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SATB2 and TLE1 Expression in *BCOR-CCNB3* (Ewing-like) Sarcoma, Mimicking Small Cell Osteosarcoma and Poorly Differentiated Synovial Sarcoma

To the Editor:

Pieron et al[1] identified recurrent gene fusions of *BCOR* (encoding Bcl-6 interacting corepressor) and *CCNB3* (cyclin B3) in a subset of primitive and, so far, undifferentiated primary bone sarcomas with predominantly Ewing sarcoma–like round cell morphology (Ewing-like tumors).[1,2] However, later series reported apart from a Ewing-like round cell morphology tumors with a prominent spindle cell, epithelioid and/or myxoid tumor component, expanding the list of differential diagnoses, including malignant peripheral nerve sheath tumors, synovial sarcomas, and myxofibrosarcomas (Figs. 1A–C).[3–5] Moreover, despite the described preference for the skeletons of male adolescents, *BCOR-CCNB3*-positive sarcomas can also occur in patients aged above 30 years and may originate in soft tissues. Of note, SATB2 (special AT-rich sequence-binding protein 2) (known as a "osteoblastic" marker) and TLE1 (transducin-like enhancer of

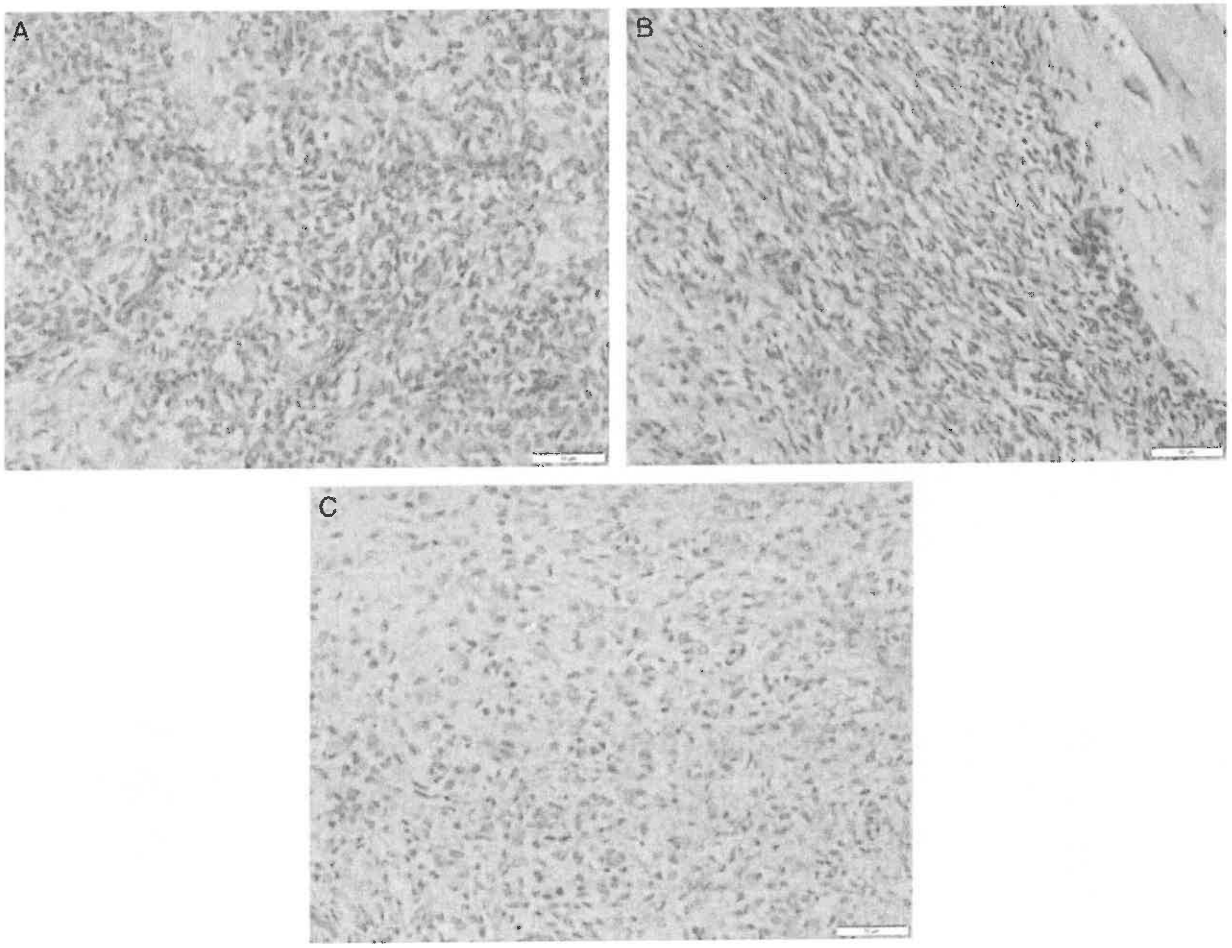

FIGURE 1. Histomorphology of a *BCOR-CCNB3* sarcoma. A, "Ewing-like" round cell morphology with compact nests of undifferentiated round-to-ovoid tumor cells with scant cytoplasm and irregular nuclei. Note the dense (osteoid like) collagen deposition between the tumor cells, mimicking small cell osteosarcoma (hematoxylin & eosin staining, original magnification ×200). B, "Synovial sarcoma-like" or malignant peripheral nerve sheath tumor-like spindle cell tumor component composed of fascicles of hypercellular plump fusiform cells (hematoxylin & eosin staining, original magnification ×200). C, Epithelioid tumor areas composed of epithelioid tumor cells with mildly atypical nuclei (hematoxylin & eosin staining, original magnification ×200).

The author declares no conflict of interest.

