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Rosai-Dorfman Disease of the Breast With Variable IgG4+ Plasma Cells

A Diagnostic Mimicker of Other Malignant and Reactive Entities

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Rosai-Dorfman Disease（RDD）

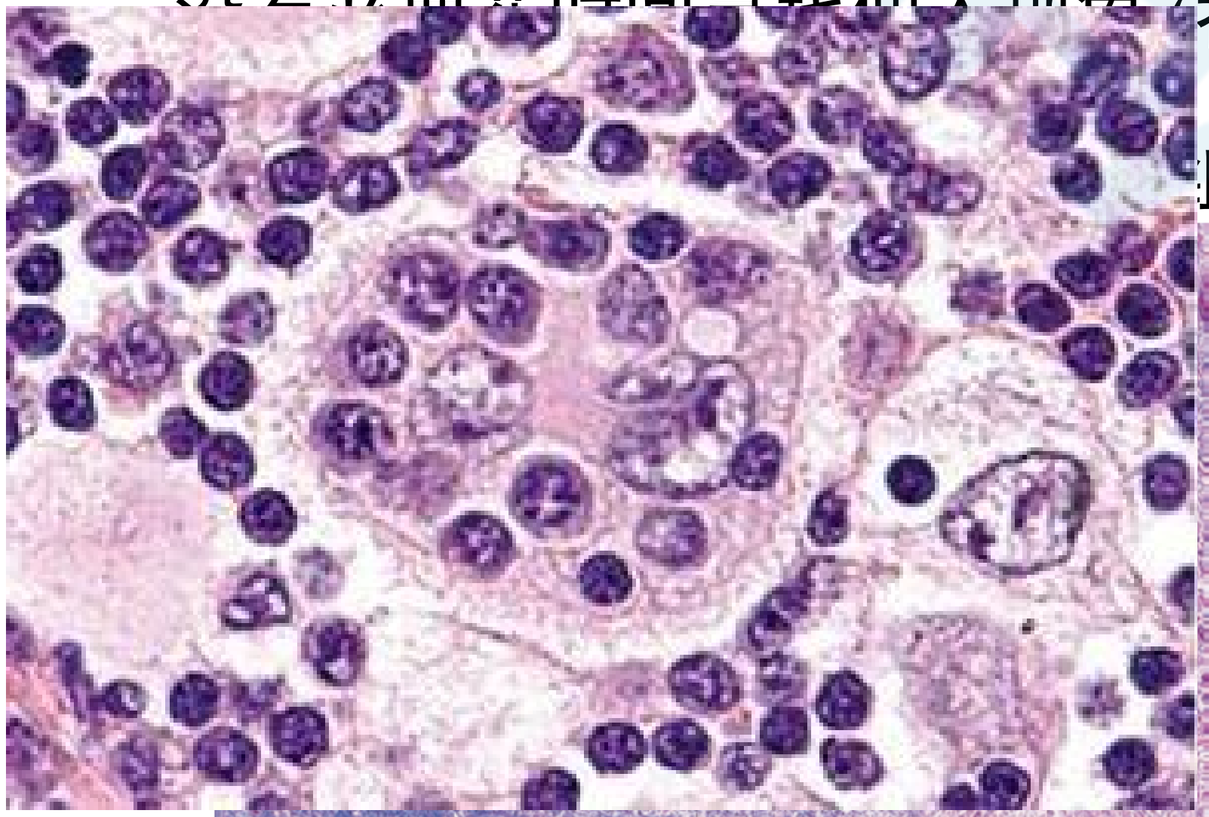
- 窦组织细胞增生伴巨大淋巴结病 (SHML)
- 反应性，特发性组织细胞增生性疾病
- 年龄: 平均20岁
- 性别: 男性稍多

