NKM Laboratório
Patologia e Citopatologia

Sociedade Brasileira de Patologia

# Caso do mês
# Janeiro/2016 - 2

Carlos Camilo Neto

# História clínica

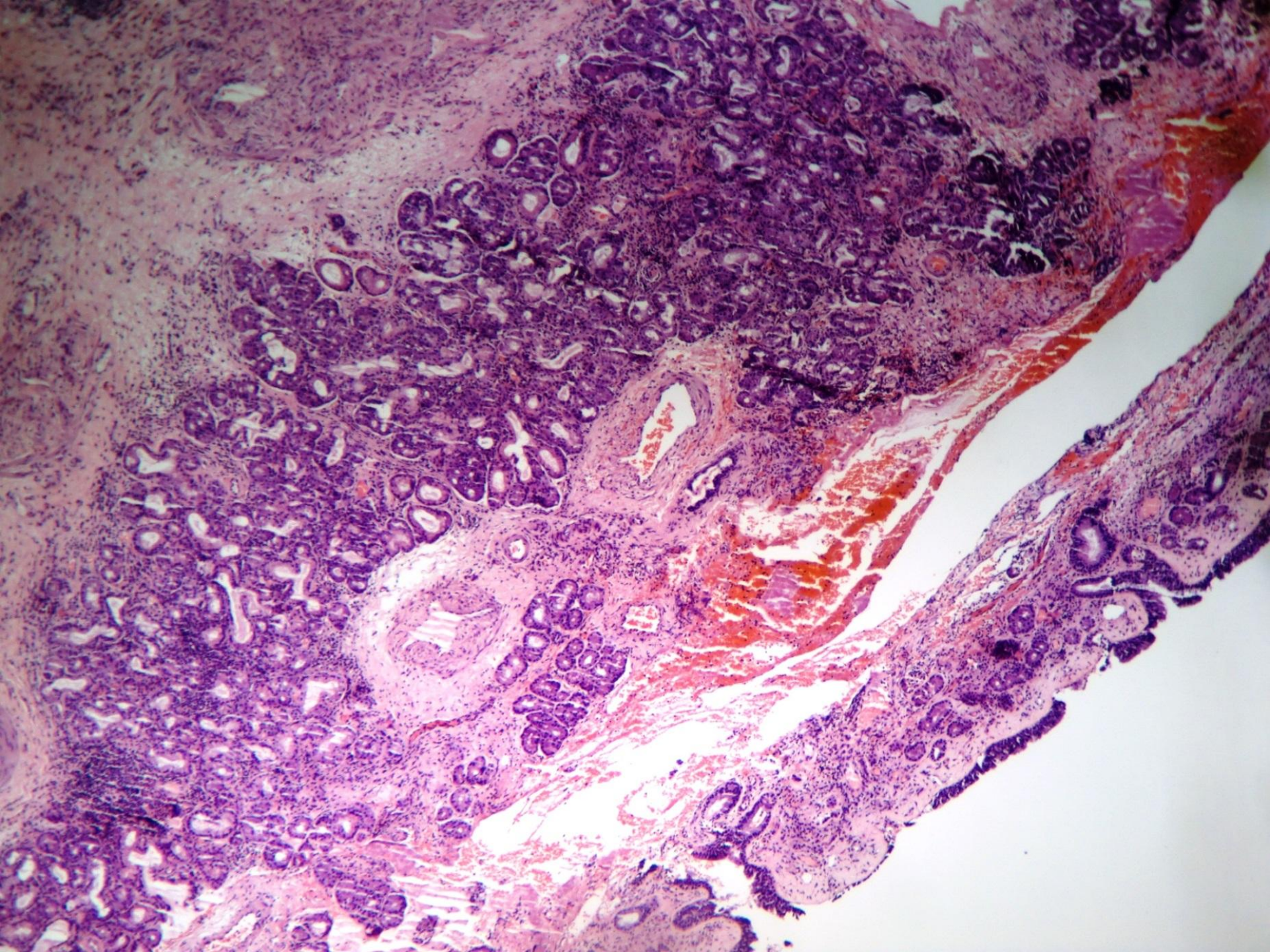
