Mediastinal Synovial Sarcoma Clinicopathologic Analysis of 21 Cases With Molecular Confirmation

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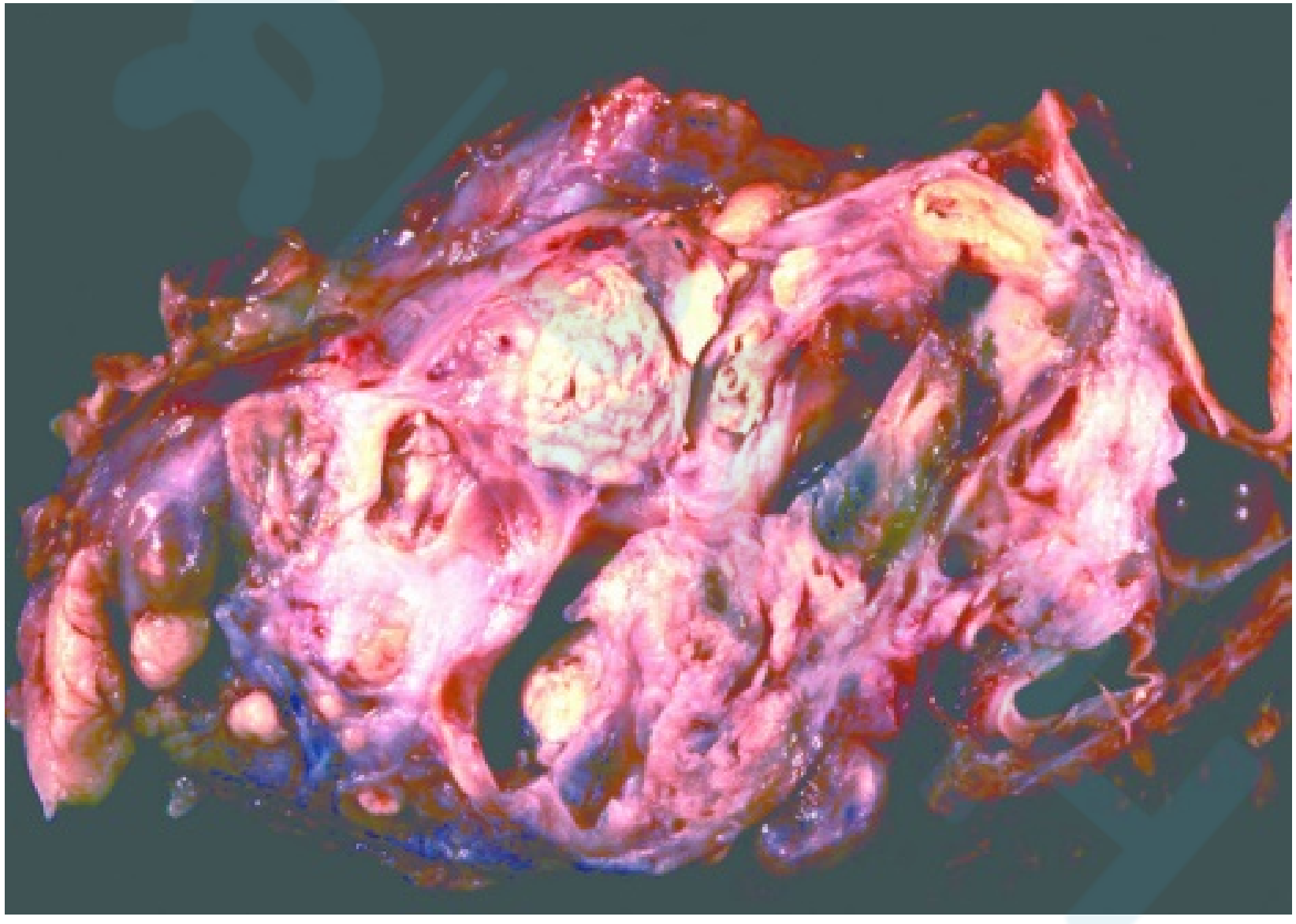
滑膜肉瘤（Synovial Sarcoma）

- 定义：具有不同程度上皮分化的间叶性肿瘤。
- t(X;18)(p11;q11)染色体易位，产生SS18-SSX1/SS18-SSX2/SS18-SSX4融合基因
- 可发生在任何年龄，15-20岁青壮年占50%以上
- 无性别差异
- 下肢膝关节 > 躯干 > 头颈部 > 生殖器官 > 肾 > 肾上腺

临床特征

- 起病隐匿，深部软组织内缓慢生长（2—4y）
- 特殊部位可出现相应症状
- 结节状、分叶状，界限较清
- 3—5cm/15cm/20cm
- 切面灰白、灰红、鱼肉状

