Pilocytic Astrocytoma Diagnosis

Diagnosis may be made on histologic features alone (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4436848/) When microscopic findings are limited/ambiguous, molecular testing may be necessary to assess for gene fusions and other alterations

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Wang et al. suggested that NCKAP1L, GPR37L1, CSPG4, PPFIA4, and C8orf46 are potential biomarkers for the pilocytic astrocytoma diagnosis [1].

Pricola Fehnel et al., report the use of urinary biomarkers as a novel, noninvasive technique to detect juvenile pilocytic astrocytomas (JPAs), capable of distinguishing JPAs from other CNS diseases, including other brain tumors. Preliminary screening of an array of tumors implicated proteases (including matrix metalloproteinases [MMPs]) and their inhibitors (tissue inhibitors of metalloproteinase [TIMPs]) as well as growth factors (including basic fibroblast growth factor [bFGF]) as candidate biomarkers. These data led the authors to hypothesize that tissue inhibitor of metalloproteinase 3 (TIMP3) and bFGF would represent high-probability candidates as JPA-specific biomarkers.

Urine was collected from 107 patients, which included children with JPA (n = 21), medulloblastoma (n = 17), glioblastoma (n = 9), arteriovenous malformations (n = 25), moyamoya (n = 14), and age- and sex-matched controls (n = 21). Biomarker levels were quantified with enzyme-linked immunosorbent assay, tumor tissue expression was confirmed with immunohistochemical analysis, and longitudinal biomarker expression was correlated with imaging. Results were subjected to univariate and multivariate statistical analyses.

Using optimal urinary cutoff values of bFGF > 1.0 pg/µg and TIMP3 > 3.5 pg/µg, multiplexing bFGF and TIMP3 predicts JPA presence with 98% accuracy. Multiplexing bFGF and MMP13 distinguishes JPA from other brain tumor subtypes with up to 98% accuracy. Urinary biomarker expression correlated with both tumor immunohistochemistry and in vitro tumor levels. Urinary bFGF and TIMP3 decrease following successful tumor treatment and correlate with changes in tumor size.

This study identifies 2 urinary biomarkers-bFGF and TIMP3-that successfully detect one of the most common pediatric brain tumors with high accuracy. These data highlight the potential benefits of urinary biomarkers and support their utility as diagnostic tools in the treatment of children with JPA [2].

Radiographic features

Preoperative MRI of the entire neuraxis (brain, cervical, thoracic, and lumbar spine) without and with contrast is recommended when possible to evaluate for dissemination through the CSF (rare) and in case it proves to be a different pathology.

On CT or MRI, PCAs are usually well-circumscribed, 94% enhance with contrast [3] (unlike most low-

grade fibrillary astrocytomas), frequently have a cystic component with a mural nodule (especially cerebellar PCAs), and have little or no surrounding edema. The cyst wall may or may not enhance. PCAs involving the optic apparatus are typically fusiform.

Although they may occur anywhere in the CNS, 82% are periventricular [4].

Calcifications are only occasionally present [5].

General

Pilocytic astrocytomas range in appearance:

large cystic component with a brightly enhancing mural nodule: 67%

non-enhancing cyst wall: 21%

enhancing cyst wall: 46%

heterogeneous, mixed solid and multiple cysts and central necrosis: 16%

completely solid: 17%

Enhancement is almost invariably present (~95%). Up to 20% may demonstrate some calcification. Hemorrhage is an uncommon complication.

MRI

T1

solid component: iso to hypointense compared to adjacent brain

cystic component: ~fluid signal unless hemorrhage

T1 C+

vivid contrast enhancement

the cyst wall enhances in ~50% cases

T2

solid component: hyperintense compared to adjacent brain

cystic component: high signal

T2*:

signal loss if calcification or hemorrhage present

[1)]

Wang G, Jia Y, Ye Y, Kang E, Chen H, Wang J, He X. Clinical and Epidemiological Study of Intracranial Tumors in Children and Identification of Diagnostic Biomarkers for the Most Common Tumor Subtype and Their Relationship with the Immune Microenvironment Through Bioinformatics Analysis. J Mol Neurosci. 2022 Mar 28. doi: 10.1007/s12031-022-02003-z. Epub ahead of print. PMID: 35347632.

[2)]

Pricola Fehnel K, Duggins-Warf M, Zurakowski D, McKee-Proctor M, Majumder R, Raber M, Han X, Smith ER. Using urinary bFGF and TIMP3 levels to predict the presence of juvenile pilocytic astrocytoma and establish a distinct biomarker signature. J Neurosurg Pediatr. 2016 Oct;18(4):396-407. PubMed PMID: 27314542.

[3)] , [4)] , [5)]

Coakley KJ, Huston J, Scheithauer BW, et al. Pilocytic Astrocytomas: Well-Demarcated Magnetic Resonance Appearance Despite Frequent Infiltration Histologically. Mayo Clin Proc. 1995; 70: 747–751