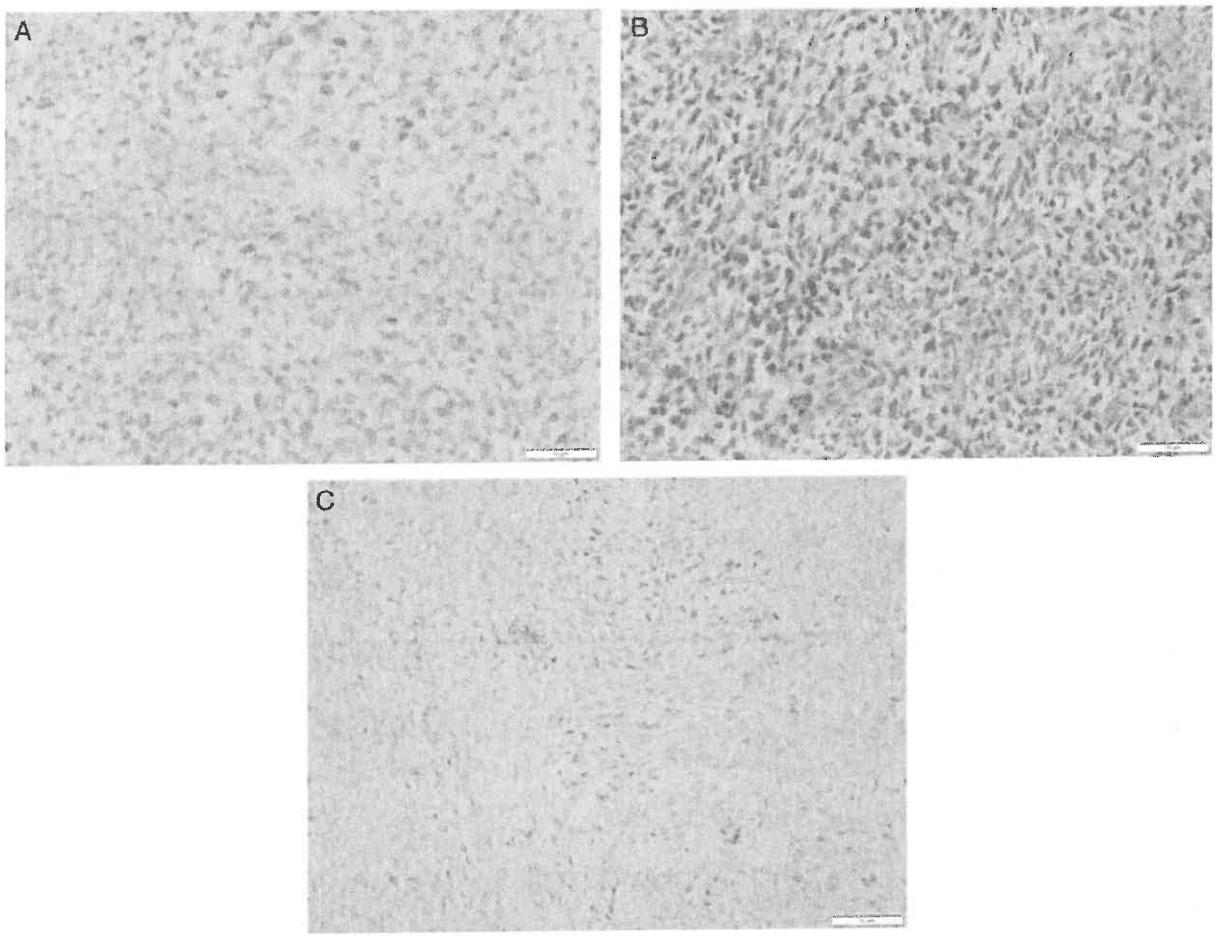

FIGURE 2. Nuclear SATB2 (A, original magnification ×400), TLE1 (B, original magnification ×400) and BCOR (C, original magnification ×200) immunoreactivity in *BCOR-CCNB3* sarcoma. full color online

split 1) (known as a sensitive and robust diagnostic marker for synovial sarcoma) are commonly expressed in this group of tumors, which could lead to the misdiagnosis of a small cell osteosarcoma or poorly differentiated synovial sarcoma, respectively.[4,6–9] Four additional BCOR-CCNB3-positive cases were analyzed at our pathology department. Immunohistochemistry was performed using an immunostainer (Benchmark XT; Ventana Medical systems, Tucson, AZ), according to the manufacturer's instructions. The 4-μm sections were immunostained with primary antibodies against SATB2 (1:250, polyclonal; Sigma, St. Louis, MO) and TLE1 (1:10, polyclonal; Santa Cruz Biotechnology, Dallas, TX).

All 4 cases showed SATB2 nuclear staining of moderate intensity in a patchy (3 cases) to diffuse manner (1 case) (Fig. 2A). Moderate to strong TLE1 nuclear staining was observed in 3 cases, focally in 1 case and diffuse in 2 cases (Fig. 2B). Hence, SATB2 and TLE1 stains should be always interpreted with caution when facing a poorly differentiated bone or soft tissue sarcoma with round cell and/or spindle cell morphology, especially in limited biopsy material. Kao et al[9] reported BCOR immunohistochemistry as a useful and highly sensitive marker for round cell sarcomas with *BCOR* genetic abnormalities. Therefore, BCOR immunohistochemistry could be used a screening tool for *BCOR-CCNB3*-positive sarcomas and other *BCOR*-driven tumors. In all 4 cases moderate, patchy to diffuse nuclear BCOR (1:100, C-10; Santa Cruz Biotechnology) immunoreactivity was demonstrated (Fig. 2C). Appropriate positive (normal colonic epithelium, synovial sarcoma samples, and testis for SATB2, TLE1, and BCOR, respectively) and negative controls were used throughout this study.

In conclusion, awareness of the broad morphologic spectrum and of the fairly common SATB2 and TLE 1 expression in these rare and recently characterized bone and soft tissue sarcomas justifies BCOR immunohistochemistry and molecular analysis for *BCOR-CCNB3* fusion in all primitive, difficult-to-classify bone and soft tissue sarcomas to avoid a misdiagnosis of a small cell osteosarcoma or poorly differentiated synovial sarcoma.

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