Craniopharyngioma Pathogenesis and Implications for Medical Management

Saksham Gupta, BA; Wenya Linda Bi, MD, PhD; Pratiti Bandopadyay, MBBS, PhD; Sandro Santagata, MD, PhD; Edward R. Laws Jr., MD; Ian F. Dunn, MD
Department of Neurosurgery, Brigham and Women’s Hospital, Boston MA

Background

- Craniopharyngiomas arise from squamous cell rests of the craniopharyngeal duct
- Two histologic subtypes: adamantinomatous and papillary craniopharyngioma (ACP and PCP)
- ACPs (A-I) and PCPs (J-O) manifest with a spectrum of appearances on MRI. The cystic nature of these lesions are highlighted on post-contrast T1-weighted MRI.
- Growing understanding of ACP/PCP biology is motivating pre-clinical and clinical studies of targeted therapies

Papillary Craniopharyngioma

Fig 1. PCP Pathogenesis and Molecular Targets

- PCP occurs predominantly in adults and generally has a more indolent clinical course
- The V600E mutation in BRAF, which are implicated in melanoma, is present in up to 95% of PCP
- A case report of B-Raf inhibitor vemurafenib in PCP demonstrated significant reduction in tumor burden
- A case report of B-Raf inhibitor dabrafenib and MEK inhibitor tramatenib also demonstrated positive response in PCP

Adamantinomatous Craniopharyngioma

Fig 2. ACP Pathogenesis and Molecular Targets

- A paracrine cancer stem cell model of pathogenesis has been proposed in ACP
- The Wnt/β-Catenin pathway is upregulated in ACP and β-Catenin expression is associated with poorer outcomes
- Multiple growth factors and their receptors are upregulated in ACP
- Extracellular matrix and immuno microenvironment factors have also been implicated
- ATRA and erlotinib have demonstrated efficacy in in vivo models of ACP; multiple targeted therapies have demonstrated efficacy in in vitro models of ACP

Citations