Slide Seminar Soft Tissue and Bone Pathology: curious, enigmatic and gorgeous bone and soft tissue lesions

CASE 1

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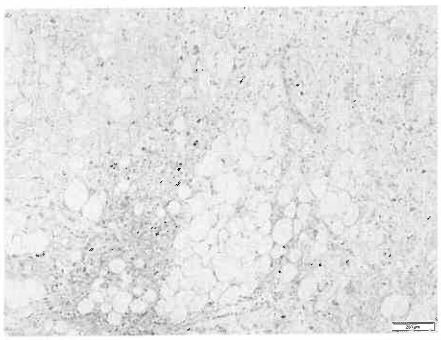
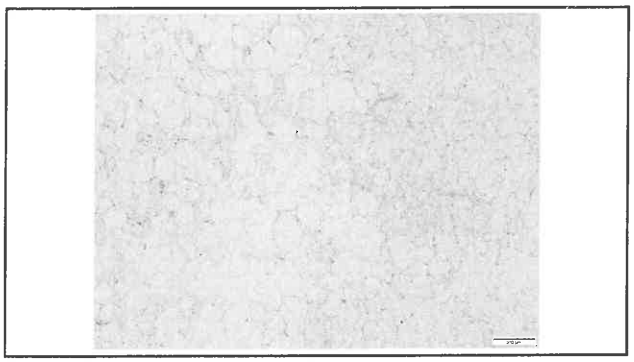
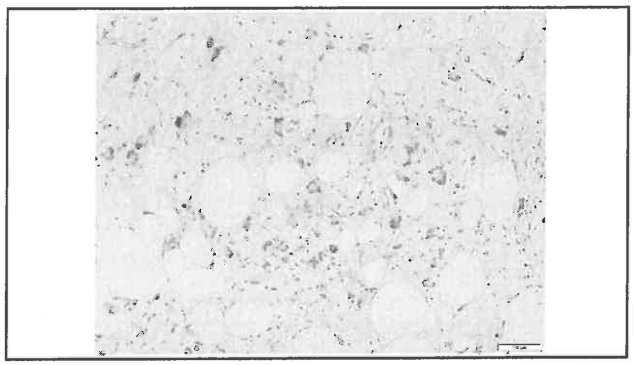
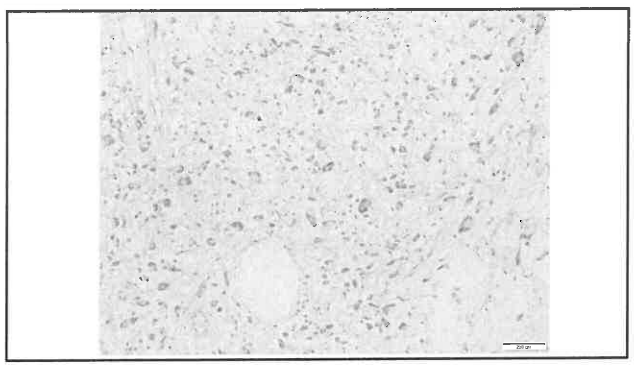
Case 1: clinical information

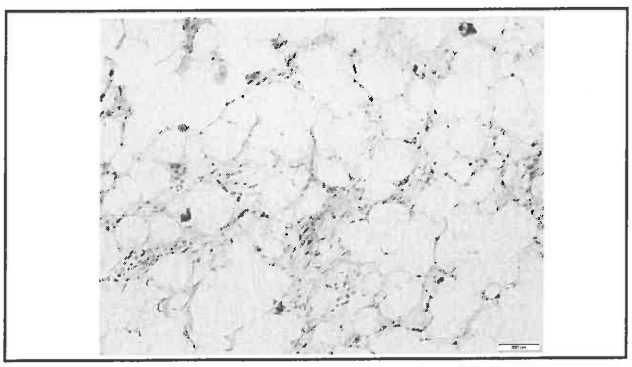
- 64y-old male patient
- Presents with a not painfull and recently enlarged nodule on the left ellbow (diameter 6,0 cm)
- No important clinical history
- The patient wants it removed

