Trichodiskomy s převahou vřetenitých buněk a lipomatózní metaplazií či vřetenobuněčné/pleomorfní lipomy s adnexální indukcí?

Květa Michalová

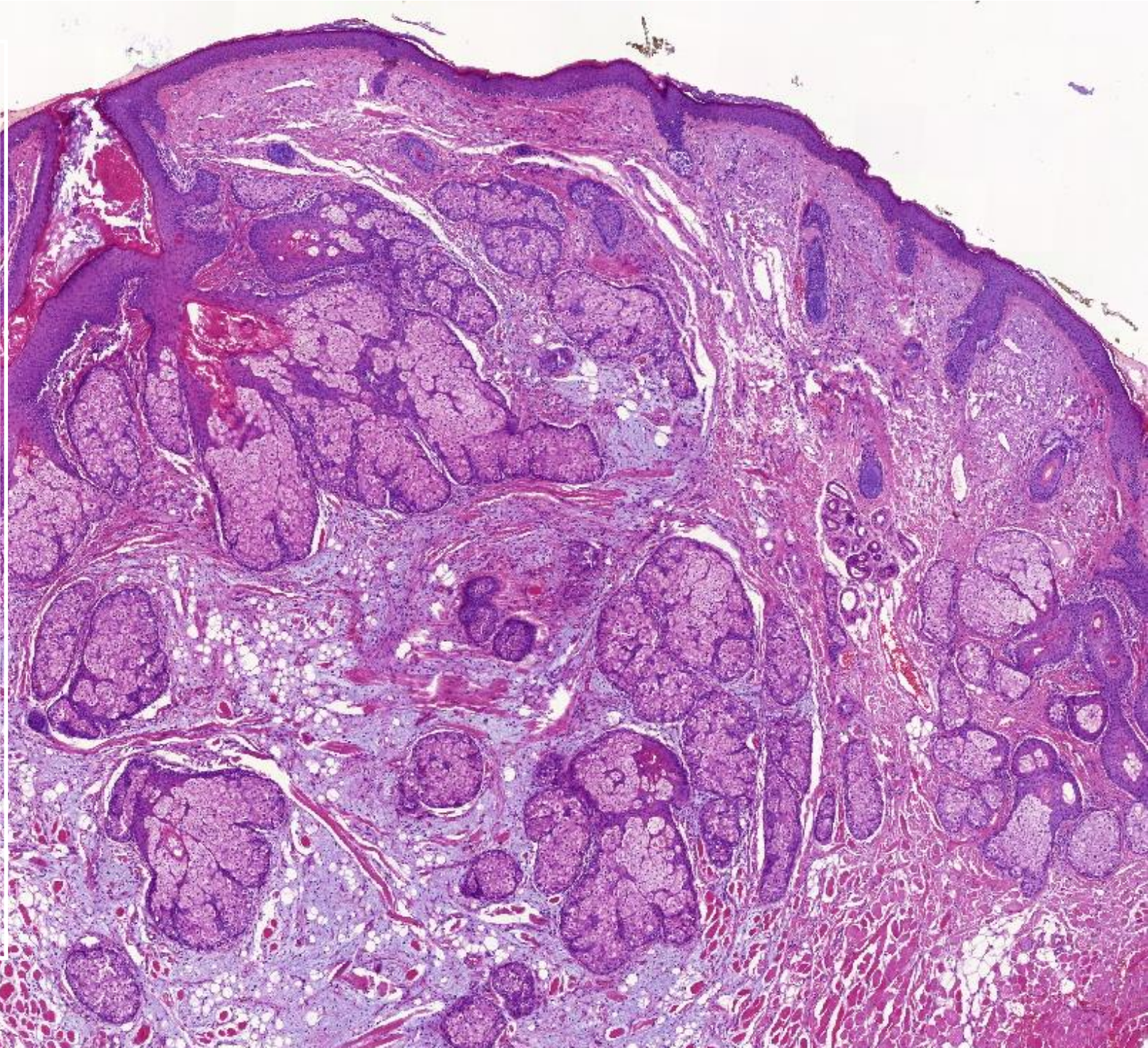
Bioptická laboratoř
CYTOLOGIE | BIOPSIE | MOLEKULÁRNÍ GENETIKA

PLZEŇ ŠIKLŮV ÚSTAV PATOLOGIE

TRICHODISKOM

- kožní adnexální léze s převážně sebaceózní diferenciací
- myxoidní vřetenobuněčné stroma s příměsí kolagenních vláken, obklopené trsy sebaceózních žláz
- do jejich morfologického spektra spadají též fibrofolikulomy (=mantleomy)

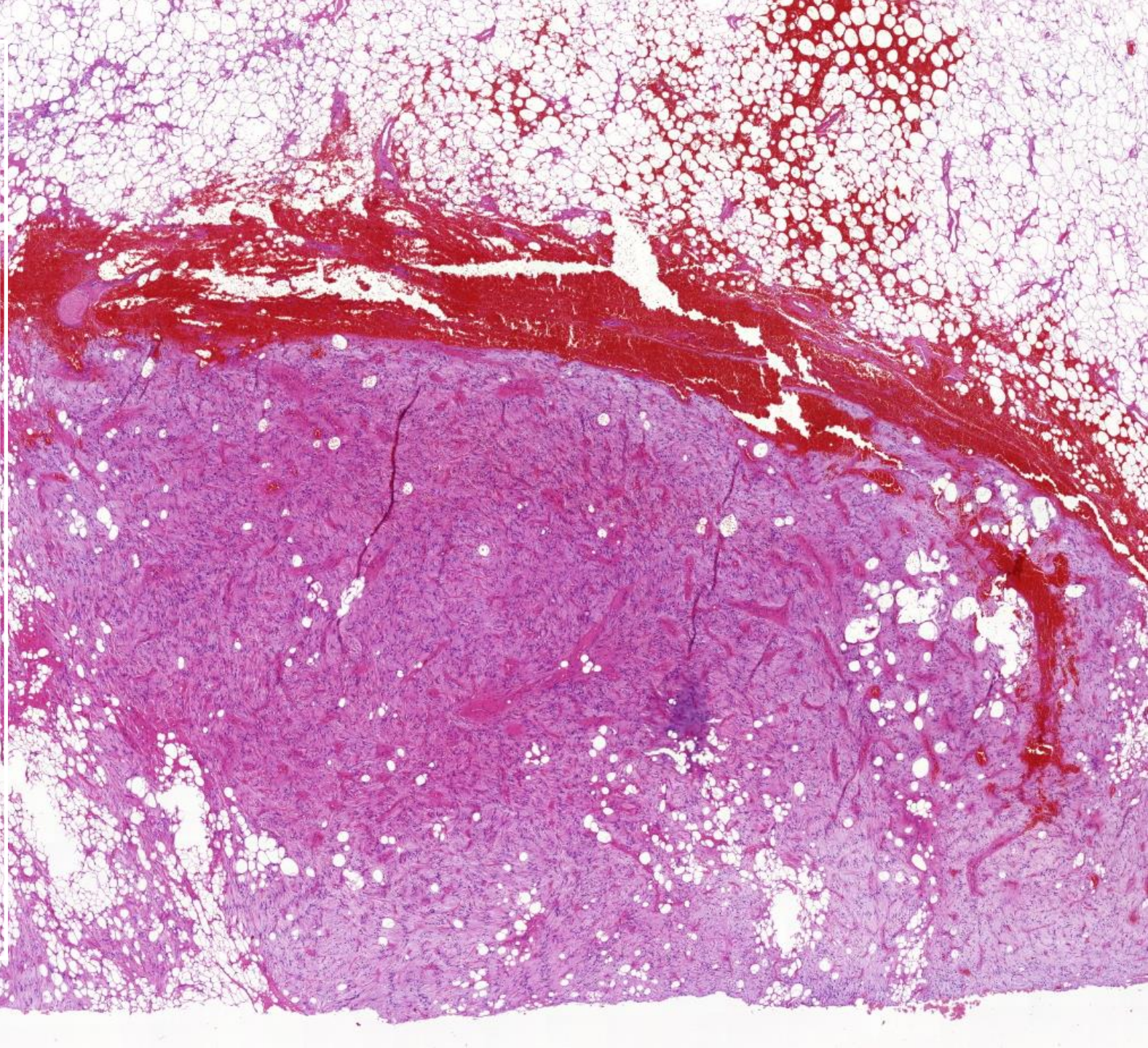
- většina na obličeji, hlavně na nose



VŘETENOBUNĚČNÝ /PLEOMORFNÍ LIPOM

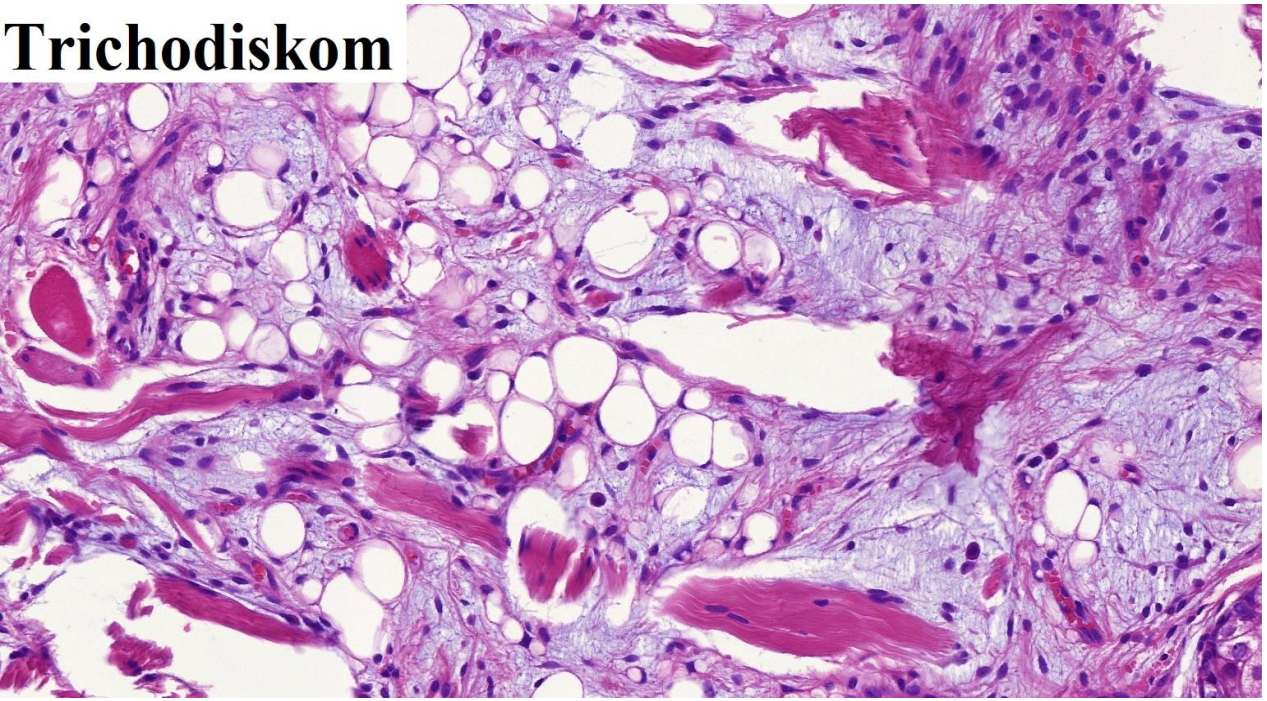
- tvořen variabilním množstvím tukové tkáně, blandními vřetenitými buňkami a silnými kolagenními vlákny
- pleomorfní lipomy mají navíc ve stromatu příměs pleomorfních buněk bizarních tvarů či mnohojaderných „floret-like cells“