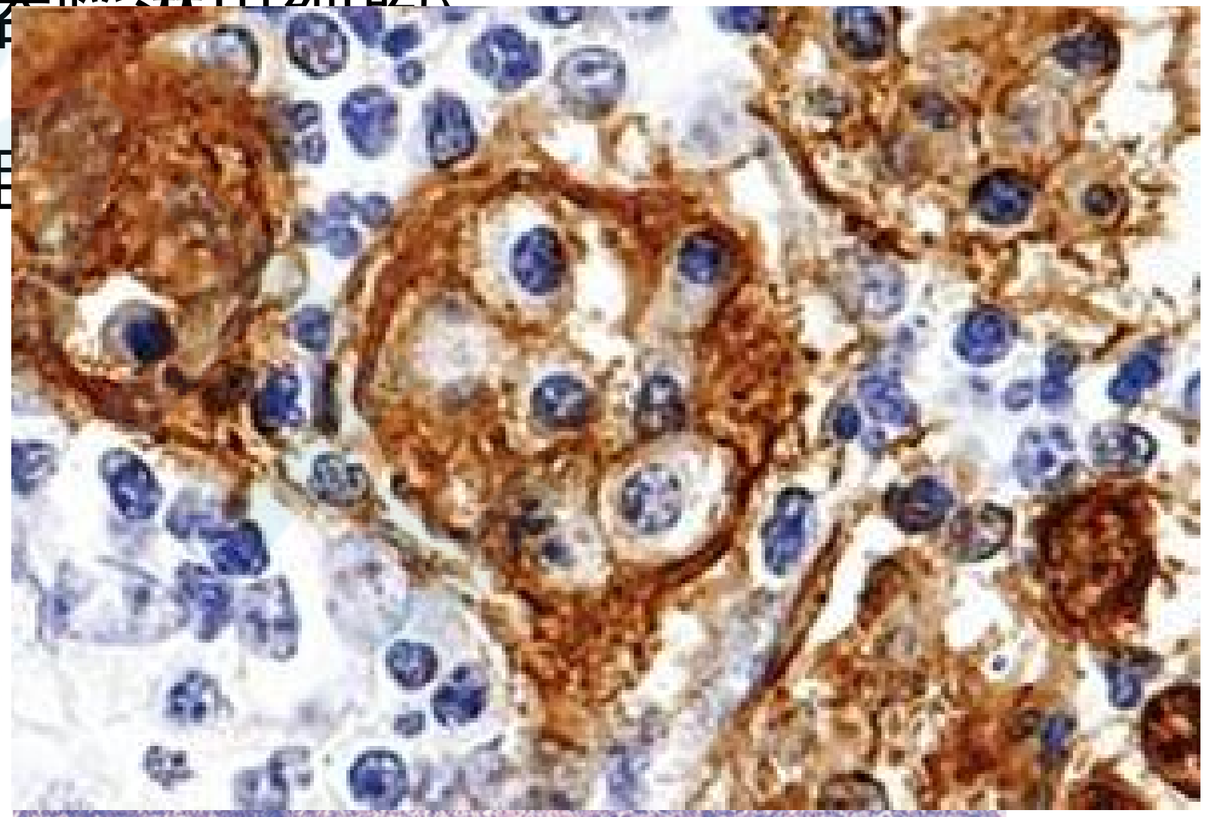
Rosai-Dorfman Disease

- 大部分患者出现淋巴结肿大 (尤其是颈部，通常是多个，较大并且融合在一起)
- 结外受累常见 (43%)
  - 伴有或不伴有同时出现的淋巴结受累
  - 最常见的部位：皮肤，上呼吸道，骨
- 大部分病例是良性经过: 自发消退或迁延不愈
- 少数病人死于累及重要器官的广泛病变或与免疫异常相关的并发症

