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CORRESPONDENCE

Inflammatory rhabdomyoblastic tumor with progression to high-grade rhabdomyosarcoma

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To the Editor:

Recently, we published our experience with inflammatory rhabdomyoblastic tumor (histiocyte-rich rhabdomyoblastic tumor, inflammatory leiomyosarcoma) [1]. As detailed in our publication, the results of this and prior studies suggest these very rare, distinctive tumors to be best considered rhabdomyoblastic tumors of borderline malignancy, having only a low risk for distant metastases. Furthermore, progression of inflammatory rhabdomyoblastic tumor to rhabdomyosarcoma has not as yet been documented.

Almost immediately after the publication of our study, however, we have encountered a morphologically and genetically classical example of inflammatory rhabdomyoblastic tumor showing morphologic progression to high-grade rhabdomyosarcoma with aggressive clinical behavior. This correspondence aims to raise awareness of this exceptionally rare event.

A 42-year-old male presented with an ~18 cm left thigh mass. A core needle biopsy was performed, showing a histiocyte-rich spindle cell neoplasm with typical morphologic and immunohistochemical features of inflammatory rhabdomyoblastic tumor, including diffuse desmin expression (DE-R-11, 1:50–1:100; Leica, Newcastle Upon Tyne, UK) and more variable expression of MyoD1 (EP212, 1:25–1:100; Cell Marque, Rocklin, CA) and myogenin (F5D, 1:25–1:50; Dako, Santa Clara, CA)(Dako Envision detection system, Dako, Carpinteria, CA, USA) (Fig. 1A–C). Owing to the large size of the mass and the rarity of this diagnosis, a second open biopsy was performed, showing areas identical to the first biopsy as well as a morphologically high-grade component comprised of markedly pleomorphic epithelioid cells with atypical mitoses and foci of tumor necrosis (Fig. 1D). This high-grade component also strongly expressed desmin, myogenin, and myoD1 (data not shown).

Single nucleotide polymorphism (SNP) chromosomal microarray testing (OncoScan CNV Assay, Thermo Fisher Scientific, Waltham, Massachusetts) was performed on both components of the tumor. As expected, the area of typical inflammatory rhabdomyoblastic tumor displayed a hyperhaploid genome with loss of most chromosomes; normal copy number with biparental disomy was limited to chromosomes 5, 18, 20, 21, and 22 (Fig. 2A). In contrast, the high-grade component was hyperdiploid with widespread loss of heterozygosity (LOH) ("pseudohyperdiploid"), consistent with whole genome duplication, following the haploidization event which had generated widespread LOH (Fig. 2B). Additional abnormalities in the high-grade tumor included LOH on chromosome 21 and numerous terminal and interstitial gains and losses throughout the genome including LOH of *RB1*, *CDKN2A*, *TP53*, and *PTEN*, multiple copy gains of *JUN* and *RICTOR*, and a complex copy number profile on chromosome 5 including *TERT*.

Taken together, these morphologic, immunophenotypic, and genetic features are those of an inflammatory rhabdomyoblastic tumor with progression to high-grade rhabdomyosarcoma. In the 4 months since presentation the patient has developed pulmonary, bone and soft tissue metastases.

We conclude that very rare instances of inflammatory rhabdomyoblastic tumors may progress to rhabdomyosarcoma, with aggressive behavior. Conceivably, the presence of areas of inflammatory rhabdomyoblastic tumor may have been overlooked in prior cases of adult soft tissue rhabdomyosarcoma, and we would certainly urge close inspection and molecular genetic study, including SNP array, of adult rhabdomyosarcomas

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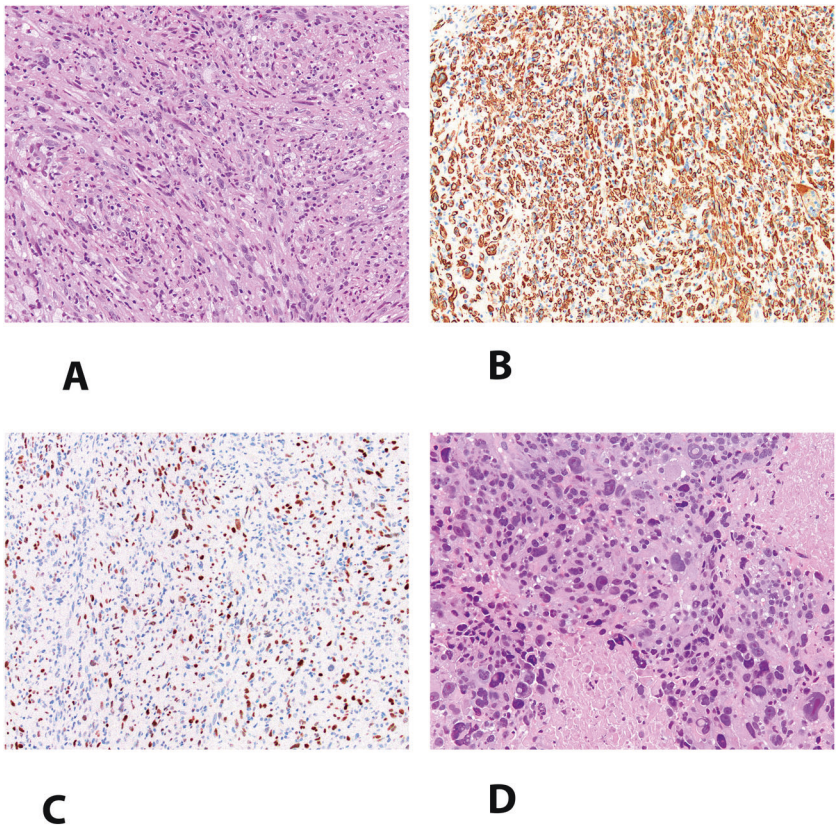