- 90% na zádech a zadní straně krku u starších mužů

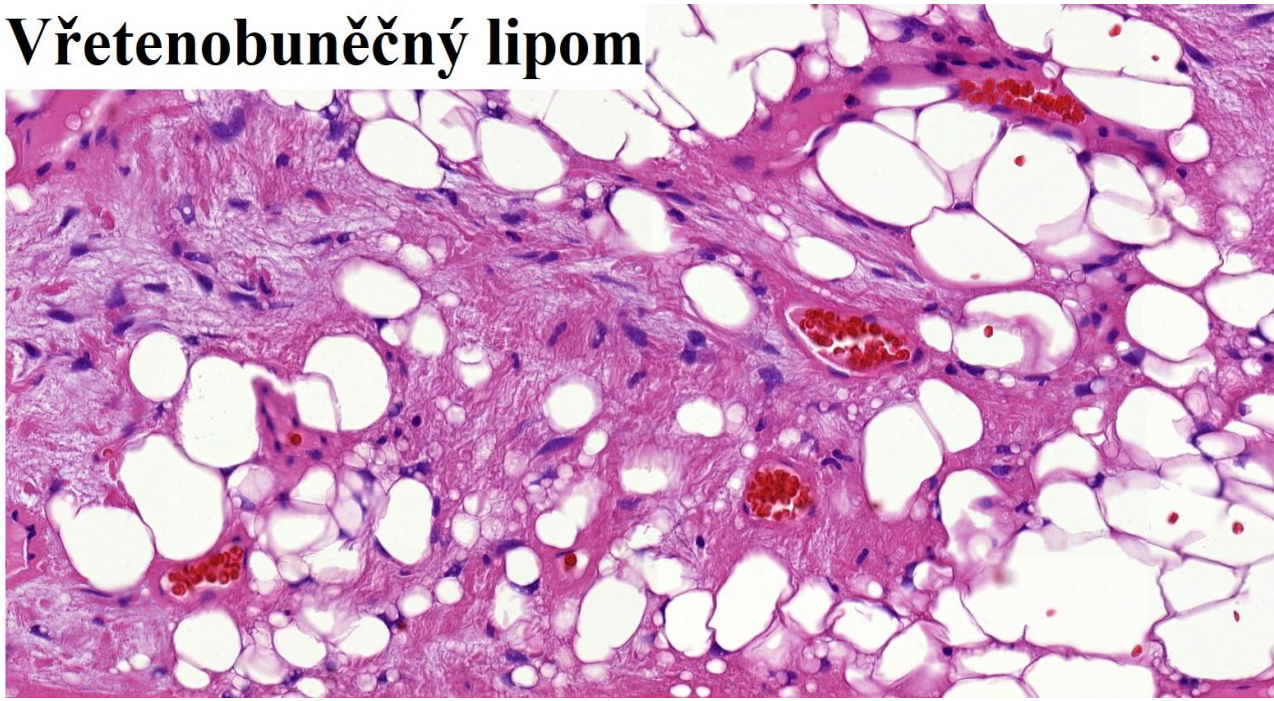


- stromální složka trichodiskomů je morfologicky identická s vřetenobuněčnými lipomy

Trichodiskom



Vřetenobuněčný lipom



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Maxime Battistella, MD, Peter Van Eeckhout, MD,† and Bernard Cribier, MD, PhD‡*

Spindle Cell Predominant Trichodiscoma or Spindle Cell Lipoma With Adnexal Induction? A Study of 25 Cases, Revealing a Subset of Cases With *RB1* Heterozygous Deletion in the Spindle Cell Stroma

Kvetoslava Michalova, MD, Heinz Kutzner, MD,† Petr Steiner, PhD,‡ Ladislav Hadravsky, MD,§ Michael Michal Jr, MD,*¶ Michal Michal, MD,* and Dmitry V. Kazakov, MD**

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Key Words: trichodiscoma, fibrofolliculoma, spindle cell lipoma, pleomorphic lipoma, epithelial induction, retinoblastoma, *RB1*gene

(*Am J Dermatopathol* 2019;00:1–7)

INTRODUCTION

Trichodiscoma is a cutaneous adnexal lesion with predominantly sebaceous differentiation which is, together with fibrofolliculoma, considered to represent a different stage of a single pathological process forming a morphological continuum that has been referred to as mantleoma.[1] In trichodiscoma, the predominant tissue element is centrally located variably myxoid spindle cell stroma admixed with collagen bundles surrounded by prominent clusters of sebaceous

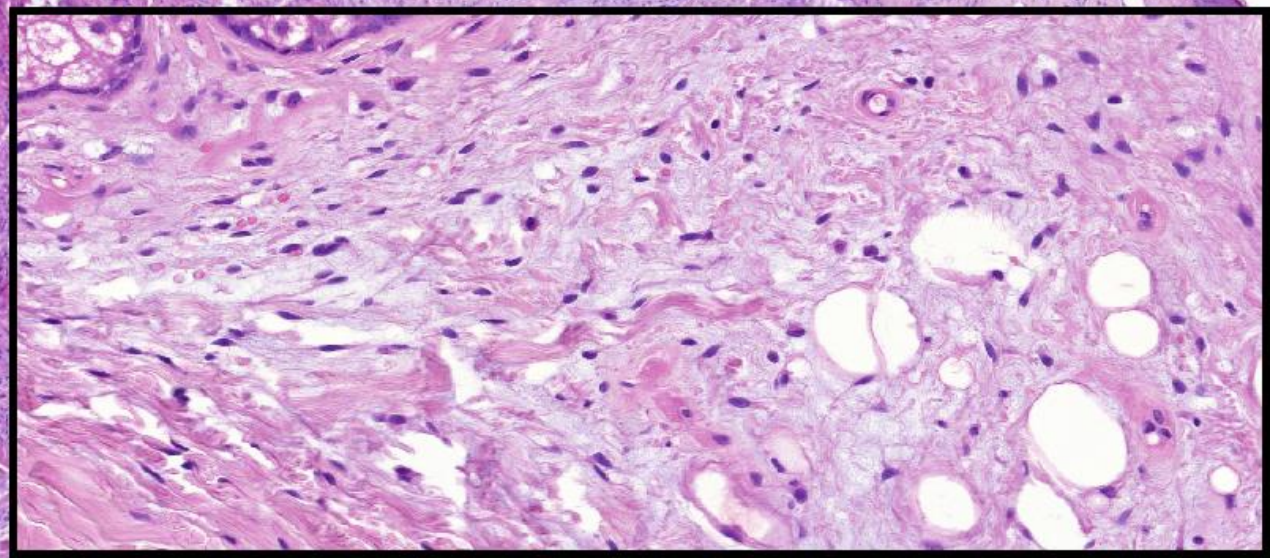
CASE NO	SCL TYPE	EPITHELIAL INDUCTION TYPE
1	MIXED	TRICHODISCOMA
2	MIXED	TRICHODISCOMA
3	MIXED	TRICHODISCOMA+FIBROFOLLICULOMA
4	MIXED	TRICHODISCOMA
5	MIXED	TRICHODISCOMA
6	FAT PREDOMINANT	TRICHODISCOMA
7	FAT PREDOMINANT	TRICHODISCOMA
8	FAT PREDOMINANT	TRICHODISCOMA
9	CLASSIC	TRICHODISCOMA
10	CLASSIC	TRICHODISCOMA
11	CLASSIC	FIBROFOLLICULOMA
12	FAT POOR	TRICHODISCOMA
13	FAT POOR	TRICHODISCOMA
14	FAT POOR	FIBROFOLLICULOMA
15	FAT POOR	TRICHODISCOMA+FIBROFOLLICULOMA
16	FAT POOR	TRICHODISCOMA
17	FAT POOR	TRICHODISCOMA
18	FAT POOR	TRICHODISCOMA
19	FAT POOR	TRICHODISCOMA
20	FAT POOR	TRICHODISCOMA
21	FAT POOR, PLEOMORPHIC LIPOMA	TRICHODISCOMA+FIBROFOLLICULOMA
22	FAT POOR	TRICHODISCOMA
23	FAT POOR	TRICHODISCOMA
24	FAT POOR	TRICHODISCOMA
25	FAT POOR	TRICHODISCOMA

<u>25 případů trichodiskomů</u>

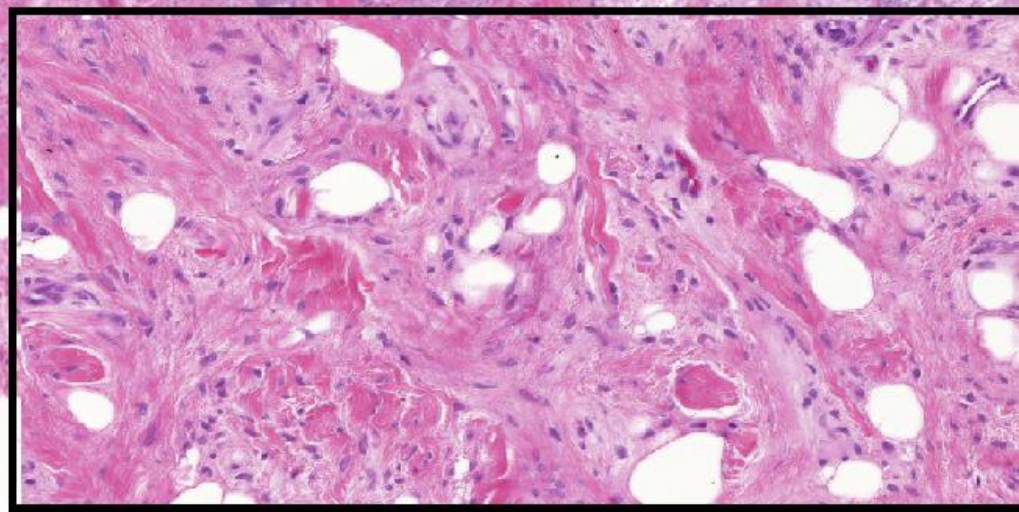
- Stroma:
  - 24 stroma jako vřetenobun.lipom (SCL), 1 jako pleomorfní lipom
    - 14 fat poor varianta SCL
    - 3 klasický SCL
    - 3 fat predominant
    - 5 „smíšených“ (fat poor+ klasický SCL)

- Epitel:
  - 20 klasických trichodiskomů
  - 3 trichodiskom i fibrofolikulom
  - 2 fibrofolikulomy

