Am J Surg Pathol 2018;42:1530–1540

Dysplastic Lipoma

A Distinctive Atypical Lipomatous Neoplasm With Anisocytosis, Focal Nuclear Atypia, p53 Overexpression, and a Lack of MDM2 Gene Amplification by FISH: A Report of 66 Cases Demonstrating Occasional Multifocality and a Rare Association With Retinoblastoma

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脂肪细胞肿瘤最新分类（WHO2013版)

良性

脂肪瘤
脂肪瘤病
神经脂肪瘤病
脂肪母细胞瘤/脂肪母细胞瘤病
血管脂肪瘤
平滑肌脂肪瘤
软骨样脂肪瘤
肾外血管平滑肌脂肪瘤
肾上腺外髓性脂肪瘤
梭形细胞/多形性脂肪瘤
冬眠瘤

中间性（局部侵袭性）

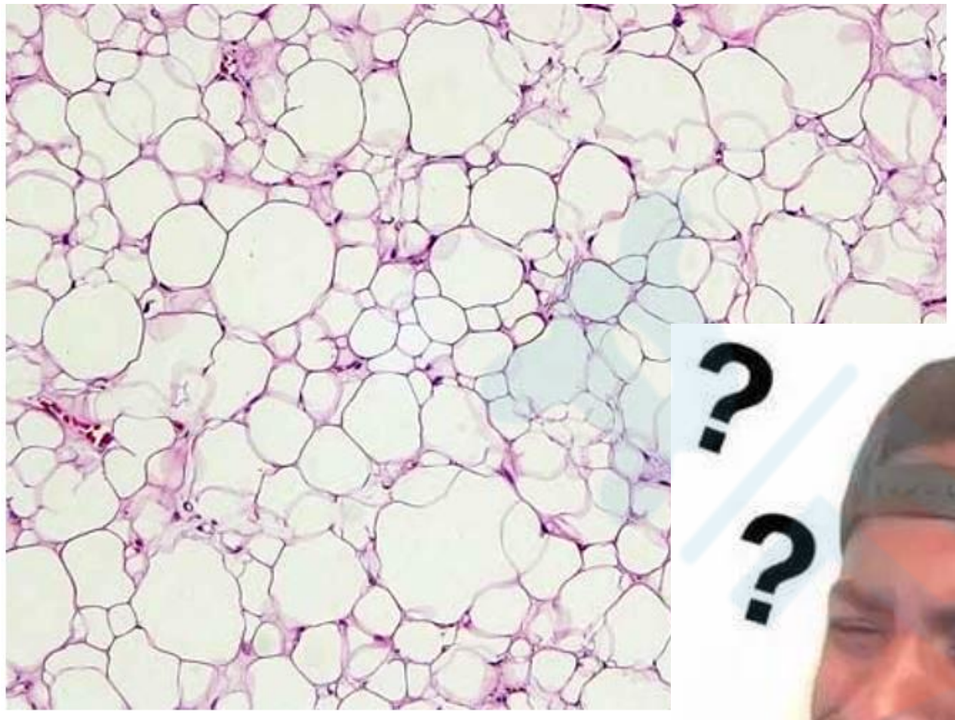
非典型脂肪瘤性肿瘤/高分化脂肪肉瘤

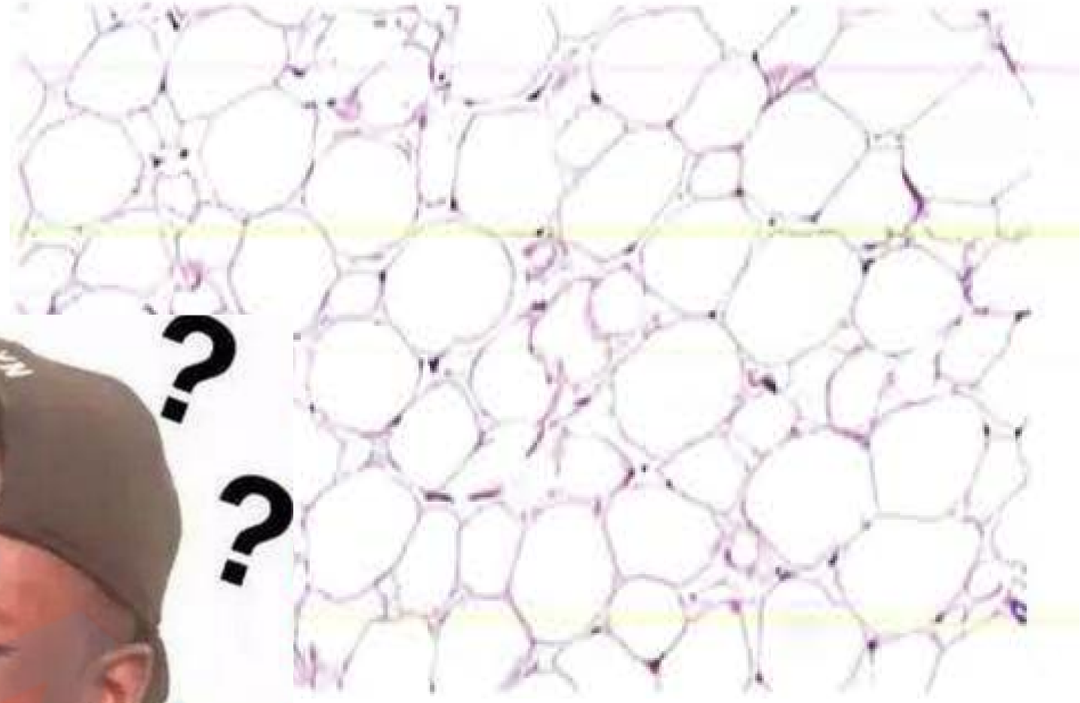
恶性

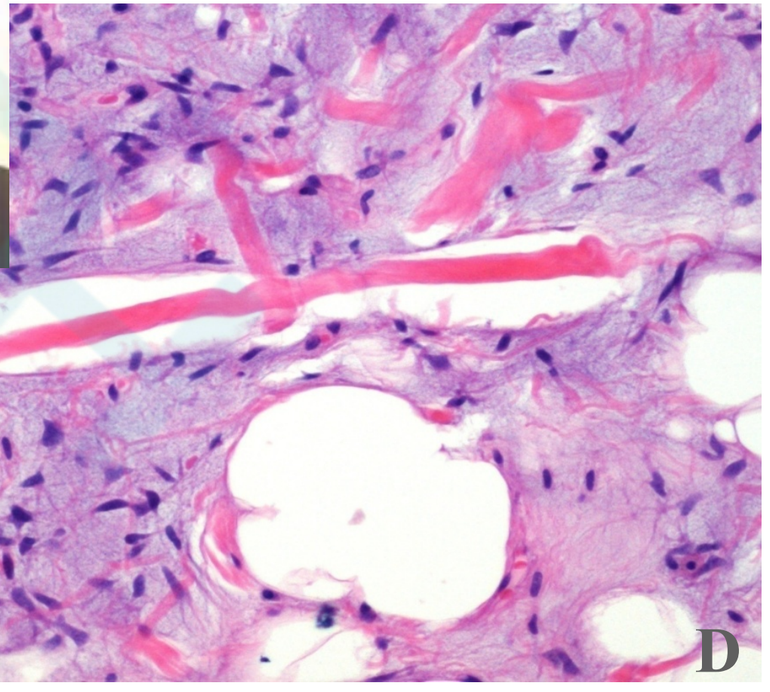
去分化脂肪肉瘤
黏液样脂肪肉瘤
多形性脂肪肉瘤
混合型脂肪肉瘤
脂肪肉瘤，NOS