. RAS, masculino, 34 anos

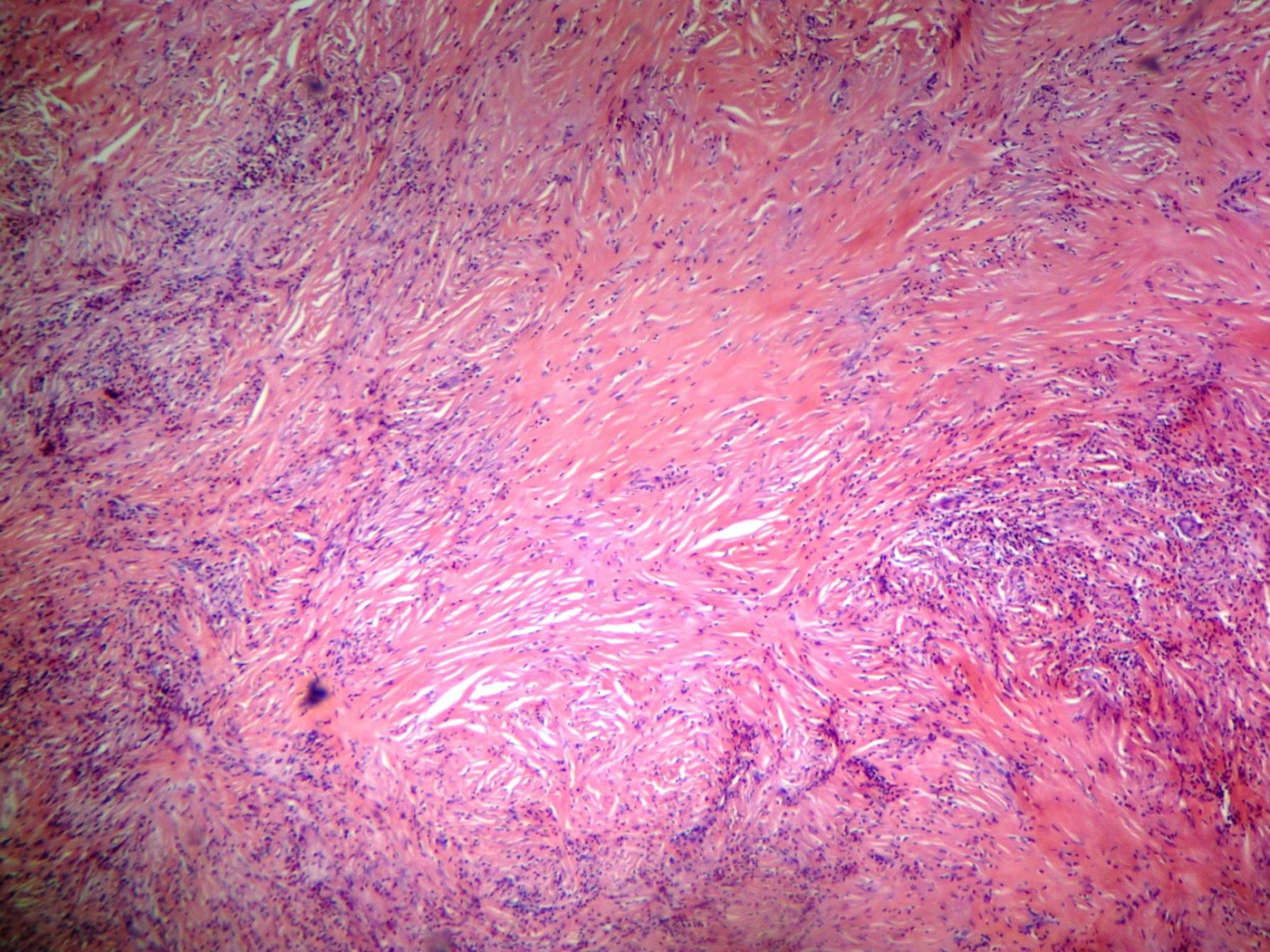
. Paciente com história de trauma nasal

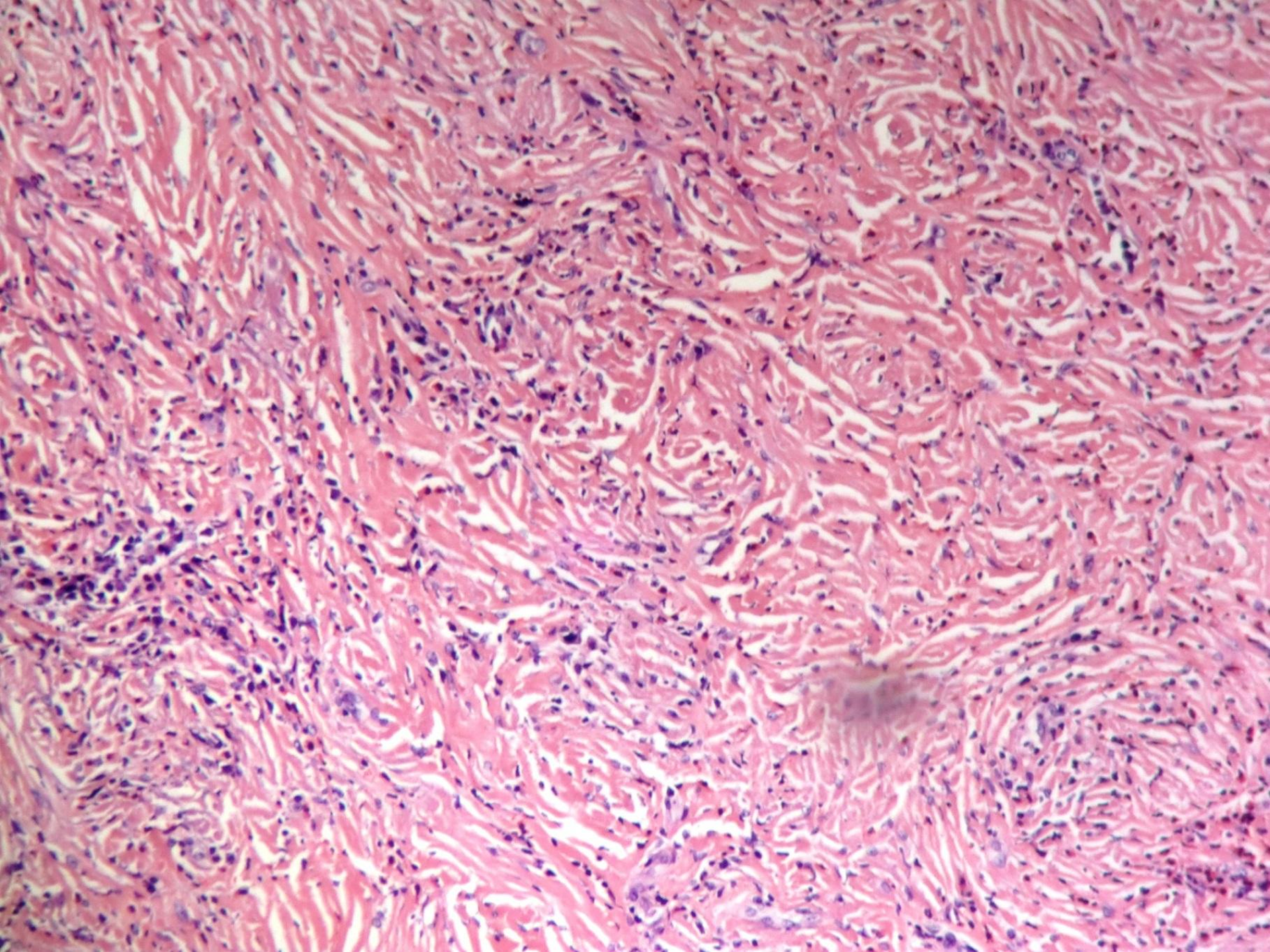
. HD: Condroma?