Rosai-Dorfman Disease

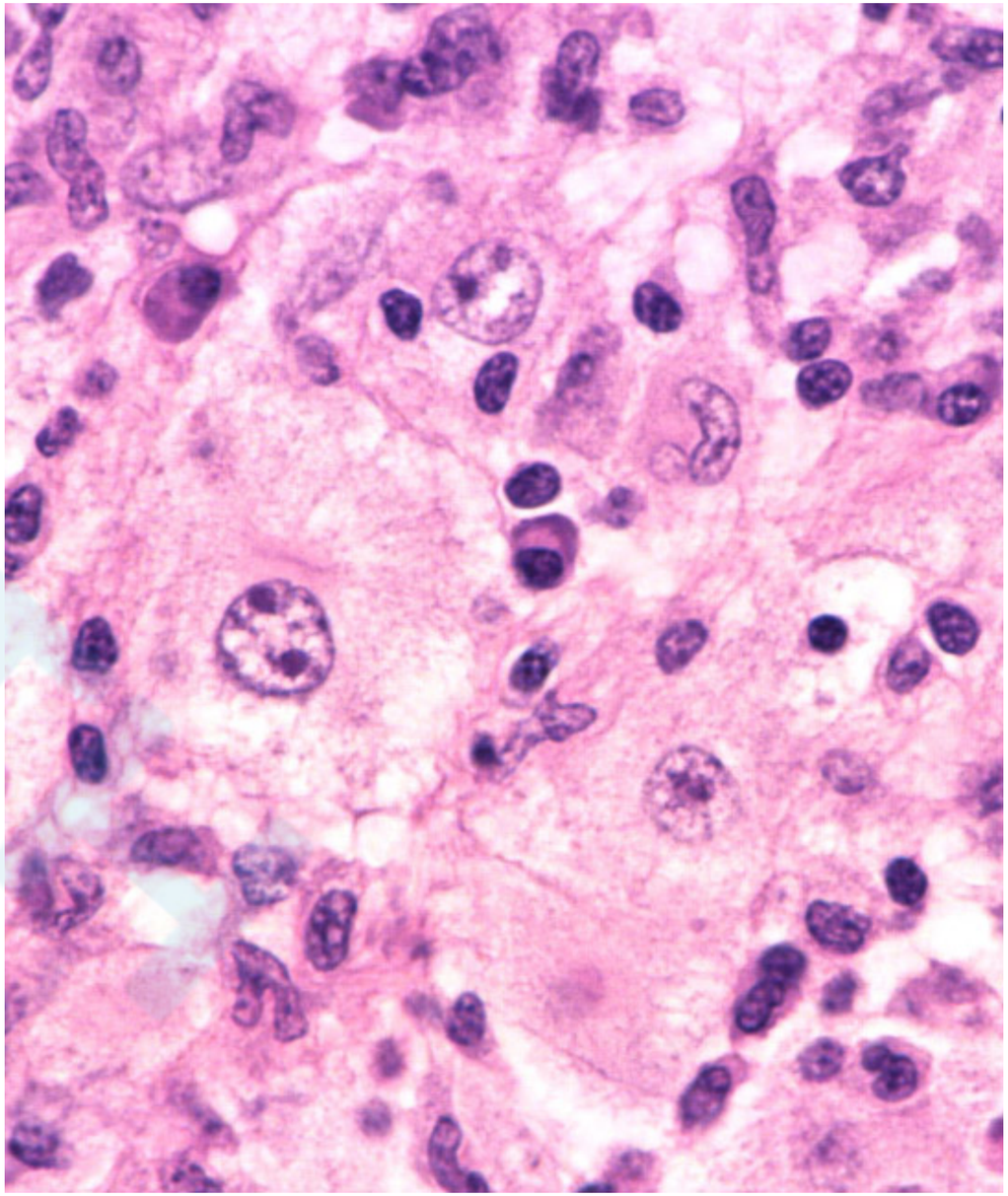
- 在淡染区寻找诊断性的组织细胞 (可存在散在的非典型细胞)
- 必然可以见到很多浆细胞
- 没有必要苛刻寻找伸入现象 (吞噬淋巴细胞)





Rosai-Dorfman Disease

- 非常大, 有大量的胞浆 (典型的淡染到透明，有时为嗜酸性)
- 核常为圆形, 泡状染色质
- 明显的核仁



乳腺RDD研究现状

- 多是个案报道，未系统性研究其临床病理特征；
- 表现为乳腺包块，可累及腋窝淋巴结，临床及影像特征与乳腺浸润性癌易混淆；
- 其他部位发生的RDD通常为良性病程，但可出现反复复发及进展；
- 乳腺RDD的预后尚不清楚

研究目的

研究并阐明乳腺RDD的临床病理特征；着重于其诊断陷阱；避免过度治疗

MATERIALS AND METHODS

Case Selection

A total of 22 cases of RDD of the breast were identified from searching the pathology archives of the Stanford University Medical Center, University of California San Francisco, University of Pennsylvania, Brigham and Women's Hospital/DFCI, Oregon Health Sciences University, Seattle Children's Hospital, University of Chicago, Washington University St Louis, PennState Health, and Medical College of Georgia between the years of 2007-2017.