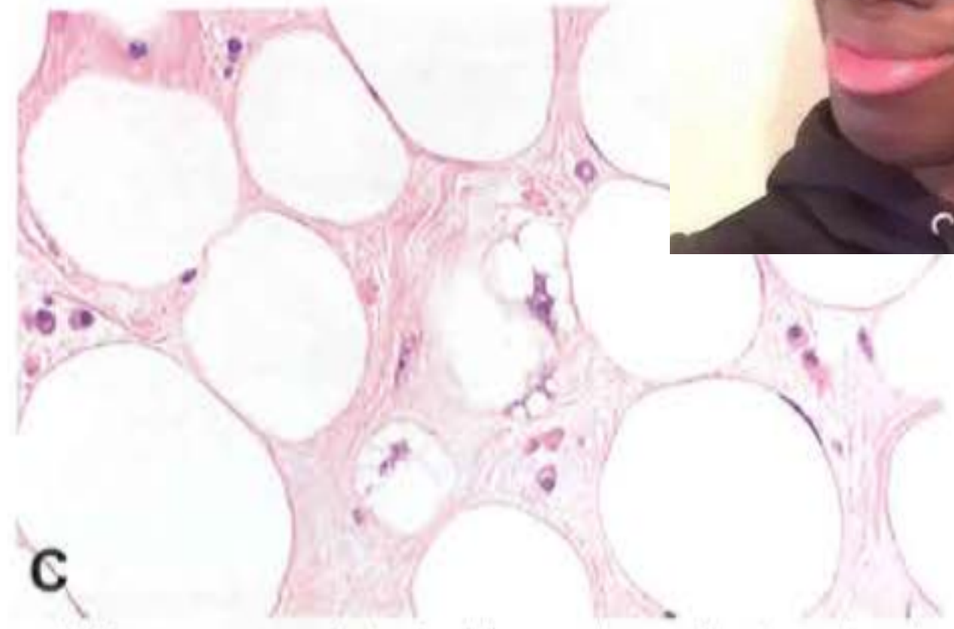
WHO Classification of Tumours of soft Tissue and Bone 4th 2013

小测验









脂肪瘤

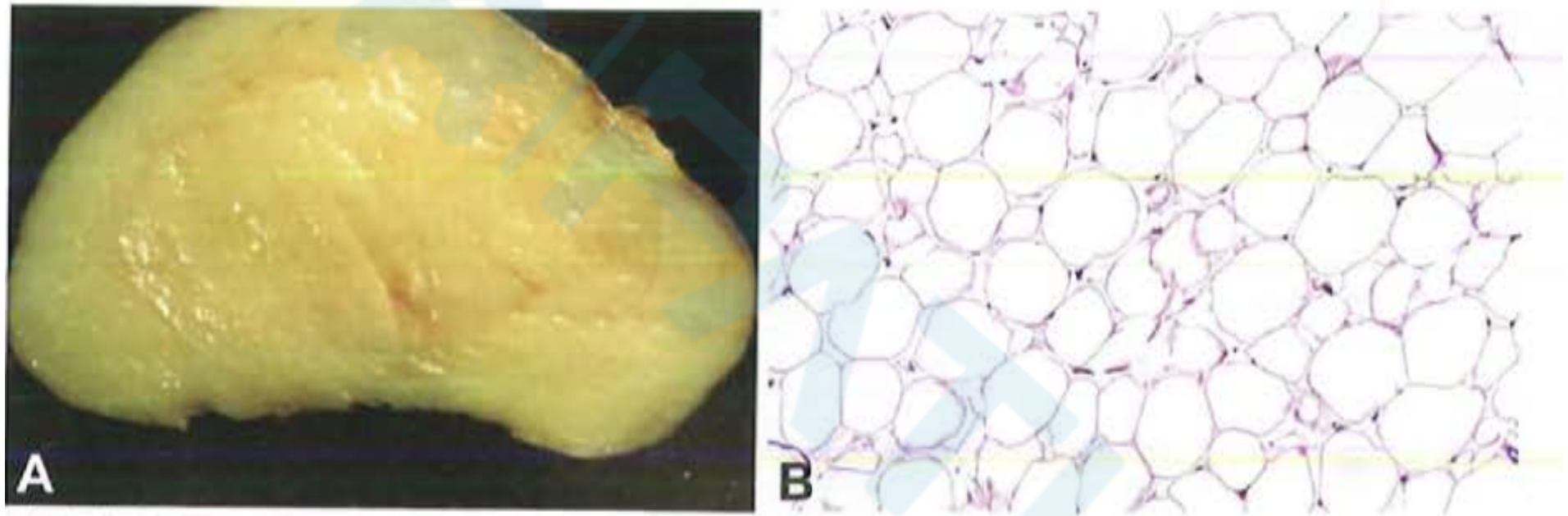


Fig. 2.01 Conventional lipoma. **A** Grossly, the tumour is well-circumscribed and has a homogeneous, yellow cut surface. **B** The mature adipocytes vary only slightly in size and shape and have small eccentric nuclei.

WHO Classification of Tumours of soft Tissue and Bone 4th 2013

非典型脂肪瘤样肿瘤/高分化脂肪肉瘤

- ICD-0编码：8850/1
- 最常见于四肢深部软组织

  其次为腹膜后、睾丸旁区和纵隔
- 组织学亚型

  脂肪细胞型

  硬化型

  炎症型

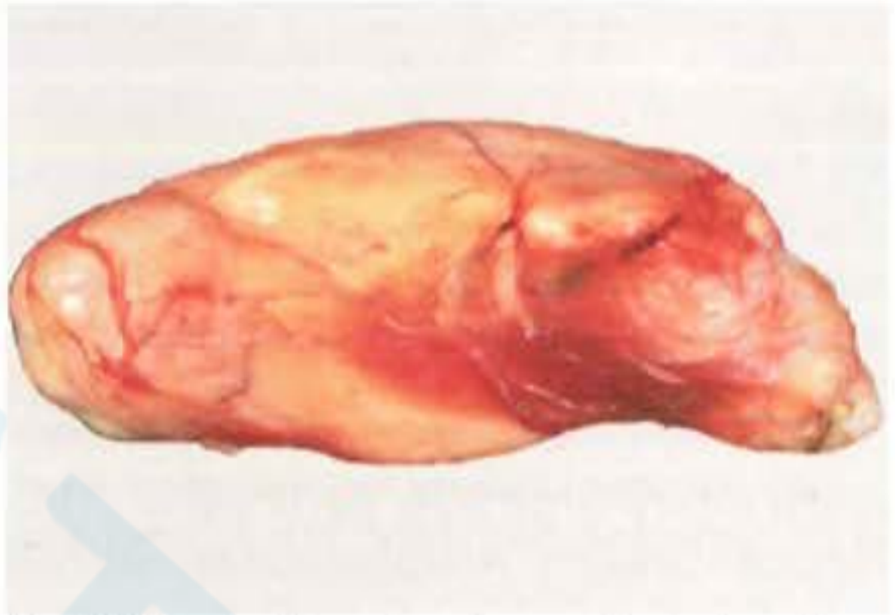
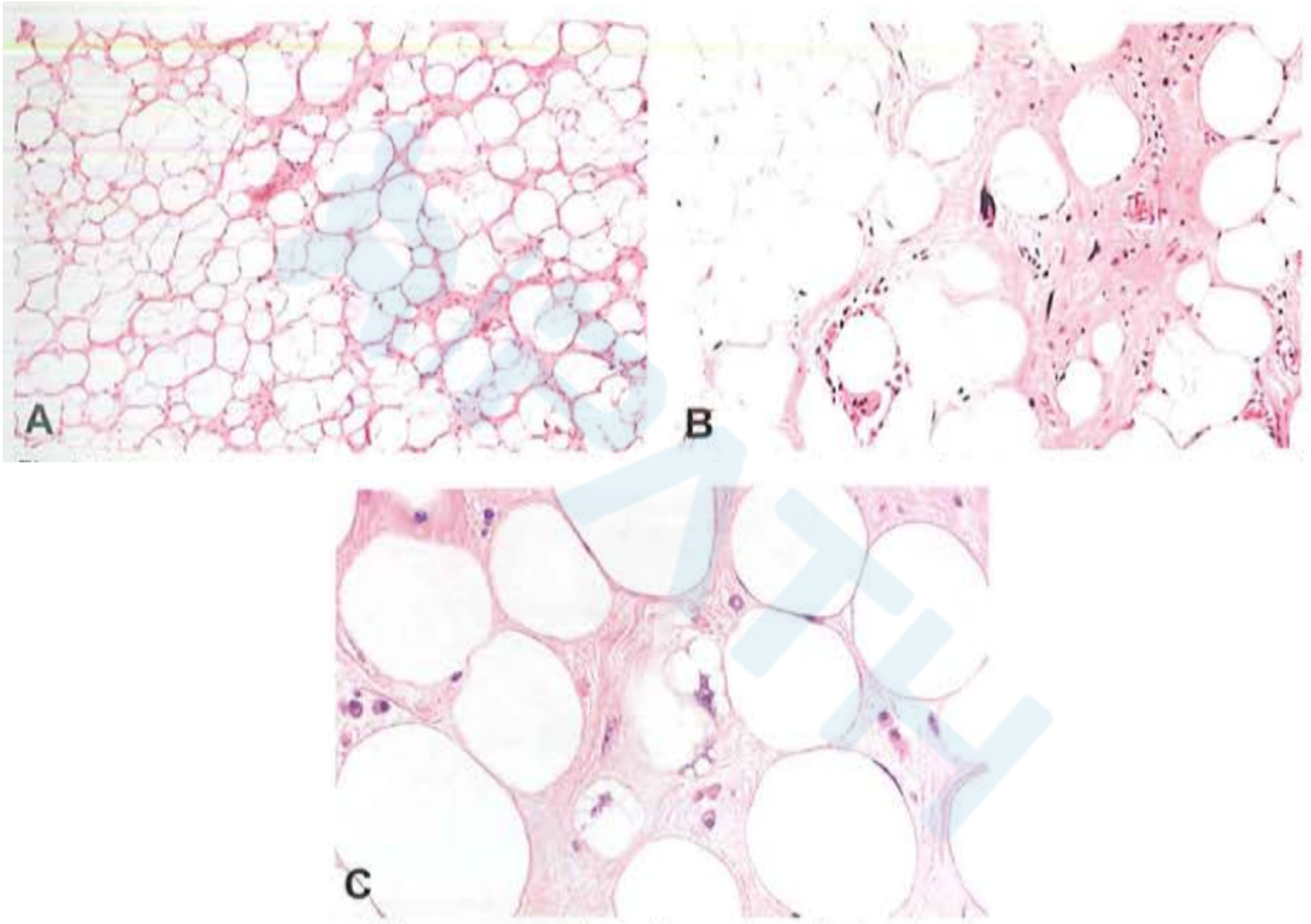