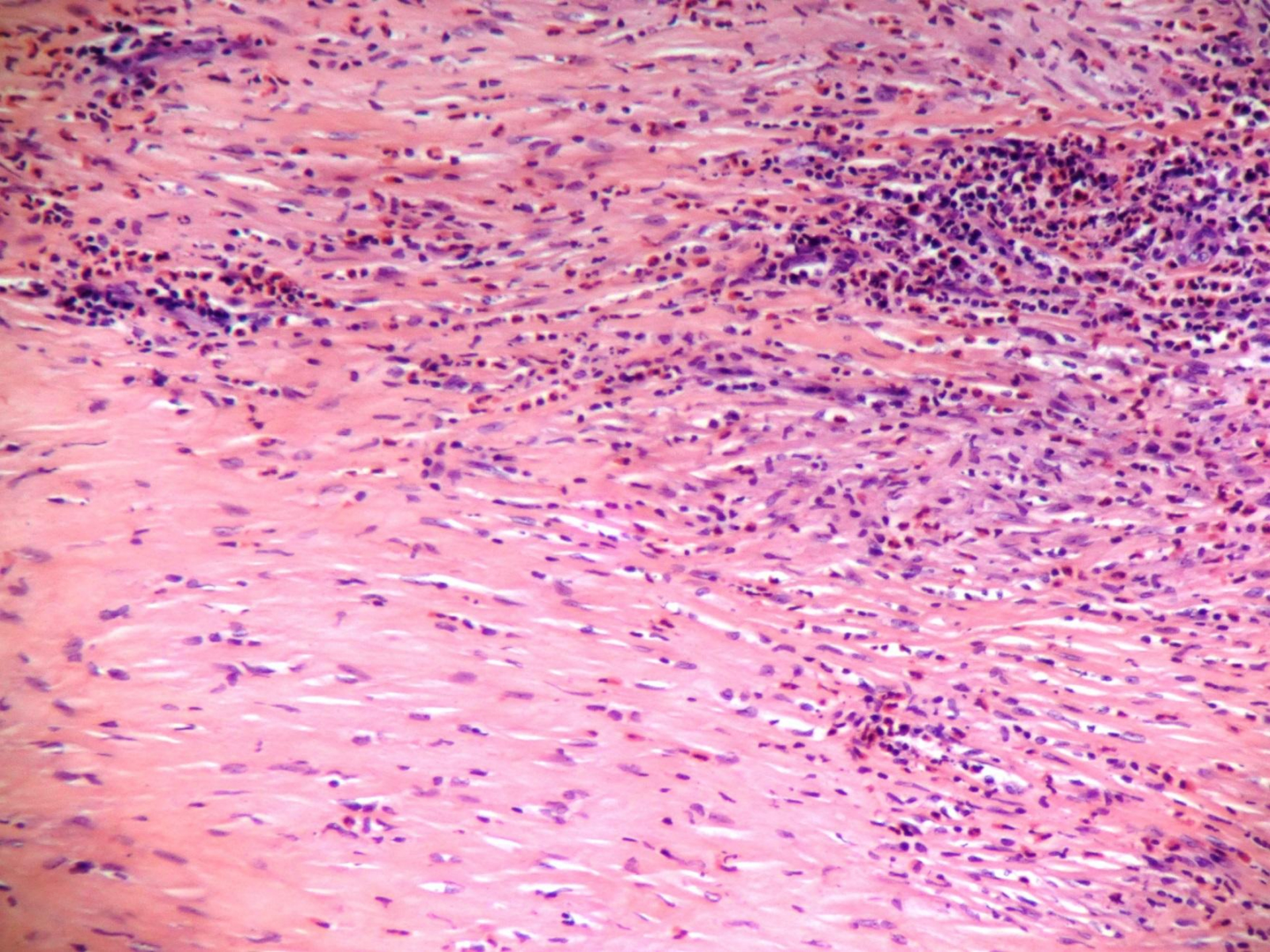
# História clínica

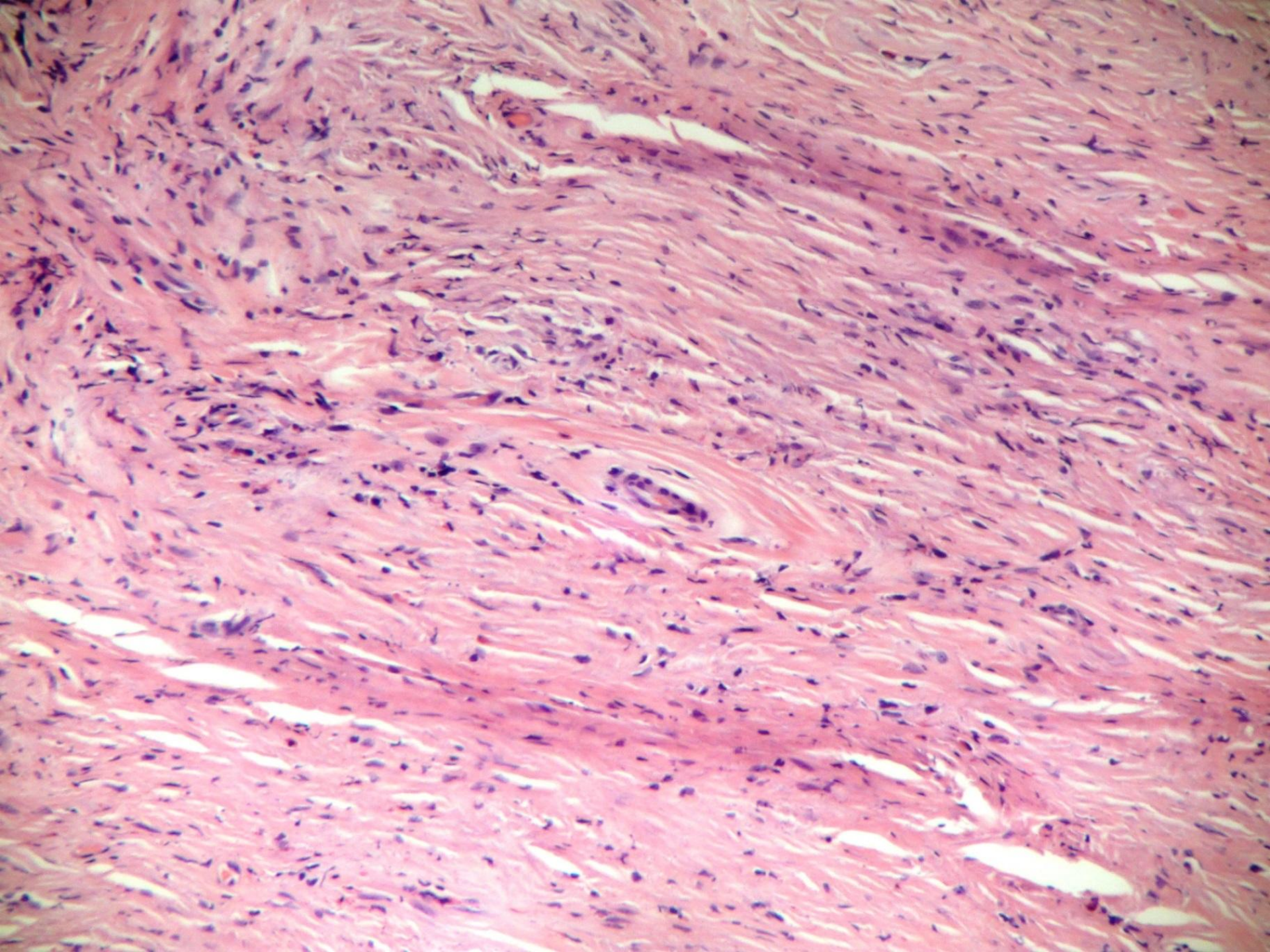
Não há informações de testes laboratoriais ou história patológica pregressa