大体



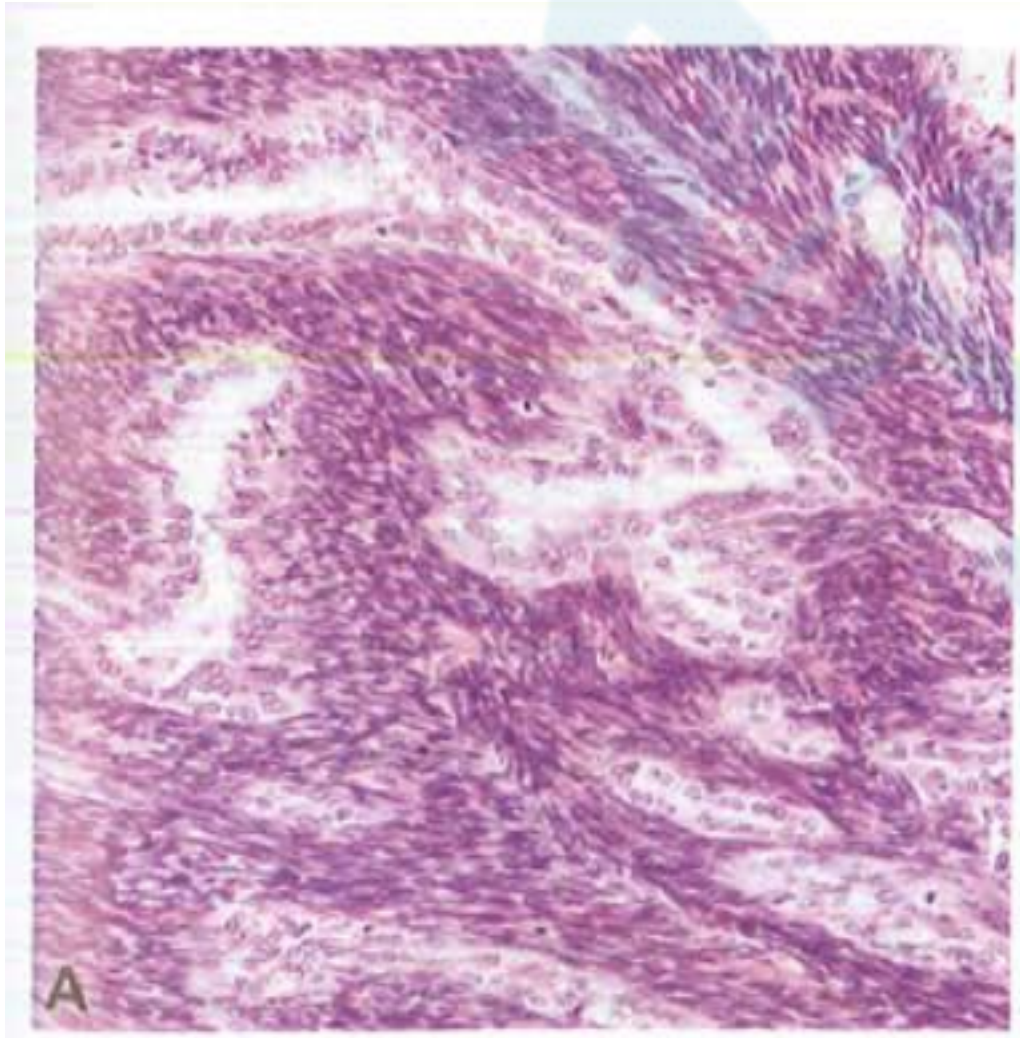
镜下

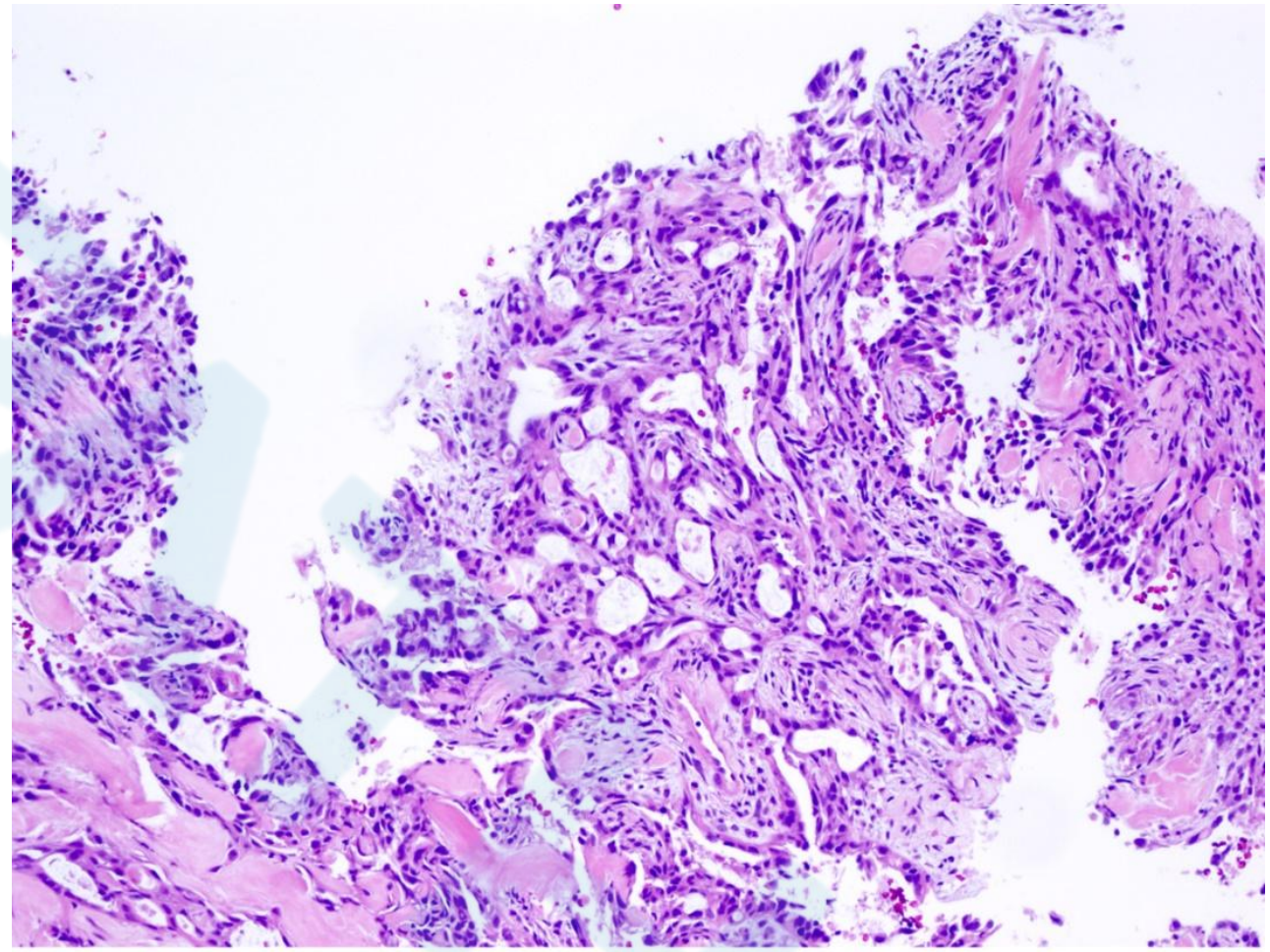
- 双相型滑膜肉瘤
- 单相梭形细胞型滑膜肉瘤
- 单相上皮型滑膜肉瘤

双相型滑膜肉瘤（混合型/经典型）

- 上皮样细胞&梭形细胞
- 上皮样细胞：立方形/柱状，胞质丰富，嗜酸，核圆形/卵圆形，空泡状，排列成腺样，小管状、条索状，实性团块状，腺泡状
- 梭形细胞：梭形，短梭形，核梭形/卵圆形，深染，核仁不明显，胞质少，不清晰，核质比大，排列成实性、束状、栅栏状、鱼骨样
- 间质局灶性粘液样变