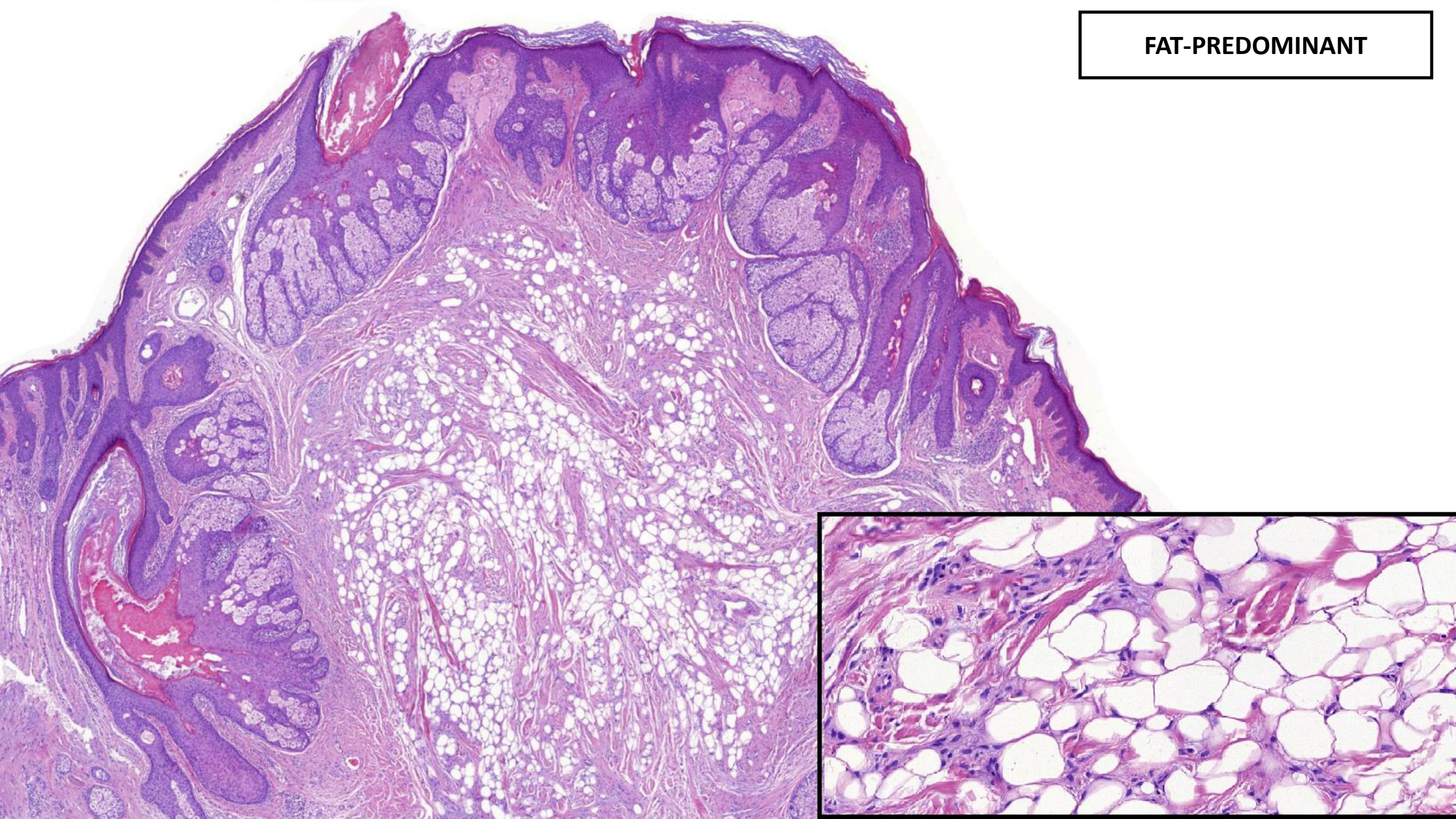
FAT-POOR



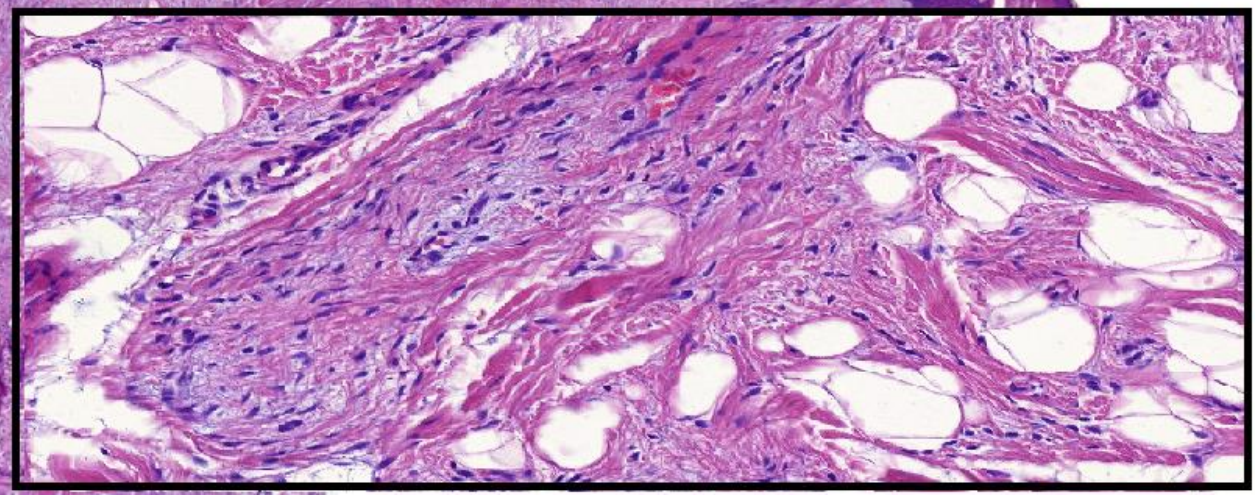
CLASSIC



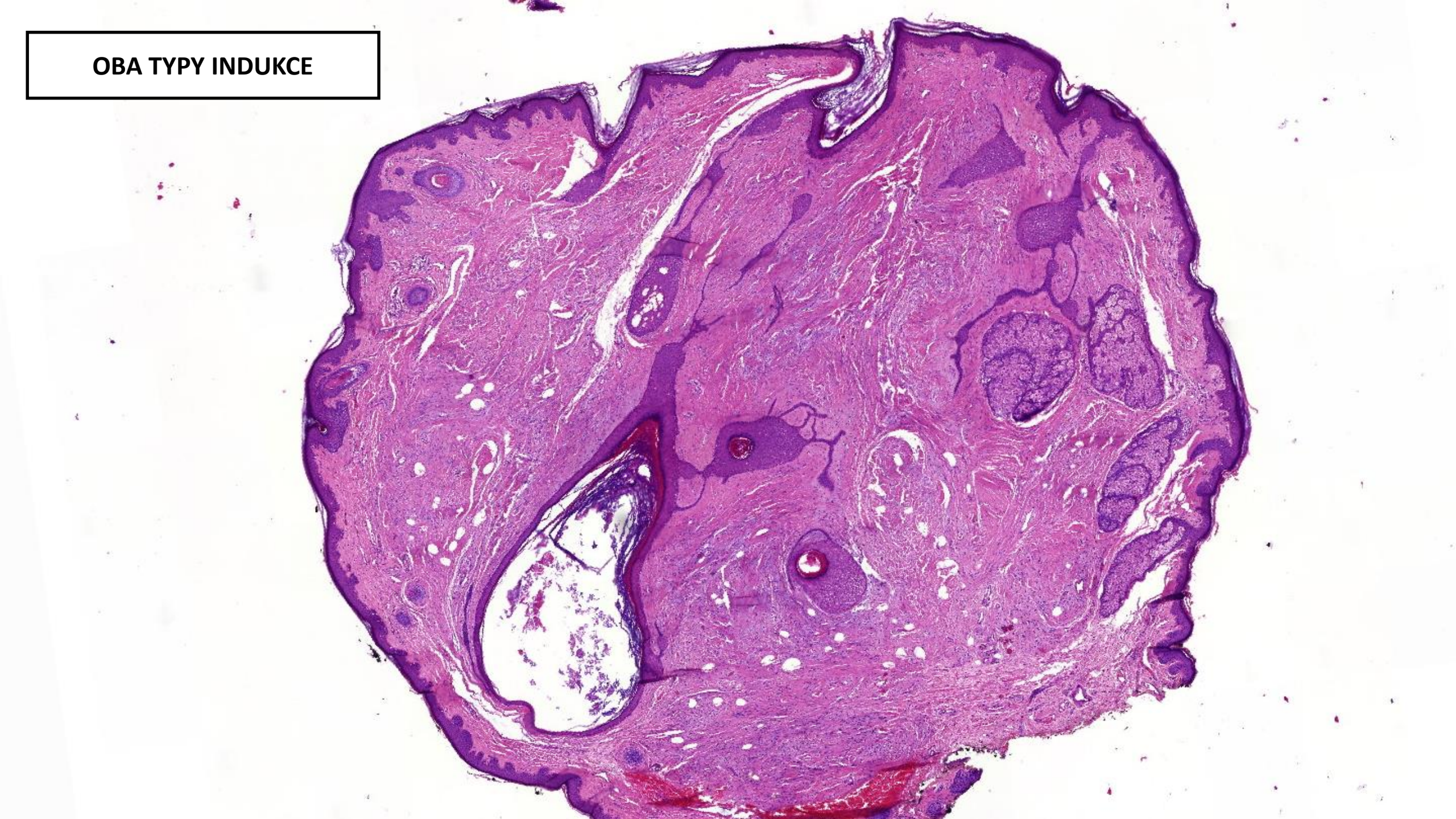
FAT-PREDOMINANT



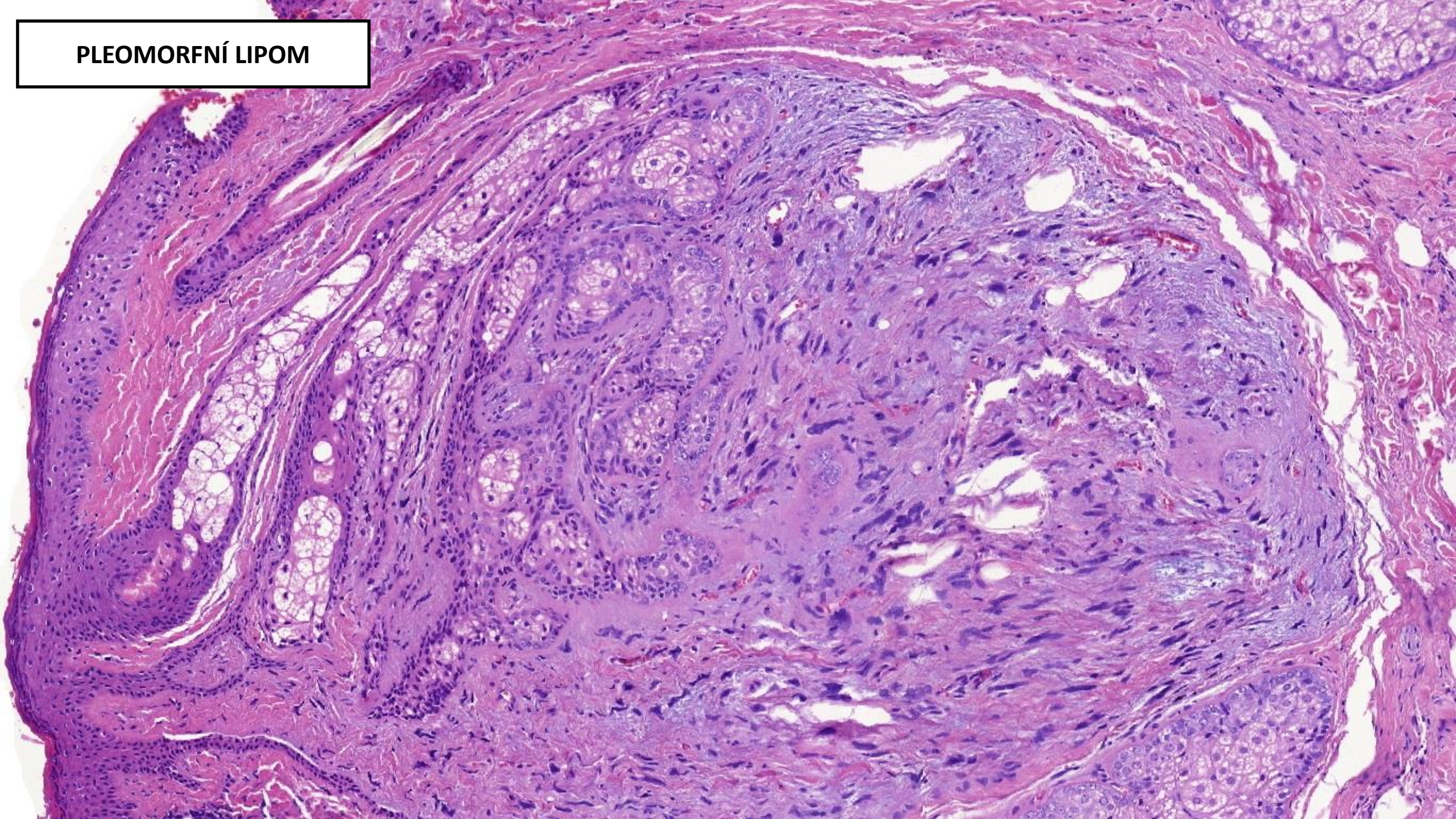
MIXED



OBA TYPY INDUKCE



PLEOMORFNÍ LIPOM



Case No	SCL type	IHC; CD34	IHC; Rb-1	FISH; Rb-1 deletion
1	MIXED			
2	MIXED			
3	MIXED			
4	MIXED			
5	MIXED			
6	FAT PREDOMINANT			
7	FAT PREDOMINANT			
8	FAT PREDOMINANT			
9	CLASSIC			
10	CLASSIC			
11	CLASSIC			
12	FAT POOR			
13	FAT POOR			
14	FAT POOR			
15	FAT POOR			
16	FAT POOR			
17	FAT POOR			
18	FAT POOR			
19	FAT POOR			
20	FAT POOR			
21	FAT POOR, PLEOMORPHIC LIPOMA			
22	FAT POOR			
23	FAT POOR			
24	FAT POOR			
25	FAT POOR			

Case No	SCL type	IHC; CD34	IHC; Rb-1	FISH; Rb-1 deletion
1	MIXED	+	loss	-
2	MIXED	-	loss	-
3	MIXED	foc.+	loss	-
4	MIXED	+	loss	NA
5	MIXED	+	loss	+
6	FAT PREDOMINANT	+	partial loss	+
7	FAT PREDOMINANT	-	loss	NA
8	FAT PREDOMINANT	+	loss	-
9	CLASSIC	+	loss	+
10	CLASSIC	NP	NP	NP
11	CLASSIC	NP	NP	NP
12	FAT POOR	+	loss	NA
13	FAT POOR	+	loss	+
14	FAT POOR	+	retained	-
15	FAT POOR	-	loss	-
16	FAT POOR	-	loss	NA
17	FAT POOR	+	loss	NA
18	FAT POOR	NP	NP	NP