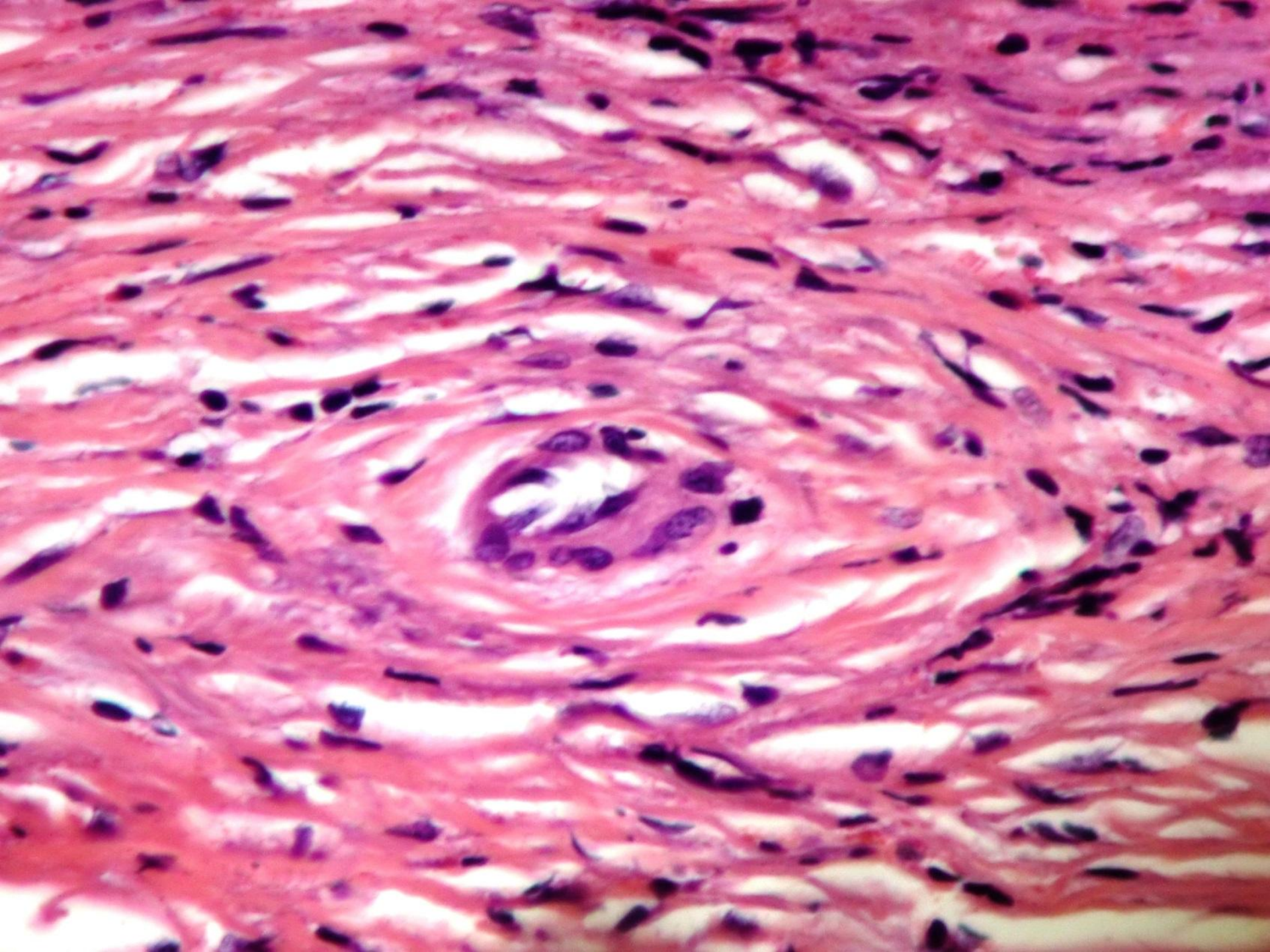


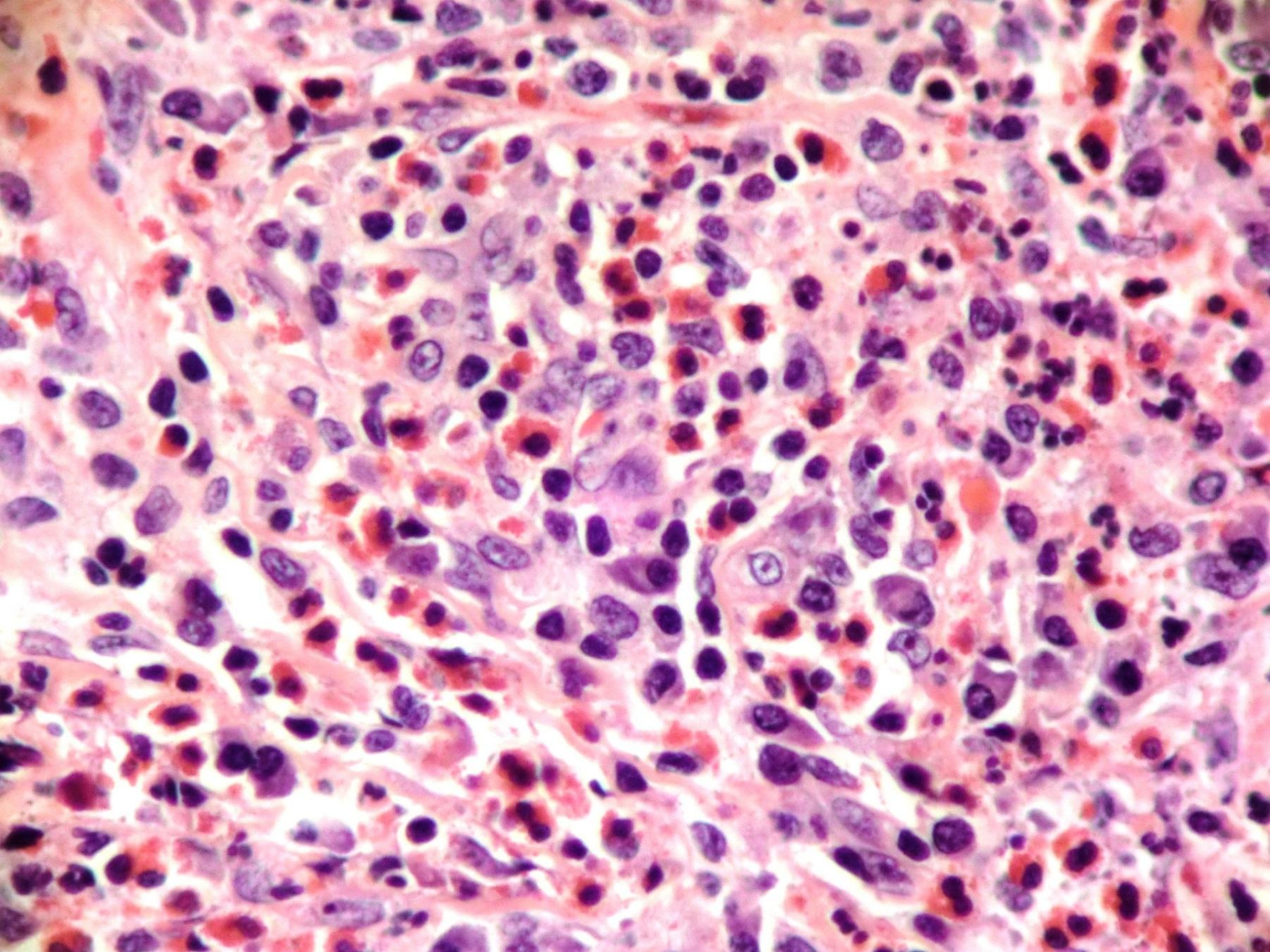












# Histologia

Ausência de:

