IDH1 & IDH2 Mutation in Glioma and Chondrosarcoma

IDH1 and IDH2 mutation tests are useful for diagnosis and prognosis of glioma and for subclassifying sarcoma. (In fresh blood or marrow, use the Myeloid Mutation Panel.)

Pathobiology: Mutation in an isocitrate dehydrogenase gene is associated with some glial neoplasms. Relevant mutations are IDH1 (c.394-396 [R132H & variants]) or less commonly in IDH2 (c.514-516 [R172K & variants]). Mutation can induce 2-hydroxyglutarate that outcompetes alpha ketoglutarate in energy metabolism, inhibiting prolyl hydroxylases that break down HIF and may spur angiogenesis. Other effects include reactive oxygen species damaging DNA, and gene promoter hypermethylation affecting expression.

Testing assists in differential diagnosis of brain lesions. Astrocytic and oligodendrogial neoplasms harboring IDH mutation generally have a better prognosis. Secondary grade IV tumors arising from low grade glioma frequently harbor IDH mutation, but primary grade IV glioblastoma does not. Benign lesions lacking IDH mutation include inflammation, infection, ischemia/infarct, demyelination, and reactive gliosis which can mimic glioma histologically.

About 60% of chondrosarcomas harbor IDH mutation which helps distinguish them from chondroblastic osteosarcomas.

Experimental targeted therapy thwarting IDH enzyme activity is available in clinical trials.

Clinical Indications: 1) To classify glioma. 2) In differential diagnosis of glioma vs other neoplastic or reactive brain lesions. 3) To help differentiate chondrosarcoma from chondroblastic osteosarcoma.

Laboratory testing: The preferred specimen is paraffin-embedded brain tissue with a high proportion of atypical/tumor cells, provided as 10 unstained slides (plain glass) and an H&E-stain marked by a pathologist to indicate the most atypical, tumor-rich region (e.g. >20% malignant cells). After macrodissection, segments of DNA containing IDH1 exon 2 and IDH2 exon 4 are amplified and pyrosequenced. Results are interpreted by a pathologist.

References:

To consult a pathologist about indications for testing or significance of results, call the Molecular Genetics Lab at (984) 974-1825 or Dr. Gulley at (919) 843-4595.
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