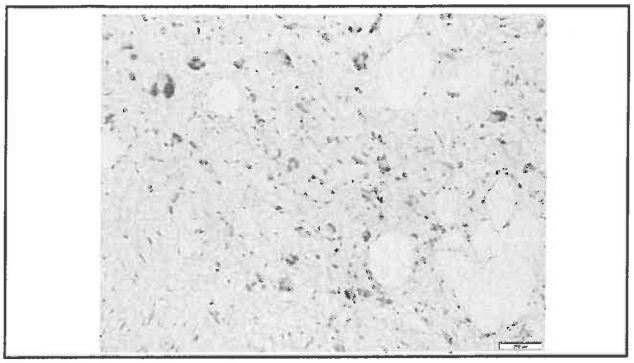


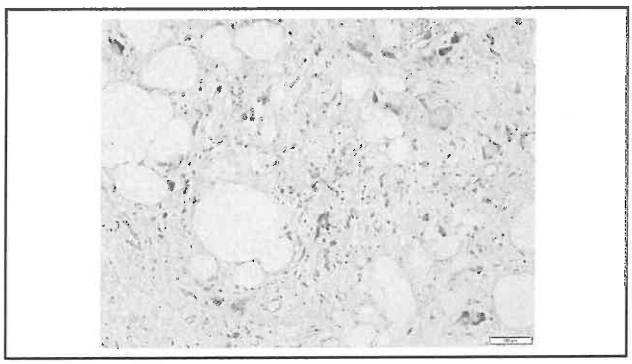


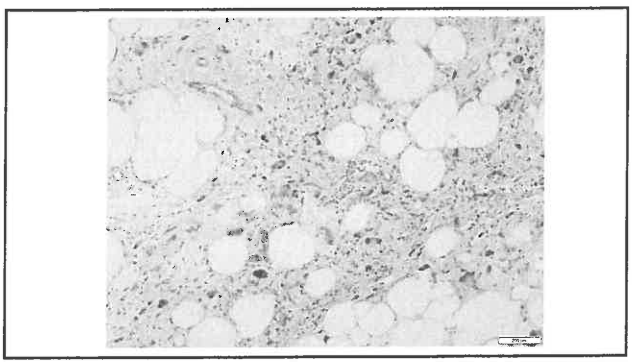


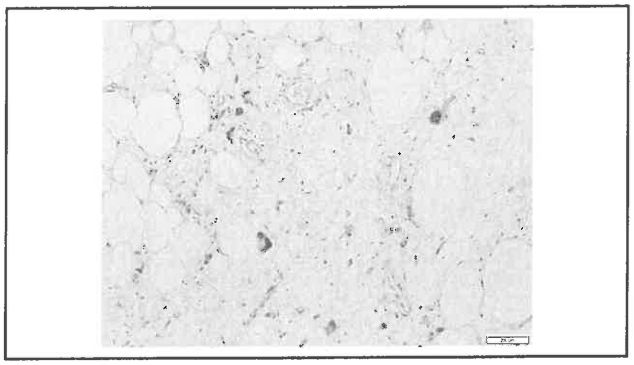


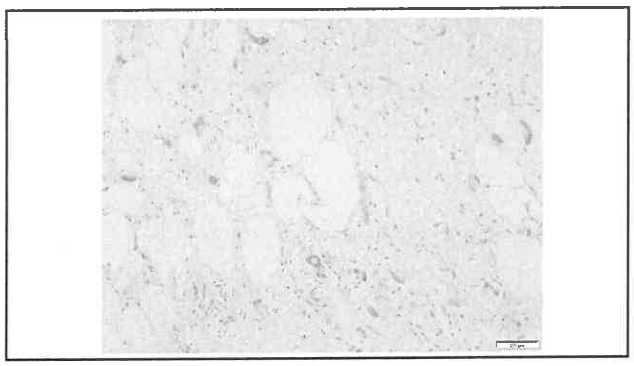


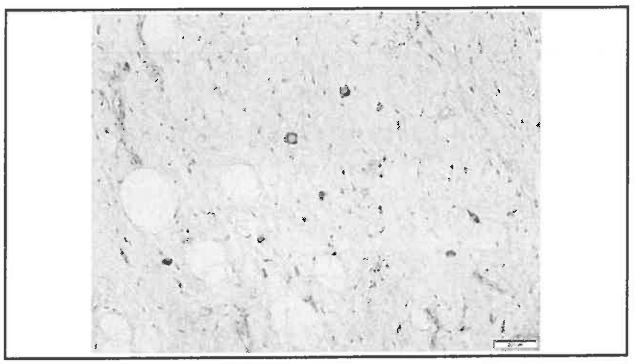


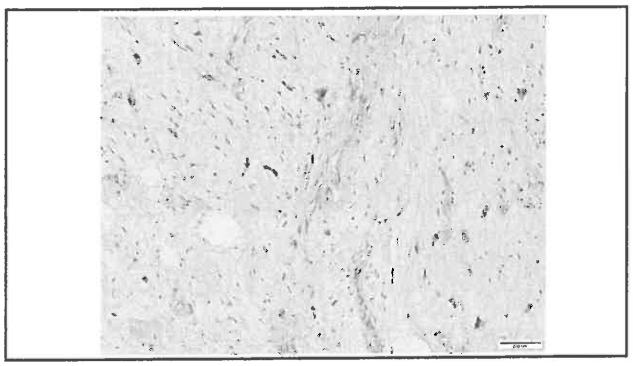


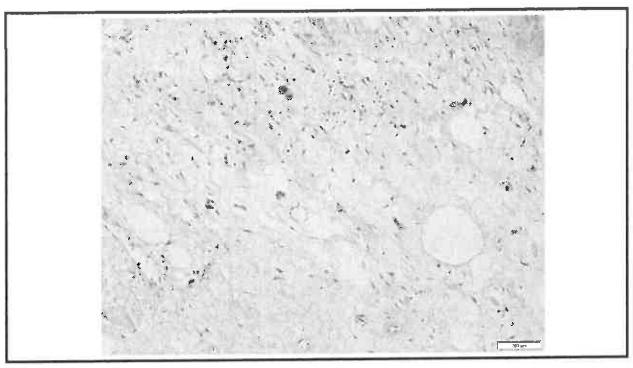


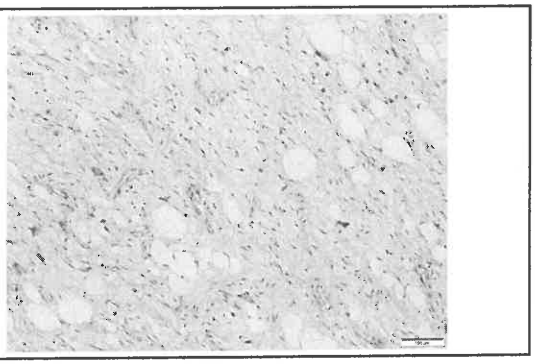


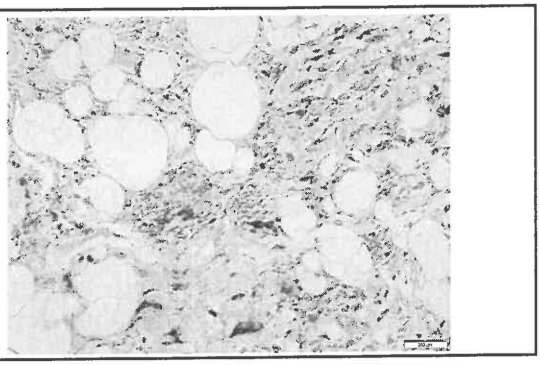