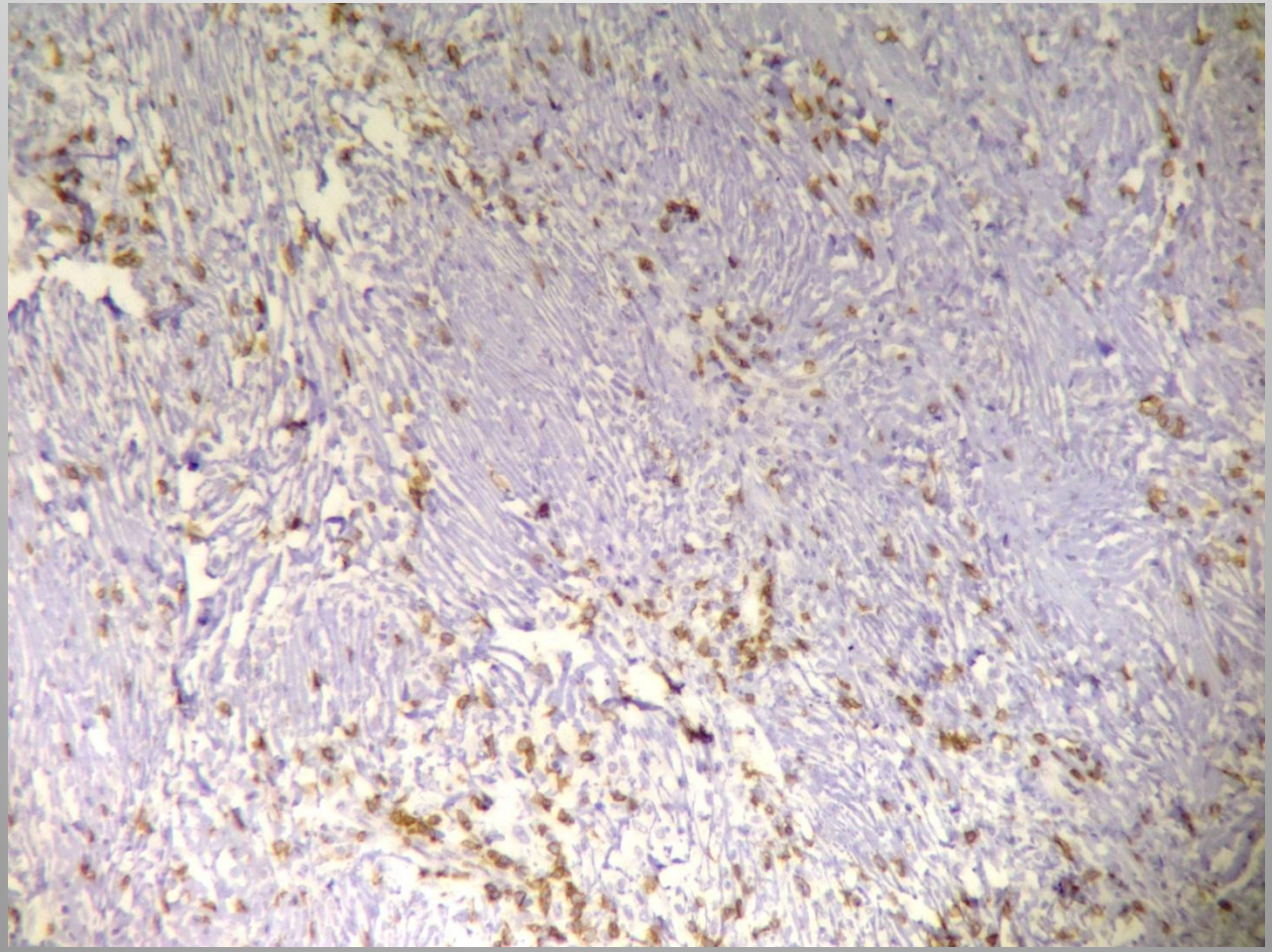
. Granulomas

. Vasculite

. Necrose

. Flebite obliterativa

# CD3



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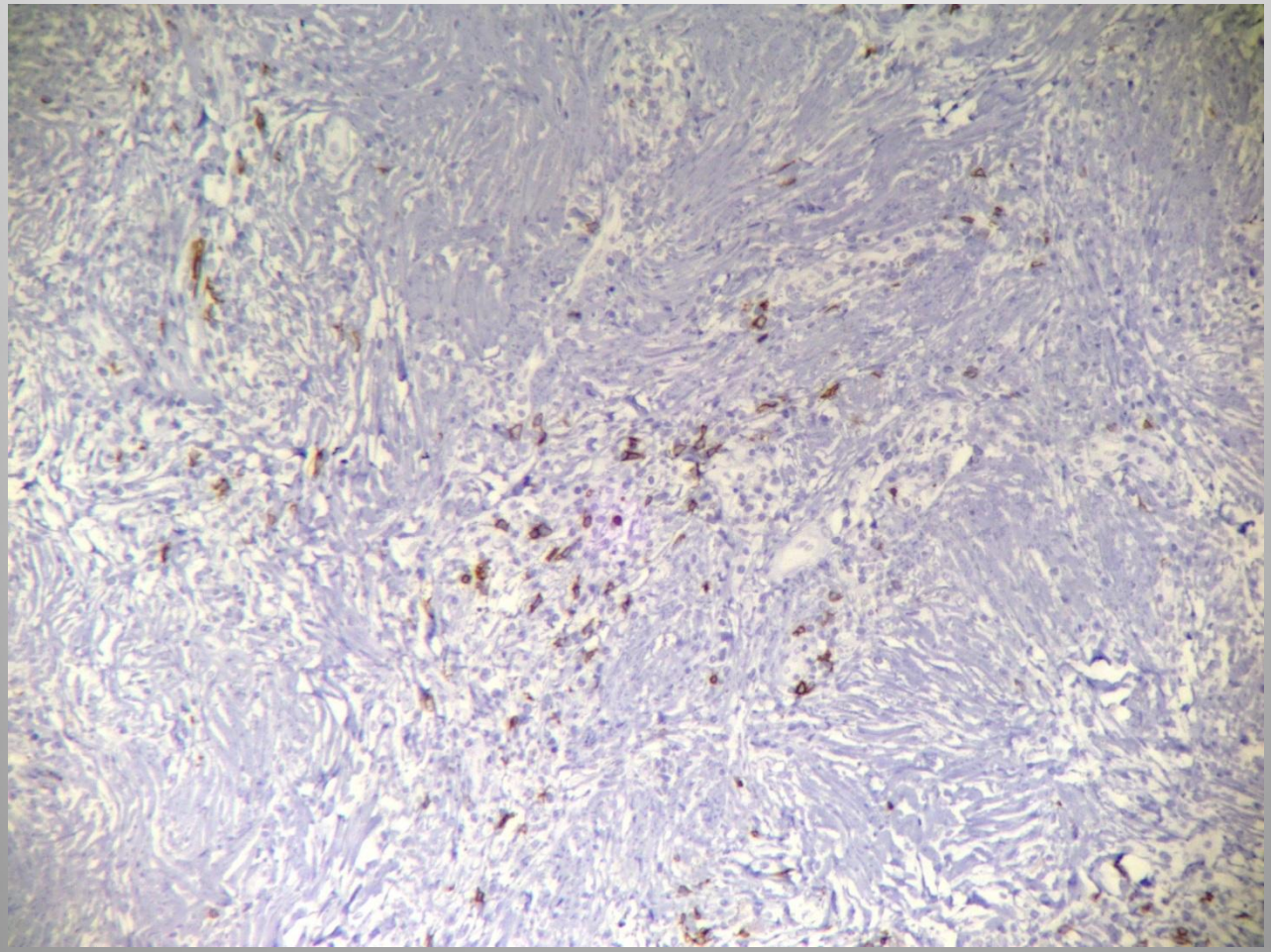

