Molecular mechanisms of brain tumor edema.

Papadopoulos MC, Saadoun S, Binder DK, Manley GT, Krishna S, Verkman AS.
Department of Neurosurgery, St. George's Hospital Medical School, London SW17 0NE, UK. mpapadop@sghms.ac.uk

Abstract

Despite their diverse histological types, most brain tumours cause brain oedema, which is a significant cause of patient morbidity and mortality. Brain tumour oedema occurs when plasma-like fluid enters the brain extracellular space through impaired capillary endothelial tight junctions in tumours. Under-expression of the tight junction proteins occludin, claudin-1 and claudin-5 are key molecular abnormalities responsible for the increased permeability of tumour endothelial tight junctions. Recent evidence suggests that the membrane water channel protein aquaporin-4 (AQP4) also plays a role in brain tumour oedema. AQP4-deficient mice show remarkably altered brain water balance after various insults, including brain tumour implantation. AQP4 expression is strongly upregulated around malignant human brain tumours in association with reduced extracellular volume, which may restrict the flow of extracellular fluid from the tumour bed into the brain parenchyma. Elimination of excess fluid leaking into brain parenchyma requires passage across three AQP4-rich barriers: a) the glia limitans externa, b) the glia limitans interna/ependyma, and c) the blood-brain barrier. Modulation of the expression and/or function of endothelial tight junction proteins and aquaporins may provide novel therapeutic options for reducing brain tumour oedema.

PMID: 15561416 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources