Pancreatic undifferentiated rhabdoid carcinoma: KRAS alterations and SMARCB1 expression status define two subtypes.

Pancreatic undifferentiated carcinoma is a heterogeneous group of neoplasms, including pleomorphic giant cell, sarcomatoid, round cell, and rhabdoid carcinomas, the molecular profiles of which have so far been insufficiently characterized. We studied 14 undifferentiated carcinomas with prominent rhabdoid cells, occurring as advanced tumors in seven females and seven males aged 44-96 years (mean: 65 years). Histologically, 10 tumors qualified as pleomorphic giant cell and 4 as monomorphic anaplastic carcinomas. A glandular component, either in the primary or in the metastases, was seen in 5 out of 14 tumors (4 out of 10 pleomorphic giant cell and 1 out of 4 monomorphic anaplastic subtypes, respectively). Osteoclast-like giant cells were absent. Immunohistochemistry revealed coexpression of cytokeratin and vimentin, and loss of membranous β-catenin and E-cadherin staining in the majority of cases. Nuclear SMARCB1 (INI1) expression was lost in 4 out of 14 cases (28%), representing all 4 tumors of the monomorphic anaplastic subtype. FISH and mutation testing of KRAS revealed KRAS amplification in 5 out of 13 (38%) and exon 2 mutations in 6 out of 11 (54%) successfully analyzed cases. A strong correlation was found between KRAS alterations (mutation...
and/or copy number changes) and intact SMARCB1 expression (7 out of 8; 87%). On the other hand, loss of SMARCB1 expression correlated with the absence of KRAS alterations (3 out of 5 cases; 60%). The results suggest that rhabdoid phenotype in pancreatic undifferentiated rhabdoid carcinomas has a heterogeneous genetic background. SMARCB1 loss is restricted to the anaplastic monomorphic subtype and correlates with the absence of KRAS alterations, whereas the pleomorphic giant cell subtype is characterized by KRAS alterations and intact SMARCB1 expression. Recognition and appropriate subtyping of these rare variants might become necessary for future therapeutic strategies.