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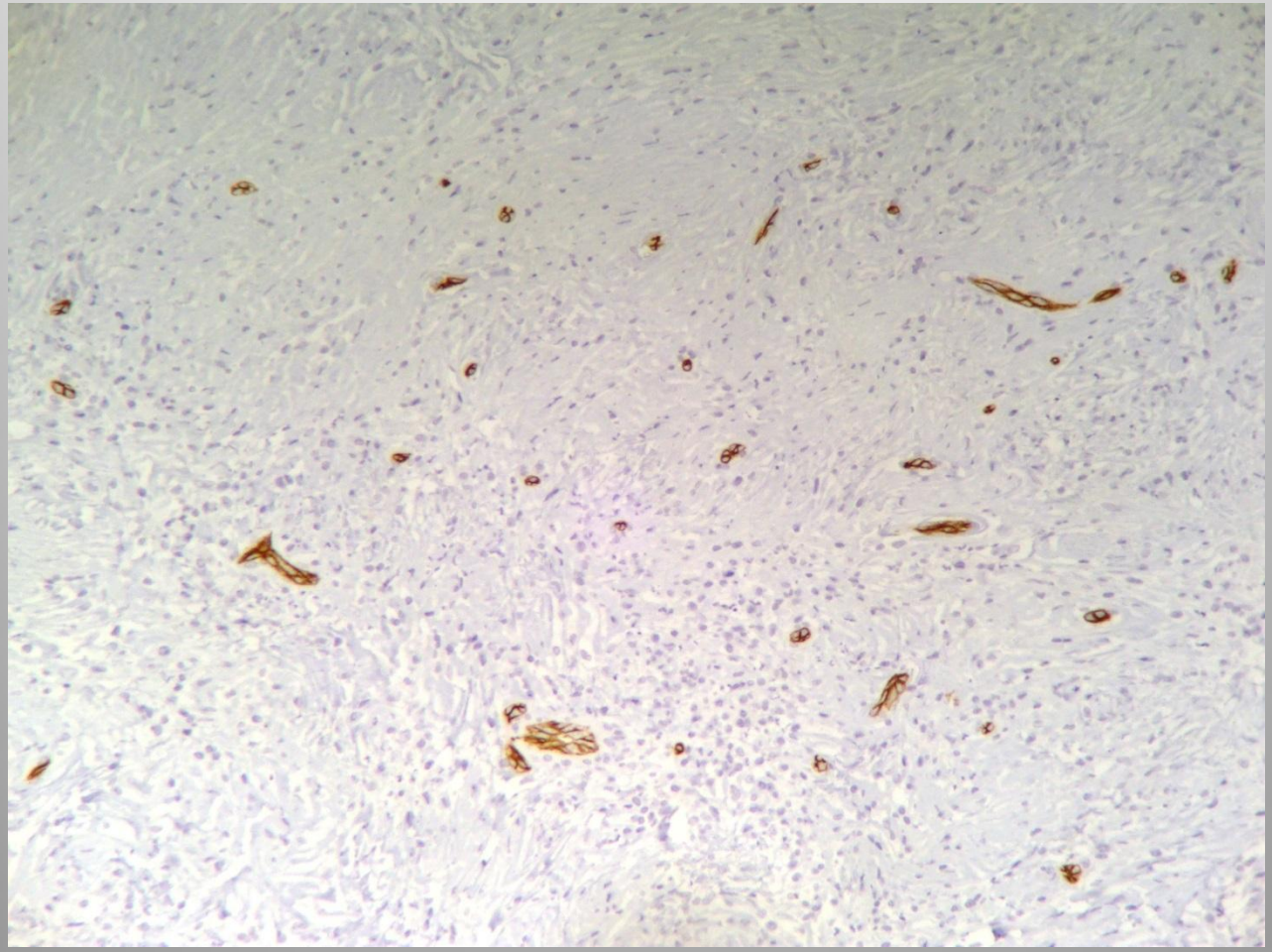
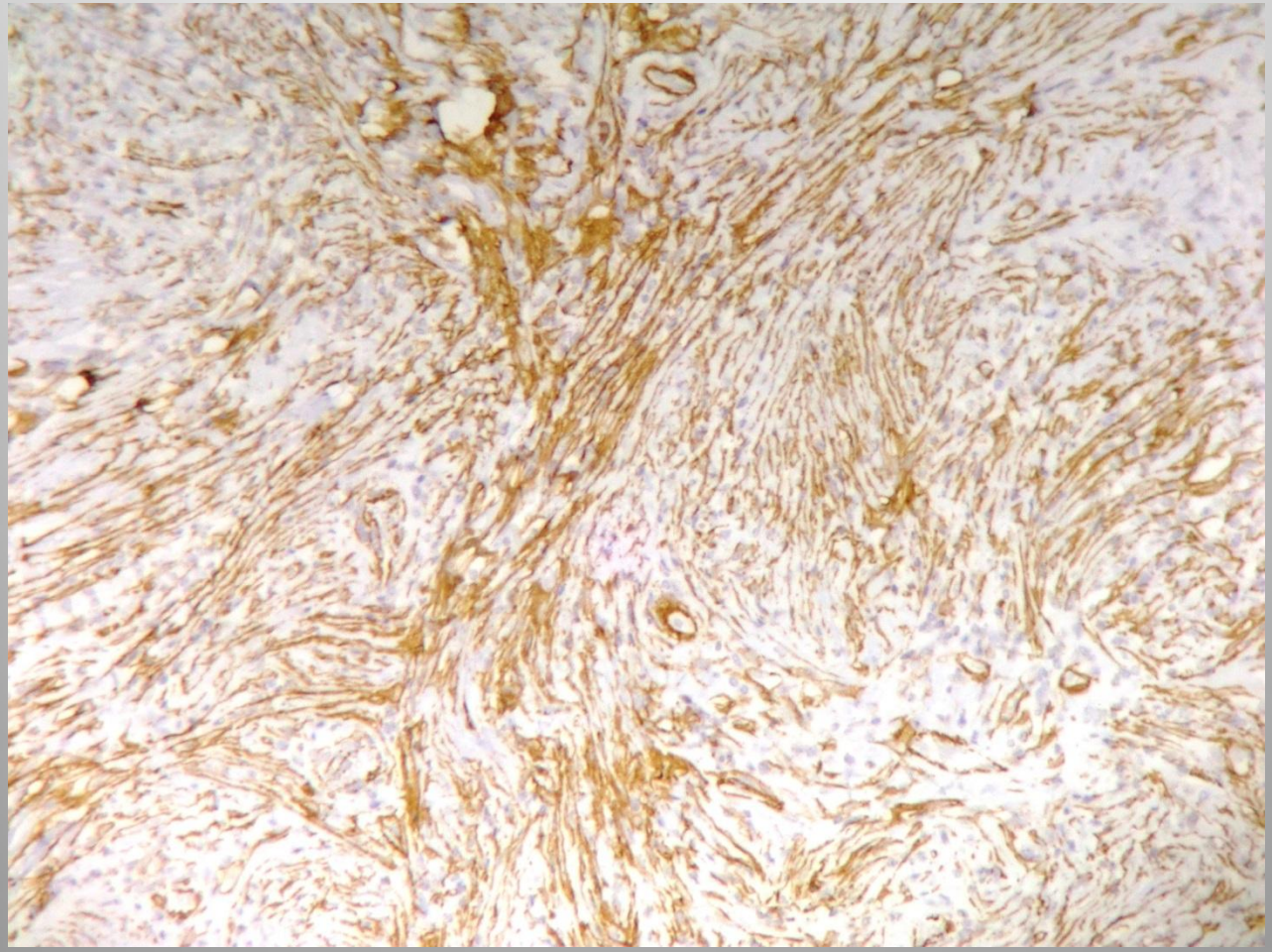
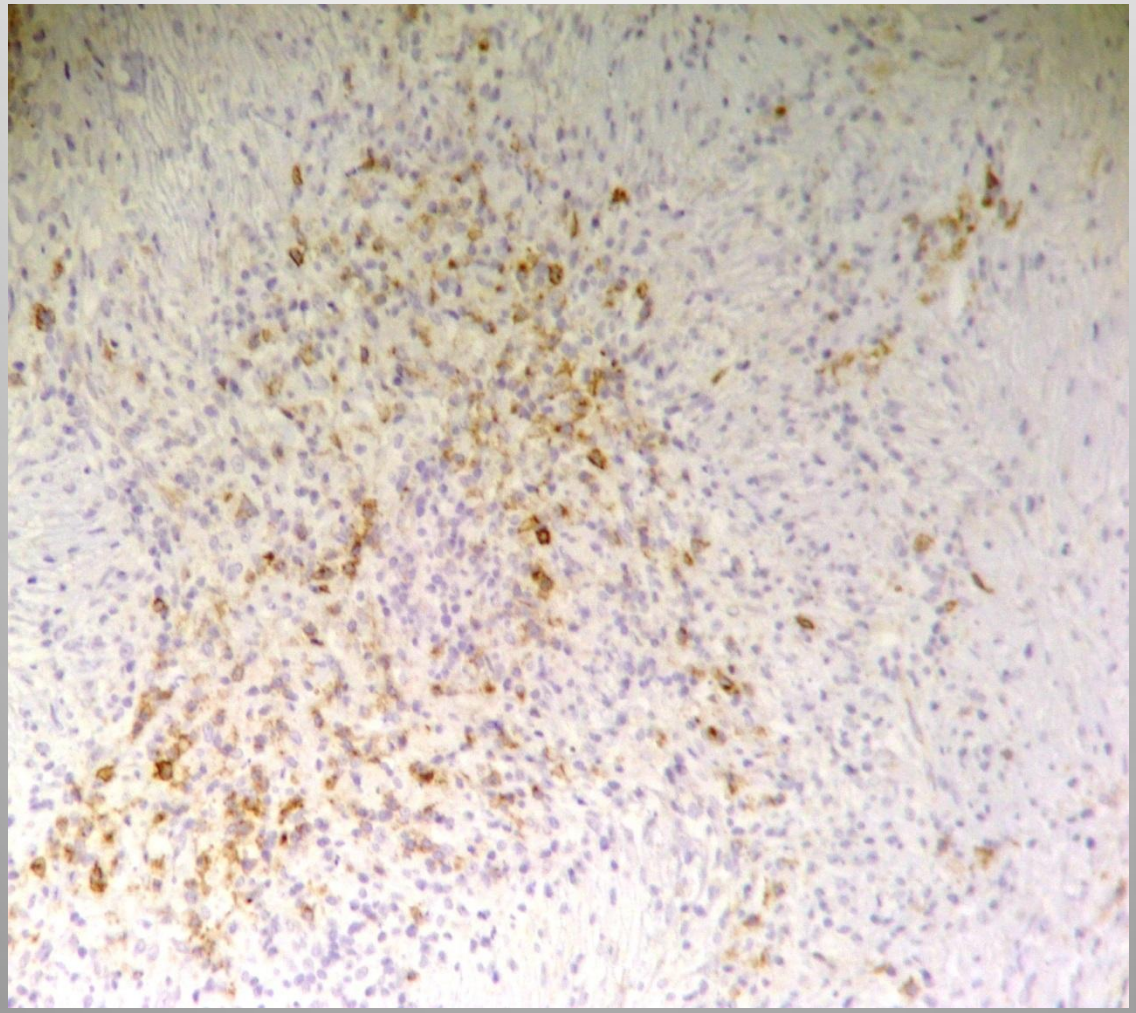