Fig. 2.22 Atypical lipomatous tumour. Surgical specimen showing a well-circumscribed, lobulated mass.

非典型脂肪瘤样肿瘤/高分化脂肪肉瘤

- 交界恶性（局部浸润）间叶组织肿瘤
- 脂肪空泡大小不一，至少局部有脂肪细胞或间质细胞的核异型性
- 出现散在的核浓染、多空泡间质细胞和数量不等的单空泡或多空泡的脂肪母细胞
- 胞浆内出现单个或多个边缘清楚的空泡压迫深染的细胞核呈扇贝样外观



WHO Classification of Tumours of soft Tissue and Bone 4th 2013

AJSP: Reviews & Reports 2016;21: 195–199

Anisometric Cell Lipoma: A Predominantly Subcutaneous Fatty Tumor With Notable Variation in Fat Cell Size But Not More Than Slight Nuclear

好发于躯干上部，男性多见

脂肪大小不一，可见核非典型性及单个脂肪细胞坏死

P53过表达，RB1蛋白缺失，无MDM2扩增

Ann Diagn Path

Anisometr
literature
role for RB1 loss and possible relationship to fat-predominant ("fat-only")
spindle cell lipoma

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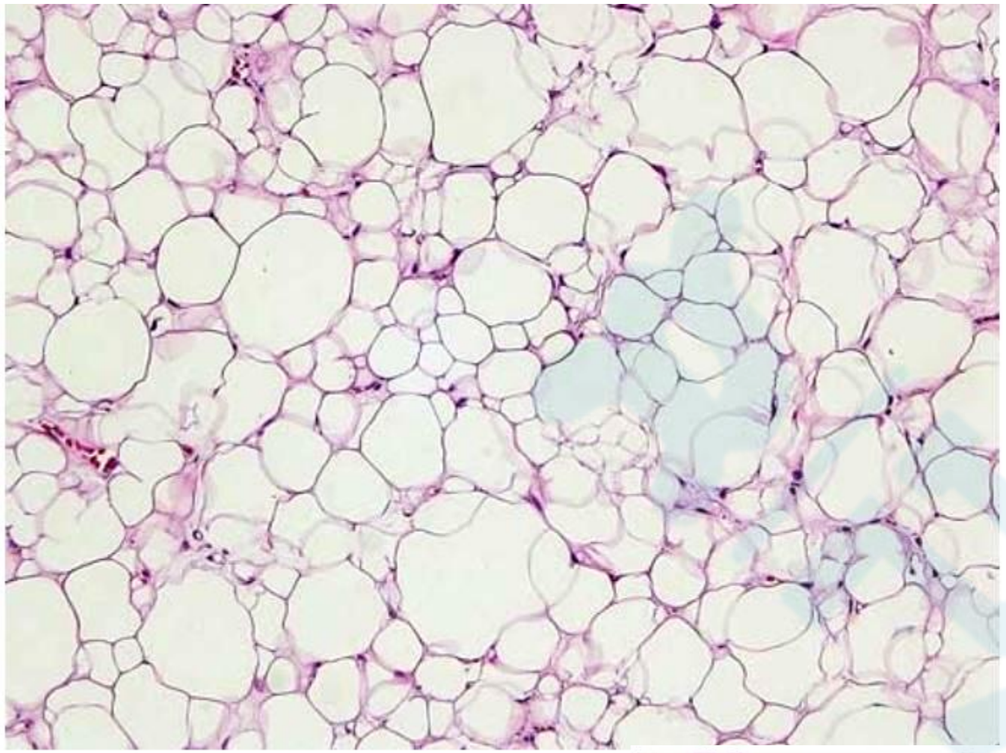
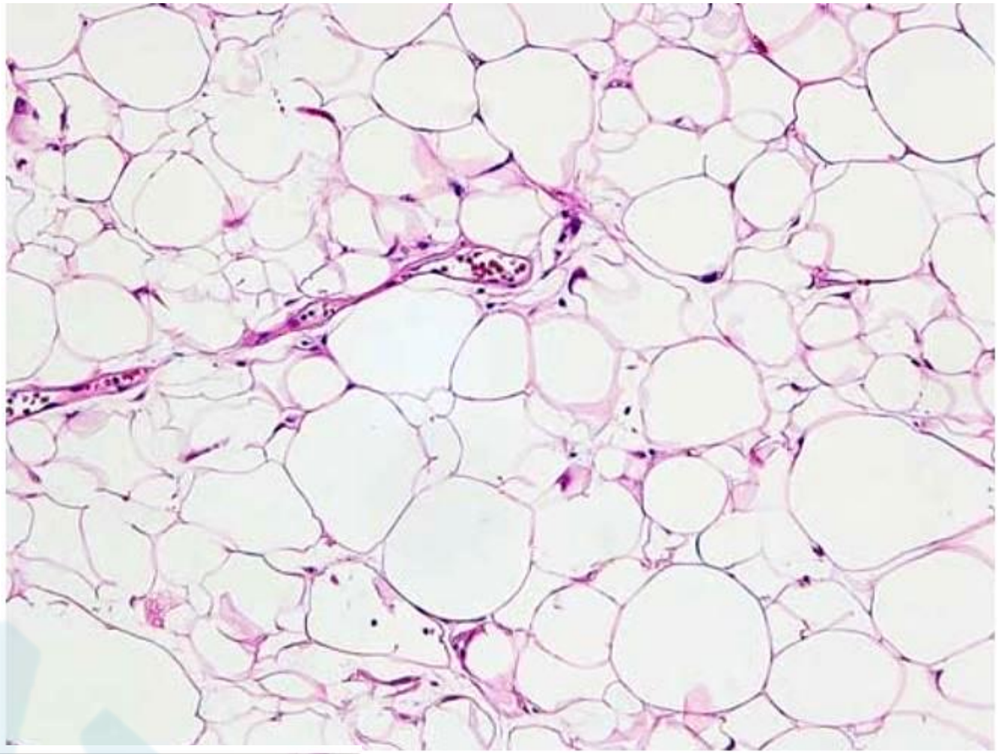
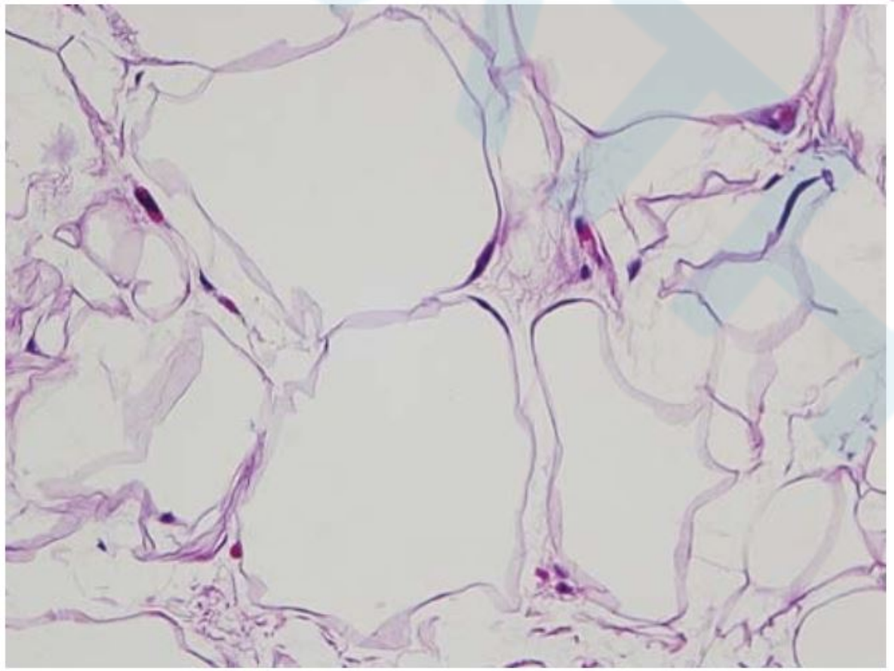
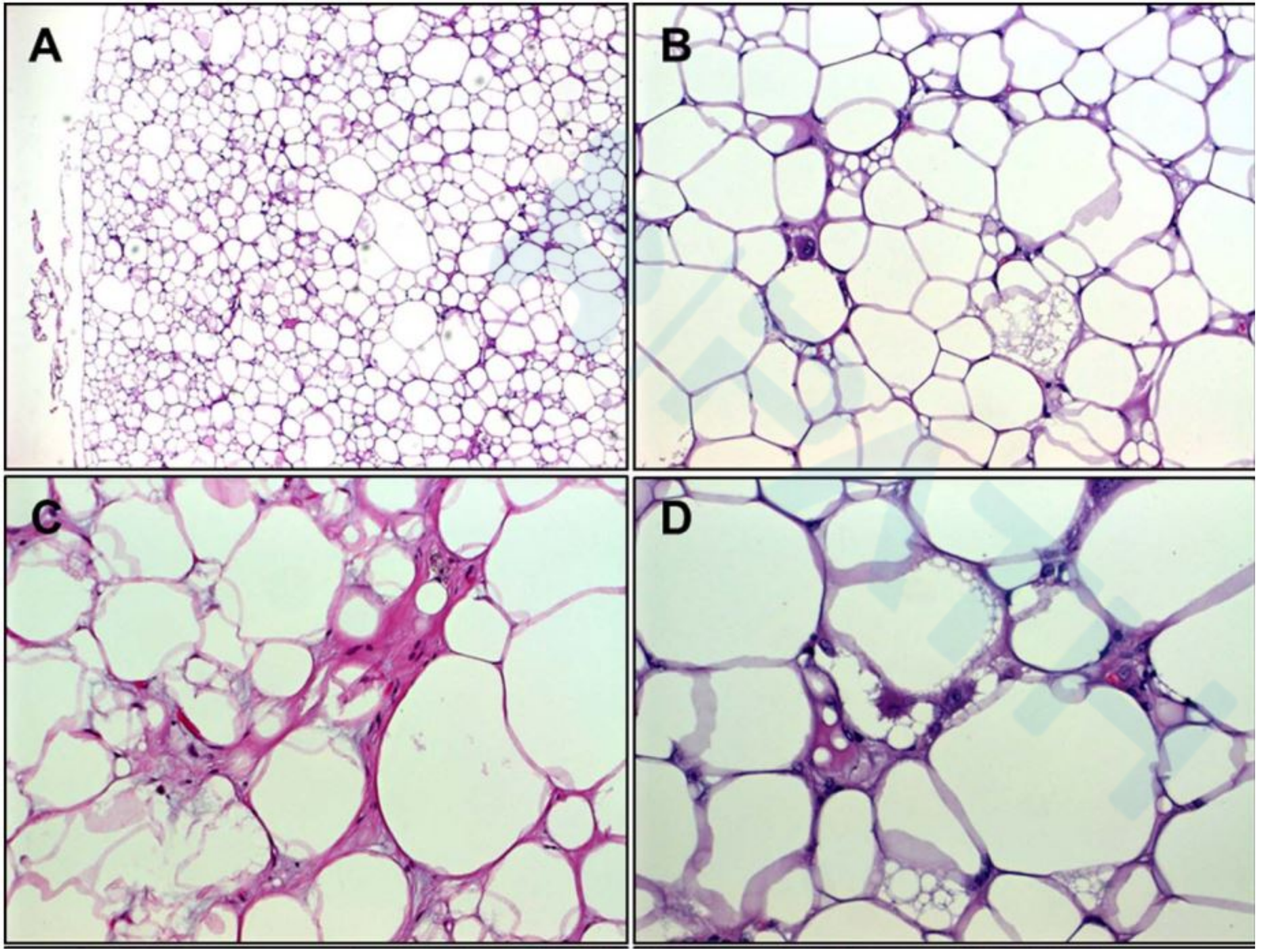