19	FAT POOR	NP	NP	NP
20	FAT POOR	+	loss	-
21	FAT POOR, PLEOMORPHIC LIPOMA	+	not done	+
22	FAT POOR	+	partial loss	-
23	FAT POOR	foc.+	loss	+
24	FAT POOR	NP	not done	NP
25	FAT POOR	foc.+	loss	-

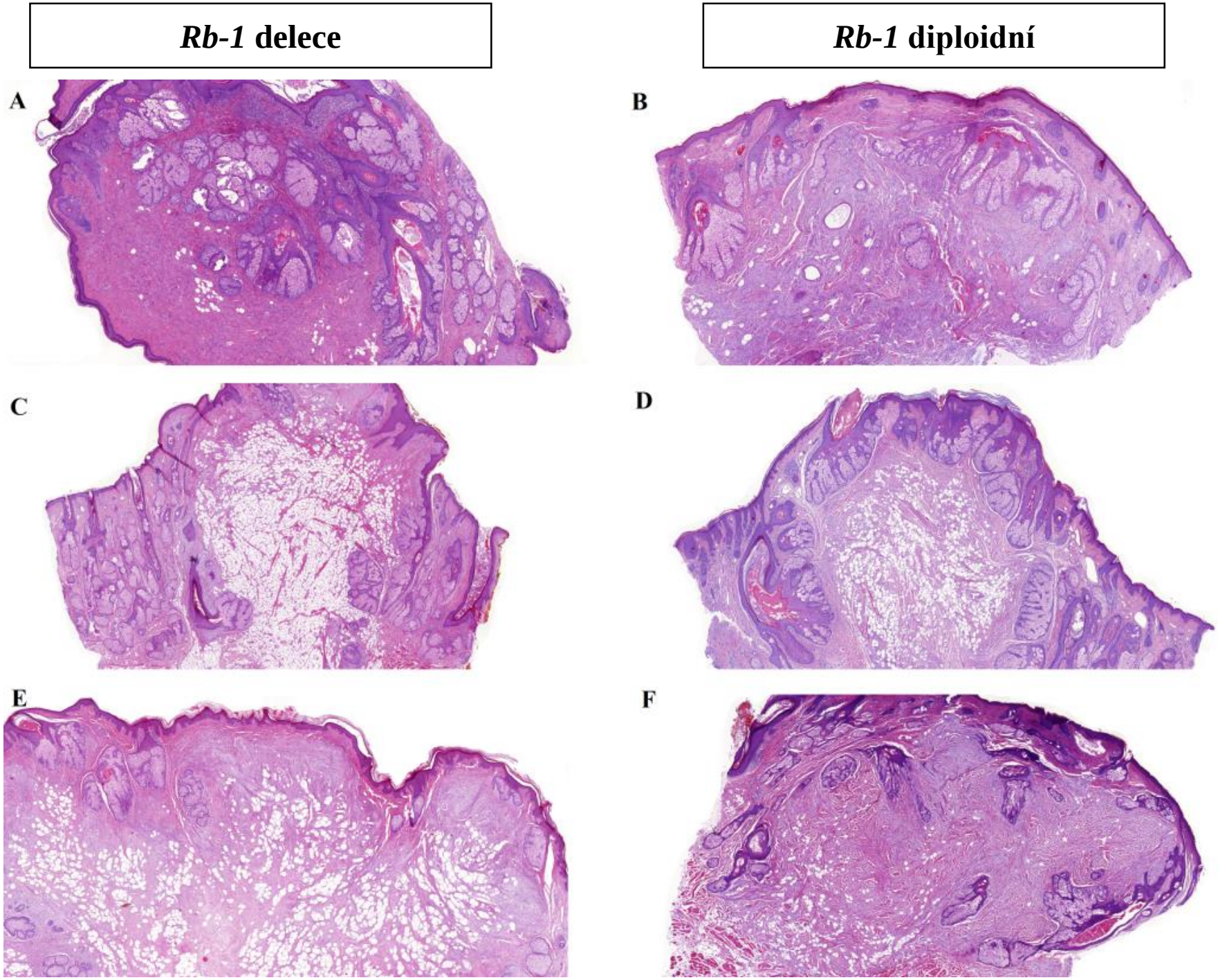
Case No	SCL type	IHC; CD34	IHC; Rb-1	FISH; Rb-1 deletion
1	MIXED	+	loss	-
2	MIXED	-	loss	-
3	MIXED	foc.+	loss	-

- Ačkoliv stromální složka některých trichodiskomů morfologicky i IHC věrně napodobuje SCL/PL, ve většině případů nebyla prokázána delece *RB-1* genu
- Většina případů jsou nejspíše „pravé“ trichodiskomy a nikoliv SCL/PL s indukcí přilehlých adnexálních struktur

18	FAT POOR	NP	NP	NP
19	FAT POOR	NP	NP	NP
20	FAT POOR	+	loss	-
21	FAT POOR, PLEOMORPHIC LIPOMA	+	not done	+
22	FAT POOR	+	partial loss	-
23	FAT POOR	foc.+	loss	+
24	FAT POOR	NP	not done	NP
25	FAT POOR	foc.+	loss	-

- Žádné morfologické ani IHC rozdíly mezi *RB-1* deletovanými a diploidními případy

- **Menšina případů s *RB-1* delecí jsou morfologicky identické léze reprezentující SCL/PL s indukcí přilehlých adnexálních struktur**



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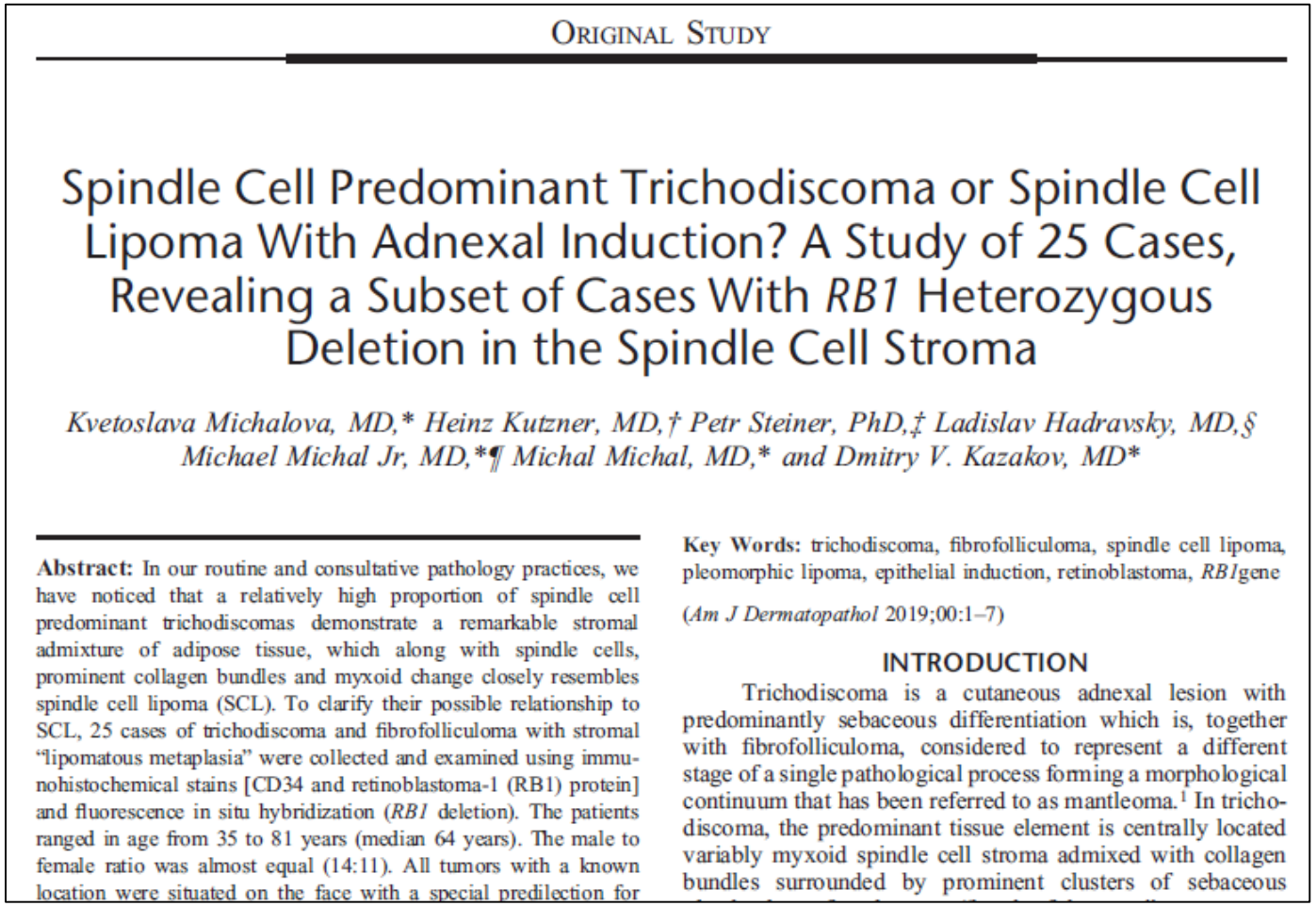
Závěr

- Protože delece *RB-1* genu charakterizuje převážnou většinu SCL/PL, je pravděpodobné, že většina případů jsou „pravé“ trichodiskomy a nikoliv SCL/PL s indukcí přilehlých adnexálních struktur



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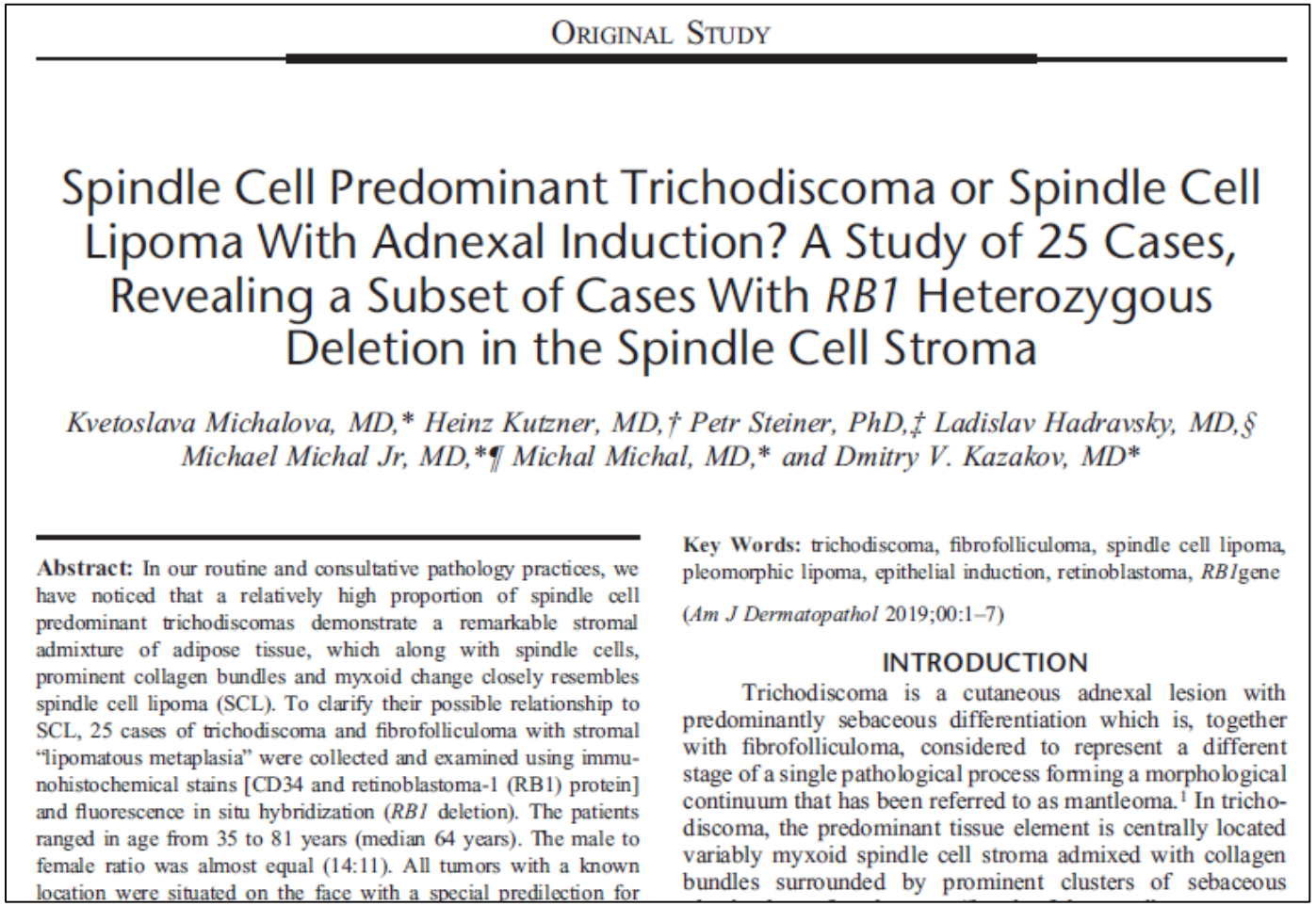

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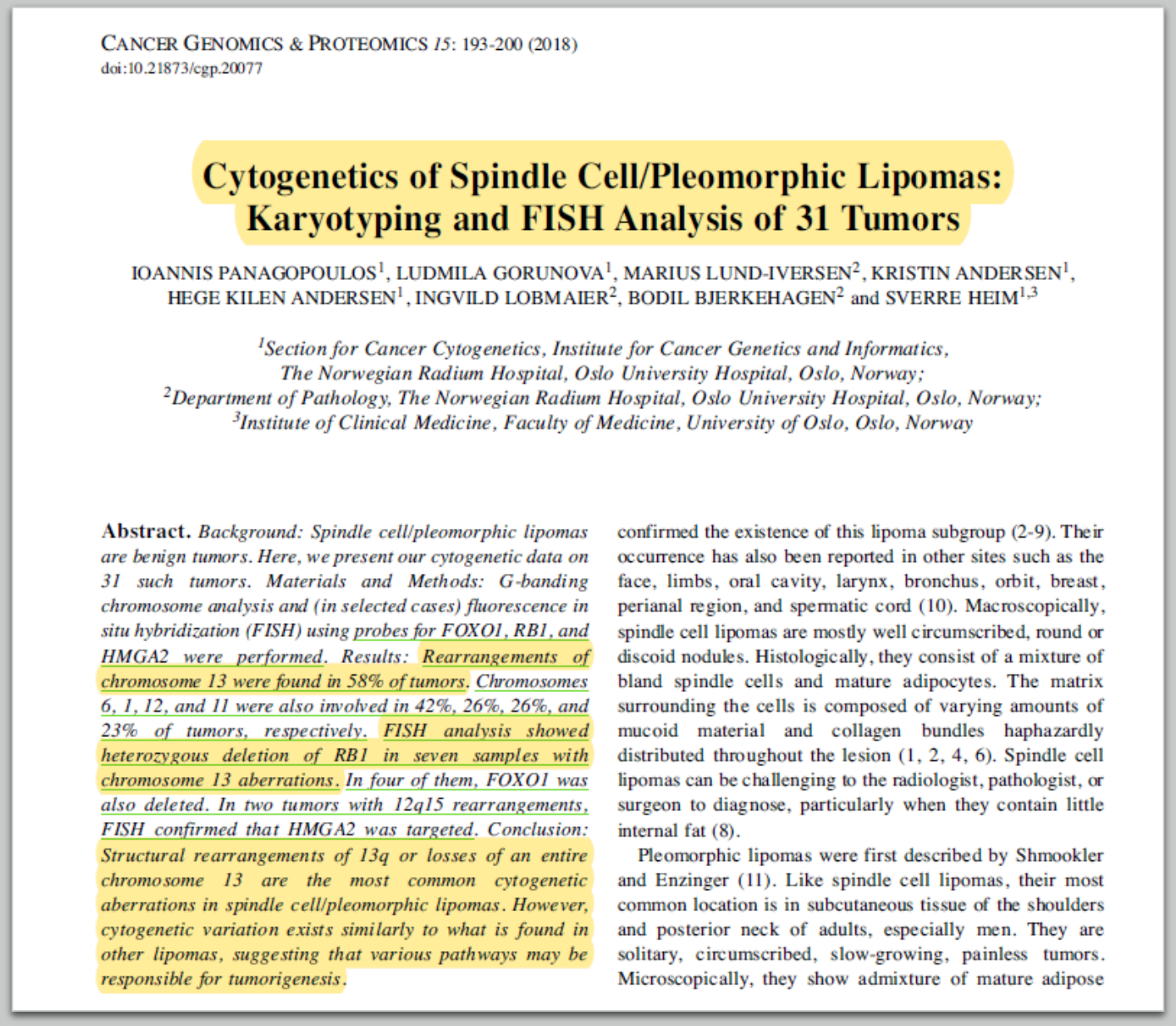
- 31 případů SCL/PL
- 58% rearanže 13.chromozomu
  - *RB1* delece v 7 z nich
  - *FOXO1* delece ve 4 z nich
- Další reanžované chromozomy: 6, 1, 12, 11 (42-23%)

- Rearanže 13.chromozomu jsou nejčastější cytogenetickou odchylkou v SCL/PL
- Cytogenetická variabilita, tumorigeneze bude pravděpodobně komplexnější



CANCER GENOMICS & PROTEOMICS *15*: 193-200 (2018)
doi:10.21873/cgp.20077

Cytogenetics of Spindle Cell/Pleomorphic Lipomas: Karyotyping and FISH Analysis of 31 Tumors

IOANNIS PANAGOPOULOS[1], LUDMILA GORUNOVA[1], MARIUS LUND-IVERSEN[2], KRISTIN ANDERSEN[1], HEGE KILEN ANDERSEN[1], INGVILD LOBMAIER[2], BODIL BJERKEHAGEN[2] and SVERRE HEIM[1,3]

[1]*Section for Cancer Cytogenetics, Institute for Cancer Genetics and Informatics, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway;*
[2]*Department of Pathology, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway;*
[3]*Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway*

Abstract. *Background: Spindle cell/pleomorphic lipomas are benign tumors. Here, we present our cytogenetic data on 31 such tumors. Materials and Methods: G-banding chromosome analysis and (in selected cases) fluorescence in situ hybridization (FISH) using probes for FOXO1, RB1, and HMGA2 were performed. Results: Rearrangements of chromosome 13 were found in 58% of tumors. Chromosomes 6, 1, 12, and 11 were also involved in 42%, 26%, 26%, and 23% of tumors, respectively. FISH analysis showed heterozygous deletion of RB1 in seven samples with chromosome 13 aberrations. In four of them, FOXO1 was also deleted. In two tumors with 12q15 rearrangements, FISH confirmed that HMGA2 was targeted. Conclusion: Structural rearrangements of 13q or losses of an entire chromosome 13 are the most common cytogenetic aberrations in spindle cell/pleomorphic lipomas. However, cytogenetic variation exists similarly to what is found in other lipomas, suggesting that various pathways may be responsible for tumorigenesis.*

confirmed the existence of this lipoma subgroup (2-9). Their occurrence has also been reported in other sites such as the face, limbs, oral cavity, larynx, bronchus, orbit, breast, perianal region, and spermatic cord (10). Macroscopically, spindle cell lipomas are mostly well circumscribed, round or discoid nodules. Histologically, they consist of a mixture of bland spindle cells and mature adipocytes. The matrix surrounding the cells is composed of varying amounts of mucoid material and collagen bundles haphazardly distributed throughout the lesion (1, 2, 4, 6). Spindle cell lipomas can be challenging to the radiologist, pathologist, or surgeon to diagnose, particularly when they contain little internal fat (8).