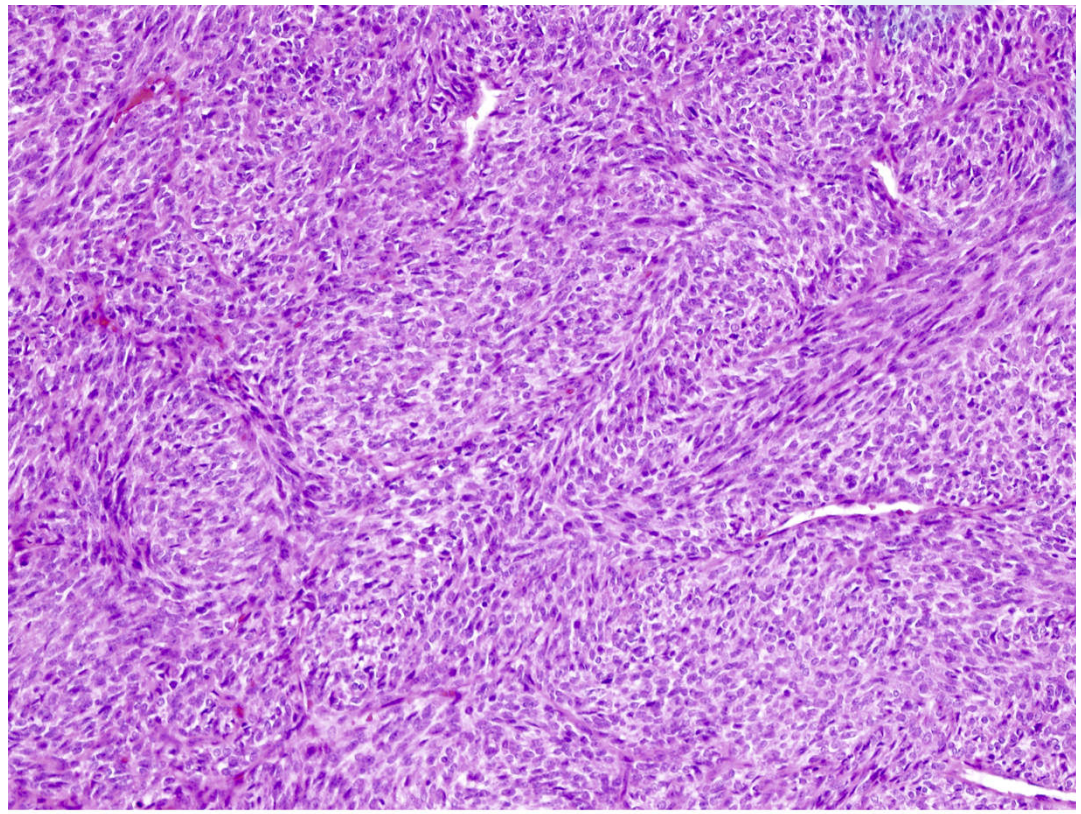
双相型滑膜肉瘤



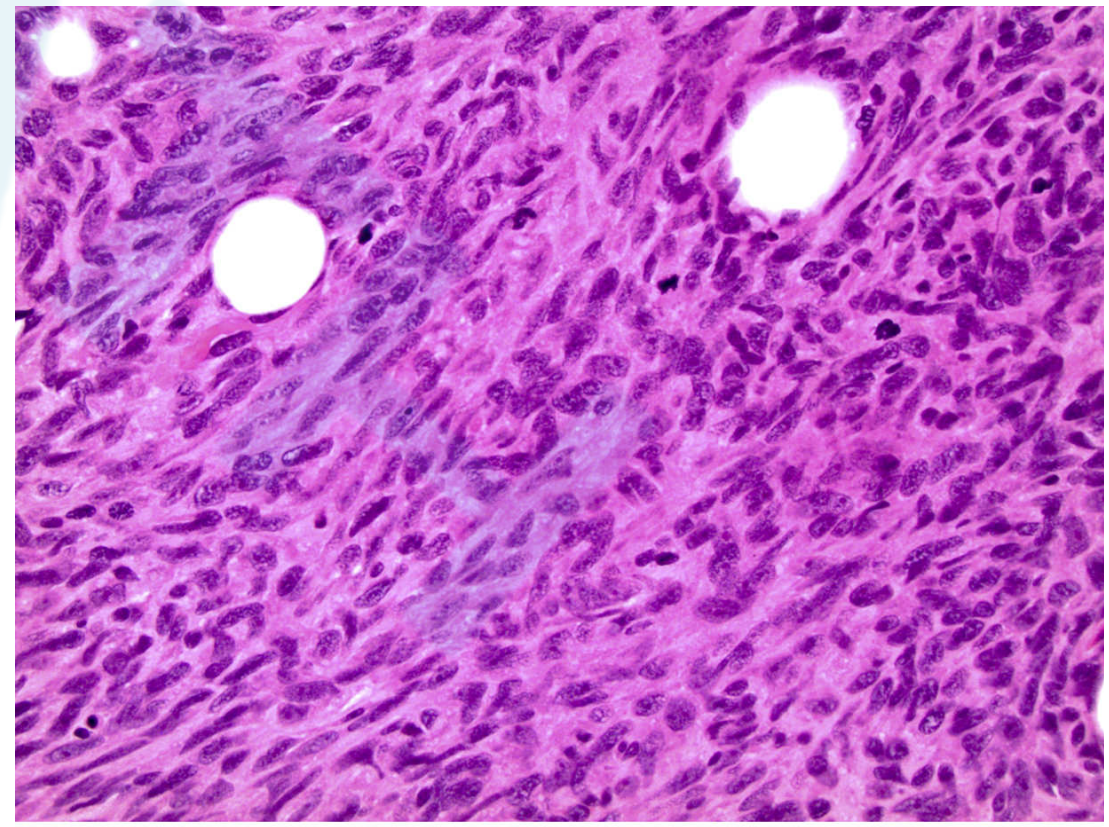


单相梭形细胞型滑膜肉瘤

- 最常见，最易误诊
- 短条束状/长条束状的梭形细胞细胞呈旋涡状/鱼骨样排列
- 散在肥大细胞（Gimesa或CD117）浸润
- 间质局灶性粘液样变



Synovial sarcoma, lung H&E



Monophasic synovial sarcoma

单相上皮样型滑膜肉瘤

- 少见，好发于四肢
- 实性片块状、腺样、小管样
- 瘤细胞为肥胖的圆形或卵圆形上皮样细胞，梭形成分少
- 很像癌，但部分区域仍可见双向分化特点
- 间质有较明显的肥大细胞及钙化

