

## Accepted Manuscript

Atypical mitoses are present in otherwise classical pleomorphic lipomas—reply

David Creytens, Thomas Mentzel, Liesbeth Ferdinande, Joost van Gorp, Jo Van Dorpe, Uta Flucke



PII: S0046-8177(18)30249-1  
DOI: doi:[10.1016/j.humpath.2018.04.032](https://doi.org/10.1016/j.humpath.2018.04.032)  
Reference: YHUPA 4635  
To appear in: *Human Pathology*  
Received date: 6 April 2018  
Accepted date: 20 April 2018

Please cite this article as: David Creytens, Thomas Mentzel, Liesbeth Ferdinande, Joost van Gorp, Jo Van Dorpe, Uta Flucke , Atypical mitoses are present in otherwise classical pleomorphic lipomas—reply. *Yhupa* (2018), doi:[10.1016/j.humpath.2018.04.032](https://doi.org/10.1016/j.humpath.2018.04.032)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## **Atypical mitoses are present in otherwise classical pleomorphic lipomas—reply**

To the Editor:

We would like to make some additional comments in response to the Letter to the Editor of Babaoglu et al in which they describe atypical mitoses in 3 interesting lipomatous tumors with a “pleomorphic lipoma/pleomorphic lipoma-like” morphology.

We agree with the authors that atypical mitoses in adipocytic tumors with a “pleomorphic lipoma/pleomorphic lipoma-like” morphology showing additional atypical morphologic features (including poor circumscription, hypercellularity, atypical hyperchromatic spindle cells, atypical multivacuolated lipoblasts) should be interpreted with caution. In such cases (like case 3), we prefer to use the recently proposed term “atypical pleomorphic lipomatous tumor” (APLT) above “atypical pleomorphic/spindle cell lipoma” (term used by Babaoglu et al) to stress the important overlap with the recently defined atypical spindle cell lipomatous tumor (ASLT), which we believe to belong to the same clinical, morphologic and genetic spectrum (“atypical spindle cell/pleomorphic lipomatous tumor”) [1,2].

Interestingly, Babaoglu described the presence of atypical mitoses in 2 cases with morphological features of classical spindle cell/pleomorphic lipoma without additional atypical morphologic features of APLT. Based on the long clinical follow-up of these cases (showing

indolent clinical behavior), the authors stated that atypical mitoses could be present in pleomorphic lipomas with otherwise classical morphology and do not necessarily predict either recurrence or malignant behavior [3]. Also in our series of APLT, some cases behaved in a benign way, which is not surprising when resected with clear margins [1]. In our experience, a broad spectrum of morphologic characteristics within the same lesion can be observed in APLT, depending on the variable proportions of adipocytes, spindle cells, pleomorphic (multinucleated) cells and an either myxoid or collagenous extracellular matrix [1]. Diagnostic atypical morphologic features (such as cytonuclear atypia of the spindle cell component and atypical lipoblasts) can be very focal in APLT and can be easily missed (eg, as a result of insufficient sampling of the large lesions). It is currently poorly understood how far pleomorphic lipomas and APLT are related lesions as they show overlapping genetic features.

Recently, we have seen a case of a 6 cm large recurrence of a “pleomorphic lipoma” (6 years after the primary diagnosis) at the posterior right knee in a 53-year-old male. Histology of the current tumor showed predominantly pleomorphic lipoma-like areas with floret-like multinucleated cells intermingled with relatively uniform spindle cells and mast cells, set in a fibrous to ropy collagenous stroma (Figure A). Low mitotic activity was observed in these areas (Figure B). However, only very focally cellular areas were seen composed of atypical spindle-shaped and pleomorphic “bizarre” tumor cells with hyperchromatic nuclei, admixed with atypical multivacuolated lipoblasts, compatible with

the diagnosis of APLT (Figure C). Revision of the histology of the originally diagnosed “pleomorphic lipoma” showed a completely resected adipocytic tumor with a pleomorphic lipoma-like morphology, however, with the presence of an atypical mitosis and sporadic atypical “bizarre” spindle cells (Figure D).

In conclusion, in our opinion, diagnosis of classical pleomorphic lipoma should always be made with caution when atypical mitoses are present [4,5]. However, the exact biological significance of atypical mitoses as a sole atypical morphologic feature in the spectrum of adipocytic tumors with a pleomorphic lipoma/pleomorphic lipoma-like morphology remains to be elucidated, as well as the biological continuum of these lesions with the recently defined APLT.

David Creytens MD, PhD

*Department of Pathology, Ghent University Hospital and CRIG, Cancer  
Research Institute Ghent, Ghent University, Ghent, Belgium*

*E-mail addresses: creytensdavid@hotmail.com,  
david.creytens@uzgent.be*

Thomas Mentzel MD, PhD

*Dermatopathology Bodensee, Friedrichshafen, Germany*

Liesbeth Ferdinande MD, PhD

*Department of Pathology, Ghent University Hospital and CRIG, Cancer  
Research Institute Ghent, Ghent University, Ghent, Belgium*

Joost van Gorp MD, PhD

*Department of Pathology, Diaconessenhuis Utrecht, The Netherlands*

Jo Van Dorpe MD, PhD

*Department of Pathology, Ghent University Hospital and CRIG, Cancer  
Research Institute Ghent, Ghent University, Ghent, Belgium*

Uta Flucke MD, PhD

*Department of Pathology, Radboud University Medical Center, Nijmegen,  
The Netherlands*

## **References**

- [1] Creytens D, Mentzel T, Ferdinande L, et al. "Atypical" pleomorphic lipomatous tumor. A clinicopathologic, immunohistochemical and molecular study of 21 cases, emphasizing its relationship to atypical spindle cell lipomatous tumor and suggesting a morphologic spectrum (atypical spindle cell/pleomorphic lipomatous tumor). *Am J Surg Pathol* 2017;41:1443-55.
- [2] Marino-Enriquez A, Nascimento AF, Ligon AH, et al. Atypical spindle cell lipomatous tumor: clinicopathologic characterization of 232 cases demonstrating a morphologic spectrum. *Am J Surg Pathol* 2017;41:234-44.
- [3] Michal M, Babaoglu B, Kazakov DV, Michal M, Kosemehmetoglu K. Atypical mitoses in pleomorphic lipomas. *HUM PATHOL* 2017;70:143.
- [4] Creytens D, Mentzel T, Ferdinande L, van Gorp J, Van Dorpe J, Flucke U. Atypical multivacuolated lipoblasts and atypical mitoses are not compatible with the diagnosis of spindle cell/pleomorphic lipoma. *HUM PATHOL* 2018;74:188-9.
- [5] Fletcher CD, Bridge JA, Hogendoorn PC, Mertens F, editors. World Health Organization Classification of Tumours. Pathology and Genetics. Tumours of Soft tissue and Bone. Lyon: IARC Press; 2013.

**Figure legend:**

**Figure A**, The recurrent lesion was predominantly composed of pleomorphic lipoma-like areas with floret-like multinucleated cells intermingled with relatively uniform spindle cells and mast cells (HE, original magnification  $\times 100$ ). **B**, Low mitotic activity was seen (HE, original magnification  $\times 200$ ). **C**, Very focal, more cellular areas were observed with atypical spindle-shaped and pleomorphic “bizarre” tumor cells admixed with atypical multivacuolated lipoblasts (HE, original magnification  $\times 40$ ). **D**, Presence of an atypical mitosis in the primary tumor with a pleomorphic lipoma-like morphology (HE, original magnification  $\times 100$ ).