Chromosomal arm 1p/19q codeletion (Non-core)

Reason/Evidentiary Support

This cytogenetic alteration refers to whole-arm codeletion of chromosome arms 1p and 19q that together with IDH mutation constitutes the diagnostic molecular criteria for *oligodendroglioma, IDH-mutant and 1p/19q-codeleted, WHO grade II*, as well as *anaplastic oligodendroglioma, IDH -mutant and 1p/19q-codeleted, WHO grade III*.[1] The whole-arm codeletion in oligodendroglial tumours is caused by an unbalanced t(1;19)(q10;p10) translocation.[2,3] Of note, only whole-arm 1p/19q codeletion combined with IDH mutation is the diagnostically relevant marker; partial deletions on either chromosome arm may be found in other types of diffuse gliomas, including IDH-wildtype glioblastomas, and are neither diagnostic for IDH-mutant and 1p/19q-codeleted oligodendroglial tumours[1] nor associated with favourable patient outcome.[4] Moreover, detection of 1p/19q codeletion in the absence of IDH mutation is suspicious of partial deletions, and by definition is not sufficient for a diagnosis of an IDH-mutant and 1p/19q-codeleted oligodendroglial tumour.

Various techniques are being used for the diagnostic assessment of 1p/19q codeletion. Commonly used methods include microsatellite analysis for loss of heterozygosity (LOH), FISH or CISH, and multiplex ligation-dependent probe amplification (MLPA). FISH/CISH can be applied on routine FFPE sections. However, analysis is often restricted to single loci on each chromosome arm, which may not reliably distinguish whole-arm losses from partial deletions. There is no standardized cut-off for determination of codeletion by FISH/CISH, with each laboratory needing to validate its assay. In addition, polysomies of chromosomes 1 or 19 may complicate diagnostic assessment and have been associated with less favourable outcome.[5-7] LOH analysis and MLPA assess multiple loci along each chromosome arm and thereby reduce the risk of false-positive findings due to partial deletions. However, extraction of tumour DNA (for MLPA) as well as tumour and leukocyte DNA (for LOH analysis) is required for these techniques. Microarray-based approaches may also be used for diagnostic purposes, including DNA methylation bead arrays that allow for simultaneous detection of 1p/19q codeletion, *MGMT* promoter methylation, and G-CIMP status indicative of IDH mutation.[8] Most recently, panel-based NGS approaches have been used for 1p/19q detection and simultaneous mutational analyses of *IDH1* and *IDH2*, a well as other alterations commonly associated with 1p/19q codeletion, such as *TERT* promoter mutation and *CIC* mutation.[9,10] Immunostaining for the proneural α-internexin protein[11,12] or NOGO-A[13] cannot substitute as a surrogate marker for 1p/19q codeletion.

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