少见亚型

- 低分化型滑膜肉瘤
- 黏液样型滑膜肉瘤
- 硬化性滑膜肉瘤

低分化型滑膜肉瘤

- 少见，20%
- 小细胞型肉瘤
- 瘤细胞为不分化的短梭形/椭圆形/圆形的幼稚间叶细胞
- 有薄壁窦样血管，血管丰富，似血管外皮瘤

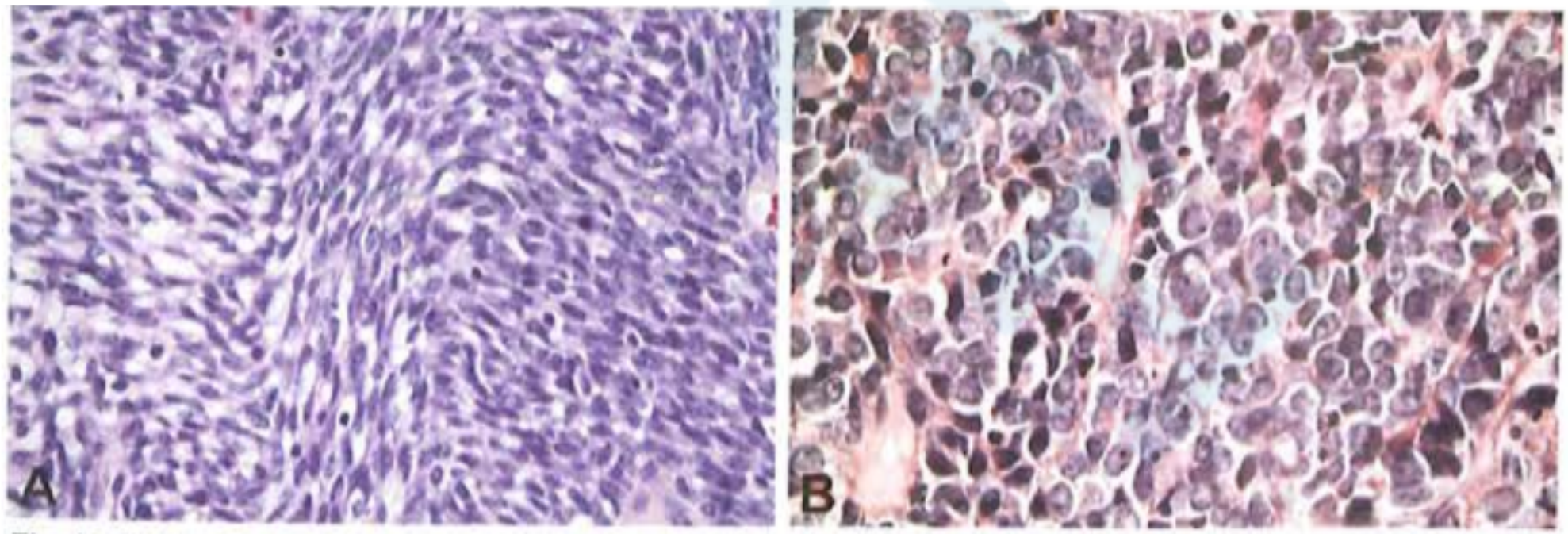
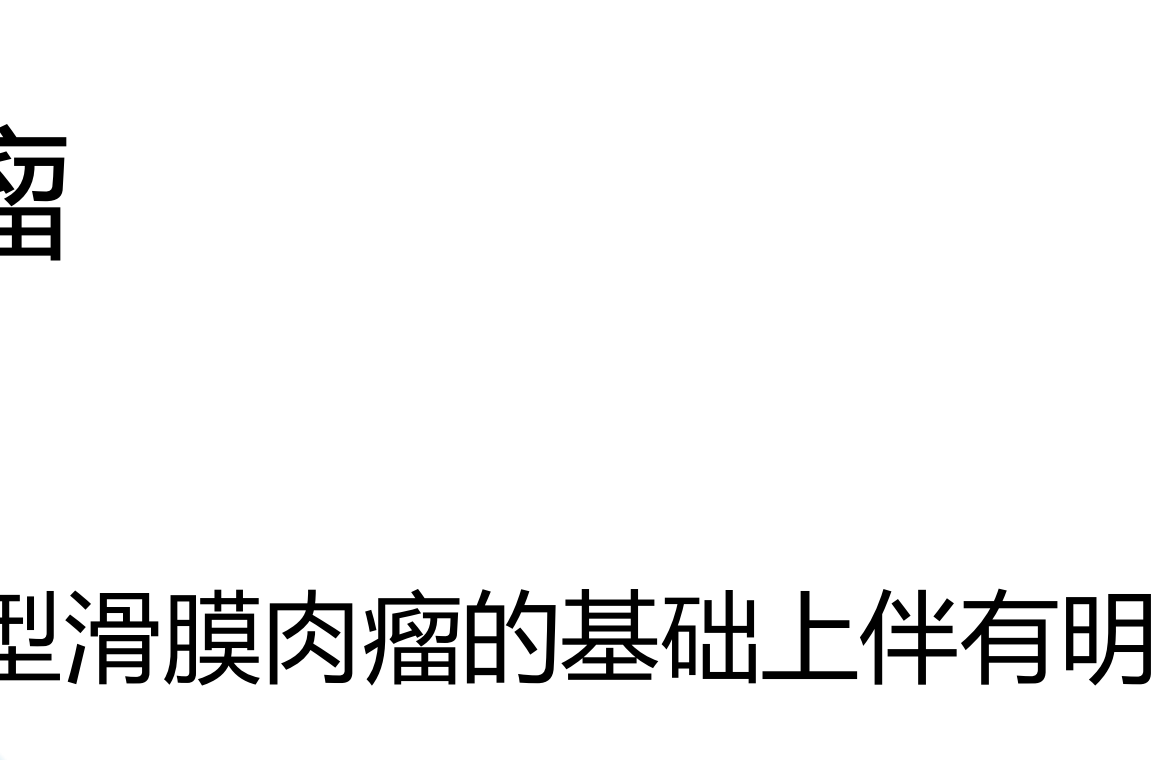


Fig. 12.45 Synovial sarcoma. **A** Poorly differentiated synovial sarcoma resembling malignant peripheral nerve sheath tumour. **B** Poorly differentiated synovial sarcoma resembling Ewing sarcoma.

