

# Dedifferentiated chordoma

Dedifferentiated [chordoma](#) is defined as a high-grade [sarcoma](#) lacking notochordal differentiation, which arises in association with conventional [chordoma](#). The mechanism underlying dedifferentiation remains unclear.

Makise et al. immunohistochemically investigated trimethylation at lysine 27 of histone 3 ([H3K27me3](#)) in nine dedifferentiated chordomas.

The tumors occurred at the skull base (N = 5) or the sacrum (N = 4) in four men and five women with a median age of 50 years. Dedifferentiation occurred de novo in four cases and at recurrence/metastasis in five cases. Five tumors retained H3K27me3, whereas four showed complete loss of H3K27me3 only in the dedifferentiated component, while the conventional chordoma component retained H3K27me3. All the H3K27me3-negative tumors showed co-loss of dimethylation at H3K27 (H3K27me2), consistent with the inactivation of polycomb repressive complex 2. Two genetically analyzed tumors harbored EED homozygous deletions. All four H3K27me3-negative dedifferentiated chordomas affected the skull base of young or middle-aged women. Unlike dense proliferation of highly pleomorphic spindle or epithelioid cells in the H3K27me3-positive dedifferentiated chordomas, all H3K27me3-negative tumors displayed swirling fascicles of relatively uniform spindle cells with alternating cellularity and perivascular accentuation, resembling malignant peripheral nerve sheath tumor (MPNST). Rhabdomyoblastic differentiation was present in one H3K27me3-negative tumor.

Makise et al. identified a novel group of dedifferentiated [skull base chordoma](#) that lost [H3K27me3/me2](#) only in the dedifferentiated component, which was associated with EED homozygous deletion and [malignant peripheral nerve sheath tumor](#) (MPNST)-like histology. This data suggest a distinct “[polycomb](#)-type” dedifferentiation pathway in [chordoma](#), similar to a recently described dedifferentiated [chondrosarcoma](#) with H3K27me3 loss <sup>1)</sup>

<sup>1)</sup>

Makise N, Shimoi T, Sunami K, Aoyagi Y, Kobayashi H, Tanaka S, Kawai A, Yonemori K, Ushiku T, Yoshida A. Loss of [H3K27](#) trimethylation in a distinct group of dedifferentiated [chordoma](#) of the [skull base](#). Histopathology. 2022 Oct 11. doi: 10.1111/his.14823. Epub ahead of print. PMID: 36217885.

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