高雄榮民總醫院
Kaohsiung Veterans General Hospital

Clinicopathological Conference

A 45y/o man with progressive general weakness (four limbs) with difficult walking for 3 weeks

202011

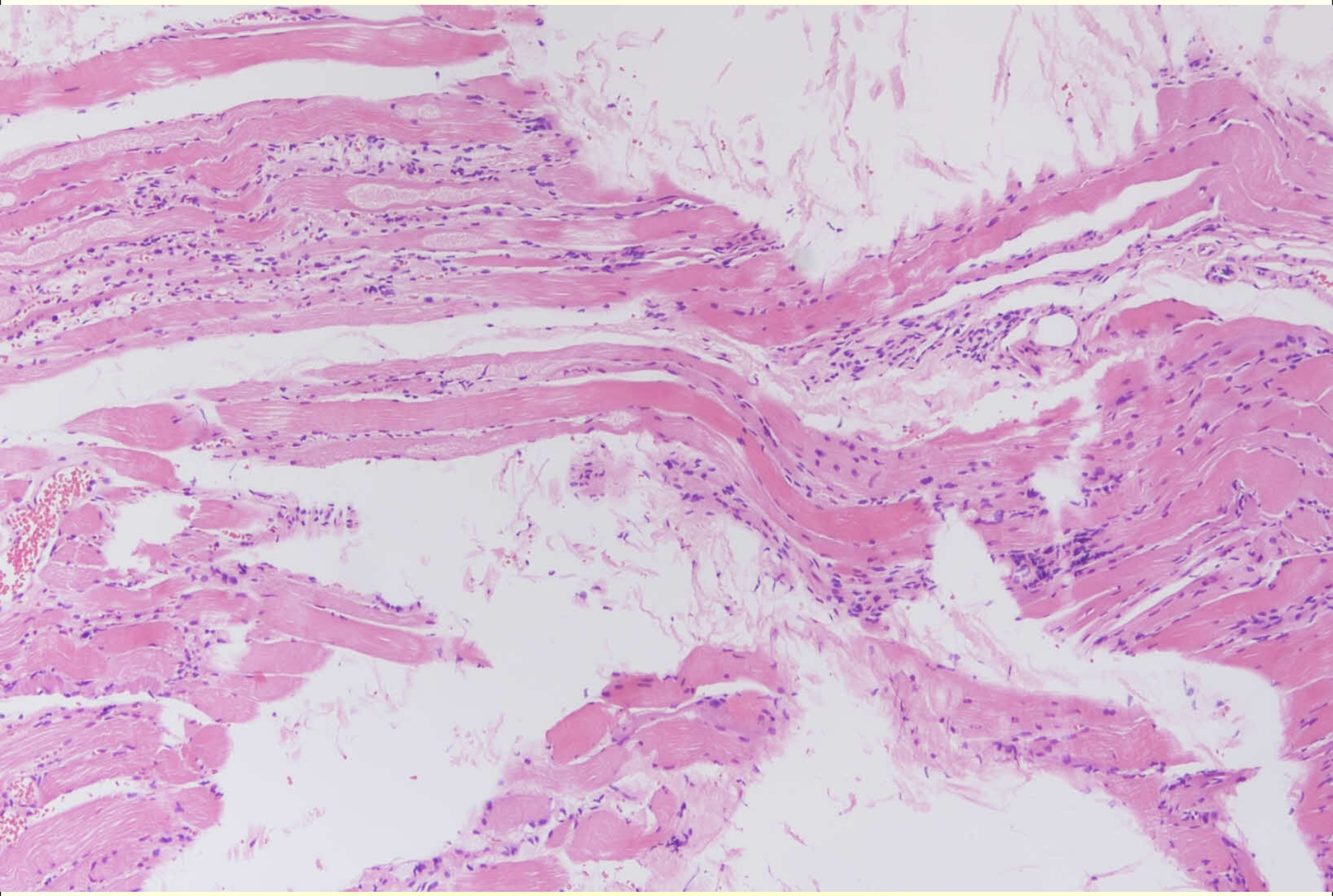
病理檢驗部

李懷寶

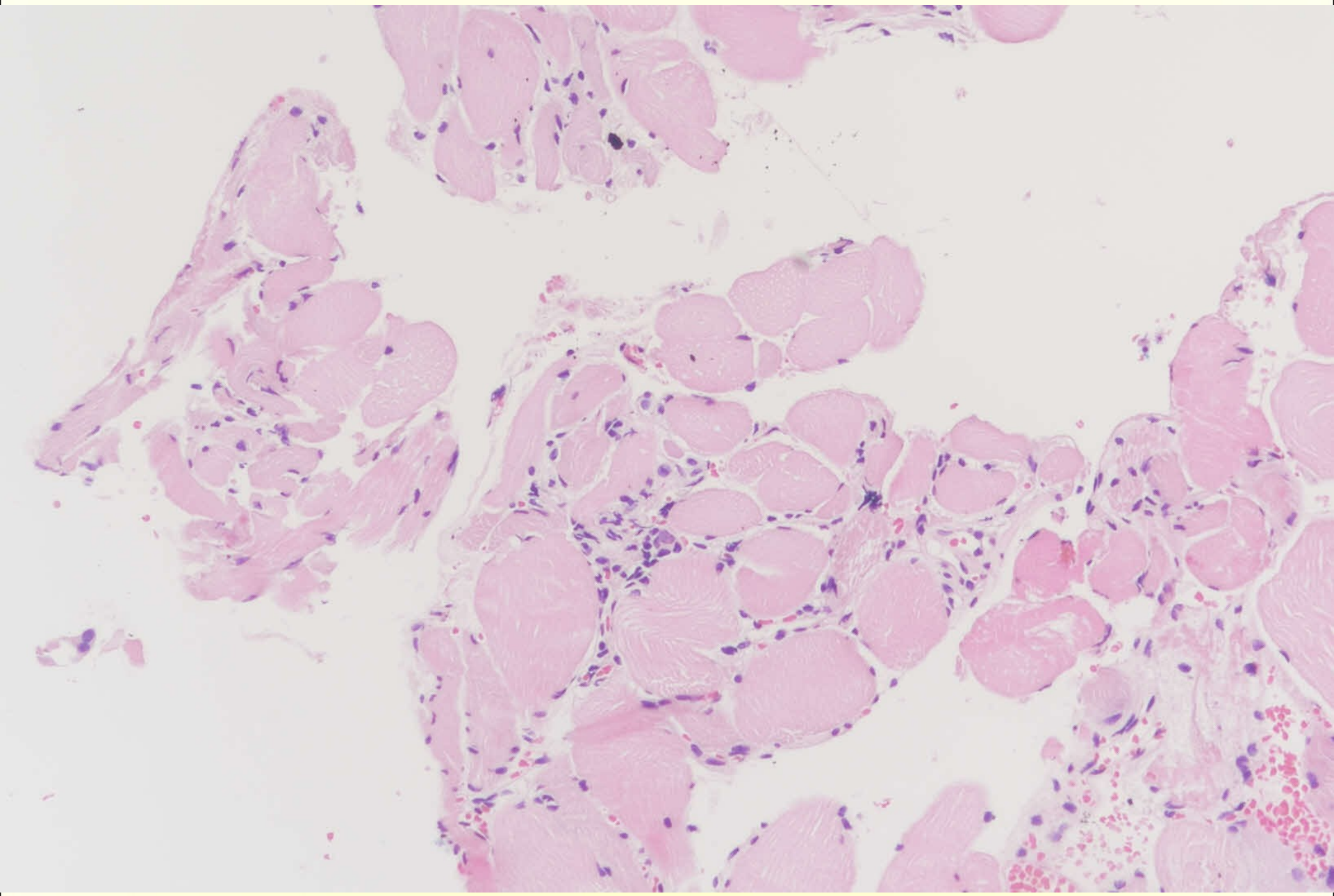
Muscle, biopsy (09-16125)