Pleomorphic lipomas were first described by Shmookler and Enzinger (11). Like spindle cell lipomas, their most common location is in subcutaneous tissue of the shoulders and posterior neck of adults, especially men. They are solitary, circumscribed, slow-growing, painless tumors. Microscopically, they show admixture of mature adipose

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Neplatí, že absence *RB1* delece vylučuje diagnózu SCL/PL

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Abstract. *Background: Spindle cell/pleomorphic lipomas are benign tumors. Here, we present our cytogenetic data on 31 such tumors. Materials and Methods: G-banding chromosome analysis and (in selected cases) fluorescence in situ hybridization (FISH) using probes for FOXO1, RB1, and HMGA2 were performed. Results: Rearrangements of chromosome 13 were found in 58% of tumors. Chromosomes 6, 1, 12, and 11 were also involved in 42%, 26%, 26%, and 23% of tumors, respectively. FISH analysis showed heterozygous deletion of RB1 in seven samples with chromosome 13 aberrations. In four of them, FOXO1 was also deleted. In two tumors with 12q15 rearrangements, FISH confirmed that HMGA2 was targeted. Conclusion: Structural rearrangements of 13q or losses of an entire chromosome 13 are the most common cytogenetic aberrations in spindle cell/pleomorphic lipomas. However, cytogenetic variation exists similarly to what is found in other lipomas, suggesting that various pathways may be responsible for tumorigenesis.*

confirmed the existence of this lipoma subgroup (2-9). Their occurrence has also been reported in other sites such as the face, limbs, oral cavity, larynx, bronchus, orbit, breast, perianal region, and spermatic cord (10). Macroscopically, spindle cell lipomas are mostly well circumscribed, round or discoid nodules. Histologically, they consist of a mixture of bland spindle cells and mature adipocytes. The matrix surrounding the cells is composed of varying amounts of mucoid material and collagen bundles haphazardly distributed throughout the lesion (1, 2, 4, 6). Spindle cell lipomas can be challenging to the radiologist, pathologist, or surgeon to diagnose, particularly when they contain little internal fat (8).

Pleomorphic lipomas were first described by Shmookler and Enzinger (11). Like spindle cell lipomas, their most common location is in subcutaneous tissue of the shoulders and posterior neck of adults, especially men. They are solitary, circumscribed, slow-growing, painless tumors. Microscopically, they show admixture of mature adipose

Alternativní závěr

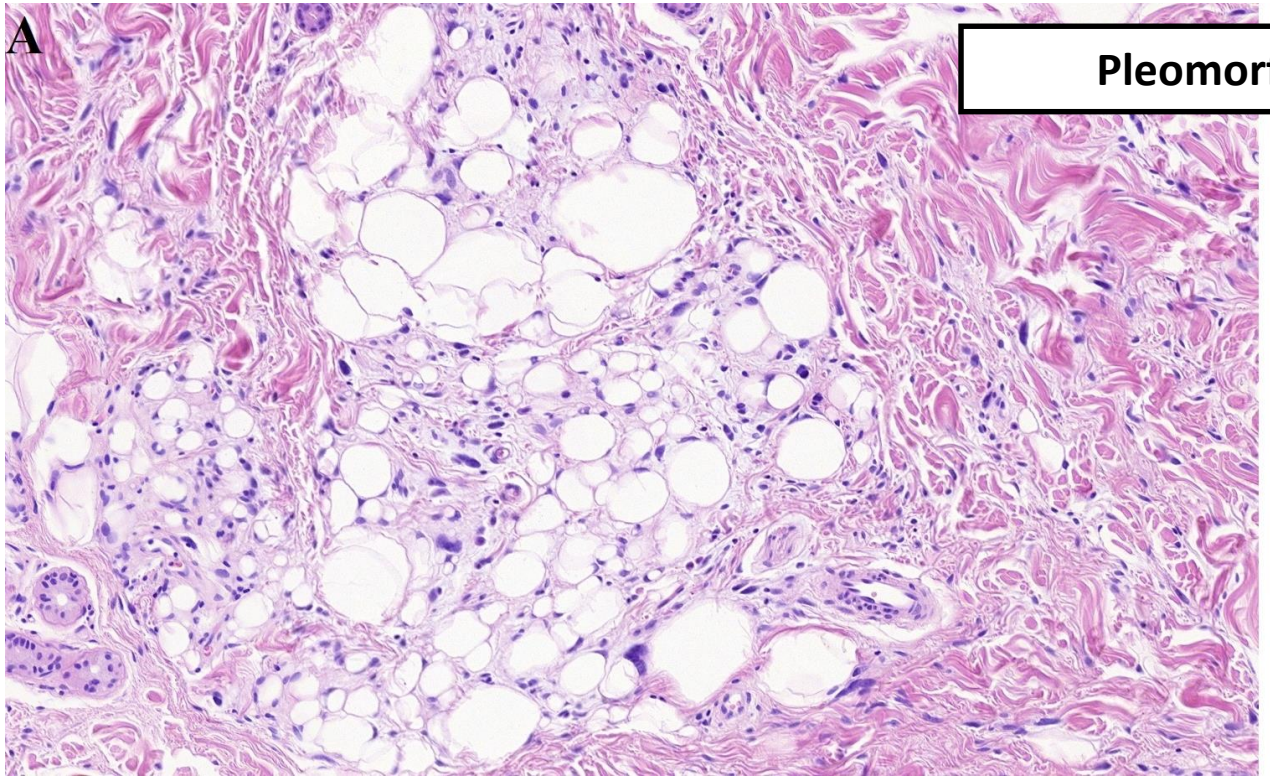
- Je možné, že ve skutečnosti jde ve všech případech o vřetenobuněčné/pleomorfní lipomy s indukcí adnexálních struktur a nikoliv o trichodiskomy s převahou vřetenitých buněk a „lipomatózní metaplazií“

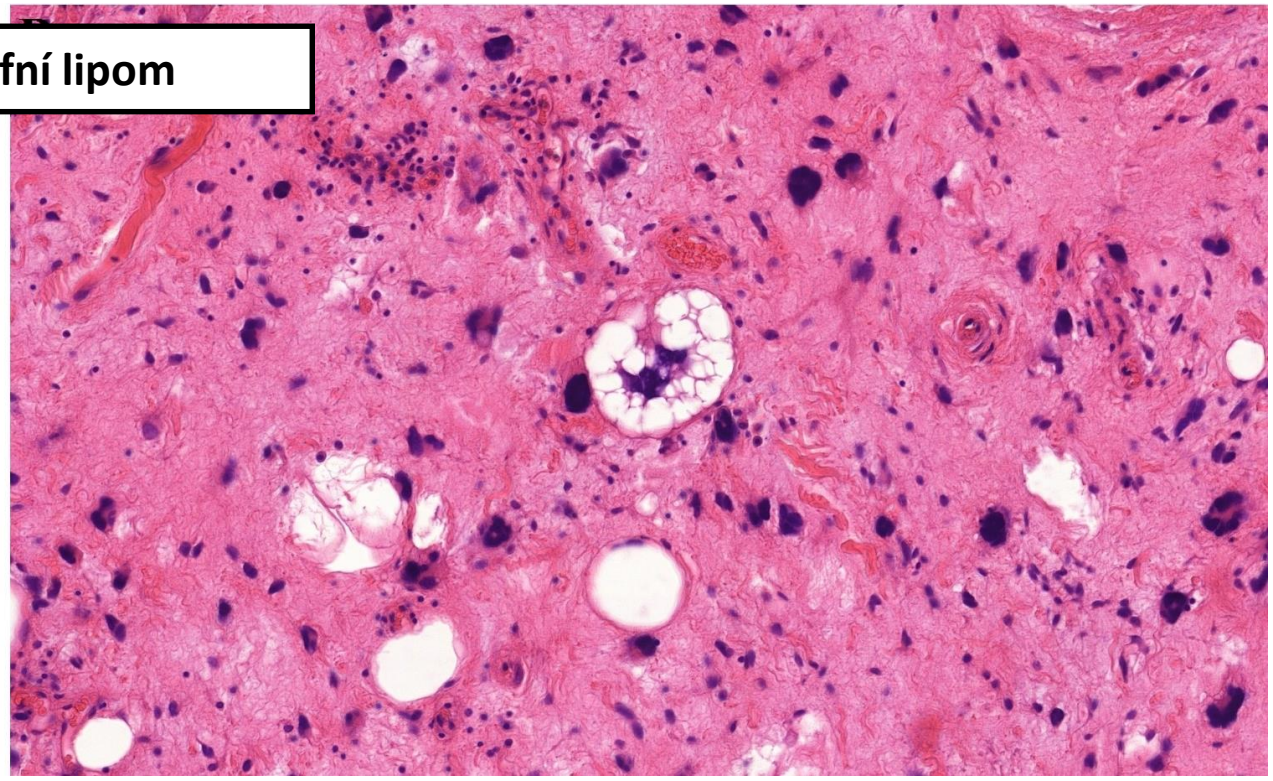
- Cytogenetická analýza detekce změn na 13., 6., 1., 12. a 11. chromozomu

Case No	SCL type	epithelial induction type	other histological features
1	mixed	trichodiscoma	lipoblasts
2	mixed	trichodiscoma	lipoblasts
3	mixed	trichodiscoma+fibrofolliculoma	lipoblasts
4	mixed	trichodiscoma	lipoblasts
5	mixed	trichodiscoma	lipoblasts
6	fat predominant	trichodiscoma	
7	fat predominant	trichodiscoma	
8	fat predominant	trichodiscoma	lipoblasts
9	classic	trichodiscoma	lipoblasts
10	classic	trichodiscoma	lipoblasts
11	classic	fibrofolliculoma	lipoblasts
12	fat poor	trichodiscoma	
13	fat poor	trichodiscoma	
14	fat poor	fibrofolliculoma	
15	fat poor	trichodiscoma+fibrofolliculoma	
16	fat poor	trichodiscoma	
17	fat poor	trichodiscoma	
18	fat poor	trichodiscoma	
19	fat poor	trichodiscoma	
20	fat poor	trichodiscoma	
21	fat poor, pleomorphic lipoma	trichodiscoma+fibrofolliculoma	
22	fat poor	trichodiscoma	
23	fat poor	trichodiscoma	
24	fat poor	trichodiscoma	
25	fat poor	trichodiscoma	

Lipoblast

- nezralá forma lipocytu
- v cytoplazmě jedna či více tukových vakuol
- hyperchromní, zvlněné či zoubkované jádro
- **často mylně považován za diagnostické kritérium maligního ALT/dobře diferencovaného liposarkomu**





- Na častou přítomnost lipoblastů v pleomorfních lipomech poukázáno už při jeho prvopopisu
- V odborné literatuře posledních letech opomíjeno, že i benigní lipomatózní léze mohou lipoblasty obsahovat

Pleomorphic Lipoma: A Benign Tumor Simulating Liposarcoma

A Clinicopathologic Analysis of 48 Cases

BARRY M. SHMOOKLER, MD, LTC, MC, USAR,* AND FRANZ M. ENZINGER, MD†

A clinicopathologic study of 48 cases of pleomorphic lipoma from the files of the Armed Forces Institute of Pathology reveals that this tumor occurs principally in males (83%) in the fifth to seventh decades (mean 57 years) and shows a predilection for the posterior neck, shoulder, and back. Typically, the lesion appears as a painless, circumscribed subcutaneous mass that, on gross examination, resembles an ordinary lipoma. However, microscopically, in contrast to the uniform appearance of the mature adipose tissue cells of an ordinary lipoma, this neoplasm is characterized by an *intimate* admixture of variably-sized fat cells, and bizarre, pleomorphic, multinucleated giant cells. Many of the latter cells show a distinctive floret-like arrangement of the nuclei and are associated with interlacing bundles of dense birefringent collagen. Despite this pleomorphic picture, which not infrequently leads to a misdiagnosis of liposarcoma, follow-up data obtained for 34 patients (median follow-up period of three years) establish the invariably benign clinical behavior of this unusual tumor.