MATERIALS AND METHODS

Histopathologic and Immunohistochemical Features

✓Sclerosis was graded as minimal (not visibly present), moderate (thin bands of fibrosis), and prominent (thick bands of fibrosis)；

✓RDD cells were defined as rare (< 1/50 HPF), occasional (1 to 50/50 HPF), numerous (> 50/50 HPF)；

RESULTS

TABLE 1. Histopathologic Features of RDD Biopsies of the Breast

Case No.	Lymphocytic Infiltrate	Plasma Cell Infiltrate	Sclerosis	RDD Cells (on H&E)	Breast Epithelium
1	Prominent, in nodules w/GCs	Prominent	Prominent	Occasional	Absent
2	Prominent, in nodules w/GCs	Prominent	Prominent	Numerous	Absent
3	Prominent, diffuse	Prominent	Prominent	Occasional	Present
4	Prominent, in nodules, w/o GCs			Occasional	Absent
5	Prominent, diffuse			Occasional	Absent
6*	Moderate, in nodules w/o GCs			Rare	Absent
7*	Prominent, in nodules w/o GCs			Occasional	Absent
8	Prominent, in nodules w/o GCs			Numerous	Absent
9	Prominent, diffuse			Numerous	Present
10	Prominent, in nodules w/GCs			Numerous	Absent
11	Prominent, diffuse			Occasional	Present
12	Prominent, diffuse			Occasional	Absent
13	Prominent, in nodules w/o GCs			Occasional	Absent
14	Prominent, in nodules w/o GCs			Occasional	Absent
15	Prominent, in nodules w/o GCs			Rare	Absent
16	Prominent, in nodules w/GCs			Occasional	Absent
17	Prominent, in nodules w/GCs, dispersed in other areas	Moderate	Prominent	Occasional	Present
18	Prominent, in nodules w/o GCs	Prominent	Moderate	Numerous	Absent
19	Prominent, in nodules w/o GCs	Prominent	Moderate	Occasional	Present
20	Prominent, in nodules w/o GCs	Prominent	Prominent	Occasional	Absent
21	Prominent, in nodules w/GCs	Moderate	Prominent	Occasional	Absent
22	Prominent, in nodules w/GCs	Moderate	Prominent	Occasional	Absent