Light Microscopy

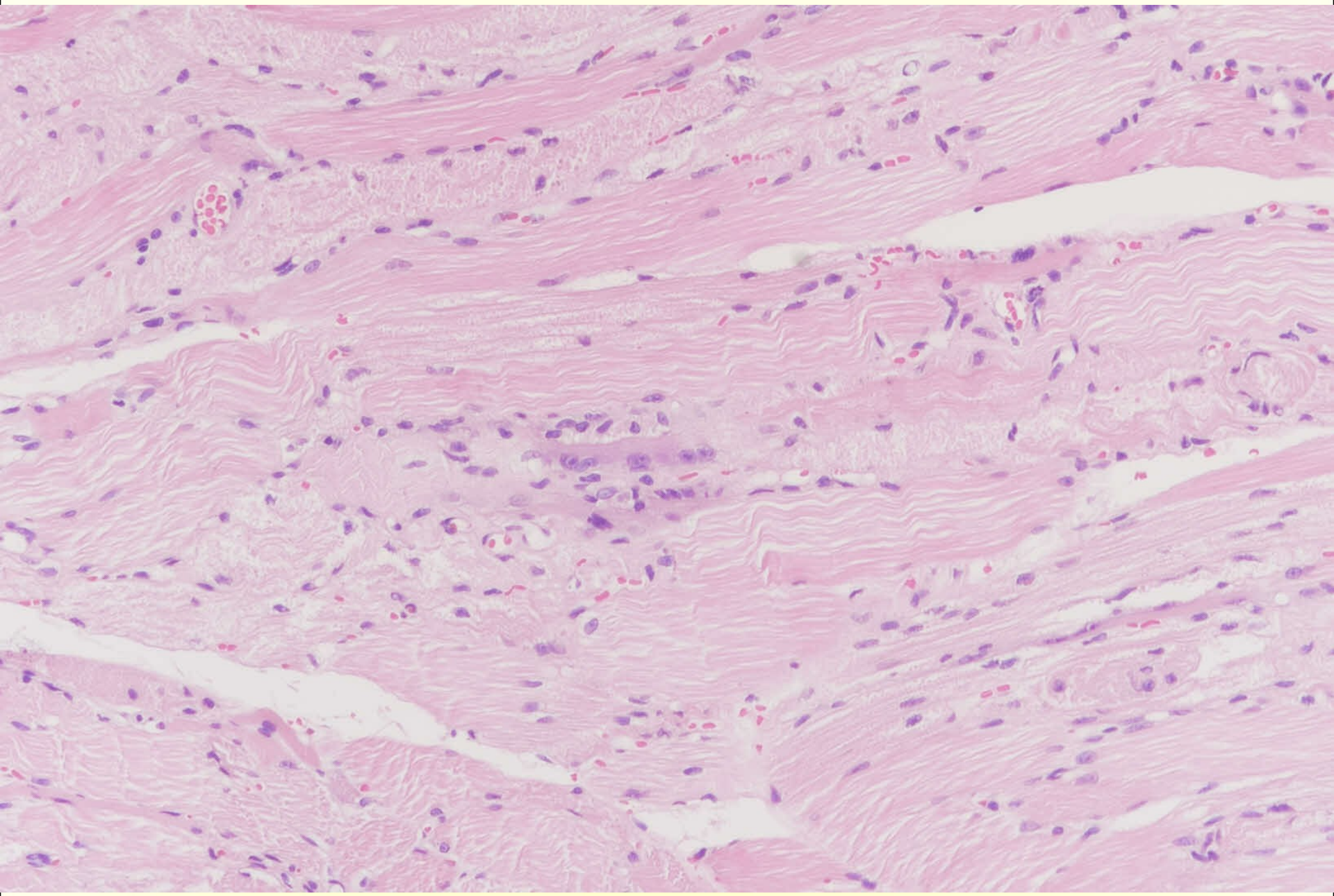
Intra-fascicular (endomysial) inflammation