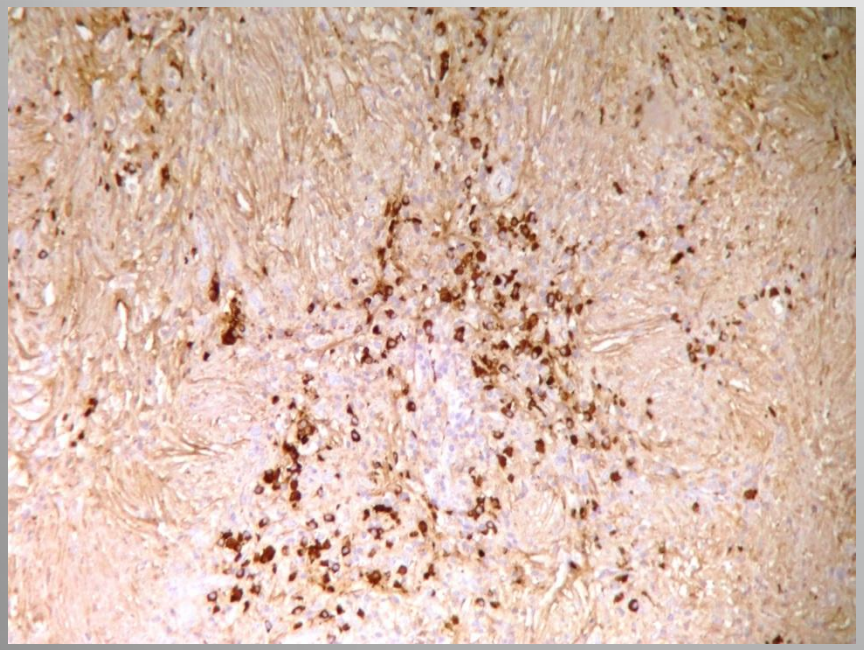
# AML



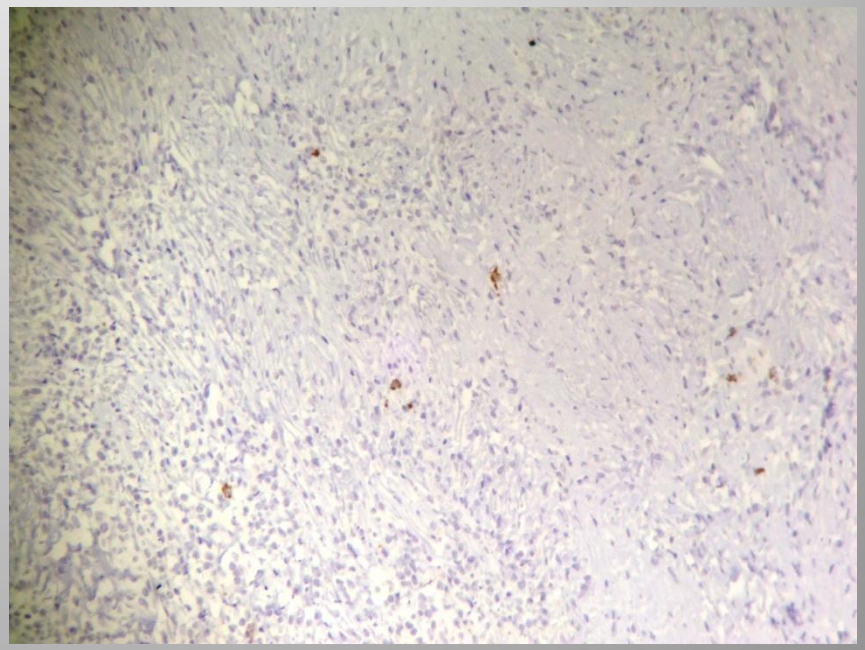
# CD 138



IgG



IgG4



# Anticorpos pesquisados

. CD30 - negativo

. Desmina - negativo

. EBV - negativo

. EMA - negativo

. S100 - negativo

. AE1/AE3 – negativo

. CD15 – positivo nos granulócitos

. Ki-67 – baixo índice proliferativo

Com base nestes aspectos, qual o diagnóstico?

# Diagnóstico

Fibrose angiocêntrica eosinofílica

(que pode estar no espectro da doença esclerosante associada a IgG4)

# History of IgG4-related disease

- 1892 Mikulicz's disease
- 1961 Hyper-gammaglobulinemia in CP
- 1967 Familial multifocal fibrosclerosis
- 1972 Kuttner tumor
- 1991 Lymphoplasmacytic sclerosing pancreatitis
- 1995 Autoimmune pancreatitis
- 2001 High IgG4 levels in sclerosing pancreatitis (N Eng J Med)
- 2002 Japan Pancreas Society-Clinical diagnostic criteria for AIP
- 2003 Doença sistêmica relacionada ao *IgG4*
- 2006 Clinical diagnostic criteria for AIP
- 2006 Mayo criteria
- 2006 IgG4-related sclerosing disease
- 2006 IgG4-related plasmacytic disease
- 2008 IgG4-multiorgan lymphoproliferative syndrome (MOLPS)
- 2011 International Consensus
- Diagnostic Criteria (ICDC) for AIP
- 2012 Concept and comprehensive Diagnostic Criteria for IgG4-related disease
- 2012 International Pathological Consensus for IgG4-RD
- 2012 Nomenclatures of individual organ manifestation of IgG4- RD

# Mayo Clinic Diagnostic Criteria for Autoimmune Pancreatitis (IgG4-related Sclerosing Pancreatitis): The HISORt Criteria

- **Criterion H-Histology**
- (at least one of the following)
- 1. Periductal lymphoplasmacytic infiltrate, obliterative phlebitis, storiform fibrosis
- 2. Lymphoplasmacytic infiltrate, storiform fibrosis, abundant IgG4+ cells (≥10 HPF)

- **Criterion I-Imaging of pancreas**
- 1. Typical-diffusely enlarged gland with delayed (rim) enhancement; diffusely irregular, attenuated main pancreatic duct
- 2. Others-Focal pancreatic mass/enlargement; focal pancreatic duct stricture; pancreatic atrophy; pancreatic calcification; pancreatitis

- **Criterion S-Serology**
- Elevated serum IgG4 (normal: 8-140 mg/dL)
-
- **Criterion O-Other organ involvement** (can be confirmed by biopsy or resolution/ improvement with steroid therapy)
- Hilar/intrahepatic biliary strictures; persistent distal biliary stricture; parotid/lacrimal gland involvement; mediastinal lymphadenopathy;
- retroperitoneal fibrosis

- **Criterion R-Response to steroid therapy**
- Resolution or marked improvement of pancreatic/extrapancreatic manifestation with steroid therapy

- Diagnostic of autoimmune pancreatitis when any of the following is fulfilled
- **1. Criterion H**
- 2. Criterion I+S
- 3. Strong clinical suspicion of autoimmune pancreatitis
- (idiopathic pancreatic disease+Criterion S and/or O)+Criterion R

# Doença esclerosante IgG4 relacionada

IgG4: >10 células / CGA

Relação IgG4/IgG: > 40%

Esclerose do parênquima

Presença de flebite obliterativa

Boa resposta ao corticoide

Recidivante (20-60% dos casos)

OBS: Após Vias pancreatobiliares, cabeça e pescoço é sítio mais comum de Dç IgG4 relacionada

# Fibrose angiocêntrica eosinofílica

. Doença rara e benigna, descrita em 1983 por Holmes e Pajes

. Pode acometer cav. nasal, órbita e laringe

. Etiologia desconhecida

. Há artigos que relatam pacientes com história prévia de trauma nasal e alergia

# Fibrose angiocêntrica eosinofílica

. Estudos recentes mostram relação com Doença IgG4-relacionada (ainda não estabelecido)

. Artigos com casuísticas pequenas

. Não há artigos relatando Fibrose angiocêntrica eosinofílica com outras doenças esclerosantes IgG4

# Fibrose angiocêntrica eosinofílica

Histologia:

. Fibrose angiocêntrica (arteriolar)

. Fibrose estoriforme

. Infiltrado inflamartório constituído por eosinófilos, linfócitos, plasmócitos e alguns neutrófilos

Head and Neck Pathol (2008) 2:309–315
DOI 10.1007/s12105-008-0077-y

CASE REPORT

# Sinonasal Eosinophilic Angiocentric Fibrosis: A Report of Four Cases and Review of Literature

Reena Jain · Jennifer V. Robblee · Emerald O'Sullivan-Mejia · Jane Lea · Andrew Heller · William C. Faquin · Celeste N. Powers

| C | Age/sex | Clinical symptoms | Site | Laboratory tests | Radiological findings | Treatment | Follow-up |
|---|---|---|---|---|---|---|---|
| 1 | 31/F | Right epiphora, left orbital mass | Sinuses (left maxillary & ethmoid), orbit | ANCA, p29, MPO | Not done | Multiple biopsies, steroids, single resection | Rec. × 3,4 years; SOB |
| 2 | 57/M | Nasal congestion, epiphora, proptosis, decreased sense of smell | Nose (bilateral lateral wall), multiple sinuses, lacrimal gland | ANCA, p29, MPO, ANA, anti-DNA, peripheral eosinophilia | Mass involving lacrimal gland and multiple sinus cavities | Steroids, single resection | Rec. × 2 years; SOB |
| 3 | 27/F | Nasal obstruction | Nose (bilateral lateral wall) | ANA, ANCA | Not done | Biopsy | Lost to follow-up |
| 4 | 51/F | Nasal mass, obstruction & epiphora | Nose (right lateral wall) | Not done | Mass involving right nasal cavity, medial canthus and nasolacrimal duct | Single resection (debulking) | Persistent mass; small increase in size |

Rec., recurrence; SOB, shortness of breath

Não pesquisado Imunoglobulinas neste artigo de 2008
Testes laboratoriais negativos

# Eosinophilic Angiocentric Fibrosis Is a Form of IgG4-related Systemic Disease

*Vikram Deshpande, MD,* Arezou Khosroshahi, MD,† Gunnlaugur P. Nielsen, MD,* Daniel L. Hamilos, MD,† and John H. Stone, MD, MPH†*