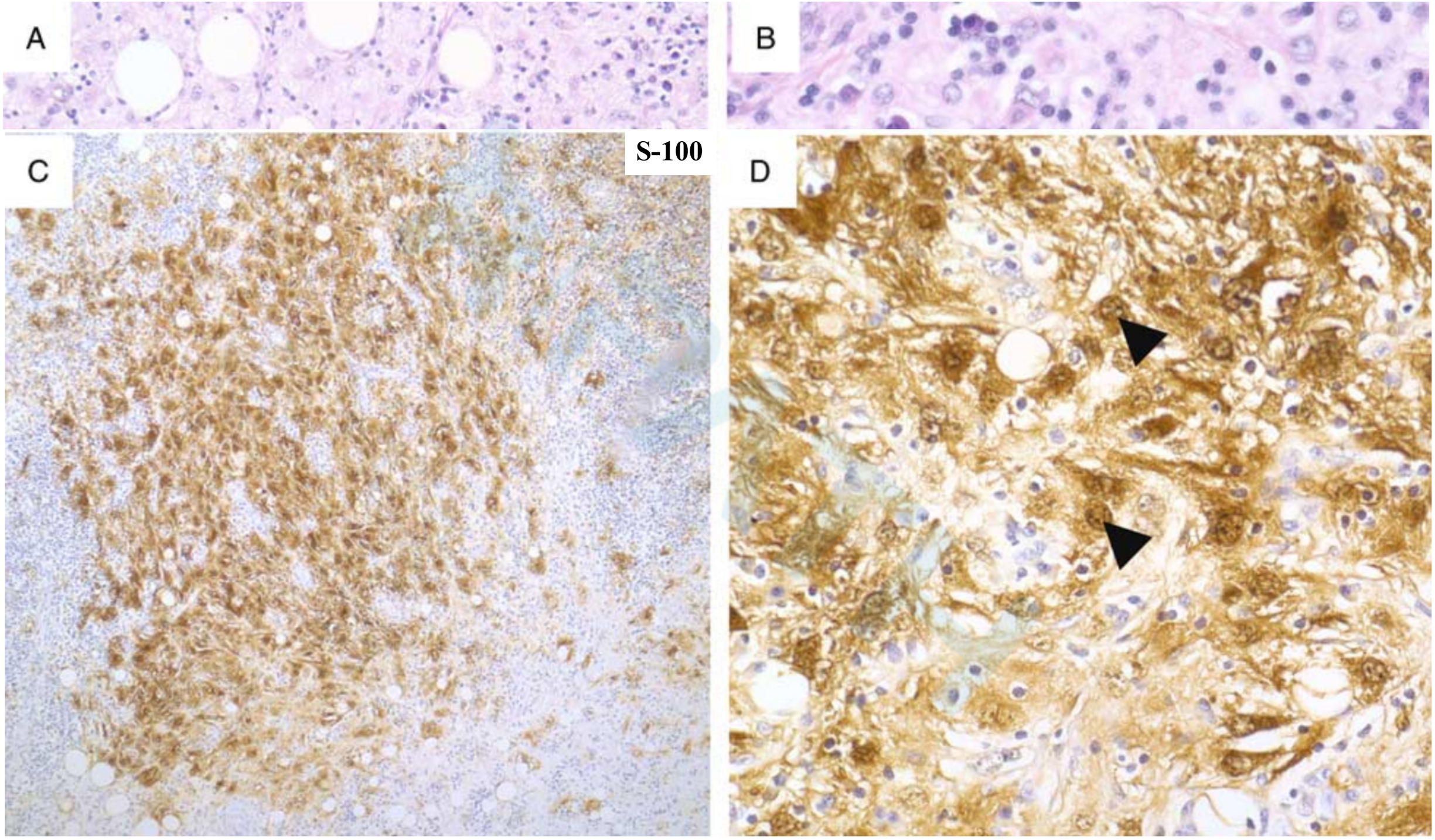
1）淋巴细胞：显著，22/22；

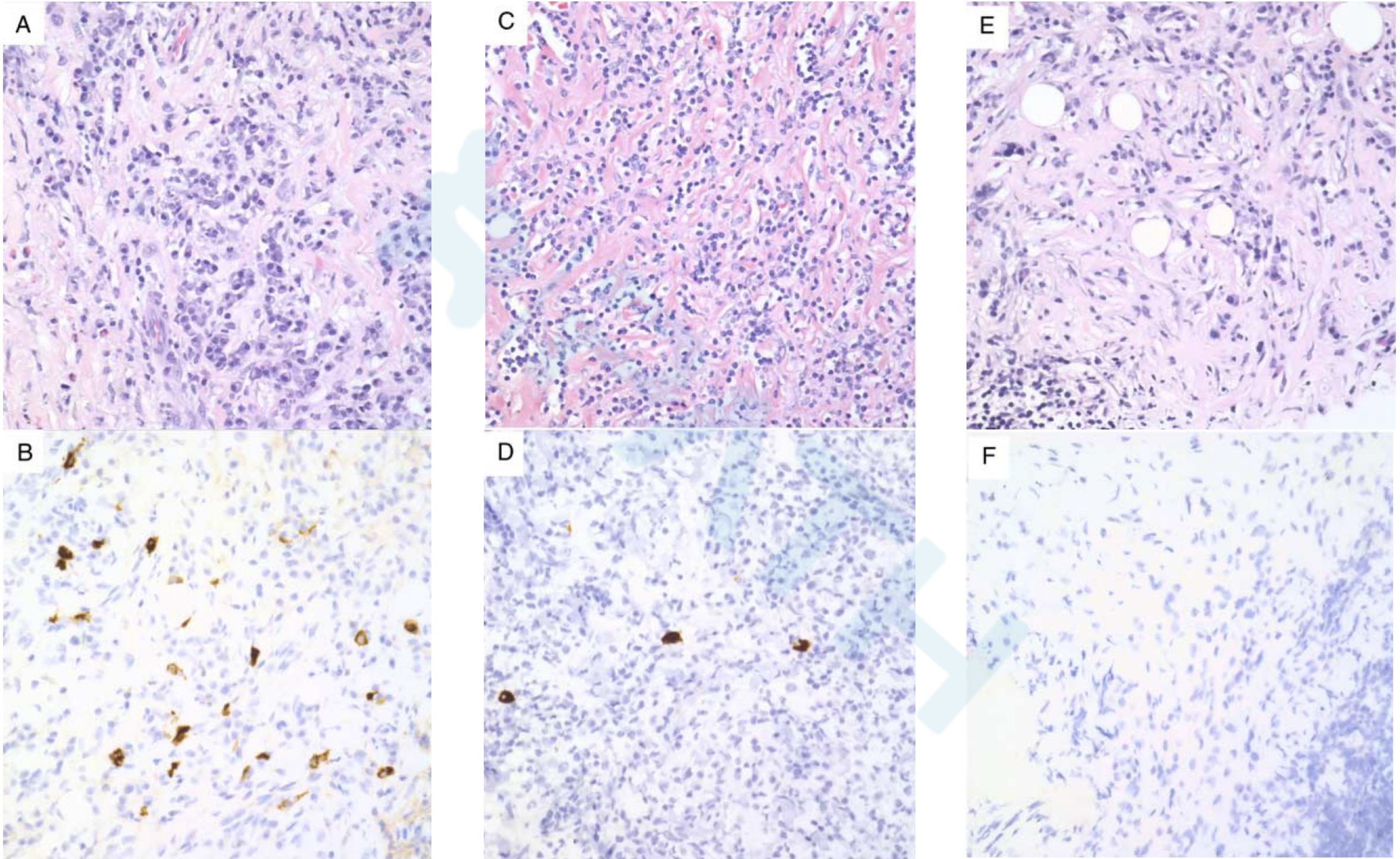
2）浆细胞：中等-弥漫，19/22；

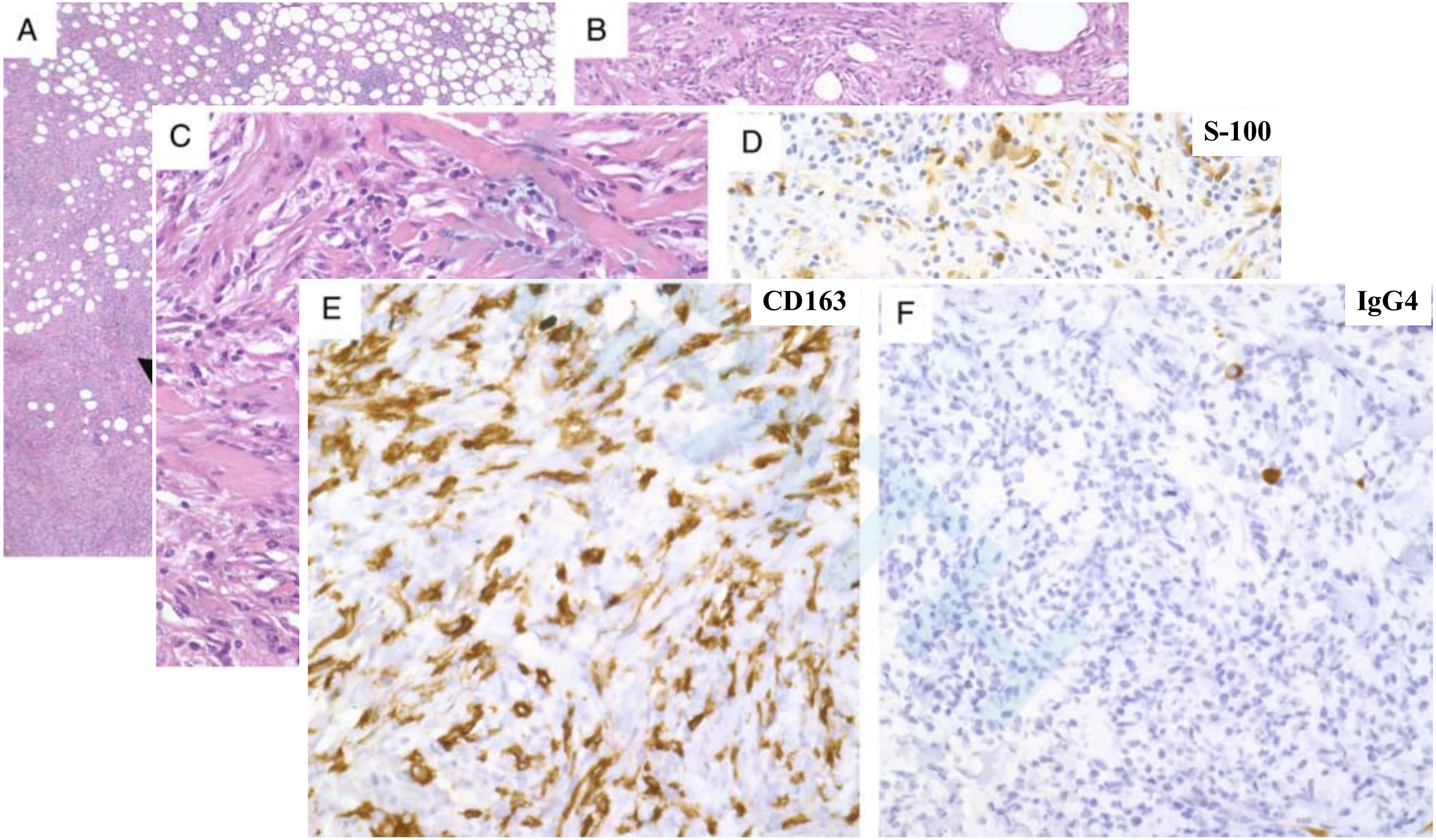
3）硬化：中等-显著，19/22；

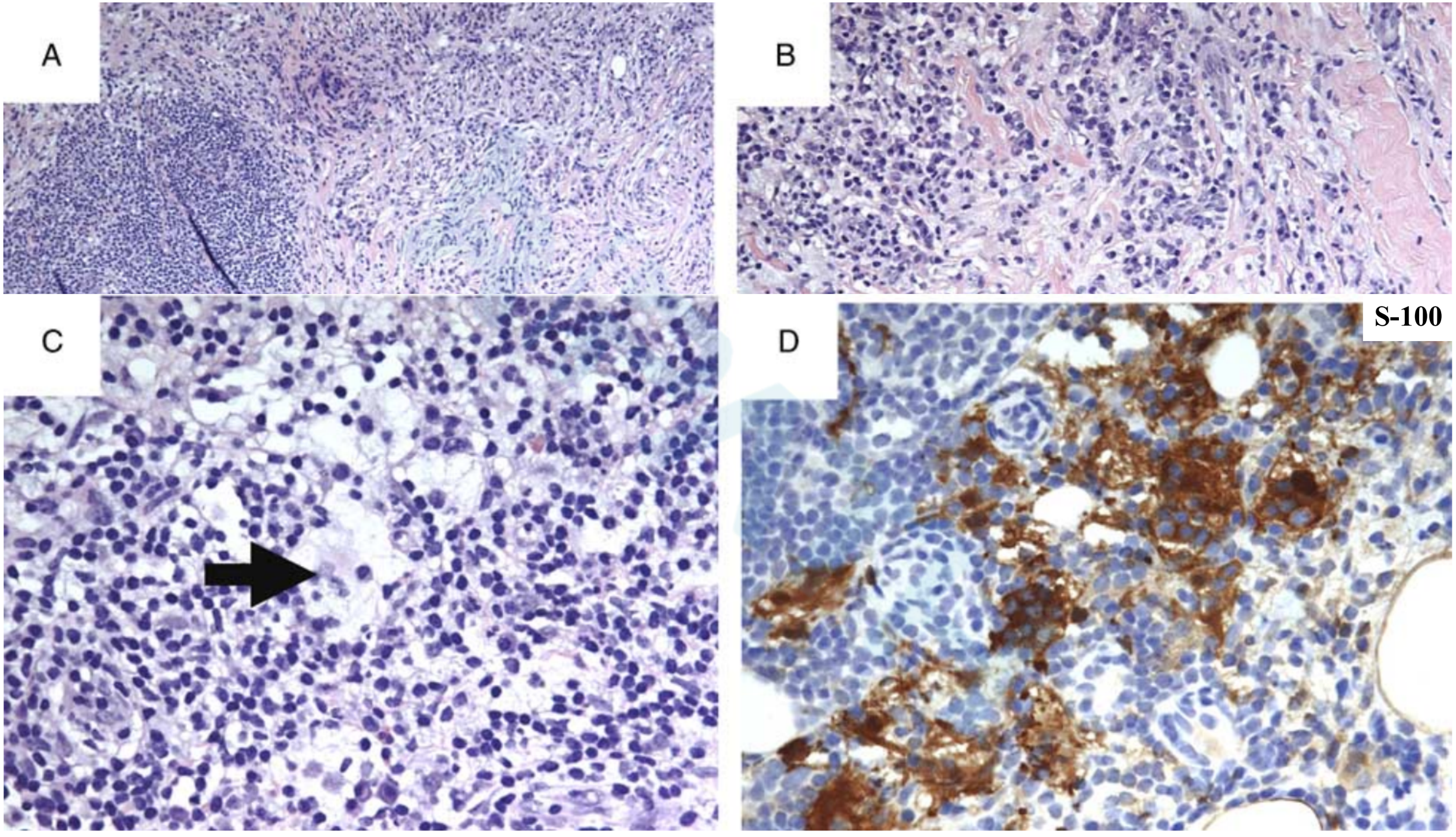
4）RDD细胞：偶见或罕见，17/22；

5）乳腺上皮：缺失，17/22


A
B
C
S-100
D


A
B
C
D
E
F


A
B
C
D
S-100
E
CD163
F
IgG4


A
B
C
D
S-100

Clinical Features

- The median age was 54(15-79), with 18 females and 4 males;
- Ten patients presented with a mass lesion, ranging in size from 0.4 to 6.0 cm, 3 of which were discovered by mammography.
- Of all 22 cases, 4 were diagnosed on a core biopsy, whereas the remaining 18 were diagnosed on an excision specimen;

Clinical Features

- Follow-up information was available for 6 patients. Case 7, as described above, had an initial simple mastectomy which was diagnosed as inflammatory