Ann Diagn Pathol. 2017;29:52–56.

研究目的

提出不典型脂肪瘤（dysplastic lipoma）的概念，并通过大量病例研究揭示该肿瘤的临床病理学及分子遗传学特征

MATERIALS AND METHODS

材料与方法

病例来源

5例常规病例，61例会诊病例

免疫组化

CD34、RB1、MDM2、P16、CDK4、CD163、S100、P53

分子遗传学研究

FISH：*MDM2*、*RB1*

Sanger Sequencing：*TP53*

NGS：271 cancer-related genes panel including *TP53, RB1, and MDM2*

RESULTS

TABLE 1. Clinical Features for Selected Patients With Dysplastic Lipoma*

Case	Age (y)/ Sex	Location	Duration (mo)	Tumor Size (cm)	Submitting Diagnosis	Multiple Sites	Recurrence	Follow-up (mo)	Other
9	55/M	L shoulder-upper arm	NA	4	Lipoma vs. ALT	Yes—1 DL	No	10	
15	63/M	Posterior neck	NA	4.5×4×2	ALT	Ordinary lipoma—R upper arm	No	36	
23	34/M	Neck/trunk/ upper arm/ bilateral scrotal area	NA	~9	NA	Multiple DL, excisions since the age 26	No	17	Retinoblastoma at the age 1
25	43/M	Posterior neck	NA	4.5	Lipoma vs. ALT	No	Yes (in 7 mo)	7	
36	22/F	R shoulder	Months	7.5	LN with rare atypical cells	Another LN—NR	No	25	
37	49/M	R hip/L upper arm	>11	5×4.3×1.8	ALT	Yes	No	28	First tumor with increased atypia
43	45/M	R back over scapula	12	4.8×4×2.2	LN—ALT?	LN on L neck (4.5×3.2×2.5 cm) NR	No	19	Pheochromo-cytoma
45	28/M	L shoulder	NA	4×2.2×1.5	LN—ALT×lipoblasto-ma×pleomorphic lipoma?	Other LN—R side 5 y prior, NR	No	19	
46	37/M	R neck	>28	4.2×3.8×2.6	Lipoma with mild atypia	No	Yes	44	Multiple nevi
62	51/M	L inferior back	NA	6.2×3.6×2.6	Lipoma with mild atypia	2 other LN, superior back (6.6 cm) and L chest (3.4 cm), NR	NA	NA	
64	43/M	Posterior neck	NA	3.3×2.6×1.5	Fibroadipose tissue—lipoma?	SQ LN 14 y prior in both biceps; 7 y prior in R forearm, 4.8×3×1.5, NR	NA	NA	
65	70/M	R shoulder	NA	3.2×2.6×1.5	LN	Yes—2 DL+other SQ LN 10 y prior—NR	NA	NA	

临床特征

- 男：女=57：8，年龄22-87岁（51.2岁）
- 所有肿物均位于皮下，仅一例侵及胸锁乳突肌
- 62/64位于头颈部、上肢躯干，好发于上背部、肩部、颈背部
- 最大径1.5-14cm（5.2cm）
- 10例同时或异时多发脂肪肿瘤

Supplementary Table 1：http://links.lww.com/PAS/A666

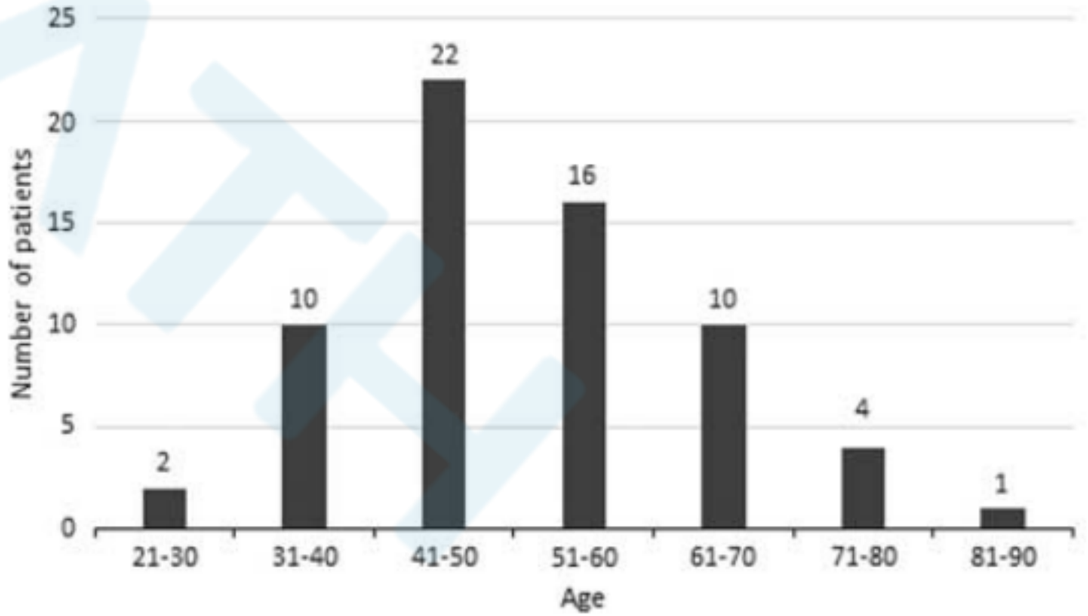


FIGURE 1. The graph shows age distribution of patients with dysplastic lipoma.

临床特征

- 所有肿瘤均行单纯切除术
- 47例随访病例（1-192月）只有2例发生局部复发，其中1例于术后7个月复发，另1例于术后44个月复发
- 所有病例在随访期间均未发生转移及死亡

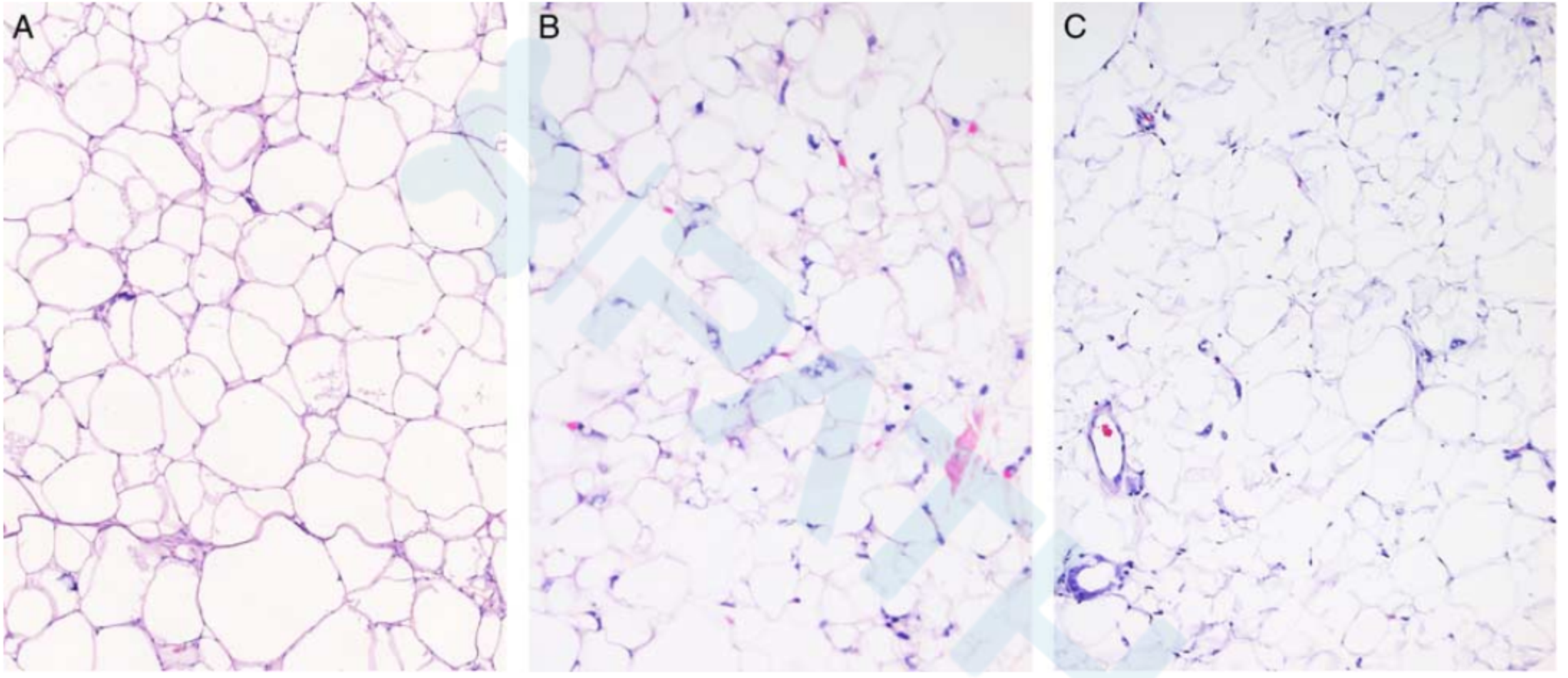


FIGURE 2. Low power pictures of dysplastic lipomas. Note substantial adipocytic size variation, patchy single-cell fat necrosis, and scattered hints of mild adipocytic atypia. Case 12 (A). Two different tumors in the same patient (case 37): the first tumor with a more pronounced adipocytic atypia (B) and the recurrence (C).