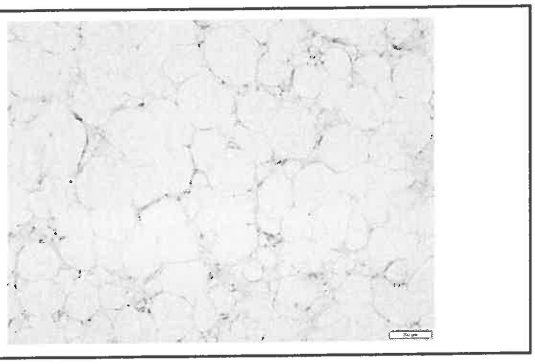


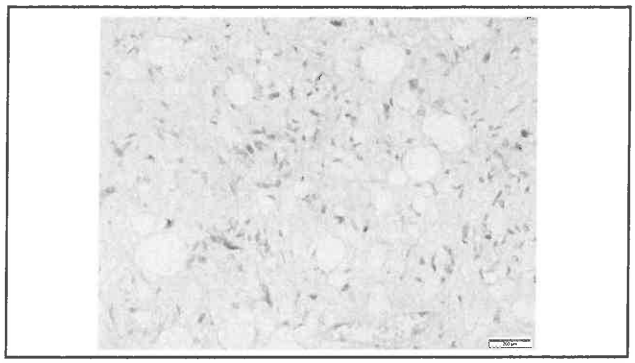


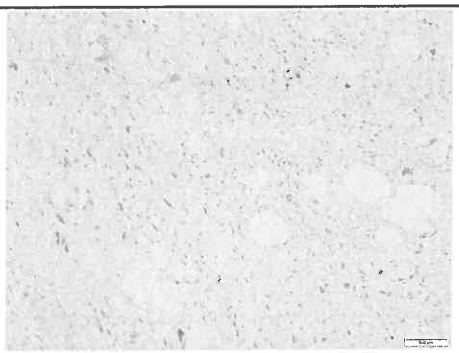




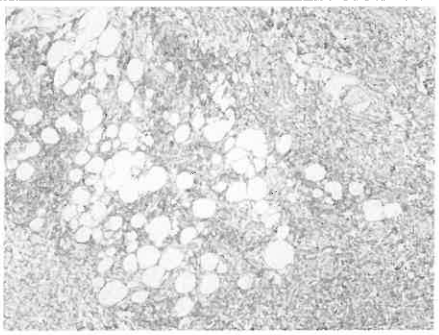




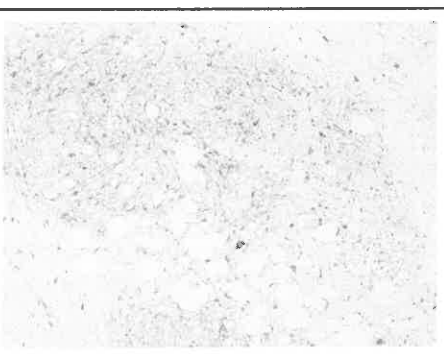




IMMUNOHISTOCHEMISTRY

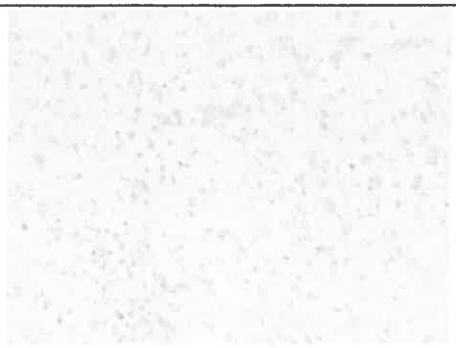


CD34



p16

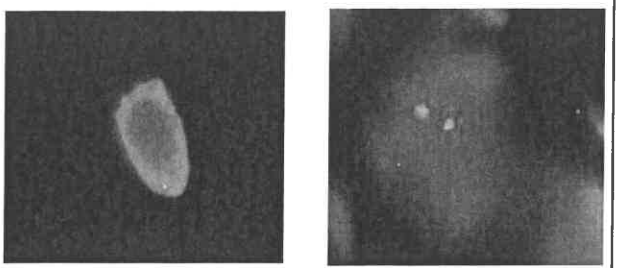
MDM2



Rb1

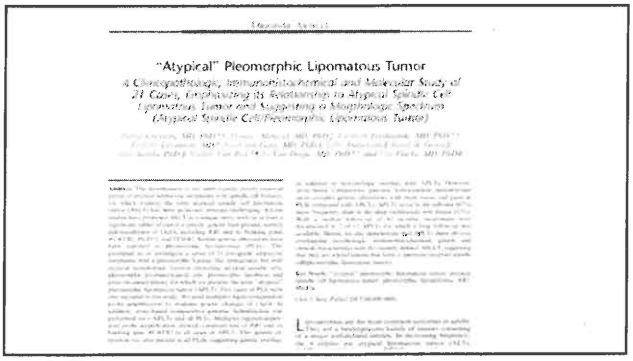
MOLECULAR DIAGNOSTICS

- No amplification of *MDM2* or *CDK4* gene (FISH)