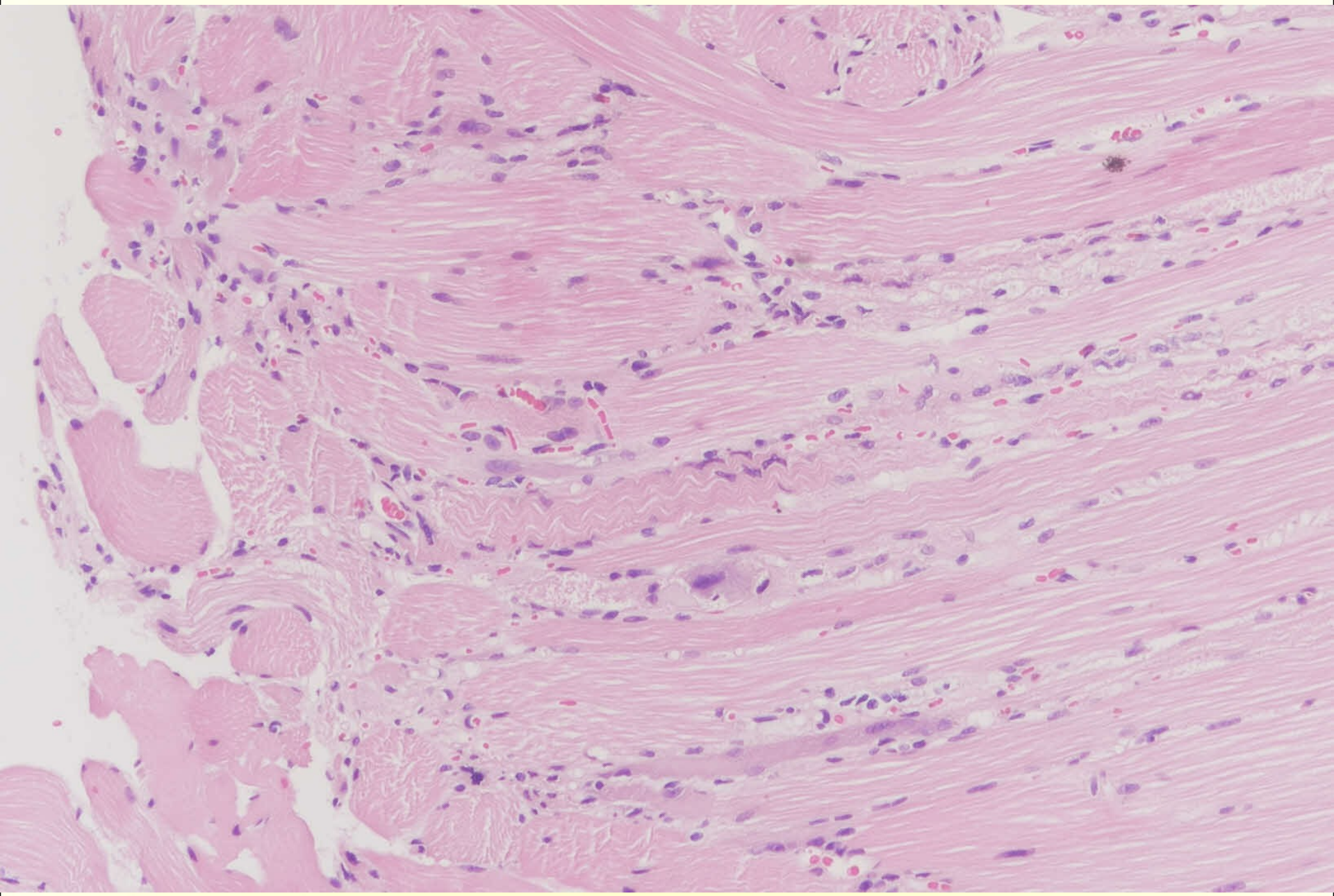
Intra-fascicular (endomysial) mononuclear inflammatory infiltrate