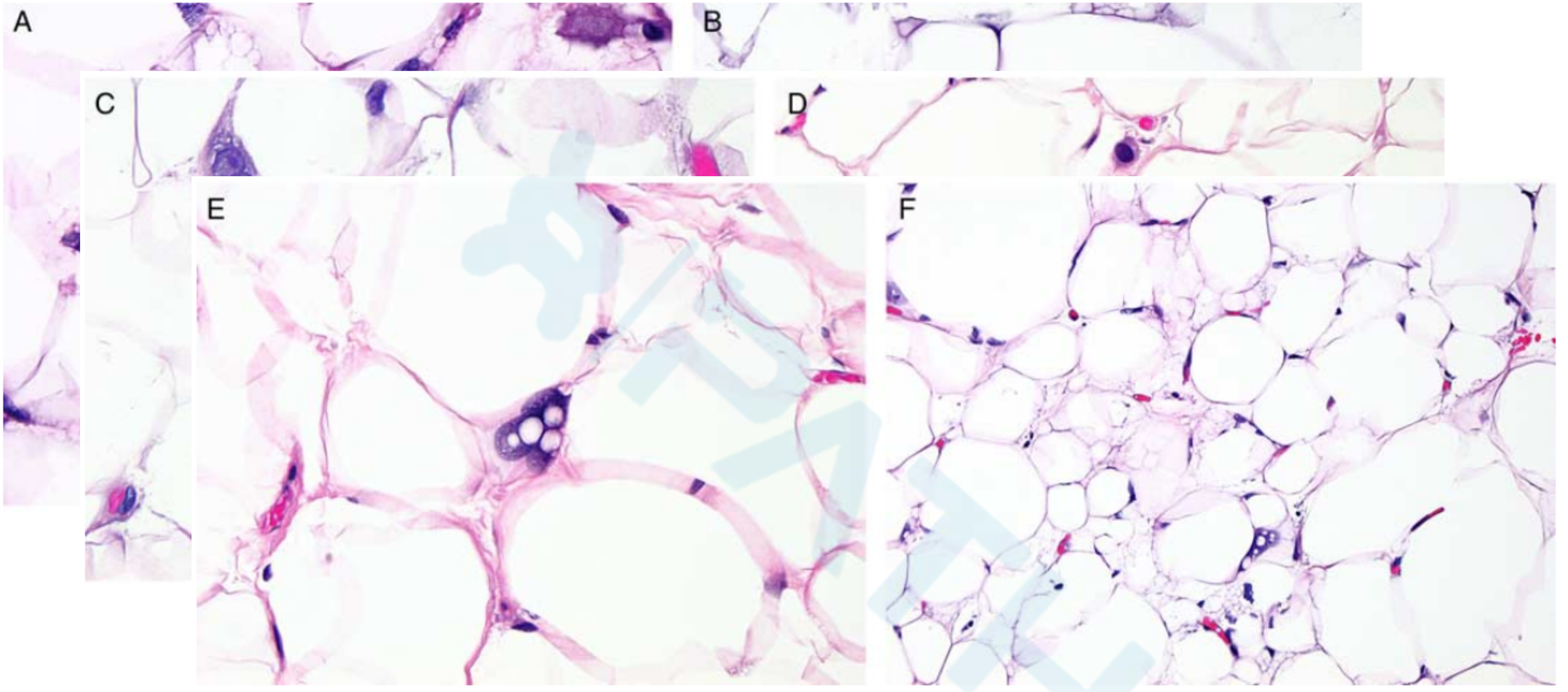


FIGURE 3. Intermediate and high-power views demonstrating adipocytic atypia (A–F). Binucleation (C, arrow) and multinucleation were a common finding (A, B, E). Nuclear enlargement, hyperchromasia with chromatin coarsening, and one or more small nucleoli (A) were frequently present. Reactive histiocytes were a common finding (C, arrowhead). *Lochkern* change was also encountered with some regularity (A, B, E, F).

免疫组化

抗体	表达情况
P53	所有病例均表达（阳性率2%-20%），尤其具有非典型核的脂肪细胞
S-100	大部分脂肪细胞表达
MDM2	20/50表达，大部分表达<1%
CDK4	所有检测病例均阴性
RB1	22/32显示所有肿瘤细胞表达缺失，10/32显示部分细胞表达缺失
CD163	组织细胞阳性，有助于区分非典型脂肪细胞

Supplementary Table 2：http://links.lww.com/PAS/A667

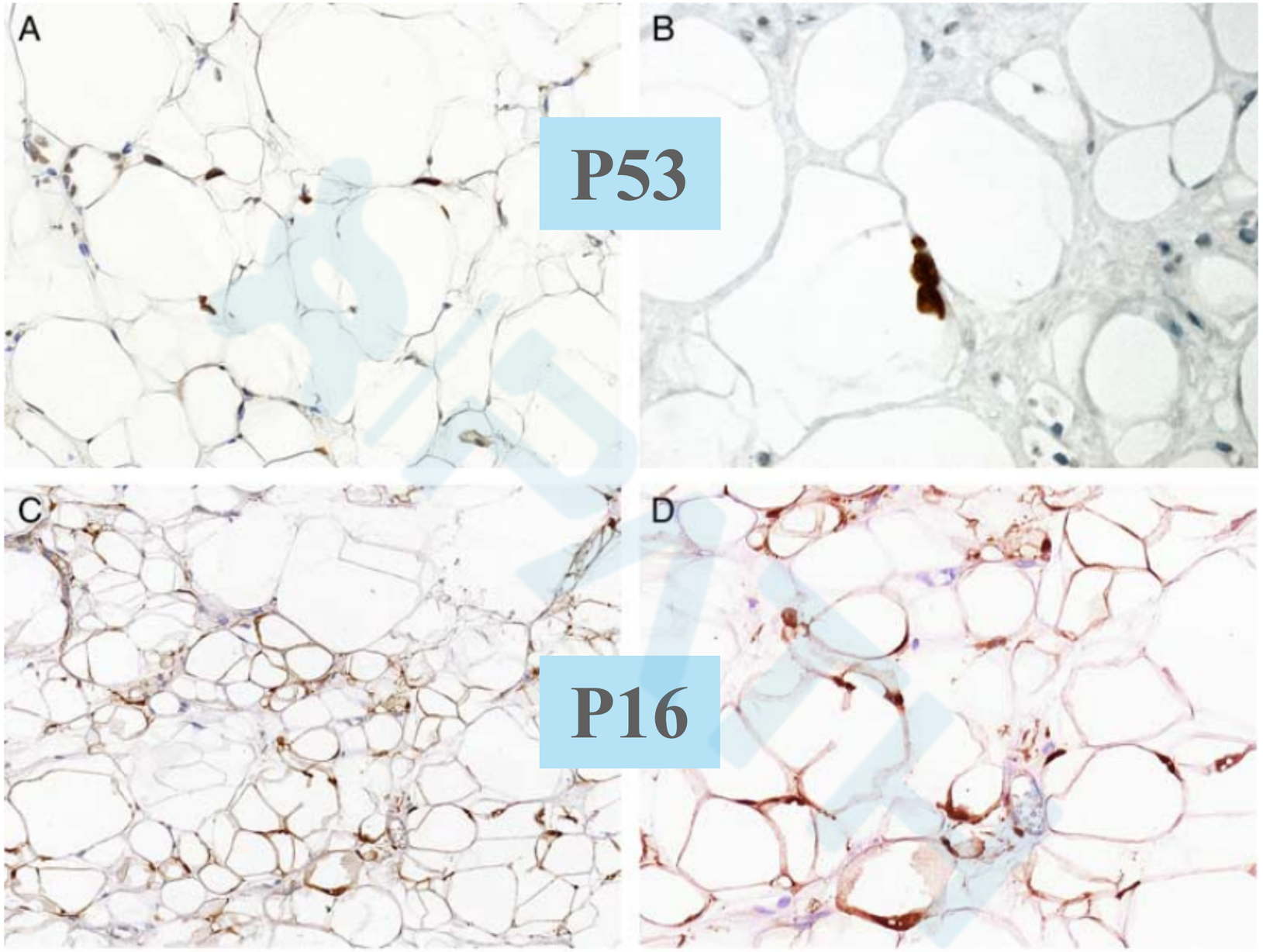
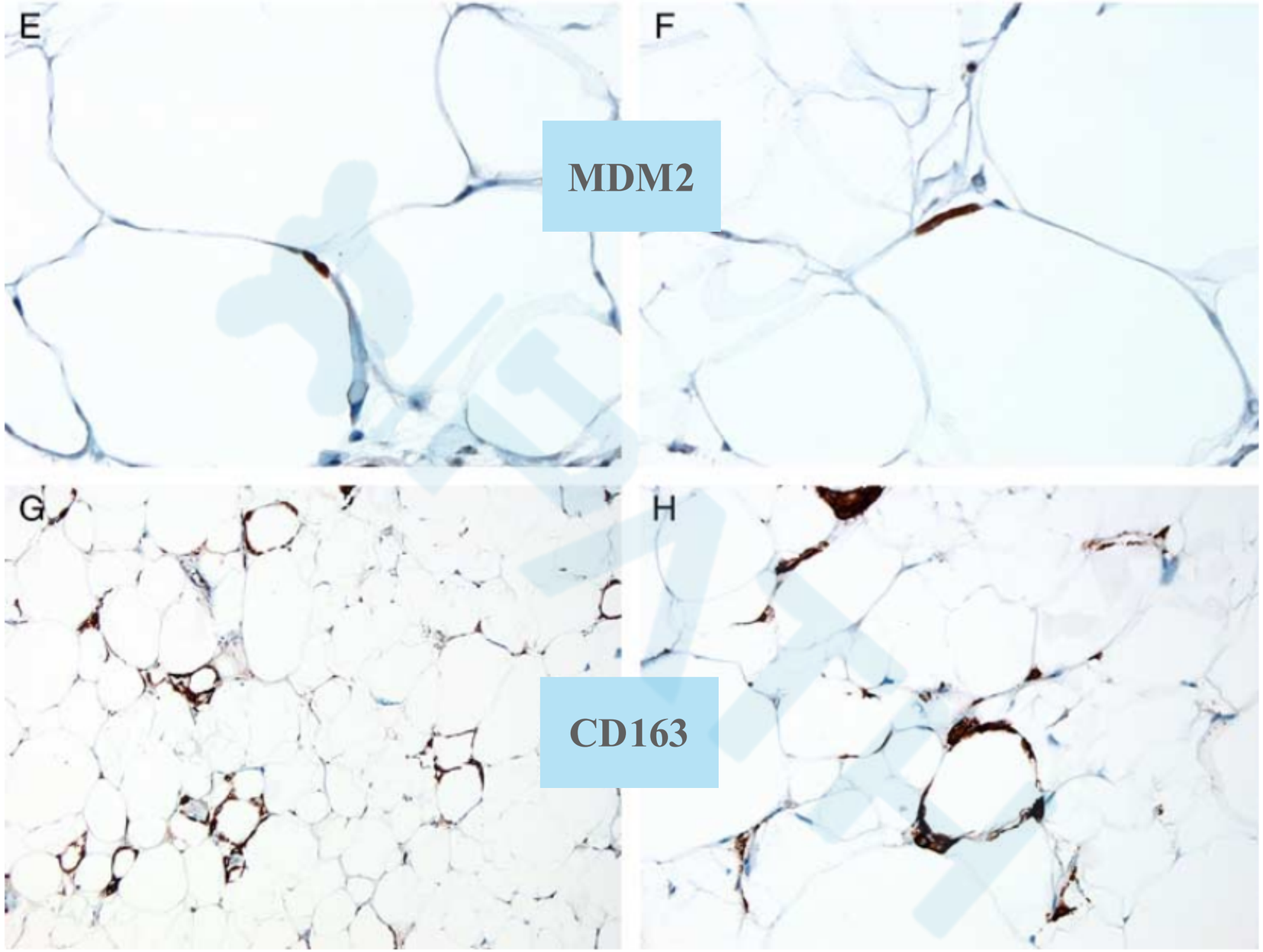