***Cancer* 47:126–133, 1981.**

LIPOSARCOMA—THE MALIGNANT TUMOR OF LIPOBLASTS*

ARTHUR PURDY STOUT, M.D

NEW YORK, N. Y.

FROM THE LABORATORY OF SURGICAL PATHOLOGY, COLUMBIA UNIVERSITY, AND THE DEPARTMENT OF SURGERY, PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

Histopathology

Histopathology

Pleomorphic lipoma: a tumour simulating liposarcoma

J.G. AZZOPARDI, J. IOCCO, R. SALM

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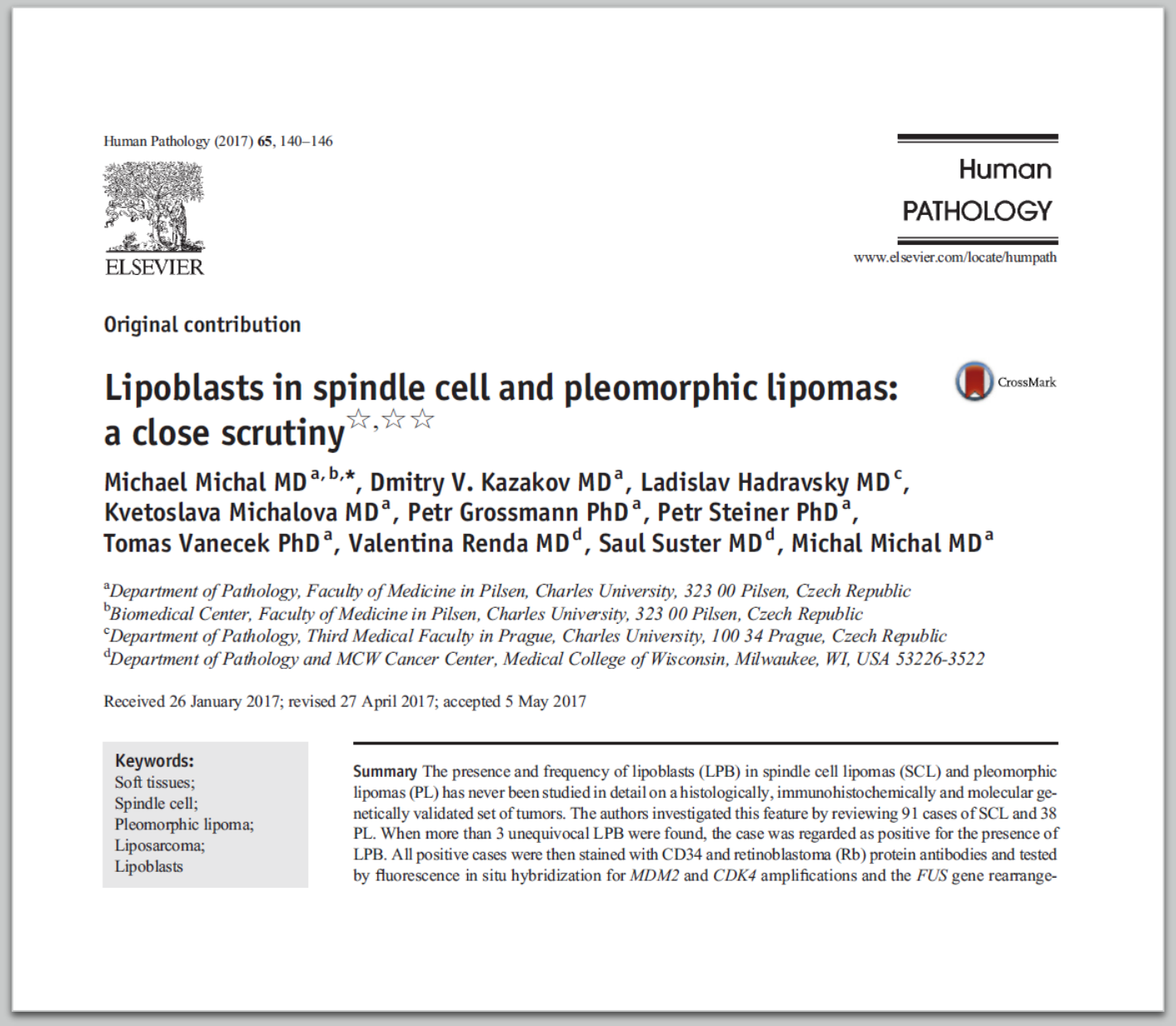
- 129 případů SCL/PL
- 91 SCL, 38 PL
- Inkluzní kritérium: alespoň 3 lipoblasty

- IHC protilátky CD34 a RB-1
- FISH próby MDM2, CDK4 a FUS



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Original contribution

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

Michael Michal MD[a,b,*], Dmitry V. Kazakov MD[a], Ladislav Hadravsky MD[c], Kvetoslava Michalova MD[a], Petr Grossmann PhD[a], Petr Steiner PhD[a], Tomas Vanecek PhD[a], Valentina Renda MD[d], Saul Suster MD[d], Michal Michal MD[a]

[a]*Department of Pathology, Faculty of Medicine in Pilsen, Charles University, 323 00 Pilsen, Czech Republic*
[b]*Biomedical Center, Faculty of Medicine in Pilsen, Charles University, 323 00 Pilsen, Czech Republic*
[c]*Department of Pathology, Third Medical Faculty in Prague, Charles University, 100 34 Prague, Czech Republic*
[d]*Department of Pathology and MCW Cancer Center, Medical College of Wisconsin, Milwaukee, WI, USA 53226-3522*

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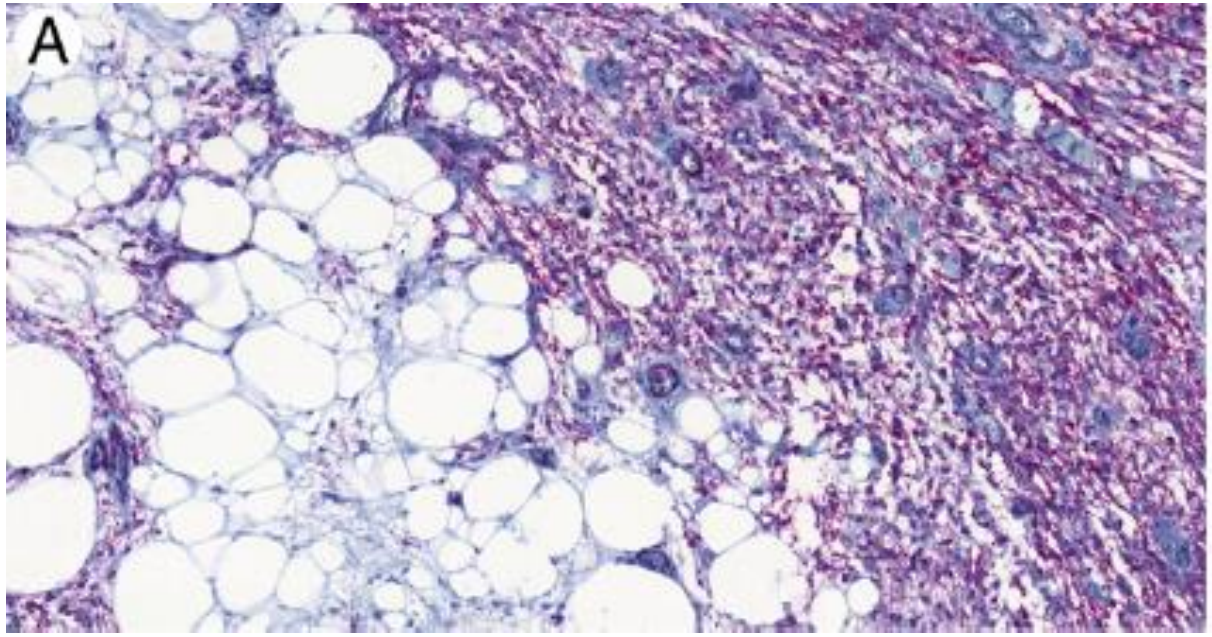
Pleomorphic lipoma;
Liposarcoma;
Lipoblasts

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 rearrange-

- SCL
  - 37/91 případů (41%) obsahovalo lipoblasty
  - Většinou málo, viditelné až po pečlivějším hledání

- PL
  - 25/38 případů (66%) obsahovalo lipoblasty
  - Značně častější, i difuzně přítomné

IHC pozitivita CD34, ztráta Rb-1, FISH analýza bez průkazu amplifikace genů MDM2, CDK4 či FUS



