SMARCB1 in Atypical teratoid rhabdoid tumor

Identification of loss of SMARCB1/INI1 expression in poorly differentiated (PD) chordoma in pediatric patients suggests that PD chordoma is an entity molecularly distinct from conventional chordoma or Atypical teratoid rhabdoid tumor, which is also characterized by loss of SMARCB1/INI1 expression by inactivating mutation of the SMARCB1/INI gene. So far, around 20 cases of pediatric PD chordoma with loss of SMARCB1/INI1 expression have been reported.

Cha et al. report two cases of pediatric PD chordoma with loss of SMARCB1/INI1 expression, which is very rare among the pediatric chordoma types. Both patients presented clival masses on preoperative MRI. Histologically, both tumors had nonclassic histologic features for conventional chordoma: sheets of large epithelioid to spindle cells with vesicular nuclei and prominent nucleoli. Both cases revealed nuclear expression of brachyury, loss of SMARCB1/INI1 expression and lack of embryonal, neuroectodermal, or epithelial component. One case showed heterozygous loss of EWSR1 gene by break-apart fluorescence in situ hybridization that reflected loss of SMARCB1/INI1 gene. Based on the clival location and histologic findings along with the loss of SMARCB1/INI1 expression and positivity for nuclear brachyury staining, the final pathologic diagnosis for both cases was PD chordoma [1].

In a study, Torchia et al analyzed 191 primary Atypical teratoid rhabdoid tumor ATRTs and 10 ATRT cell lines to define the genomic and epigenomic landscape of ATRTs and identify subgroup-specific therapeutic targets. They found ATRTs segregated into three epigenetic subgroups with distinct genomic profiles, SMARCB1 genotypes, and chromatin landscape that correlated with differential cellular responses to a panel of signaling and epigenetic inhibitors. Significantly, they discovered that differential methylation of a PDGFRB-associated enhancer confers specific sensitivity of group 2 ATRT cells to dasatinib and nilotinib, and suggest that these are promising therapies for this highly lethal ATRT subtype [2].

References

[1]
Cha YJ, Hong CK, Kim DS, Lee SK, Park HJ, Kim SH. Poorly differentiated chordoma with loss of SMARCB1/INI1 expression in pediatric patients: A report of two cases and review of the literature. Neuropathology. 2017 Aug 15. doi: 10.1111/neup.12407. [Epub ahead of print] PubMed PMID: 28812319.

[2]
Torchia J, Golbourn B, Feng S, Ho KC, Sin-Chan P, Vasiljevic A, Norman JD, Guilhamon P, Garzia L, Agamez NR, Lu M, Chan TS, Picard D, de Antonellis P, Khuong-Quang DA, Planello AC, Zeller C, Barsyte-Lovejoy D, Lafay-Cousin L, Letourneau L, Bourgey M, Yu M, Gendoo DM, Dzamba M, Barszczyk M, Medina T, Riemenschneider AN, Morrissy AS, Ra YS, Ramaswamy V, Remke M, Dunham CP, Yip S, Ng HK, Lu JQ, Mehta V, Albrecht S, Pimentel J, Chan JA, Somers GR, Faria CC, Roque L, Fouladi M, Hoffman LM, Moore AS, Wang Y, Choi SA, Hansford JR, Catchpoole D, Birks DK, Foreman NK, Strother D, Klekner A, Bognár L, Garami M, Hauser P, Hortobágyi T, Wilson B, Hukin J, Carret AS, Van Meter TE, Hwang EI, Gajjar A, Chiou SH, Nakamura H, Toledano H, Fried I, Fults D, Wataya T, Fryer C, Eisenstat DD, Scheinemann K, Fleming AJ, Johnston DL, Michaud J, Zelcer S, Hammond R, Afzal S, Ramsay DA, Sirachainan N, Hongeng S, Larbcharoensub N, Grundy RG, Lulla RR, Fangusaro JR, Druker H, Bartels U, Grant R, Malkin D, McGlade CJ, Nicolaides T, Tihan T, Phillips J, Majewski J, Montpetit A, Bourque G, Bader GD, Reddy AT, Gillespie GY, Warmuth-Metz M, Rutkowski S, Tabori U, Lupien M, Brudno M, Schüller U, Pietsch T, Judkins AR, Hawkins CE, Bouffet E, Kim SK, Dirks PB, Taylor MD, Erdreich-Epstein A, Arrowsmith CH, De Carvalho DD, Rutka JT, Jabado N, Huang A. Integrated (epi)-Genomic Analyses

Identify Subgroup-Specific Therapeutic Targets in CNS Rhabdoid Tumors. Cancer Cell. 2016 Dec 12;30(6):891-908. doi: 10.1016/j.ccell.2016.11.003. PubMed PMID: 27960086.