- No rearrangement of *FUS*, *EWSR1* or *DDIT3* genes (FISH)
- Deletion of *RB1* gene (FISH and MLPA)



RB1 FISH

'atypical' pleomorphic lipomatous tumor ('atypical spindle cell/pleomorphic lipomatous tumor')



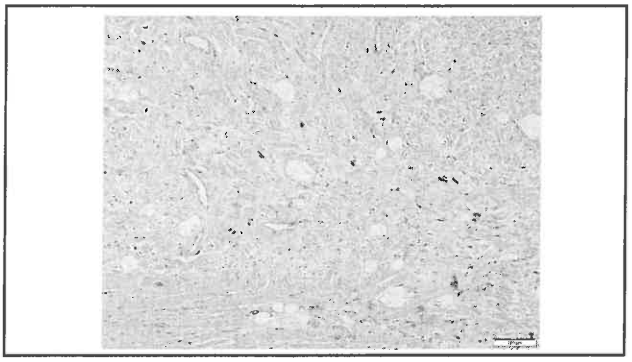
"Atypical" Pleomorphic Lipomatous Tumor

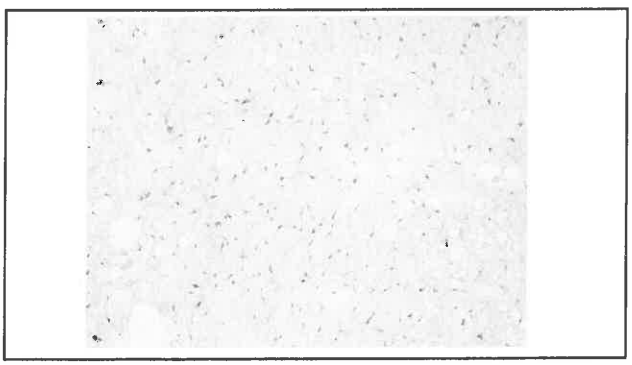
'atypical' pleomorphic lipomatous tumor (APLT) ('atypical spindle cell/pleomorphic lipomatous tumor')

