Embryonal tumor with multilayered rosettes

Previously embryonal tumors with multilayered rosettes (ETMR) where known as embryonal tumor with abundant neuropil and true rosettes (ETANTR). This term has, however, been removed from the World Health Organization Classification of Tumors of the Central Nervous System 2016 in favour of embryonal tumours with multilayered rosettes (ETMR) which incorporates not only ETANTR but also ependymoblastoma and CNS PNET which have also been removed from the classification.

This has resulted due to the presence of amplification of the C19MC region on chromosome 19 in both CNS PNET and ETANTR, suggesting that these are the one entity with variable growth pattern [1)]

Embryonal tumor with multilayered rosettes (ETMR) is a rare and aggressive embryonal brain tumor that solely occurs in infants and young children and has only recently been recognized as a separate brain tumor entity in the World Health Organization Classification of Tumors of the Central Nervous System 2016.

Patients have a very dismal prognosis with a median survival of 12 months upon diagnosis despite aggressive treatment. The aim of a study was to develop novel treatment regimens in a pre-clinical drug screen in order to inform potentially more active clinical trial protocols.

BT183 cells are very sensitive to the topoisomerase inhibitors topotecan and doxorubicin, to the epigenetic agents decitabine and panobinostat, to actinomycin D, and to targeted drugs such as the PLK1 inhibitor volasertib, aurora kinase A inhibitor alisertib, and the mTOR inhibitor MLN0128. In xenograft mice, monotherapy with topotecan, volasertib, and actinomycin D, led to a temporarily response in tumor growth and a significant increase in survival. Finally, using multi-agent treatment regimens of topotecan or doxorubicin combined with methotrexate and vincristine the response in tumor growth and survival was further increased compared to mice receiving single treatments [2)].

The presence of C19MC amplification results in a diagnosis of embryonal tumor with multilayered rosettes (ETMR), C19MC-altered. In the absence of C19MC amplification, a tumor with histological features conforming to ETANTR/ ETMR should be diagnosed as embryonal tumor with multilayered rosettes, NOS, and a tumor with histological features of medulloepithelioma should be diagnosed as medulloepithelioma (recognizing that some apparently bona fide medulloepitheliomas do not have C19MC amplification).

1)
Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016 Jun;131(6):803-20. doi: 10.1007/s00401-016-1545-1. Epub 2016 May 9. Review. PubMed PMID: 27157931.
2)
Schmidt C, Schubert NA, Brabetz S, Mack N, Schwalm B, Chan JA, Selt F, Herold-Mende C, Witt O, Milde T, Pfister SM, Korshunov A, Kool M. Pre-clinical drug screen reveals topotecan, actinomycin D and volasertib as potential new therapeutic candidates for ETMR brain tumor patients. Neuro Oncol. 2017 May 8. doi: 10.1093/neuonc/nox093. [Epub ahead of print] PubMed PMID: 28482026.