myofibroblastic tumor, subsequently had recurrence 2 years later, and was re-excised at which point a diagnosis of RDD was made. Case 18 had an excisional biopsy that recurred 6 years later, while cases 19 to 22 have all been disease free after excision with follow-up ranging from 6 months to 6 years.
- No histopathologic features correlated with recurrence (density of RDD infiltrate, degree of sclerosis, density of lymphoplasmacytic cells, or IgG4+ plasma cells).

DISCUSSION

DISCUSSION

- Our findings demonstrate that RDD of the breast can be easily overlooked especially in the setting in which the emperipolesis is inconspicuous.
- The majority of our cases (16/22) lacked prominent emperipolesis, and histologically closely resembled other diagnostic entities, including inflammatory myofibroblastic tumor, IgG4-related sclerosing mastitis, granulomatous disease, and marginal zone lymphoma with plasmacytic differentiation.

DISCUSSION

- Of note, in a single case in our series, IgG4 staining was positive in ~ 30% of the IgG+ plasma cells, which is still far below what would be expected in an IgG4-related sclerosing mastitis (49% to 85%).
- The significance of this finding is unclear, and further investigation with correlation of clinical features (eg, serum IgG4 levels, response to steroids) is required to elucidate whether these 2 entities are related.

DISCUSSION

- Recently molecular abnormalities in BRAF, KRAS, MAP2K1, ARAF, and PIK3CA have been identified in RDD. Clearly it would be of interest in future work to assess for any commonalities associated with phenotype and genotype in such cases. This can be a focus of future prospective studies where tissue is available.