*Am J Surg Pathol* • Volume 35, Number 5, May 2011

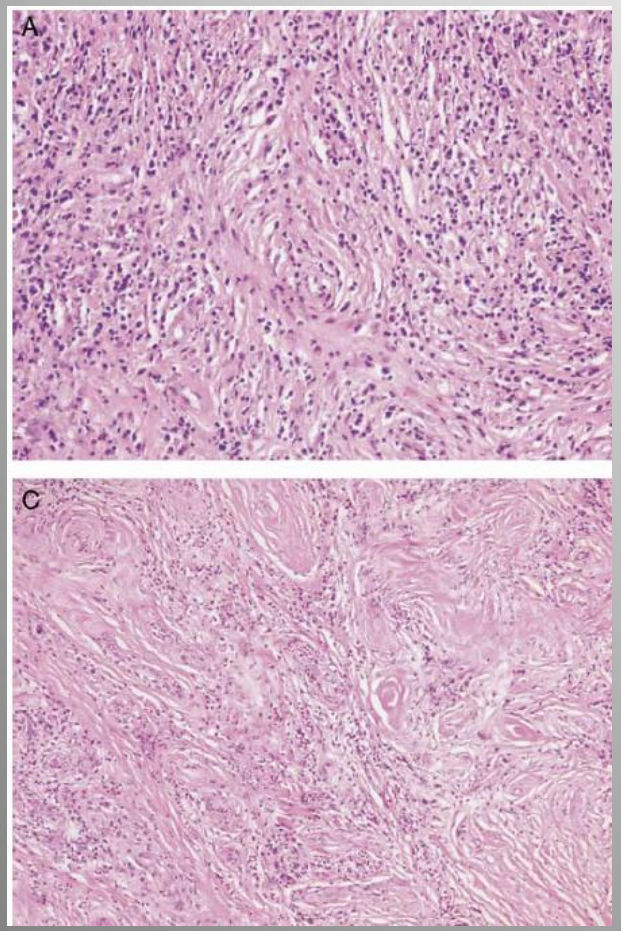



TABLE 1. Clinical and Immunohistochemical Data on 5 Cases of EAF

| No. | Age/ Sex | Site(s) | Duration of Disease | Surgical Procedures | Allergy History | ANCA | Tissue IgG4/ HPF | Tissue IgG4/ IgG Ratio |
|---|---|---|---|---|---|---|---|---|
| 1 | 63/M | Nasal and lacrimal glands, lung | 6 y | 2 | None | Negative | 118 | 0.8 |
| 2 | 81/F | Left nasal | 3 y | 2 | Allergic rhinitis | NA | 43 | 0.87 |
| 3 | 31/F | Orbit, maxillary sinus, ethmoid, nasal | 20 y | 7 | None | NA | 0 | 0 |
| 4 | 54/F | Right lacrimal gland | Unknown | 1 | None | NA | 115 | 0.97 |
| 5 | 55/M | Orbit | 6 mo | 1 | None | Negative | 59 | 0.68 |

ANCA indicates antineutrophil cytoplasmic antibodies; F, female; M, male; NA, not applicable.

. Não detectada venulite obliterativa em nenhum caso

. Caso 3 poderia ser uma fase tardia da dç com pouca inflamação e consequente falta de expressão de IgG4?

*The Journal of Laryngology & Otology (2014), **128**, 1071–1077.*

doi:10.1017/S0022215114002552

MAIN ARTICLE

# Eosinophilic angiocentric fibrosis of the nose and sinuses

TABLE I
SUMMARY OF NINE CASES OF SINONASAL EOSINOPHILIC ANGIOCENTRIC FIBROSIS

| Patient no | Age | Sex | Presentation | Management | Follow up |
|---|---|---|---|---|---|
| 1 | 37 | F | Frontonasal swelling; frontonasal/intranasal mass (first excised 18 years earlier) | Surgical excision: lateral rhinotomy ×2; oral steroids & azathioprine | NSR, 18 years |
| 2 | 68 | M | Frontonasal swelling & nasal obstruction 5 years; frontonasal/septal mass | Surgical excision: extended lateral rhinotomy | NSR, 15 years |
| 3 | 52 | F | Nasal mass extending into midface/orbit, 25 years | Surgical excision: lateral rhinotomy ×2; dapsone, hydroxychloroquine, azathioprine, oral steroids | Residual disease in orbit |
| 4 | 58 | F | Nasal swelling, 1 year | Surgical excision: lateral rhinotomy | NSR, 8 years |
| 5 | 47 | M | Nasal obstruction, 1 year; septal thickening | Surgical excision: external rhinoplasty | NSR, 8 years |
| 6 | 46 | F | Nasal obstruction & swelling, 2 years: septal/lateral wall thickening | Surgical excision: external rhinoplasty | NSR, 3 years |
| 7 | 65 | F | Nasal obstruction & swelling, 2 years; septal/alar cartilage mass with subcutaneous extension | Surgical excision: subtotal rhinectomy | Developed GPA after 17 months |
| 8 | 43 | M | Nasal obstruction & shape change, 2 years | Surgical excision: external rhinoplasty | NSR, 9 months |
| 9 | 63 | M | Nasal obstruction & pain, 7 years; shape change post-septoplasty, 6 years; septal thickening | Surgical excision: external rhinoplasty | NSR, 5 months |

No = number; NSR = no sign of recurrence; GPA = granulomatosis with polyangiitis (Wegener's granulomatosis)

. Caso 7: Gran. Wegener após 17 meses com ANCA negativo no primeiro teste
. Caso 9: ANCA e IgG4 negativos
. Casos 7,8 e 9: IgG4 sérico negativo
. Não realizado estudo IH
. Sem relação com trauma nasal prévio

Head and Neck Pathol (2008) 2:309–315
DOI 10.1007/s12105-008-0077-y

CASE REPORT

# Sinonasal Eosinophilic Angiocentric Fibrosis: A Report of Four Cases and Review of Literature

**Reena Jain · Jennifer V. Robblee · Emerald O'Sullivan-Mejia · Jane Lea · Andrew Heller · William C. Faquin · Celeste N. Powers**

Table 3 Differential diagnosis of eosinophilic angiocentric fibrosis in sinonasal and upper respiratory tract

| Disease | Sites | Clinical presentation | Laboratory tests | Histopathological features |
|---|---|---|---|---|
| Eosinophilic angiocenteric fibrosis | Upper respiratory tract, lacrimal sac, orbit | Nasal obstruction, epiphora, proptosis | None | Dense fibrosis with perivascular 'onion-skin' whorling pattern, eosinophil-rich inflammatory infiltrate |
| Wegener's granulomatosis | Upper respiratory tract, lungs, kidneys | Nasal pain, stuffiness, rhinitis, hearing loss, saddle-nose deformity (later stage) | Cytoplasmic (antiproteinase 3) c-ANCA positive (85%) | Geographic zones of bionecrosis, foreign-body giant cells, granuloma (rare) |
| Churg-Strauss syndrome | Upper and lower respiratory tract, skin, kidney, gastrointestinal tract, heart, nerve | Asthma, sinusitis | Blood eosinophilia, perinuclear (anti-myeloperoxidae) p-ANCA positive | Fibrinoid necrosis, extravascular granulomas with eosinophilia |
| Kimura's disease | Skin (head and neck) | Subcutaneous nodules, lymphadenopathy, salivary gland enlargement | Blood eosinophilia, raised ESR and serum IgE levels | Dense lymphoid aggregates with prominent germinal centers, fibrous tissue |
| Granuloma faciale | Skin (face) | Plaques and nodules | None | Polymorphous infiltrate (N, E) in the dermis, fibrosis, Grenz zone |

ANCA, antineutrophil cytoplasmic antibodies; ESR, erythrocyte sedimentation rate; N, neutrophils; E, eosinophils

# Tratamento

- Cirúrgico
- Alta taxa de recidiva
- Baixa resposta ao corticoide
- Acompanhamento a longo prazo
- Reconsiderar o diagnóstico no caso de mudanças clínicas

# Questionamentos

- Alguns casos da literatura são IgG4 negativos
- Flebite obstrutiva?
- Outras doenças IgG4 relacionadas a FEA concomitantes?
- Pouca resposta ao corticoide
- Conclusão: Estudos futuros serão necessários para relacionar a FAE como Dç IgG4 relacionada

# OBRIGADO

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