黏液样型滑膜肉瘤

- 少见
- 双相型或单相纤维性典型滑膜肉瘤的基础上伴有明显的黏液间质
- 较易复发（3/7）



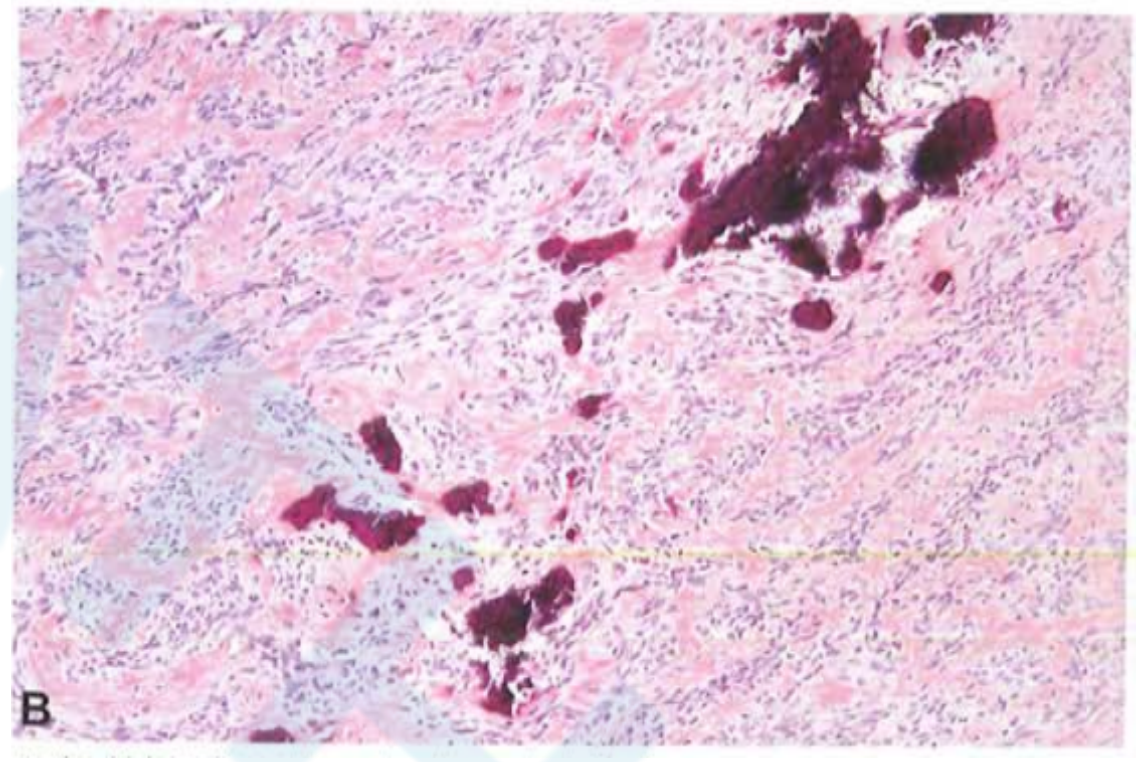
Mod Pathol. 1999 May;12(5):456-62.

Myxoid synovial sarcoma: an underappreciated morphologic subset.

Krane JF[1], Bertoni F, Fletcher CD.

硬化型滑膜肉瘤

- 细胞团索之间有明显的梁状胶原或硬化型间质
- 有单相纤维型/单相上皮样型/双向型滑膜肉瘤的结构
- 可有黏液细胞和透明细胞分化



免疫组化

- CK，EMA， Vimentin 阳性
- TLE-1 阳性
- S-100，CD99 ，bcl-2，SMA，MSA可有不同程度的表达
- CD34、desmin阴性

分子遗传学

- t(X；18)（p11；q11），涉及SS18-SSX基因融合

预后

- 低分化成分＞20%，预后差
- 瘤直径＜5cm，核分裂象＜10个/10HPF、瘤组织伴有广泛钙化和无坏死，预后好
- 儿童患者优于成人，四肢优于躯干和头颈部
- 青少年患者的5年生存率为83%。

BACKGROUND

•Most thoracic examples occur in the pleuropulmonary parenchyma, while the heart and **mediastinum** are exceptionally **rare** primary sites.

•The literature on mediastinal SS is composed of cases reports and small series, many **lacking molecular confirmation**.

•Goal : decreasing misdiagnosis and highlighting the utility of confirmatory molecular testing at this uncommon site.

MATERIALS AND METHODS

- Mayo Clinic (1993 to 2016)
- Cases which did not have molecular confirmation were excluded
- The cases were confirmed to be of mediastinal primary site
- Molecular studies:RT-PCR , FISH

Demographics and Clinical Presentation

TABLE 1. Clinical and Pathologic Features of 21 Cases of Mediastinal Synovial Sarcoma

Case	Sex	Age (y)	Histology	Molecular	Location	Size (cm)
1	Male	21	Poorly differentiated monophasic	*SS18-SSX1*	Anterior	15
2	Male	22	Poorly differentiated monophasic	*SS18-SSX2*	Posterior	
3	Male	23	Poorly differentiated monophasic	*SS18-SSX*	Mediastinum	
4	Female	27	Monophasic	*SS18-SSX2*	Superior, anterior	23
5	Male	30	Poorly differentiated monophasic	*SS18-SSX*	Anterior	
6	Male	30	Poorly differentiated monophasic	*SS18-SSX*	Anterior	29
7	Male	33	Monophasic	*SS18* FISH	Anterior	11
8	Male	33	Poorly differentiated monophasic	*SS18* FISH	Superior, posterior	
9	Male	35	Poorly differentiated monophasic	*SS18-SSX*	Mediastinum	
10	Female	36	Biphasic	*SS18-SSX1*	Posterior	"Large"
11	Male	37	Poorly differentiated monophasic	*SS18-SSX*	Mediastinum	
12	Male	42	Poorly differentiated monophasic	*SS18* FISH	Mediastinum	
13	Male	43	Monophasic	*SS18-SSX2*	Mediastinum	
14	Male	43	Monophasic	*SS18* FISH	Anterior	8.3
15	Female	43	Monophasic	*SS18-SSX1*	Posterior	16
16	Male	44	Monophasic	*SS18* FISH	Anterior	9
17	Male	44	Poorly differentiated monophasic	*SS18-SSX2*	Mediastinum	
18	Female	46	Monophasic	*SS18-SSX2*	Mediastinum	
19	Male	47	Monophasic	*SS18* FISH	Mediastinum	
20	Female	50	Monophasic	*SS18-SSX1*	Anterior	10
21	Female	75	Poorly differentiated	*SS18-SSX2*	Anterior, posterior	Multiple nodules

AWD indicates alive with disease; chemo, chemotherapy; DOD, dead of disease; XRT, external beam radiation therapy.

