

ABSTRACT

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Atypical Teratoid/Rhabdoid Tumor (AT/RT) With Molecular Features of Pleomorphic Xanthoastrocytoma.

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Atypical teratoid/rhabdoid tumor (AT/RT) is a highly malignant central nervous system tumor predominantly occurring in infants that may also arise in older children and adults. Rare secondary AT/RT developing from other tumors such as pleomorphic xanthoastrocytoma (PXA) are on record, but AT/RT presenting with molecular features of PXA have not been described. Here, we report 3 malignant central nervous system tumors in children (10, 13, and 18 y old). All tumors were located in the temporal lobe. In 2 cases, there was no history of a low-grade precursor lesion; in 1 case anaplastic PXA had been diagnosed 3 months earlier. Histopathologically, all tumors were composed of RT cells and showed frank signs of malignancy as well as loss of nuclear SMARCB1/INI1 protein expression. Two cases displayed homozygous deletions of the SMARCB1 region while the third case showed an exon 7 mutation (c.849_850delGT; p.Met283Ilefs*77). Of note, DNA methylation profiles did not group with AT/RT or other tumor entities using the Heidelberg Brain Tumor Classifier (version v11b4). By unsupervised t-distributed stochastic neighbor embedding analysis and hierarchical clustering analysis, however, all tumors clearly grouped with PXA. Genome-wide copy number analysis revealed homozygous CDNK2A/B deletions and gains of whole chromosome 7. BRAF V600E mutations could be demonstrated in all cases. In conclusion, the possibility of AT/RT with molecular features of PXA needs to be taken into account and warrants molecular characterization of AT/RT especially in older children. Since treatments targeting mutated BRAF are available, identification of such cases may also have therapeutic consequences.

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