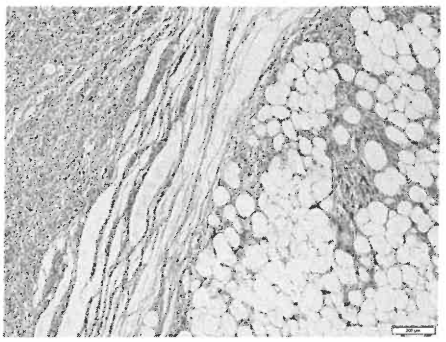
- The 21 APLT cases originated from 17 male and 4 female patients, aged between 28 to 81 years (mean, 63 years; median, 64 years).
- The tumors were located in the upper arm (n=5), shoulder (n=4), lower arm/elbow (n=2), neck (n=3), back/neck (n=1), back (n=2), gluteal region (n=1), and thigh (n=3). Tumor size ranged from 2 to 10 cm (mean, 6.4 cm).
- APLTs arose in the subcutis (67%) more frequently than in the deep (subfascial) soft tissues (33%)
- With a median follow-up of 42 months, recurrences were documentated in 2 out of 12 APLTS for which a long enough follow-up was available

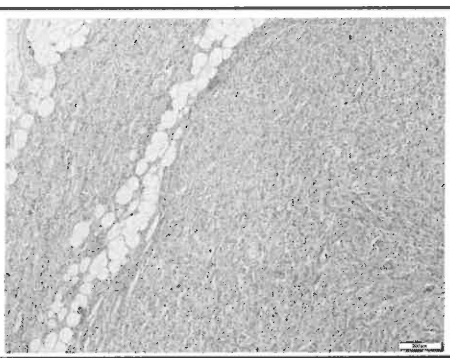
'atypical' pleomorphic lipomatous tumor (APLT) ('atypical spindle cell/pleomorphic lipomatous tumor'): DIAGNOSTIC CRITERIA

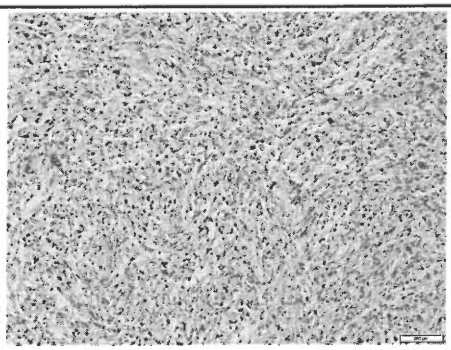
- Pleomorphic lipoma-like morphology with floret-like multinucleated cells (at least focally)
- The presence of atypical (hyperchromatic) spindle cells
- Pleomorphic (multinucleated) cells
- Pleomorphic uni- and plurivacuolated lipoblasts
- Adipocytic component showing atypical adipocytes with variation in size and shape
- Variably myxoid or collagenous stroma
- IHC: CD34+, p16+, Rb1 loss, MDM2-, STAT6-
- Molecular: loss of *RB1* and its flanking genes *RCBTB2*, *ITM2B* and *DLEU1*, no *MDM2/CDK4* amplification
- APLTs can exhibit a wide range of microscopic appearances, depending on the varying cellularity, as well as the proportion and the aspect of the extracellular matrix, which can be myxoid or more collagenous

