ATRX mutation (Non-core)

Reason/Evidentiary Support

In the setting of a diffuse glioma with an IDH mutation, the diagnosis of an IDH-mutant astrocytoma (including diffuse astrocytoma, anaplastic astrocytoma, and glioblastoma) is supported by the presence of a *TP53* mutation or alteration (mutation or deletion) of the α-thalassemia/mental retardation syndrome X-linked gene (*ATRX*; chromosome Xq21.1).[1-3] Evaluation for these two markers is also commonly used to rule out the possibility of an oligodendroglioma.

Among IDH-mutant tumours, inactivating mutations of *ATRX* appear restricted to those carrying *TP53* mutations and this combination is almost mutually exclusive with codeletion of 1p/19q.[2,4-6] Nearly all diffuse gliomas with IDH and *ATRX* mutations are associated with the alternative lengthening of telomeres (ALT) phenotype. Less commonly, *ATRX* mutations co-occur with H3.3 mutations in paediatric high-grade gliomas, most often in those with G34R/V-mutations.[7]

Documentation of *ATRX* loss/mutations can be achieved in a number of ways, with a practical and cost-effective manner being immunohistochemistry. The loss of nuclear ATRX immunostaining in neoplastic cells, with its maintained expression in non-neoplastic cells, such as endothelial cells or normal glia, is strongly associated with *ATRX* deletion or mutation and can be reliably used as a surrogate of genetic alteration.[6,8,9] Mosaic staining patterns have also been reported, but these are not always associated with ATRX mutation.[10] In combination with immunohistochemistry for IDH1 R132H and p53, ATRX immunohistochemistry provides definitive results in the majority of cases, with the added benefit of preserving cytoarchitecture for microscopic examination.[1,8]

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