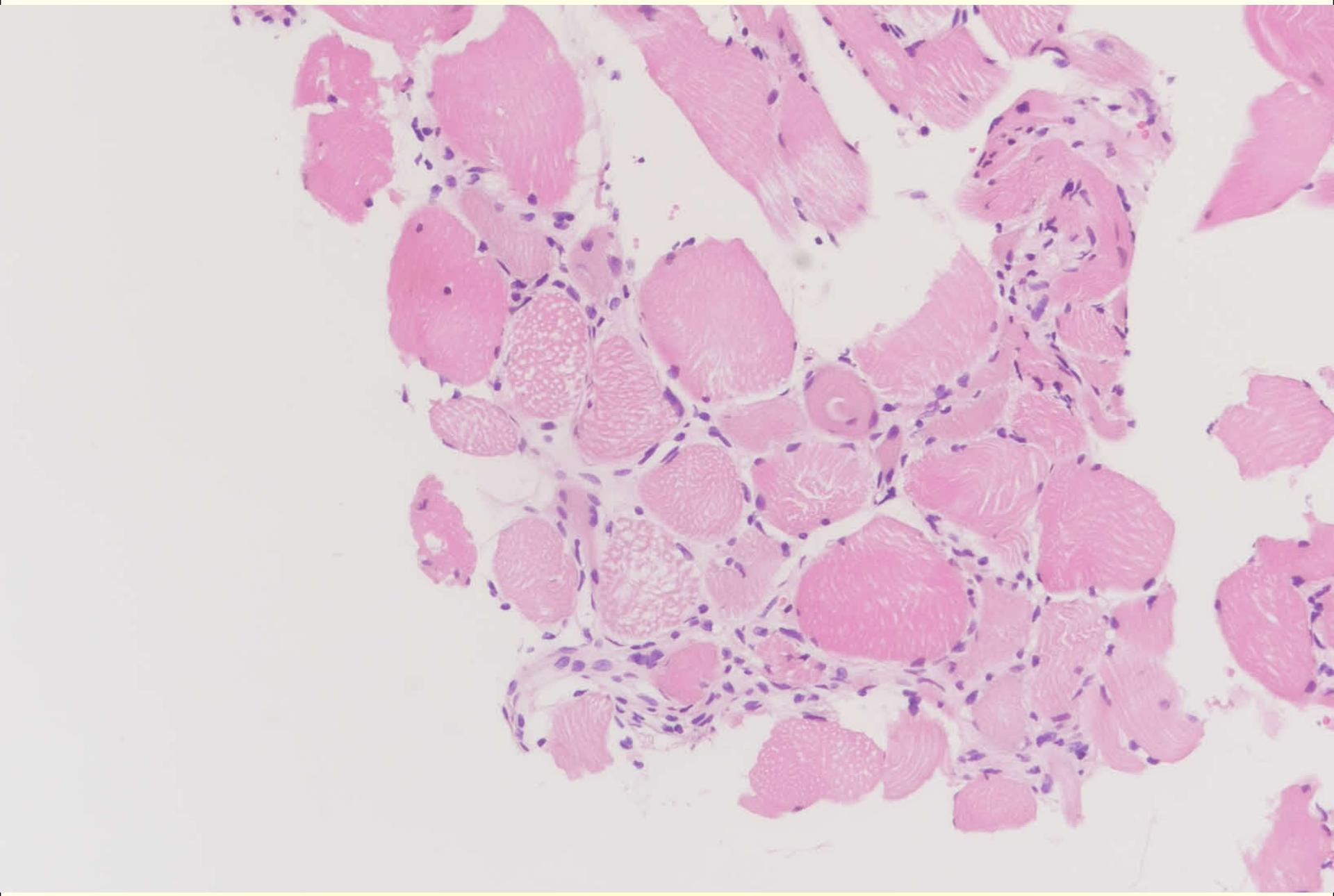
Atrophic muscle fibers



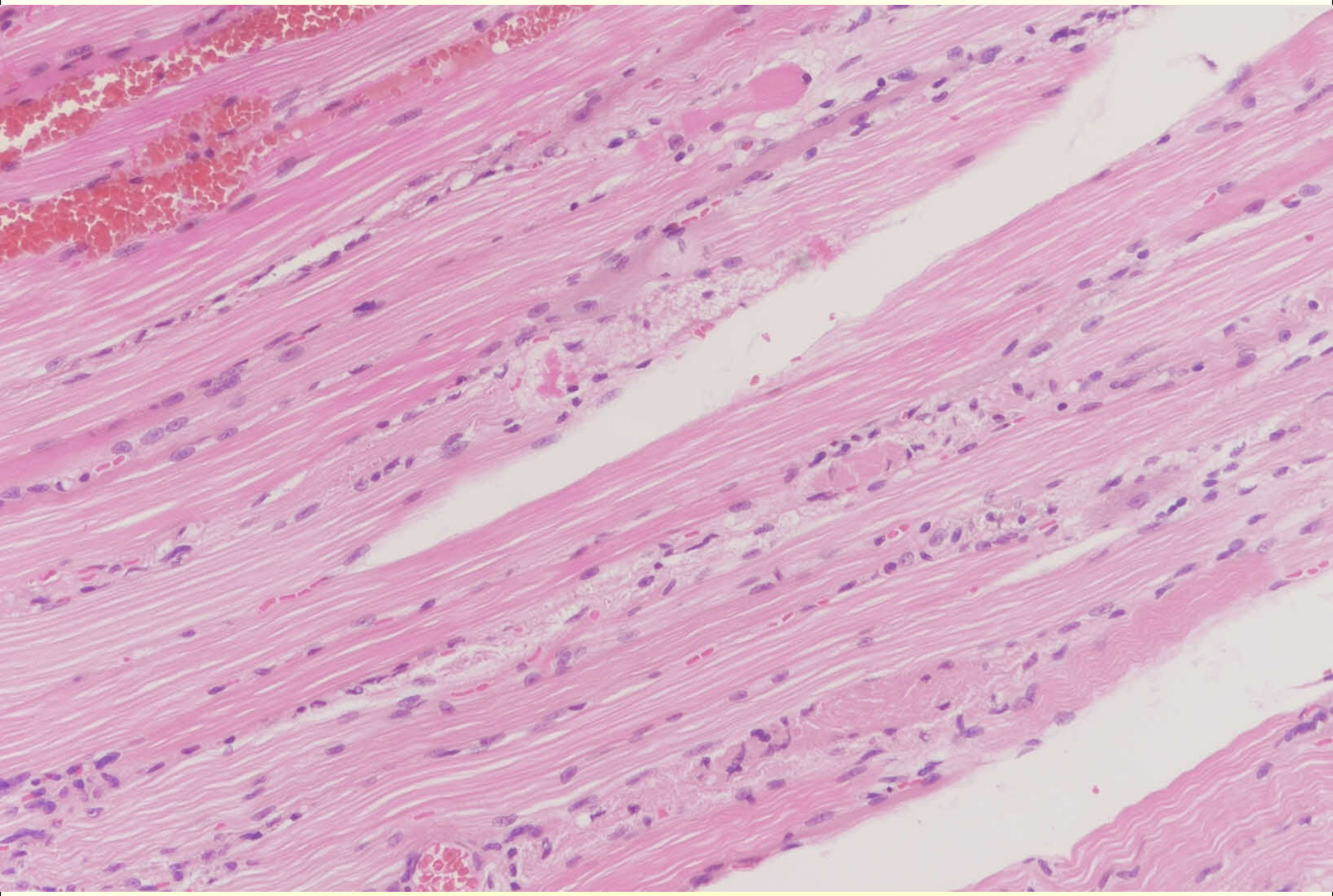
Scattered individual atrophic muscle fibers



