expression and was associated with IDHmut gliomas. Mitochondrial DNA copy number was increased in IDHmut tumours and did not change in recurrent tumours.Hierarchical clustering based on metabolism panel IHC revealed distinct subclasses of IDHmut and IDHwt gliomas with an impact on patient outcome. Further quantification of these markers allowed for the prediction of survival under antiangiogenic therapy.

A mitochondrial signature was associated with increased survival in all analyses, which could indicate tumour subgroups with specific metabolic vulnerabilities [1].

Gemistocytic astrocytoma IDH-mutant (WHO grade II).

Clinical features

The most common presenting feature (~40% of cases) is a seizure. This is particularly the case in adults. Headaches are often also present. Depending on the size of the lesion and its location, other features may be present, such as hydrocephalus and focal neurological dysfunction, including personality changes.

Diagnosis

T2-Fluid-attenuated inversion recovery (FLAIR) mismatch sign is now known to be a specific yet insensitive image feature for IDH-mutant, 1p19q non-codeleted astrocytoma. The current study revealed that lesion presenting T2-FLAIR mismatch exhibited extremely long T1- and T2-relaxation time while T2-FLAIR matched lesions showed low to moderate values. On the other hand, IDH-wildtype tumors presented noticeably short T1- and T2-relaxation time. These different relaxation time characteristics seemed to render T2-FLAIR mismatch sign of becoming such a unique and specific image feature for IDH-mutant, 1p19q non-codeleted astrocytoma [2].

Pediatric diffuse astrocytoma

see Pediatric diffuse astrocytoma

Pathology

Histology

Low degrees of cellularity with highly differentiated cells and preservation of normal brain elements within the tumor. Calcifications are rare. Anaplasia and mitoses are absent (single mitosis is allowed). Blood vessels may be slightly increased in number. These tumors stain positive for GFAP. In the absence of 1p/19q co-deletion, areas of cells resembling oligodendrogliomas are compatible with the diagnosis.

Molecular genetics

IDH mutation present by definition. ATRX & TP53 mutations support the diagnosis. Prognostically distinct subgroups based on a number of genetic markers have been tentatively identified.

IDH1 / 2 mutated well differentiated diffusely infiltrating glioma with astrocytic features without 1p / 19q codeletion and usually with p53 and / or ATRX mutations.

In the absence of 1p / 19q codeletion, a component morphologically resembling oligodendroglioma is compatible with this diagnosis.

Intrinsic capacity for malignant progression to IDH-mutant anaplastic astrocytoma and eventually to IDH-mutant glioblastoma (Glia 1995;15:211) Accounts for approximately 11 - 15% of all astrocytic brain tumors

Neuroradiology

Usually hypodense on CT. Most are hypointense on T1WI MRI, and show high-intensity changes on T2 weighted image that extend beyond the tumor volume.

Most do not enhance on CT or MRI (although up to 40% do, and these may have a worse prognosis).

Differential diagnosis

Possible imaging differential considerations include:

glioblastoma

may be indistinguishable from grade 4 astrocytoma, IDH-mutant

tends to be in older patients

tends to have a less sizable non-enhancing component

infarction: major vascular territory

cerebritis/encephalitis: herpes simplex encephalitis, ADEM

cortical based tumors: oligodendroglioma, angiocentric glioma

Treatment

Astrocytoma IDH-mutant treatment

Outcome

Diffuse astrocytoma IDH Mutant outcome.

1)
Braun Y, Filipski K, Bernatz S, Baumgarten P, Roller B, Zinke J, Zeiner PS, Ilina E, Senft C, Ronellenfitsch MW, Plate KH, Bähr O, Hattingen E, Steinbach JP, Mittelbronn M, Harter PN. Linking epigenetic signature and metabolic phenotype in IDH mutant and IDH wildtype diffuse glioma. Neuropathol Appl Neurobiol. 2020 Oct 20. doi: 10.1111/nan.12669. Epub ahead of print. PMID: 33080075.
2)
Kinoshita M, Uchikoshi M, Sakai M, Kanemura Y, Kishima H, Nakanishi K. T(2)-FLAIR Mismatch Sign Is Caused by Long T(1) and T(2) of IDH-mutant, 1p19q Non-codeleted Astrocytoma. Magn Reson Med Sci. 2020 Feb 27. doi: 10.2463/mrms.bc.2019-0196. [Epub ahead of print] PubMed PMID: 32101817.