Fig. 1 Morphology and immunohistochemistry. Morphologically typical inflammatory rhabdomyoblastic tumor, consisting of short fascicles of pleomorphic but amitotic spindled cells with eosinophilic cytoplasm, surrounded by foamy histiocytes (**A**). The neoplastic cells were uniformly positive for desmin (**B**) and more variably positive for myogenin (**C**) and MyoD1 (data not shown). Caldesmon and smooth muscle actin were negative (data not shown). Much of the second biopsy consisted of sheets of markedly atypical epithelioid and spindled cells, with necrosis and mitotic activity (**D**). This high-grade component also expressed skeletal muscle markers (data not shown).

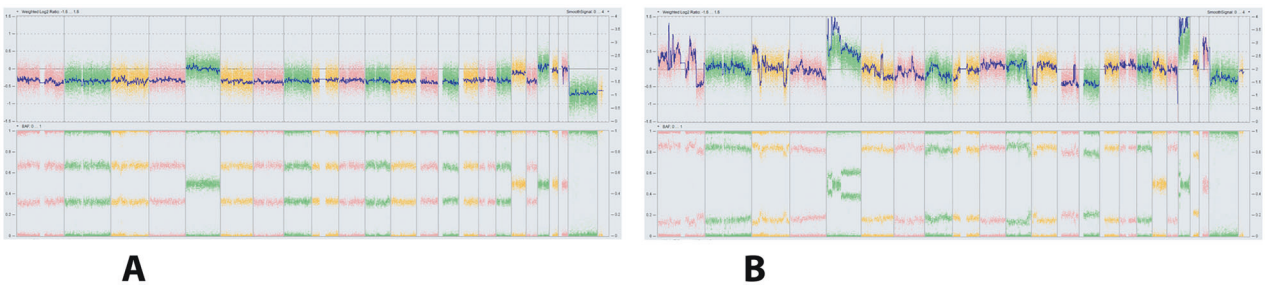

Fig. 2 Genome-wide copy number profiles. Chromosomal microarray profiles for the inflammatory rhabdomyoblastic tumor (**A**) and high-grade rhabdomyosarcoma (**B**). Copy number is displayed on the weighted log2 ratio plot (above) and allele pattern is displayed on the B allele frequency plot (below) for chromosomes 1–22, X, and Y, from left to right. Whole genome view of the inflammatory rhabdomyoblastic tumor shows loss of most chromosomes with resulting allelic imbalance (loss of heterozygosity, LOH). Only chromosomes 5, 18, 20, 21, and 22 are at the baseline normal copy state of 2 with a normal allele pattern (**A**). **B** In contrast, the whole genome view of the high-grade rhabdomyosarcoma shows widespread LOH with a markedly abnormal copy number profile, particularly on chromosomes 1, 3, 5, 13, and 20 (**B**). The allele profile resembles that of the inflammatory rhabdomyoblastic tumor, with additional copy neutral LOH of chromosome 21 in the rhabdomyosarcoma.

showing unusual morphologic features in order to identify similar cases.

Compliance with ethical standards

Conflict on interest The authors declare no competing interests.

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Reference

1. Cloutier JM, Charville GW, Mertens F, Sukov W, Fritchie K, Perry KD, et al. "Inflammatory leiomyosarcoma" and "histiocyte-rich rhabdomyoblastic tumor": a clinicopathological, immunohistochemical and genetic study of 13 cases, with a proposal for reclassification as "Inflammatory Rhabdomyoblastic Tumor". Mod Pathol. 2020. https://doi.org/10.1038/s41379-020-00703-8. [Online ahead of print].