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Original contribution

Lipoblasts in spindle cell and pleomorphic lipomas: a close scrutiny☆,☆☆

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Summary The presence and frequency of lipoblasts (LPB) in spindle cell lipomas (SCL) and pleomorphic lipomas (PL) has never been studied in detail on a histologically, immunohistochemically and molecular genetically validated set of tumors. The authors investigated this feature by reviewing 91 cases of SCL and 38 PL. When more than 3 unequivocal LPB were found, the case was regarded as positive for the presence of LPB. All positive cases were then stained with CD34 and retinoblastoma (Rb) protein antibodies and tested by fluorescence in situ hybridization for *MDM2* and *CDK4* amplifications and the *FUS* gene rearrangements. The patients with SCL and PL containing LPB were 14 women and 47 men, the rest were of unknown gender. The cases usually presented as superficial, well-circumscribed soft tissue masses and most commonly occurred in the upper back and neck. CD34 was expressed in all cases, while Rb protein was consistently absent in all. Molecular genetic results, when available, were in concordance with the morphological diagnosis of SCL/PL. LPB were found in 37 (41%) cases of SCL and 25 cases of PL (66%). While in many cases they are inconspicuous, in some others they constitute a very prominent component of the tumor. It is important to be aware of this fact in order to avoid misinterpretation as liposarcoma.

1. Introduction

Spindle cell lipomas (SCL) and pleomorphic lipomas (PL) are distinctive soft tissue tumors, originally described as 2 separate entities by Enzinger et al [1,2]. Based on similar clinicopathological, immunohistochemical as well as molecular genetic features, these neoplasms are today considered as opposite ends in a morphological spectrum of one single entity [3]. This is further supported by a frequent occurrence of cases showing characteristic morphological features of both SCL and PL in the same specimen. In their seminal paper by

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Shmookler and Enzinger in 1981, it was noted that almost one half of PL exhibited lipoblasts (LPB). Two years later, this finding was confirmed by another group [4]. However, contemporary reports often fail to mention this frequent and important feature of PL; and with respect to SCL, this feature is clearly underrecognized. After a review of the literature, including the major soft tissue pathology textbooks, we have found only 3 publications [3,5,6] acknowledging the presence of LPB in SCL. This situation is in stark contrast with our own experience. Over the years, we have encountered many cases of both SCL and PL with a prominent admixture of LPB. Since many of these cases were sent to us because of the concern for liposarcoma by the submitting pathologist, we decided to undertake this study on a large series of cases. To our knowledge, this is the first study which attempts to rigorously assess the frequency of LPB on a histologically, immunohistochemically, and molecular genetically validated set of SCL/PL.

2. Materials and methods

The 129 cases of SCL/PL constituting the subject of this study were retrieved from the routine biopsy archive and the authors' consultation files; they came from the period between years 1993 and 2016. The clinical information was extracted from the medical records, and follow-up data were obtained from the attending clinicians. To identify cases, we searched our consultation registry files for tumors diagnosed as SCL, PL or SCL/PL. This search yielded altogether 151 specimens, which were reviewed to confirm the diagnosis. Upon revision, 5 cases were excluded because they did not meet the diagnostic criteria for SCL/PL [3]. Another 11 cases of SCL were not included because they featured a prominent myxoid change, which made a reliable recognition of LPB very difficult. Five cases were omitted because they represented the fat-free variant of these tumors. One case diagnosed as PL was removed from the series due to the presence of *MDM2* amplification.

The 129 cases were divided into categories of SCL and PL based on the presence of PL component. If present even in a small amount, the case was already considered as PL. When more than 3 unequivocal fat cells having hyperchromatic, indented, or sharply scalloped nuclei were found, the case was regarded as positive for the presence of LPB. Areas where it was difficult to ascertain whether fat necrosis was present were not evaluated. Similarly, adipocytes showing Lochkerne, Ringkerne, and Kerbenkerne [7,8] (ie, different variations of an intranuclear vacuole) were disregarded. All tumors were reviewed without the knowledge of clinical features (ie, localization, gender, age). In negative cases, all available blocks of tissue were reviewed. When a case was scored as positive, the remaining blocks were not further assessed. This was also the reason why one case was misdiagnosed as PL and where later *MDM2* amplification was found. When reviewed again, the remaining blocks revealed characteristic features of atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL).

Except for 8 cases (Cases 5, 10, 26, 30, and 34 of SCL and 19, 20, and 21 of PL), paraffin blocks or unstained reserve slides were available for the study. For conventional microscopy, tissues were fixed in formalin, routinely processed, embedded in paraffin, cut into 4-μm-thick sections, and stained with hematoxylin-eosin.

2.1. Immunohistochemistry

The immunohistochemical analysis was performed using a Ventana BenchMark ULTRA (Ventana Medical System, Inc, Tucson, AZ). The following primary antibodies were used: CD34 (QBEnd/10, 1:200; Dako, Glostrup, Denmark) and Rb protein (G3–245, 1:50; BD Biosciences, Franklin Lakes, NJ). The primary antibodies were visualized employing the enzymes alkaline phosphatase or peroxidase as detecting systems (both purchased from Ventana Medical System, Inc, Tucson, AZ).

2.2. Molecular genetic studies

2.2.1. Detection of amplifications of MDM2 and CDK4 and break of *FUS* by fluorescence in situ hybridization

Specimens representing 4-μm-thick FFPE section on positively charged slides were routinely deparaffinized and processed. An appropriate amount of probe mix, Probe Vysis *FUS* Break Apart fluorescence in situ hybridization (FISH) Probe Kit (Abbott Molecular, Abbott Park, IL), mixed according to the manufacturer's protocols and factory premixed probes ZytoLight® SPEC *MDM2*/CEN 12 Dual Color Probe and ZytoLight® SPEC *CDK4*/CEN 12 Dual Color Probe (ZytoVision GmbH, Bremerhaven, Germany) were applied to the specimens. The slides were then routinely incubated, washed, and counterstained with 4′,6′-diamidino-2-phenylindole DAPI (Abbott).

2.2.2. Fluorescence in situ hybridization interpretation

One hundred randomly selected nonoverlapping tumor cell nuclei were evaluated in all analyzed samples. Samples were considered positive for amplification [9] when the ratio of signals of *MDM2* and *CDK4* probes to corresponding chromosome 12 centromeric probe signals was ≥2.0. The cut-off value of *FUS* break-apart probe was set to 10% of nuclei with chromosomal break.

3. Results

The clinical features are summarized in Tables 1 (SCL) and 2 (PL). The patients were 14 women and 47 men; and in one case, the gender was unknown. The age of the patients at the time of diagnosis ranged from 27 to 90 years (mean, 60.1 years). Twenty-two cases were retrieved from the routine