FIGURE 4. A–H, Immunohistochemical results for dysplastic lipomas. Intermediate and high-power views of atypical adipocytes with p53 expression (A and B). Intermediate and high-power views of p16 expression (C and D). Rare scattered adipocytic nuclei with immunoreactivity for MDM2 (E and F). Intermediate and high-power views showing CD163 immunoreactivity in the histiocytic population within dysplastic lipomas (G and H).



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分子遗传学

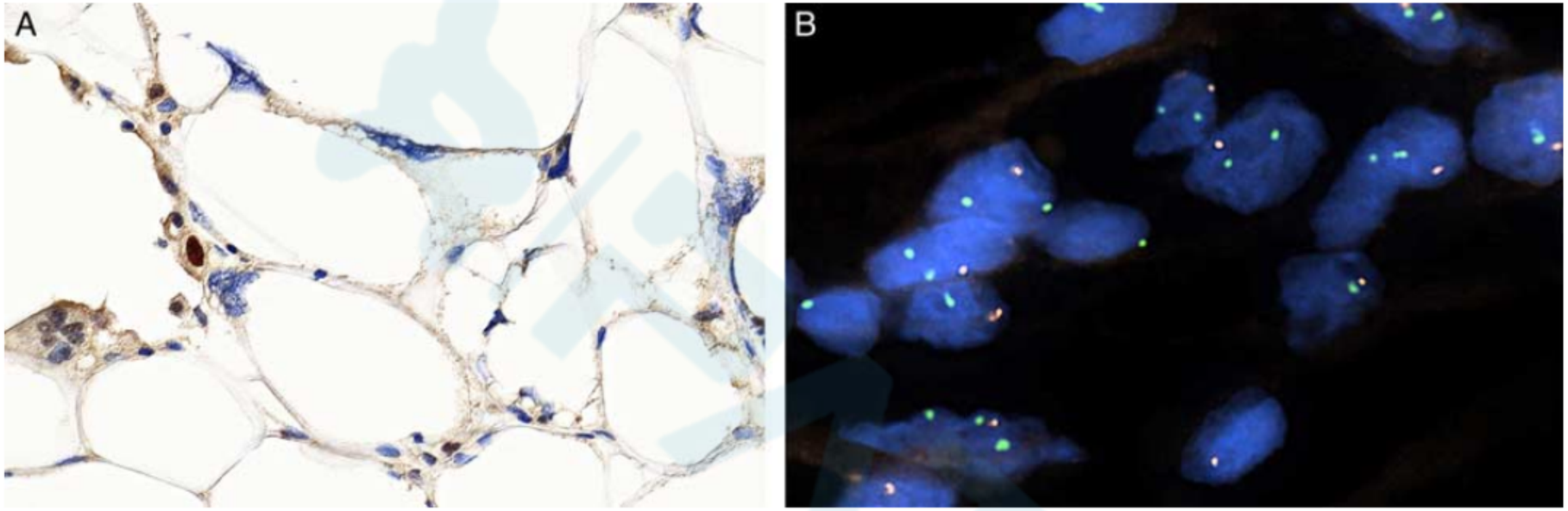


FIGURE 5. Immunohistochemical loss of *RB1* expression in a dysplastic lipoma (A), and FISH showing a heterozygous *RB1* gene deletion (B).

- *MDM2*：所有病例均无扩增
- *RB1*：3/13杂合性缺失
- *TP53*：Sanger测序检测5例均无突变
- NGS：*KMT2D, PAK3, SETD2, SUZ12, PDGFRA, FGFR4, ATM*

DISCUSSION

不典型脂肪瘤

- 男性好发，男：女=7:1
- 发病年龄广（22-87岁）
- 最常发生于背部、肩部、后颈部
- 常为多发
- 肉眼所见：界限清楚的皮下软组织包块

- 组织学：

—脂肪空泡大小不一

—可见非典型核，核拉长、染色质浓集，可见小核仁

—可见散在的单个脂肪细胞坏死

—少见梭形细胞间质及胶原基质

—罕见多空泡脂肪母细胞

不典型脂肪瘤

- 免疫组化：P53过表达，*RB1*表达缺失，MDM2可阳性
- 分子特征：

—*MDM2*无扩增

—*RB1*杂合性缺失

—*TP53*无突变

- 治疗与预后：单纯切除后长期随访罕见复发，未见转移

鉴别诊断

	脂肪瘤	不典型脂肪瘤
部位	无特殊	背部、肩部、后颈部
性别	无差异	男性多
坏死	一般为带状坏死	单个脂肪坏死
脂肪空泡	大小、形状一致	大小不一，形状各异
核不典型性	偶见核轻微拉长，但核膜轮廓清晰，染色质无浓集	可见非典型核，核拉长、染色质浓集，可见小核仁
P53	无过表达	过表达
RB1	表达正常	表达缺失

