Paraganglioma

AKA chemodectoma (obsolete), AKA glomus tumor. A WHO grade I neuroendocrine tumor that arises from specialized neural crest cells associated with autonomic ganglia, comprised of uniform cells with neural differentiation conglomerated into compact nests (Zellballen) surrounded by a capillary network.

Paragangliomas in the CNS are rare, and they primarily occur in the cauda equina/filum terminale of jugulotympanic regions. Outside the CNS, paragangliomas are often designated by a name that confers the site of origin.

carotid bifurcation (most common) - carotid body tumors

auricular branch of vagus (middle ear) - glomus tympanicum

superior vagal ganglion (jugular foramen) - glomus jugulare

inferior vagal (nodose) ganglion (nasopharynx at skull base) (least common) - glomus intravagale (AKA glomus vagale)

adrenal medulla & sympathetic chain-pheochromocytoma

These tumors arise from paraganglion cells (not chemoreceptor cells as previously thought; therefore the term chemodectoma is rarely used). Slow growing tumors (< 2 cm in 5 years). Histologically benign (< 10% associated with lymph node involvement or distant spread). Most contain secretory granules on EM (mostly epinephrine & norepinephrine, and these tumors may occasionally secrete these catecholamines with risk of life-threatening HTN and/or cardiac arrhythmias).

Glomus tumors may occur in 2 patterns:

1. familial: non multicentric. Up to 50%

2. nonfamilial: may be multicentric (metachronous) 5%

Classification

see Cerebellopontine angle paraganglioma
see Jugular paraganglioma

see Jugulotympanic paraganglioma

see Vagal paraganglioma

Spinal paraganglioma: paraganglioma (of the filum terminale)

**Etiology**

These tumors arise from paraganglion cells (not chemoreceptor cells as previously thought, therefore the term chemodectoma is losing favor). Slow growing tumors (<2 cm in 5 years). Histologically benign (<10% associated with lymph node involvement or distant spread). Most contain secretory granules on EM (mostly epinephrine & nor-epinephrine, and these tumors may occasionally secrete these catecholamines with risk of life-threatening HTN and/or cardiac arrhythmias).

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SDHB mutations are found in an increasing number of neoplasms, most notably paragangliomas and pheochromocytomas (SDHB-PPGLs). SDHB-PPGLs are slow-growing tumors, but about 50% of them may develop metastasis. The molecular basis of metastasis in these tumors is a long-standing and unresolved problem. Thus, a better understanding of the biology of metastasis is needed.

A study aimed to identify gene methylation changes relevant for metastatic SDHB-PPGLs.

They performed genome-wide profiling of DNA methylation in diverse clinical and genetic PPGL subtypes, and validated protocadherin gamma-C3 (PCDHGC3) gene promoter methylation in metastatic SDHB-PPGLs.

They defined an epigenetic landscape specific for metastatic SDHB-PPGLs. DNA methylation levels were found significantly higher in metastatic SDHB-PPGLs than in SDHB-PPGLs without metastases. One such change included long-range de novo methylation of the PCDHA, PCDHB and PCDHG gene clusters. High levels of PCDHGC3 promoter methylation were validated in primary metastatic SDHB-PPGLs, it was found amplified in the corresponding metastases and it was significantly correlated with PCDHGC3 reduced expression. Interestingly, this epigenetic alteration could be detected in primary tumors that developed metastasis several years after. We also show that PCDHGC3 downregulation engages metastasis-initiating capabilities by promoting cell proliferation, migration and invasion.

This data provide the first map of the DNA methylome episignature specific to a SDHB-mutated cancer and establish PCDHGC3 as a putative suppressor gene and a potential biomarker to identify SDHB-mutated cancer patients at high risk of metastasis who might benefit from future targeted therapies 1).

**Immunohistochemical staining patterns**

GFAP -

CAM5.2 not decisive for that particular tumor
EMA -

S-100 not decisive for that particular tumor

CgA +

Syn +

**Outcome**

About 97% are benign and cured by surgical removal; the remaining 3% are malignant because they are able to produce distant metastases.

**Case series**

Shibao et al. from the Keio University School of Medicine, Tokyo, retrospectively analyzed data from patients with CBTs who underwent transarterial embolization or angiographic examination-only between July 2010 and February 2017. The arterial supply of the tumors, the number of feeder pedicles, the mean tumor size, embolization materials, complication of embolization, and extent of tumor removal were assessed. The embryological origin of feeding artery was considered based on the literature.

Eighteen patients with 20 CBTs underwent preoperative embolization or angiographic examination. The number of feeder pedicles was significantly related to the size of the CBT (p = 0.0002). The main feeding artery was the descending branch of ascending pharyngeal artery (APhA), which was hypertrophied and tortuous (18/20, 90%). Embryologically, this artery originated from the musculospinal branch and is termed the “descending musculospinal branch”.

The main feeder of the CBTs was the “descending musculospinal branch” of the APhA and needs special consideration such as dangerous anastomosis for embolization ²).

**References**