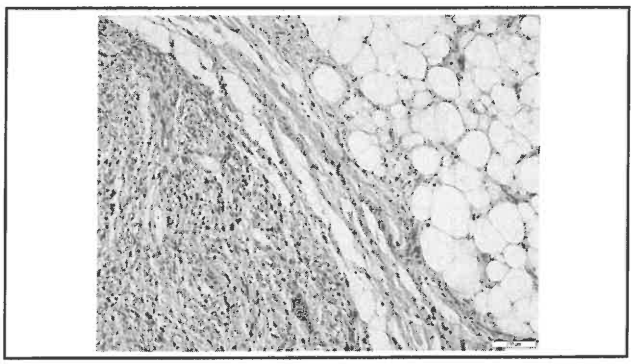


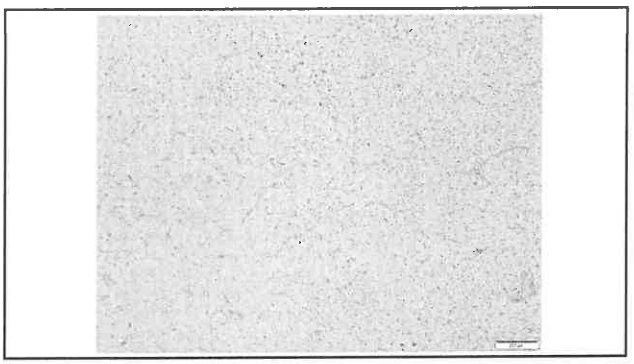


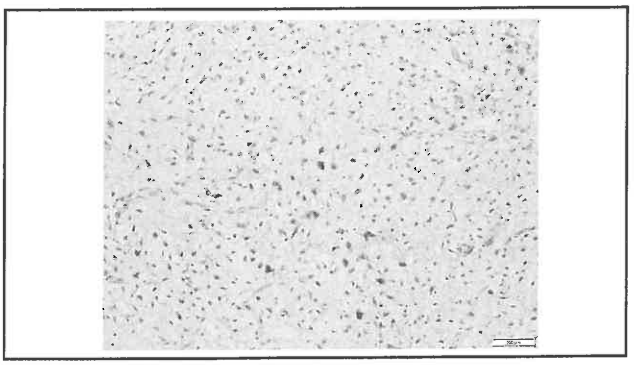


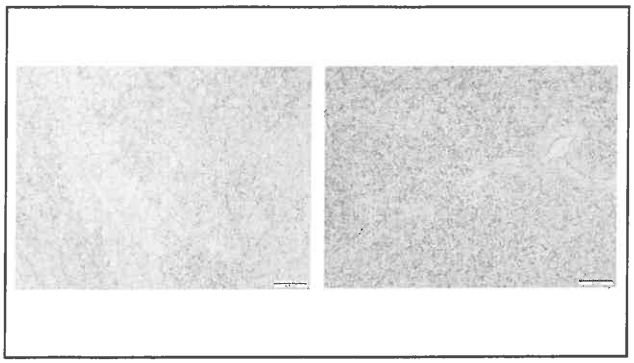


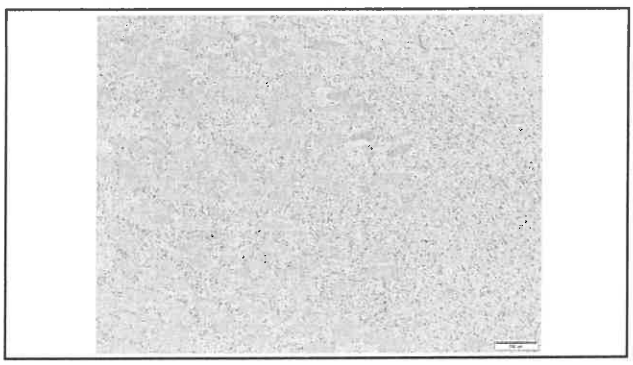












Differential diagnosis (1): pleomorphic/spindle cell lipoma

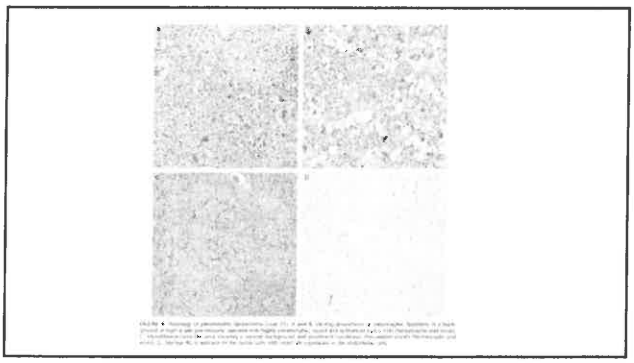
- Features of classical spindle cell/pleomorphic lipoma, including ropy collagen and/or floret-like multinucleated cells, are classically present in APLT
- APLTs, however, are characterized by a broader anatomic distribution (also locations outside neck and shoulder region), occurrence in older patients, a larger size and recurrences
- Pleomorphic and spindle cell lipoma **do not show** infiltrative growth, atypical spindle cells, 'bizarre' pleomorphic (multinucleated) cells, pleomorphic lipoblasts or mitotic activity

Lipoblasts in spindle cell and pleomorphic lipomas: a close scrutiny

Differential diagnosis (2): pleomorphic liposarcoma

- **Some overlapping morphological, immunohistochemical and genetic features between pleomorphic liposarcoma and APLT**: infiltration, pleomorphism including pleomorphic lipoblasts, *RB1* loss and its flanking genes *RCBTB2*, *ITM2B* and *DLEU1*

- **Pleomorphic liposarcoma can be differentiated from APLT by**
-a larger tumor size
-a more frequent location in deep (subfascial) soft tissues
-a higher degree of pleomorphism
-high mitotic activity
-tumor necrosis
-the absence of a pleomorphic lipoma-like component
-more complex chromosomal losses and gains (aCGH)
-an aggressive behavior with metastatic potential