- As these cases are rare, it is not surprising that some may be misdiagnosed as an inflammatory process or other spindle cell neoplasm. Therefore in the setting of sclerosis and fibrosis with a dense lymphoplasmacytic infiltrate and even with only rare histiocytic cells, one should always entertain the differential diagnosis of RDD.

鉴别诊断

- 慢性感染性疾病(如真菌感染、结核等肉芽肿性炎)：
  - ✓PAS、六胺银、抗酸；S-100阴性
- 肉芽肿性乳腺小叶炎：
  - ✓好发年龄约30岁；
  - ✓肉芽肿性炎局限于小叶内，可伴有脂肪坏死、脓肿形成及纤维化；
  - ✓S-100阴性
- 朗格汉斯细胞组织细胞增生症：
  - ✓细胞圆形、卵圆形，可见核沟；
  - ✓伴嗜酸性粒细胞浸润，部分病例可见破骨样巨细胞；
  - ✓表达S-100、CD1a、CD207

鉴别诊断

●IgG4相关硬化性疾病：

✓有自身免疫性疾病，外周血可出现自身抗体，血清IgG、IgG4升高；

✓明显纤维化伴较多浆细胞浸润；

✓IgG4+浆细胞>100/HPF，IgG4/IgG>50％

●纤维组织细胞瘤：

✓多位于肢体远端；

✓由纤维母细胞和组织细胞增生，呈旋涡状结构；

✓散在黄色瘤细胞，杜顿巨细胞、含铁血黄素性吞噬细胞；

✓S-100、CD163阴性

THANK YOU

Any questions?