性别
男性：15例
女性：6例

年龄：21-75岁
平均年龄：38岁

最大径：6-23cm
平均最大径：13.5cm

部位：
前纵膈：9例
后纵膈：5例
上纵隔：2例
不确定：8例

组织学：
双向分化：1例
单项分化：20例
（低分化：11例）

分子：
SSI8断裂：6例
SS18-SSX融合：15例

Demographics and Clinical Presentation

Case	Presenting Symptoms	Treatment	Recurrence (mo)	Metastasis (mo)	Follow-up (mo)	Outcome
1	Cough, hemoptysis, Horner syndrome	Surgery, adjuvant XRT and chemo		Lung (15)	15	DOD
2	Hemothorax				9	DOD
3						
4	Back and shoulder pain, dyspnea, fatigue, poor appetite, cough	Surgery, chemo, XRT			32	DOD
5				Brain	36	AWD
6	Chest and shoulder pain	Surgery, chemo	8	Diaphragm, lung, pleura, soft tissue (8)	10	AWD
7	Chest pain	Surgery	8		9	DOD
8		Surgery, adjuvant XRT and chemo	8	Lung (22)	24	DOD
9						
10	Supraclavicular mass	Surgery, adjuvant XRT and chemo	12	Lung (14)	27	DOD
11			6		6	AWD
12	Chest tightness, dysphagia				20	DOD
13				Pericardium (18)	18	DOD
14	Pneumonia, syncope	Surgery, chemo	3		16	AWD
15	Epigastric pain, dysphagia	Surgery, XRT			5	DOD
16	Chest pain	Surgery, XRT and chemo for recurrence	10		15	DOD
17		Unresectable at surgery; chemo and XRT			15	DOD
18						
19						
20			43		45	AWD
21	Pleuritic chest pain					