注意

单空泡或多空泡组织细胞误认为脂肪母细胞，组织细胞具有深染的肾形或卵圆形核，胞浆内可见空泡及弱嗜酸性颗粒；CD68、CD163阳性

梭形细胞/多形性脂肪瘤

◈ 发生部位及年龄

颈后部和肩部多见，面部、前额、头皮、口腔和口腔周围区以及上臂也可见

老年较多，10%为女性

◈ 组织学

梭形细胞脂肪瘤：

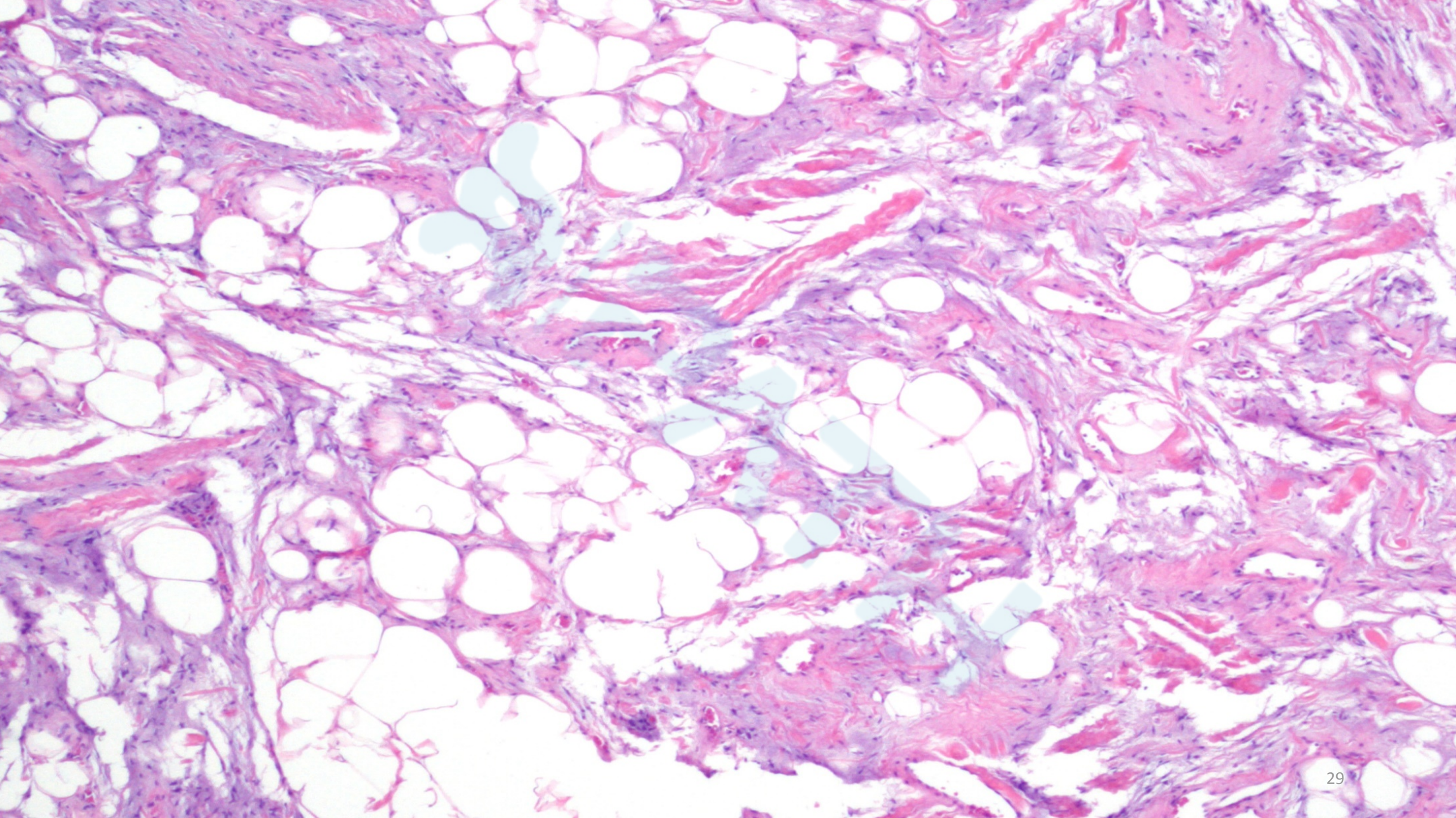
—无异形的梭形细胞在脂肪细胞和条索状胶原束之间平行排列

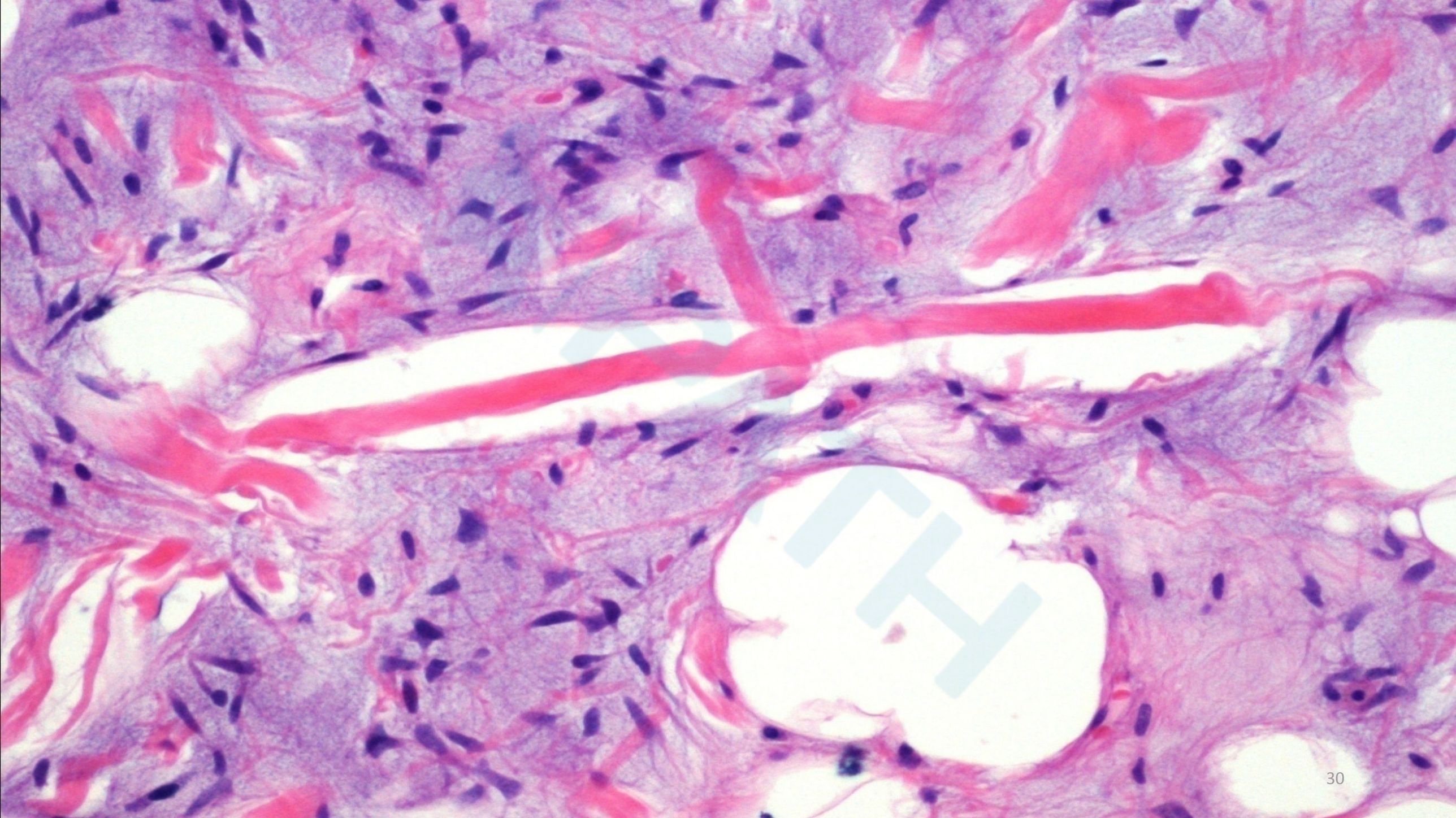
—间质大量肥大细胞，也可见到淋巴细胞和浆细胞

—部分可有间质黏液样变

多形性脂肪瘤：

以短梭形和圆形浓染的细胞和细胞核排列成“小花状”的多核巨细胞为特征





Am J Surg Pathol 2012;36:1119–1128

Loss of Retinoblastoma Protein Expression in Spindle Cell/Pleomorphic Lipomas and Cytogenetically Related Tumors: An Immunohistochemical Study With Diagnostic Implications

Benjamin J. Chen, MD, PhD, Adrián Mariño-Enríquez, MD, Christopher D.M. Fletcher, MD, FRCPath, and Jason L. Hornick, MD, PhD

梭形细胞/多形性脂肪瘤中RB蛋白表达缺失

标准：<10% 阳性细胞

皮下非典型脂肪瘤样肿瘤ALT

- 可见非典型非脂肪源性梭形细胞，且FISH检测出*MDM2*扩增
- 免疫组化MDM2在两者中均可阳性，无鉴别意义
- P16可阳性，但无特异性
- 大部分P53弥漫阳性，而不典型脂肪瘤仅为局灶阳性

预后

	复发	转移	死亡
脂肪瘤	无	无	无
梭形细胞/多形性脂肪瘤	少见	无	无
不典型脂肪瘤	4.2%	无	无
皮下ALT	<15%	无	无
深部软组织高分化脂肪肉瘤	30-50%	很少	罕见

总结

本文收集66例特殊的皮下脂肪肿瘤，作者命名其为“不典型脂肪瘤（Dysplastic lipoma）”，并通过对其临床病理学、免疫组化及分子遗传学研究，将其归为介于普通脂肪瘤与非典型脂肪瘤样肿瘤之间的脂肪肿瘤，关于本瘤的其他特点还需更多病例进行研究


恍然大悟

C

D

THANK YOU

Any questions?

Q&A