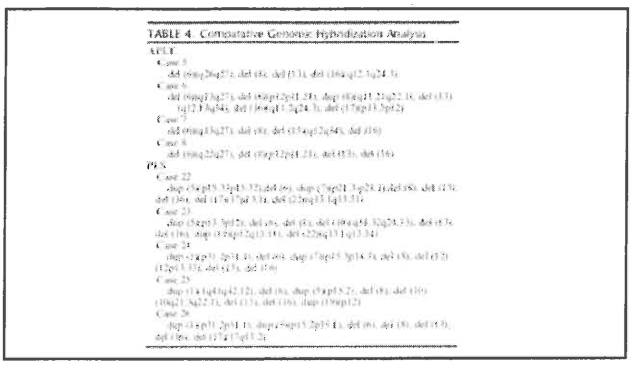


TABLE 4. Comparative Genomic Hybridization Analysis

APLT

Case 5

del (6)(q23q27), del (8), del (13), del (16)(q12.1q24.3)

Case 6

del (6)(q21.3q27), del (6)(q12p21.2)x2-3, dup (6)(q21.2)q22.1), del (13)(q12.3q34), del (16)(q11.2q24.3), del (17)(p13.3p12)

Case 7

del (6)(q13q27), del (8), del (17)(q12q24), del (16)

Case 8

del (6)(q22q27), del (8)(p12p21.2), del (13), del (16)

PLS

Case 22

dup (5)(p15.33p15.32),del (6), dup (7)(q21.3q22.1),del (8), del (12), del (16), del (17)(p13.1), del (22)(q13.1q13.31)

Case 23

dup (5)(p15.3p12), del (6), del (8), del (10)(q24.32q26.2), del (12), del (16), dup (17)(p12q23.1), del (22)(q13.1q13.31)

Case 24

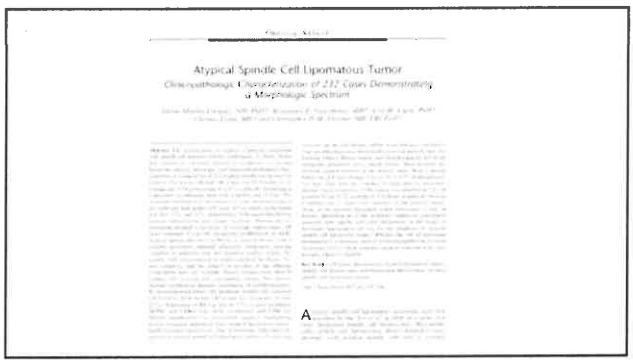
dup (2)(p11.2p13.1), del (6), dup (7)(p15.3q34.3), del (8), del (12)(p13.1?), del (13), del (16)

Case 25

dup (1)(q41q42.12), del (6), dup (9)(p15.2), del (8), del (10)(q21.3q22.1), del (13), del (16), dup (19)(p12)

Case 26

dup (1)(p11.2p31.1), dup (5)(p15.2p35.1), del (6), del (8), del (12), del (16), del (17)(p13.2)



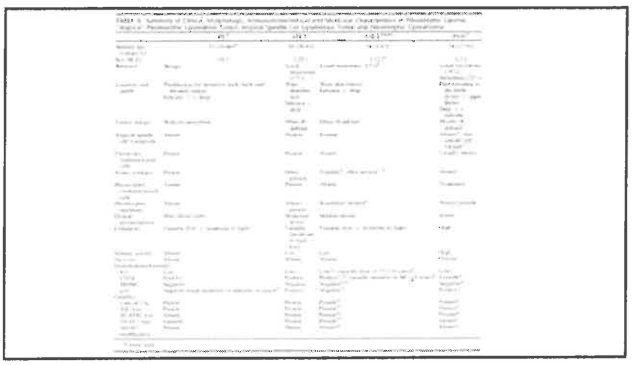
Atypical Spindle Cell Lipomatous Tumor

Clinicopathologic Characterization of 232 Cases Demonstrating a Morphologic Spectrum

A

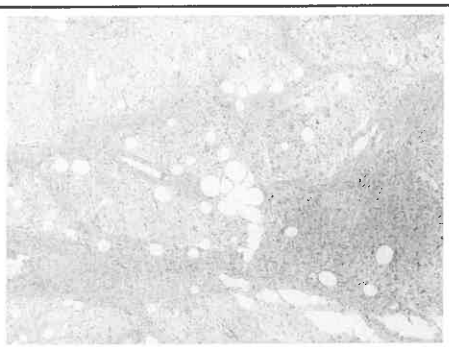
Differential diagnosis (3): atypical spindle cell lipomatous tumor (ASLT)