治疗

手术：1例

手术+化疗：2例

手术+放疗：1例

手术+放疗+化疗：5例

化疗+放疗：1例

预后：5-45个月

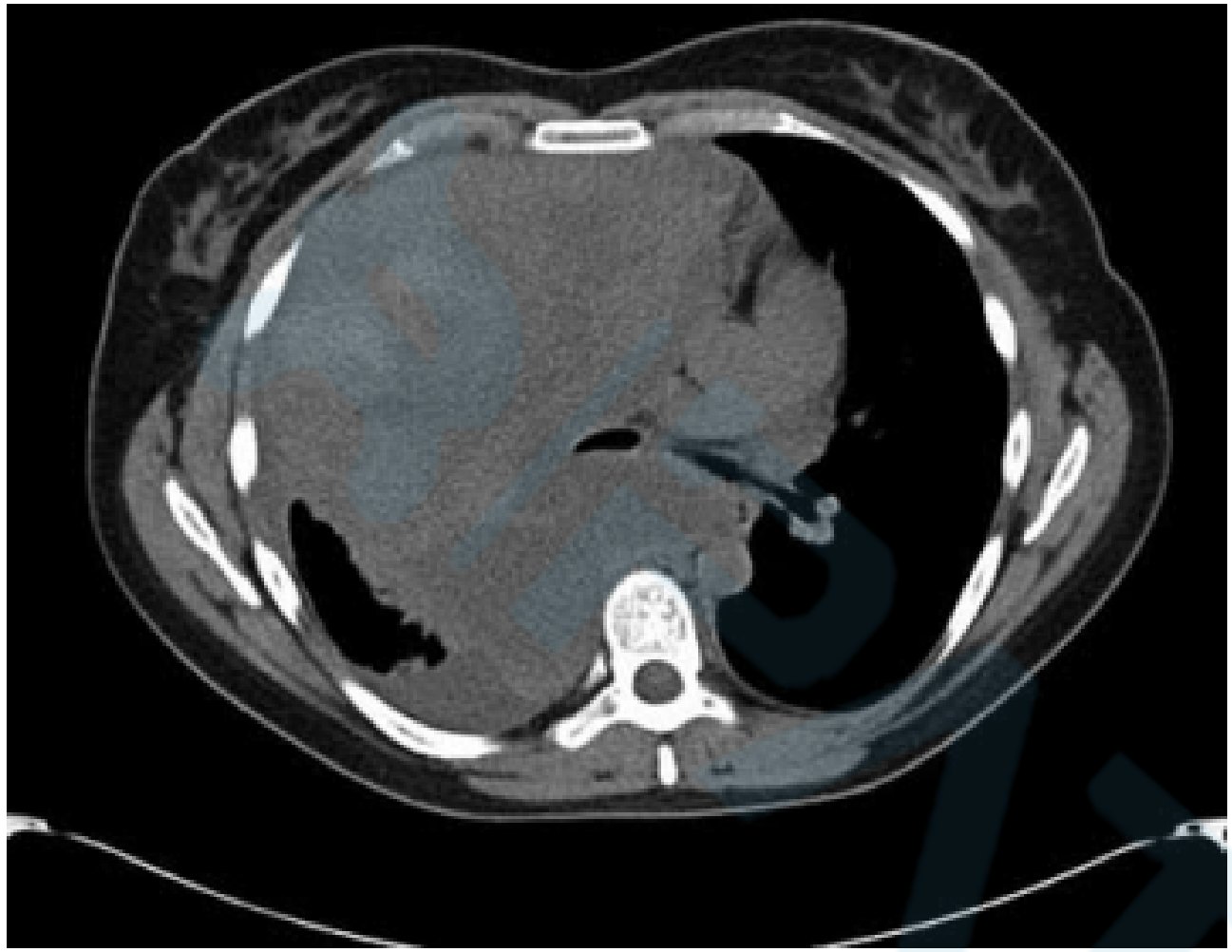
平均时间：18.9个月

复发/进展：14例

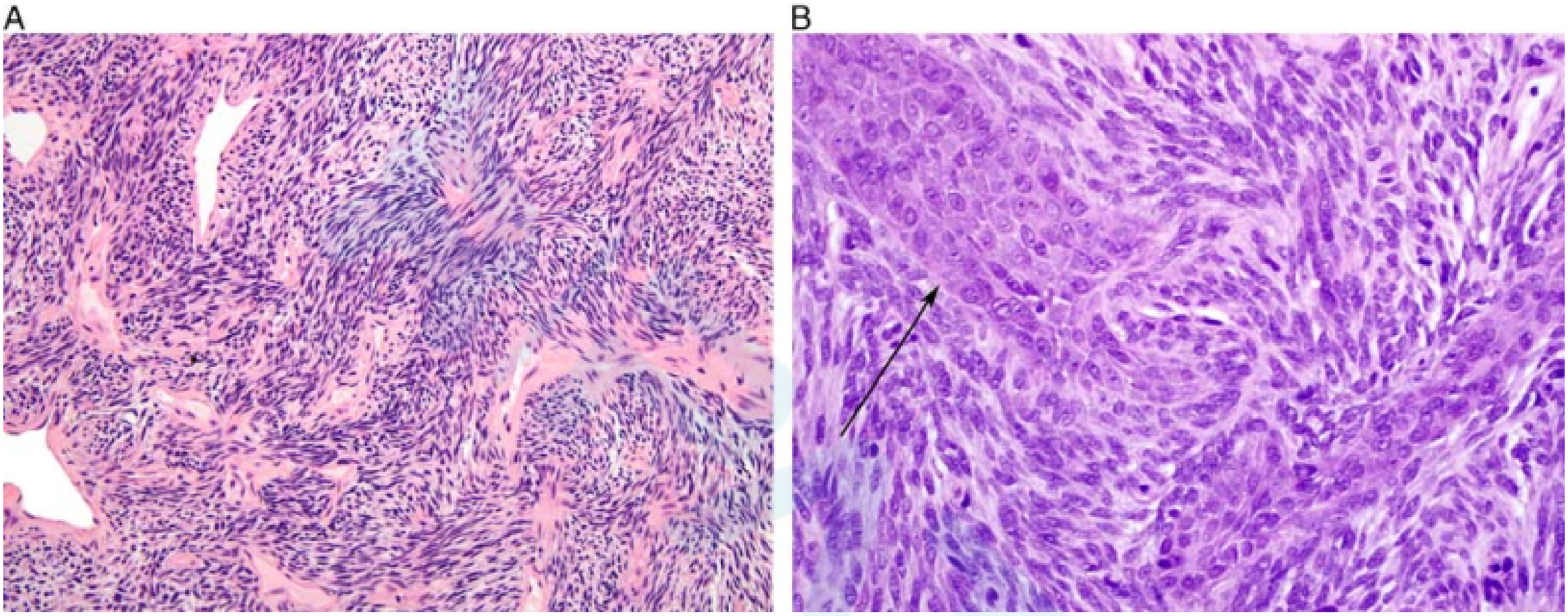
转移：6例

死亡：11例

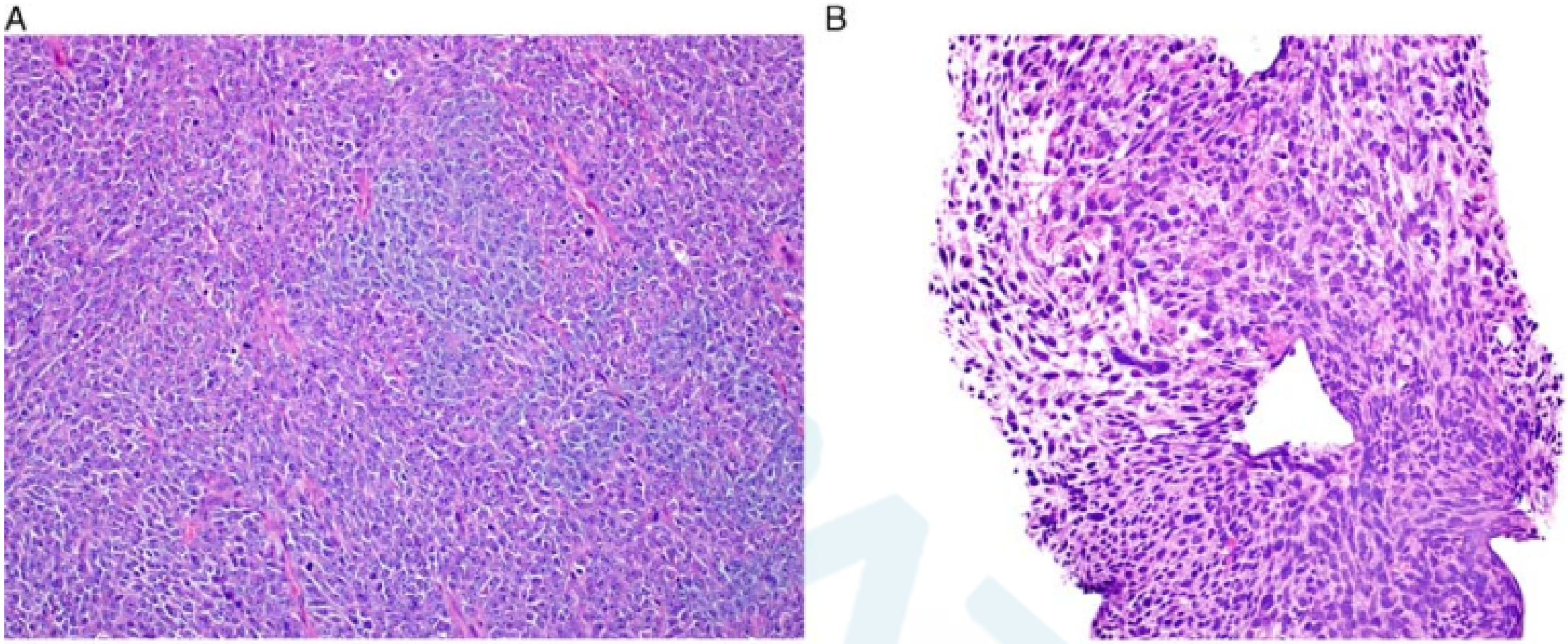
存活：5例



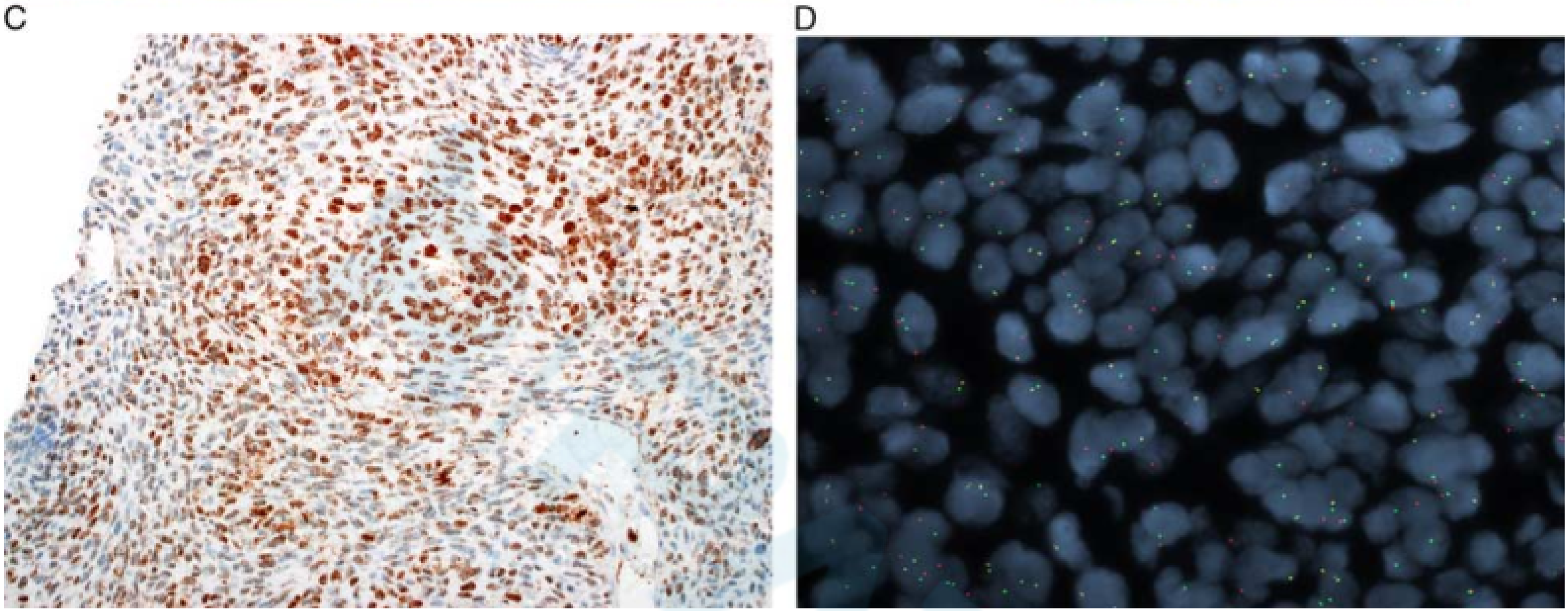
Computed tomography showing a 23 cm synovial sarcoma involving the superior and anterior mediastinum and partially filling the right chest, with compression of the right lung.



A, Monophasic mediastinal synovial sarcoma, showing monomorphic spindle cells and hemangiopericytoma-like vasculature. B, Biphasic synovial sarcoma, showing solid epithelial nests (arrow) admixed with monomorphic spindle cells.



A, Poorly differentiated mediastinal synovial sarcoma showing round cell and epithelioid morphology. B, Unusual example of synovial sarcoma showing nuclear pleomorphism.



C, Strong and diffuse nuclear positivity for TLE1 in poorly differentiated synovial sarcoma.
D, Interphase fluorescence in situ hybridization confirms rearrangement of SS18 (break apart of red and green signals).

DISCUSSION

- The occurring in the mediastinal primary site representing was slightly higher at 11.2% cases.（referral bias）

- we may be underestimating the rate of biphasic tumors（1/21）.（biopsies）

DISCUSSION

- Poorly differentiated morphology is an important clue to the correct diagnosis.

  Poorly differentiated areas with rounded or spindled cells showing severe nuclear atypia and high mitotic activity (＞15/10 HPFs) may be found. Poorly differentiated areas are at least two of the following high-grade nuclear features: nuclear crowding, nuclear irregularity, prominent nucleoli or irregular clumping of chromatin.

- Immunohistochemistry： keratins, EMA, TLE-1, CD99 and S-100.