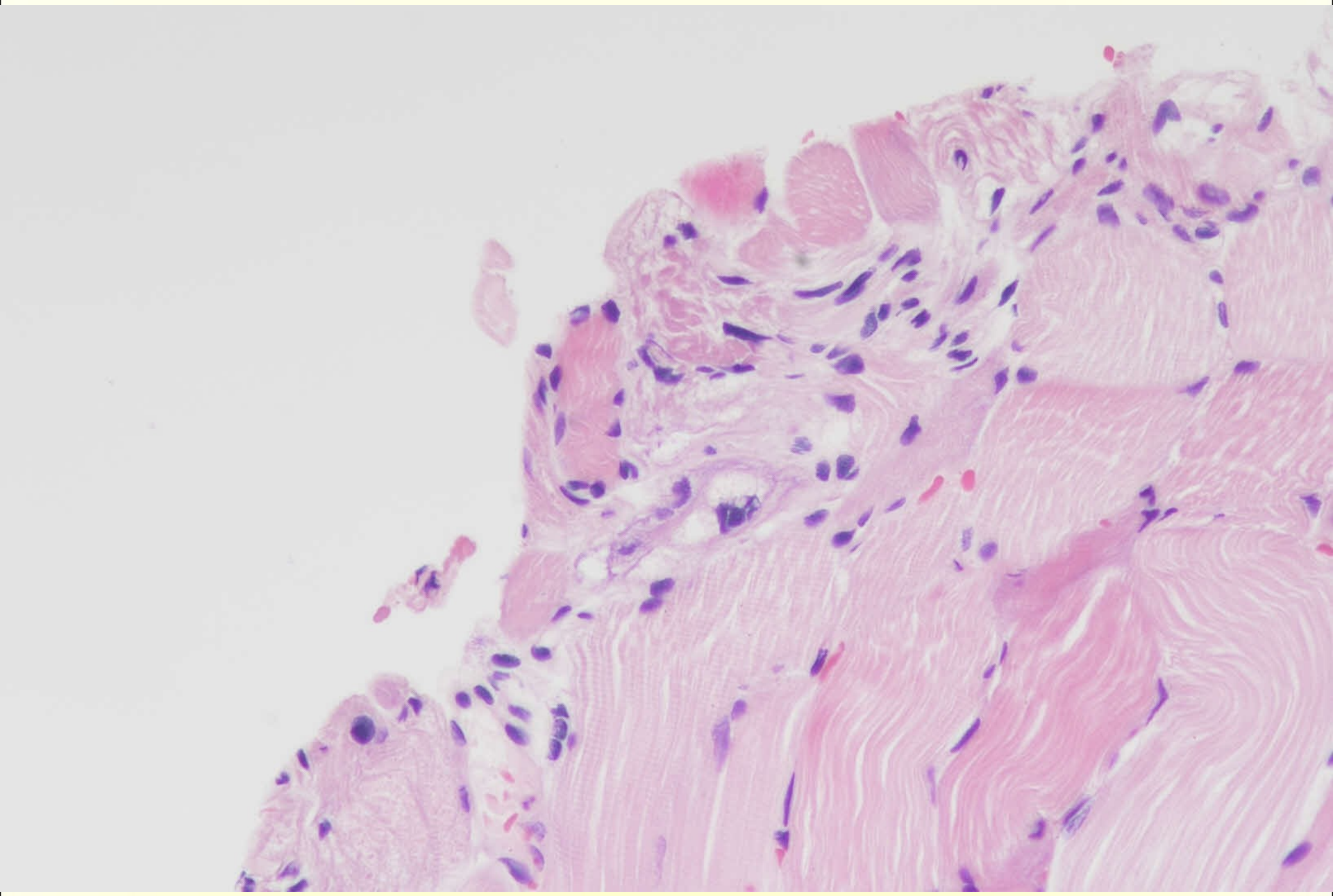
Degenerative muscle fibers, loss of myofibrils