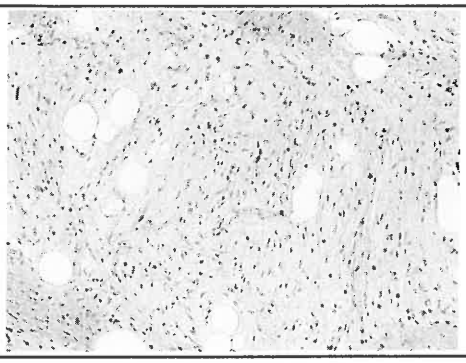
- Based on similar genetic and morphologic observations (loss of *RB1* and its flanking genes *RCBTB2*, *ITM2B* and *DLEU1*, and the presence of an atypical spindle cell component and ropey collagen), one could argue that ASLT and APLT belong to a **spectrum ('atypical spindle cell/pleomorphic lipomatous tumor')**
- **Morphologic features more characteristic for the APLT end of this spectrum are the presence of floret-like multinucleated cells, pleomorphic (multinucleated) cells and pleomorphic lipoblasts, and an overall higher degree of pleomorphism**

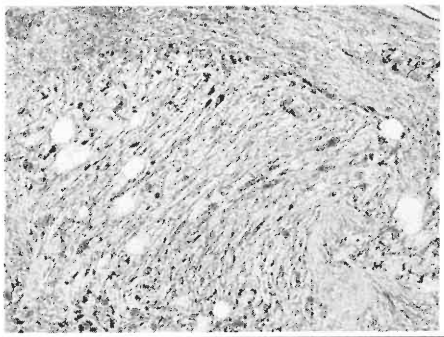


Other differential diagnoses (4)

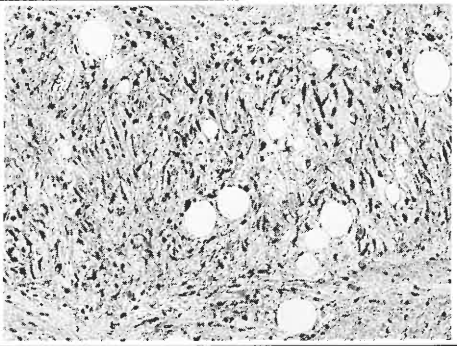
- **Atypical lipomatous tumor (ALT)**
  →pleomorphic lipoblasts less common; *MDM2/CDK4* overexpression/amplification
- **Dedifferentiated liposarcoma**
  →pleomorphic lipoblasts extremely uncommon ('homologous' lipoblastic); *MDM2/CDK4* overexpression/amplification
- **Myxoid liposarcoma** (in cases with prominent myxoid stroma, chickenwire vasculature and/or mucine pools)
  →no pleomorphism; rearrangement of *DDIT3*
- **Soft tissue angiofibroma** (in cases with prominent branching capillary network)
  →absence of nuclear atypia; absence of (pleomorphic) lipoblasts; rearrangement of *NCOA2*
- **Solitary fibrous tumor (lipomatous variant)** (in cases with staghorn-like (HPC-like) vessels; CD34+)
  →more 'patternless' pattern; STAT6 nuclear positivity; no *RB1* deletion







CD34



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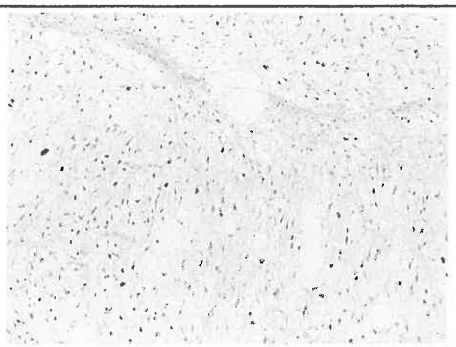

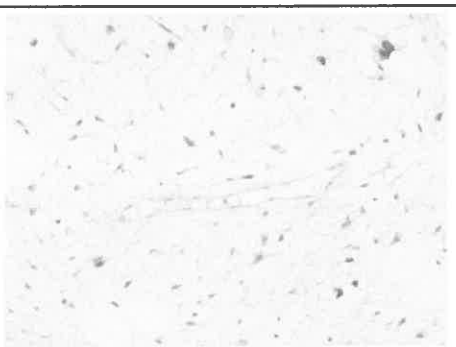

'atypical' pleomorphic lipomatous tumor (APLT): conclusion

- Importance of strict diagnostic criteria
- However, wide range of microscopic appearances (and differential diagnoses)
- APLT is different from classical spindle cel/pleomorphic lipoma
- Despite some overlapping (morphological, immunohistochemical and genetic features) between APLT and pleomorphic liposarcoma, APLT can be differentiated from pleomorphic liposarcoma
- Based on similar genetic and morphologic observations, one could suggest a morphologic spectrum with atypical spindle cell lipomatous tumor ('atypical spindle cell/pleomorphic lipomatous tumor')