Differential diagnosis

- sarcomatoid carcinoma
- mesothelioma
- thymoma
- spindle epithelial tumor with thymus-like differentiation (SETTLE)]
- malignant peripheral nerve sheath tumor
- solitary fibrous tumor

	部位	组织形态	免疫组化	分子遗传学
滑膜肉瘤	四肢深部软组织、胸膜肺实质	双相型、单相型、低分化型 一般无核的显著异型性	CK、EMA灶或弱阳 TLE-1核阳性	SS18-SSX1 SS18-SSX2
癌肉瘤	任何部位	梭形、多形性瘤细胞，异型性明显	CK强阳性	-
肉瘤样间皮瘤	胸、腹腔	梭形、多形性细胞，异型性明显	间皮性标记物阳性	P16缺失
胸腺瘤	胸腺	纤维性包膜，呈多结节生长	CD5、CK19、TdT阳性	-
SETTLE	甲状腺或颈部	似SS：梭形细胞及上皮成分	HCK强阳性 CD99、bcl-2阳性	-
mPNST	任何部位	形态多样	S-100灶阳或阴性 EMA、CK通常阴性	-
SFT	任何部位	血管外皮瘤样 有丰富的胶原纤维束	CD34、CD99(+), bcl-2(+,30%)	-
Ewing 肉瘤	长骨的骨干及干骺端、不规则骨	小蓝圆细胞 染色质细腻	CD99膜(+)、 CK(+,20%)	FLI-EWS、 ERG-EWS

Prognosis

•SSs in the lung and pleura also have a poor prognosis compared with soft tissue tumors, with approximately **half of patients dead from disease within 5 years.**

•Our data indicates that the prognosis of mediastinal SS may be even worse, with **69% of patients dying from disease in <3 years from diagnosis.**

•The poor prognosis likely relates to **site-specific** factors, including proximity to critical anatomic structures and late detection with **large tumor size** at diagnosis.

Summary

•Mediastinal SS is a rare and aggressive malignancy most common in patients **younger than 50 years.**
•Most are monophasic and reach **large size** before detection.
•SS should be included in the differential diagnosis of **spindle cell**,**biphasic** and **poorly differentiated mediastinal tumors.**
•The **prognosis** of mediastinal SS may be even **worse**, with 69%of patients dying from disease in <3 years from diagnosis.
•Because of the rarity of SS at this site, **molecular testing** is recommended to confirm the diagnosis.

THANK YOU