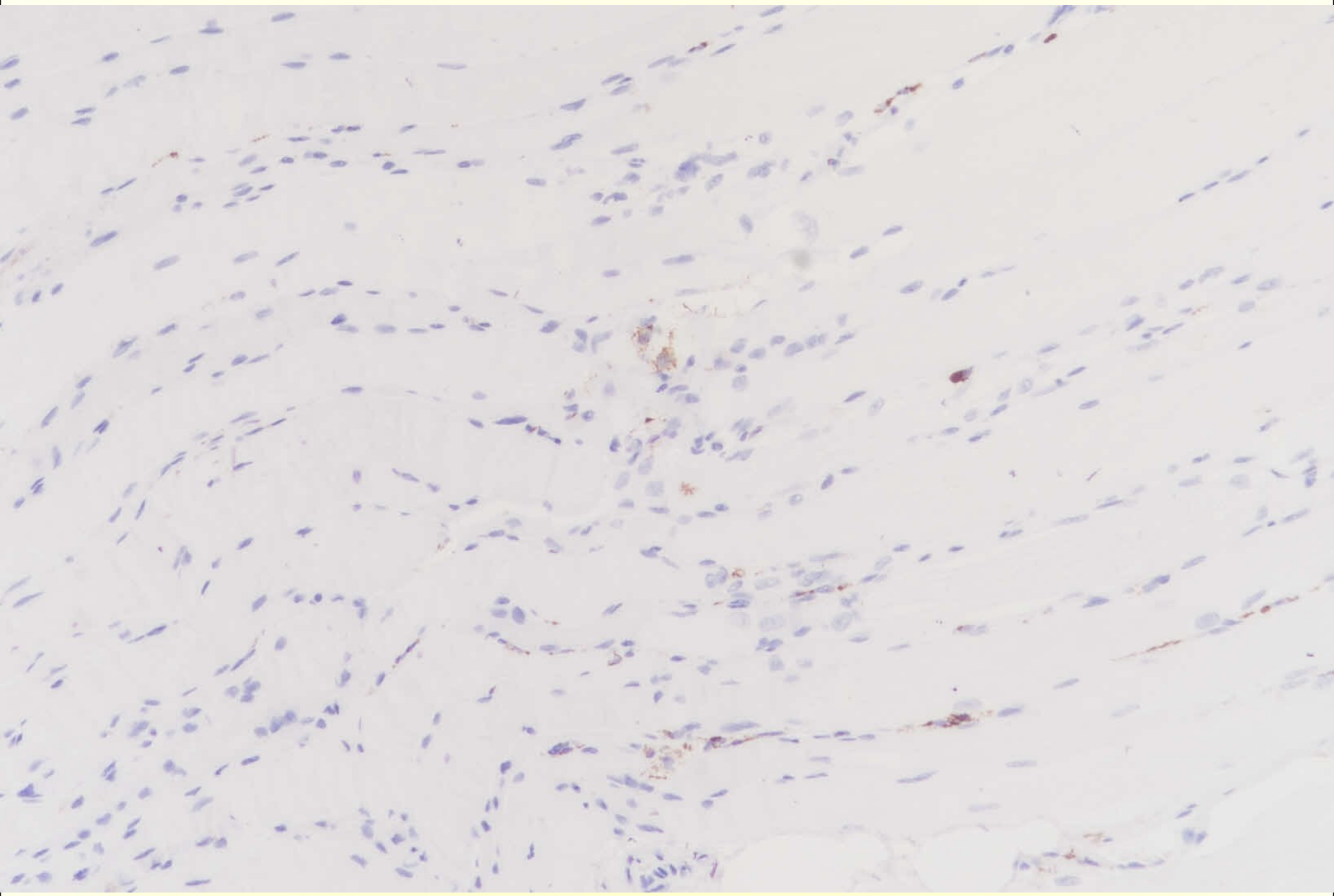
Vacuolar degeneration and segmental necrosis