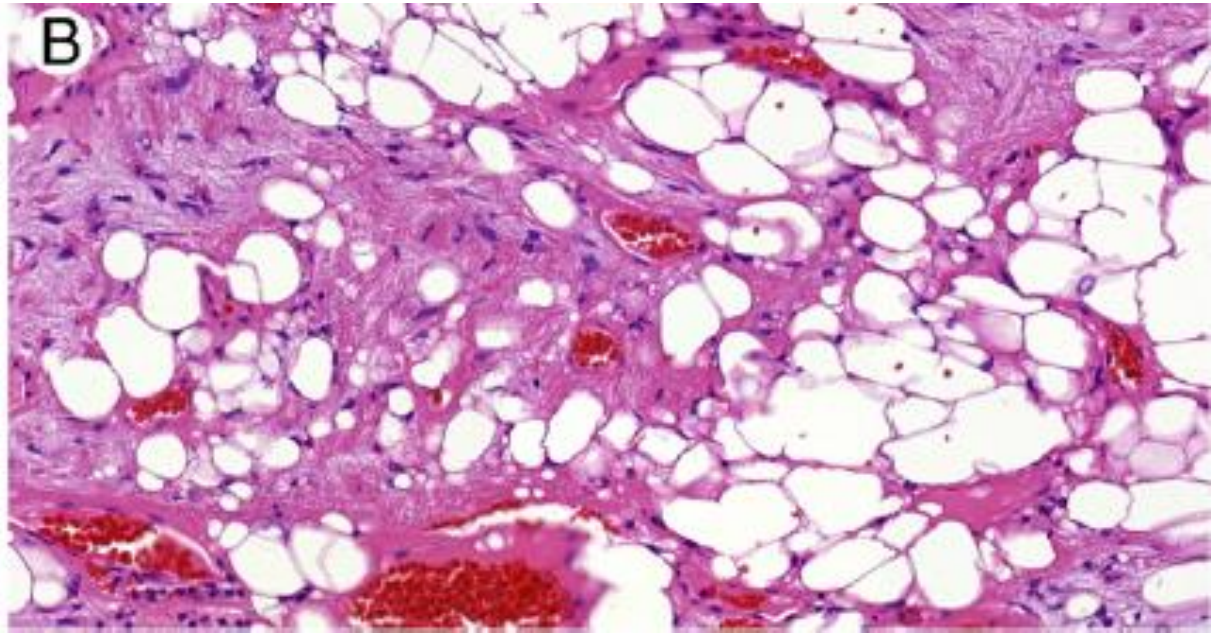


Table 1 Spindle cell lipomas

Case	Available methods	Age/sex	Location	Size (cm)	Referring diagnosis
1	All 3	70/M	Back of the neck	7 × 4 × 4	SCL/PL *vs* ALT
2	All 3	76/M	Back of the neck	Ø2	Routine case
3	*CDK4*; *MDM2*	61/M	Back of the neck	2.5 × 1.5 × 10	SCL
4	All 3	62/M	Back of the neck	6 × 5 × 3.5	Routine case
5	NT	69/F	NA	NA	Not listed
6	*CDK4*; *MDM2*	55/M	Back of the neck	6 × 4 × 2.5	Routine case
7	None	77/M	Back of the neck	Ø5	Routine case
8	None	63/M	3rd toe	3 × 2 × 2	SCL
9	None	59/M	Buccal mucosa	Ø2	Exclude ALT
10	NT	27/F	Head	Ø2	Probably SCL, uncertainty due to the clinical setting
11	None	39/M	NA	NA	NA
12	All 3	72/M	Shoulder	3 × 1.7 × 1.7	Routine case
13	All 3	57/M	Back of the neck	Ø1.5	Routine case
14	All 3	49/M	Scapula	3 × 2.5 × 1.5	Routine case
15	*CDK4*; *MDM2*	61/M	Scapula	3 × 2.5 × 1.5	NA
16	*CDK4*; *MDM2*	87/M	Back	NA	Routine case
17	*CDK4*; *MDM2*	65/M	Back	NA	Routine case
18	None	71/F	Buccal mucosa	1.5 × 1 × 1	Myxoid liposarcoma
19	None	61/F	Nose	NA	Routine case
20	All 3	62/M	Parotid gland	NA	Myoepithelioma *vs* ALT *vs* schwannoma
21	None	61/M	Back of the neck	NA	Routine case
22	*CDK4*; *MDM2*	73/M	Hypogastrium	Ø4.5	Routine case
23	All 3	62/M	Clavicle	NA	Routine case
24	All 3	55/M	Upper back	3 × 3 × 2	SCL
25	*CDK4*; *MDM2*	49/M	Upper back	15 × 14 × 4.5	Exclude liposarcoma
26	NT	59/M	Back of the neck	0.8	Angiolipoma *vs* SCL with focal regressive cellular changes
27	None	55/M	Upper back	4 × 3 × 2	Routine case
28	None	65/M	Scalp	NA	Routine case
29	None	76/M	Upper back	Ø2	Fibrolipoma
30	NT	NA	Back	NA	NA
31	None	73/M	NA	8 × 4 × 2.5	Neurofibroma
32	CDK4	90/M	Shoulder	10 × 9 × 4	Lipoma
34	NT	50/M	Back	6.5 × 6 × 5	Fibrolipoma
35	None	49/M	Forehead	NA	Routine case
36	None	87/M	NA	NA	Routine case
37	All 3	53/M	Back	1.5 × 1.5 × 0.8	Spindle cell tumor with univacuolated and focally multivacuolated lipoblasts (reminiscent of lipoblastoma but in incompatible setting).

Podstatná část případů zaslána na naše pracoviště jako konzultační biopsie s diagnózou ALT či jiný typ liposarkomu (konkrétně 5/15 SCL a 8/13 PL)

Table 2 Pleomorphic lipomas

Case	Available methods	Age/sex	Location	Size (cm)	Referring diagnosis
1	All 3	66/M	Nuchal area	No	NL
2	All 3	46/M	Upper back	6 × 3 × 3	NL
3	All 3	27/F	NA	Ø0.6	Pleomorphic fibroma, stromal areas raising concerns about ALT
4	None	66/M	Back of the neck	2.2 × 2 × 1.2	LG sarcoma—myxoid or angiomatoid variant of ALT
5	All 3	81/M	Arm	7 × 5.5 × 2	PL
6	All 3	55/M	Back of the neck	Ø2.5	PL
7	All 3	66/M	Back of the neck	2.4 × 2 × 1.4	ALT—focally more cellular but without dedifferentiation
8	All 3	63/F	Popliteal area	Ø1.3	NL
9	FUS	76/F	Back of the neck	1.5 × 0.5 × 0.5	Fibrolipoma—some nuclei irregular and hyperchromatic—probably a reactive posttraumatic change
10	All 3	62/F	Shoulder	Ø4.5	Routine case
11	None	46/F	Upper back	6 × 6 × 4	Routine case
12	All 3	40/F	Upper back	24 × 16 × 8	Atypical lipoma *vs* ALT
13	All 3	58/M	Back of the neck	3 × 3 × 3	Routine case
14	All 3	42/M	Back of the neck	8 × 6 × 2	Routine case
15	All 3	53/F	Upper back	3.5 × 3 × 3	ALT
16	All 3	60/F	Elbow	Ø2.5	PL *vs* ALT
17	None	75/M	Back of the neck	Ø2	Spindle cell liposarcoma
18	*CDK4*; *MDM2*	53/F	Back of the neck	NA	Routine case
19	NT	70/M	Back of the neck	7 × 4 × 4	PL *vs* ALT
20	NT	41/M	Parotid gland	Ø1.5	PL
21	NT	65/M	NA	Ø2	PL
22	All 3	56/F	NA	2.1	NA
23	All 3	69/M	Neck	7	NA
24	All 3	58/M	Shoulder	3.8	NA
25	All 3	71/M	Neck	12.2	NA

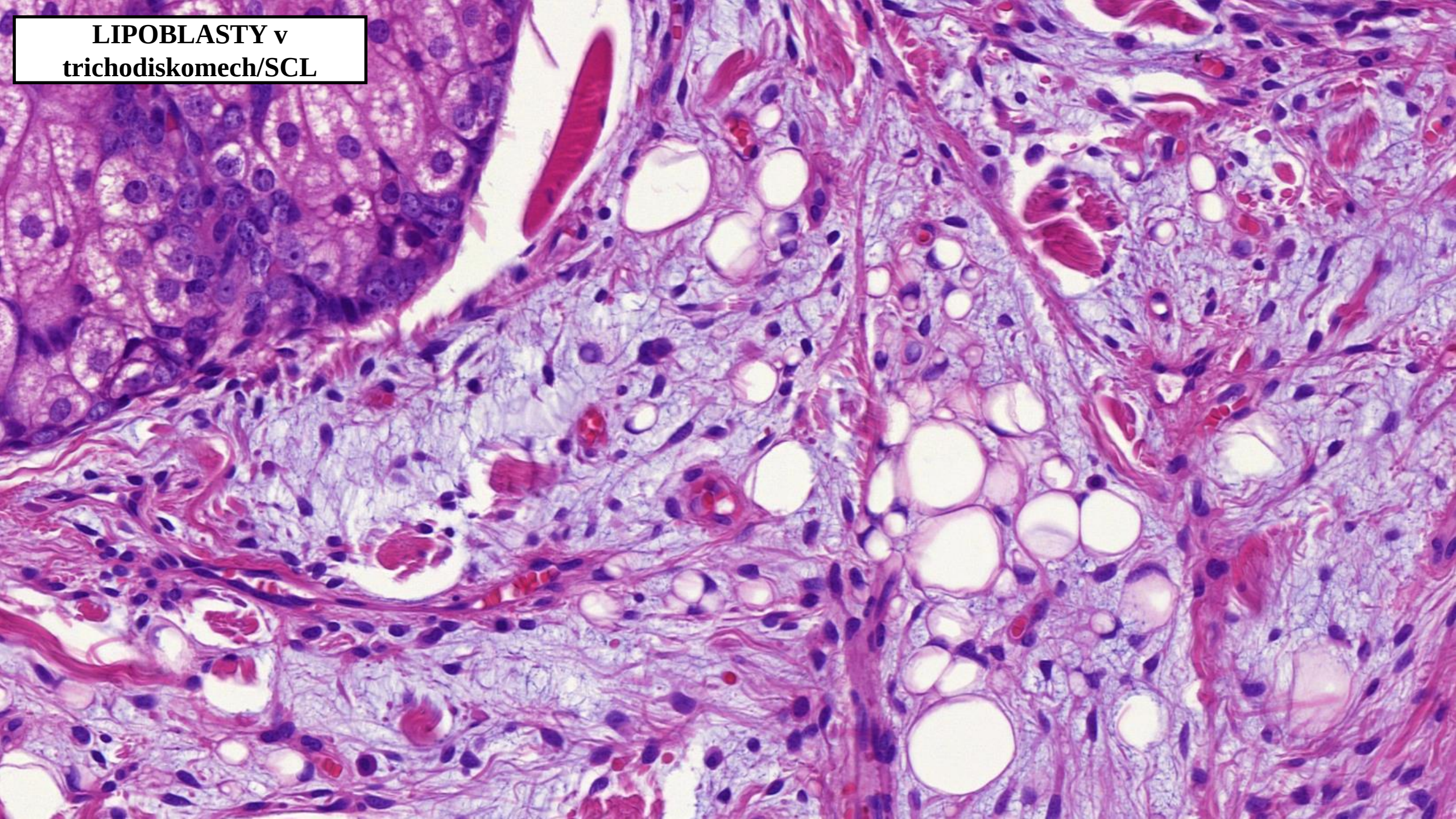
SCL/PL

- menší tumor v podkožní tkáni převážně na zádech, ramenou a zadní části krku
- **silná kolagenní vlákna**
- CD34+, ztráta exprese Rb-
- *RB1* delece

ALT/dobře diferencovaný liposarkom

- velký, infiltrativně rostoucí tumor hluboké tukové tkáně
- **jemná kolagenní vlákna**
- MDM2+
- *MDM2* amplifikace

- **Lipoblasty jsou přítomny přibližně v polovině SCL/PL**
- Dva tumory z naší studie zrecidivovaly, zbytek neměl agresivní průběh (follow-up 44 pacientů)


LIPOBLASTY v
trichodiskomech/SCL


Děkuji za pozornost
kveta.michalova@biopticka.cz