Germ cell tumor biomarker

Tumor Markers in Serum or CSF:

1. **Alpha-Fetoprotein (AFP)**: Elevated in yolk sac tumors.
1. **Beta-Human Chorionic Gonadotropin (β-hCG)**: Elevated in choriocarcinomas or some germinomas

see also Pineal germinoma serum and cerebrospinal fluid biomarkers.

Germ cell tumor characteristically (but not always) give rise to tumor markers in the CSF.

Biomarkers of Germ Cell Tumors

Tumor Subtype	Alpha-Fetoprotein	Beta Human Chorionic Gonadotropin	Placental Alkaline Phosphatase
Germinoma		+/– [b]	+
Teratoma	+/– [a]		
Embryonal carcinoma	+	+/– [b]	
Choriocarcinoma		+	
Endodermal sinus tumor (yolk sac carcinoma)	+		

a) Mature teratomas tend to be negative for serum and cerebrospinal fluid alpha-fetoprotein.

Alpha-fetoprotein (AFP) is elevated with endodermal sinus tumors, embryonal carcinoma and occasionally with teratomas. Elevated placental alkaline phosphatase (PLAP) in serum or CSF occurs with intracranial germinomas.

When positive, tumor markers can be followed serially to assess treatment and to look for recurrence (they should be checked in serum and CSF). NB: tumor markers alone are not usually sufficient for making a definitive diagnosis of a pineal region tumor since many of these tumors are mixed cell types.

Since tumors may be of mixed cell types, CSF tumor markers (β-hCG, AFP…) are not as useful for diagnosis as they are for following response to treatment.

A study aimed to establish the detectability of circulating tumor DNA (ctDNA) from cerebrospinal fluid (CSF) of children with Central Nervous System Germ Cell Tumor as a potential biomarker. They obtained CSF from patients with CNS-GCT by lumbar puncture or intra-operatively. Cell-free DNA (cfDNA) was extracted and subjected to low-pass whole genome sequencing (LP-WGS). Copy-number alterations (CNAs) were inferred and served as a marker of measurable residual disease (MRD). Comparisons with imaging findings and tumor marker levels were made. A total of 29 CSF samples from 21 patients (16 with germinoma, 5 with non-germinomatous GCT) were sequenced. Twenty samples from 19 patients were collected at diagnosis, and 9 samples from 7 patients were collected during or after therapy. Among the diagnostic samples, CNAs were detected in samples from 17/19

patients (89%), which included 8 with marker-negative tumors. Specific clinical scenarios suggested that serial cfDNA analysis may carry utility in tracking treatment responses as well as clarifying indeterminate imaging findings. Our results provide evidence for the high sensitivity in detecting ctDNA from CSF of CNS-GCT patients using LP-WGS, with potential utility for non-invasive diagnosis and disease monitoring in upcoming CNS-GCT studies [1)].

1)
Nakano Y, Burns I, Nobre L, Siddaway R, Rana M, Nesvick C, Bondoc A, Ku M, Yuditskiy R, Ku DTL, Shing MMK, Cheng KKF, Ng HK, Das A, Bennett J, Ramaswamy V, Huang A, Malkin D, Ertl-Wagner B, Dirks P, Bouffet E, Bartels U, Tabori U, Hawkins C, Liu APY. High detection rate of circulating-tumor DNA from cerebrospinal fluid of children with central nervous system germ cell tumors. Acta Neuropathol Commun. 2024 Nov 20;12(1):178. doi: 10.1186/s40478-024-01886-w. PMID: 39568077.