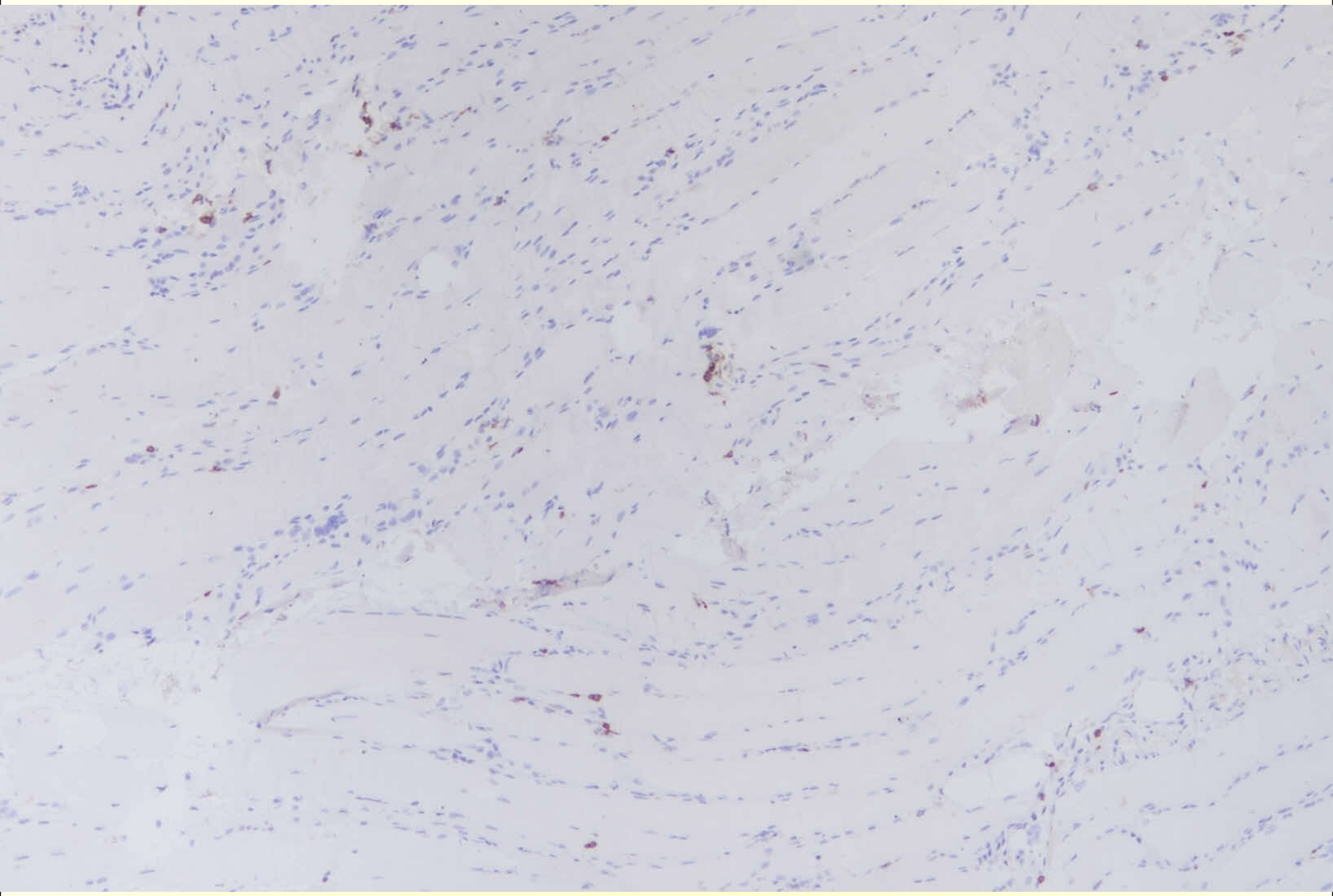
Vacuolar degeneration



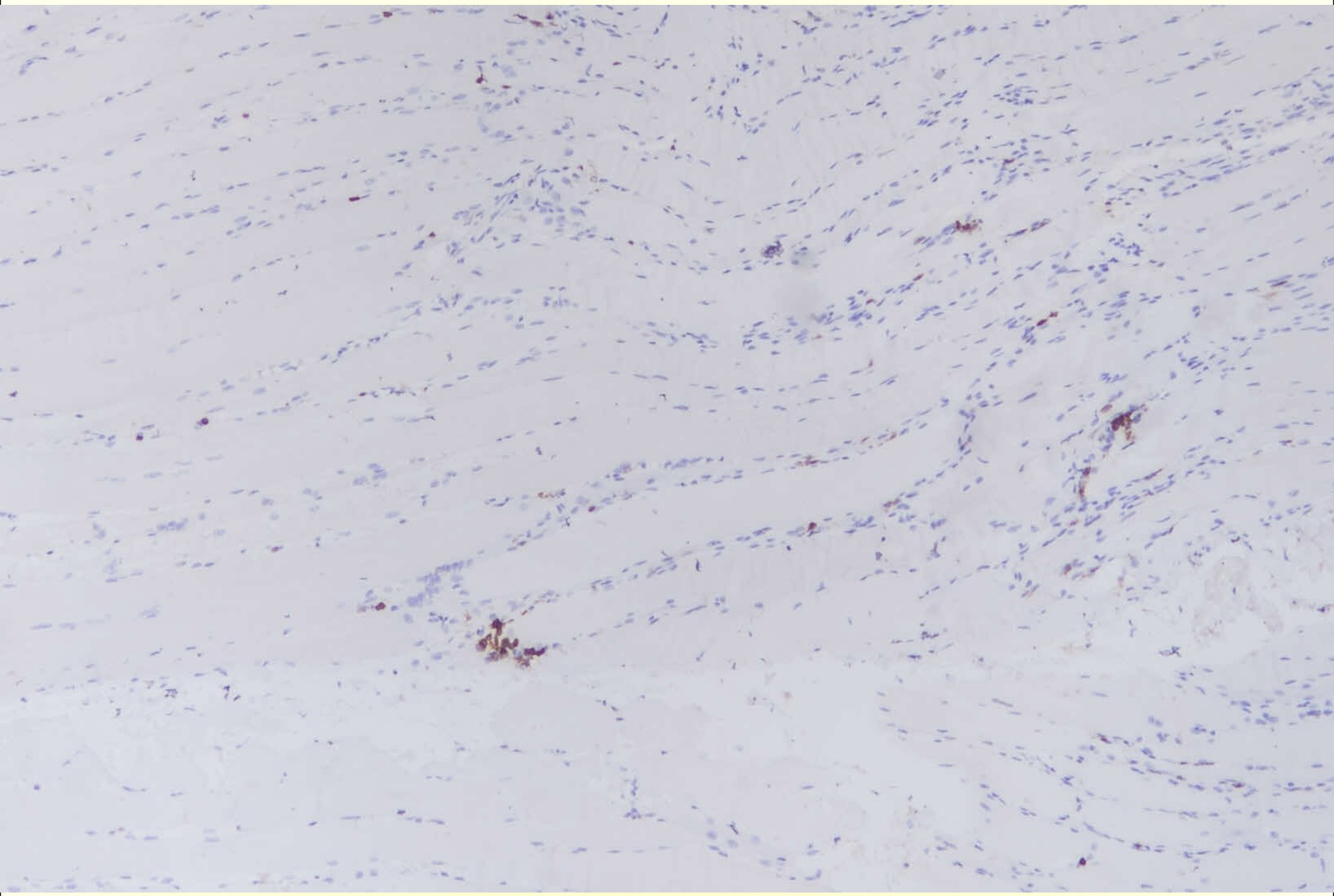
Phagocytosis of the degenerative/necrotic cells by CD68(+) macrophages



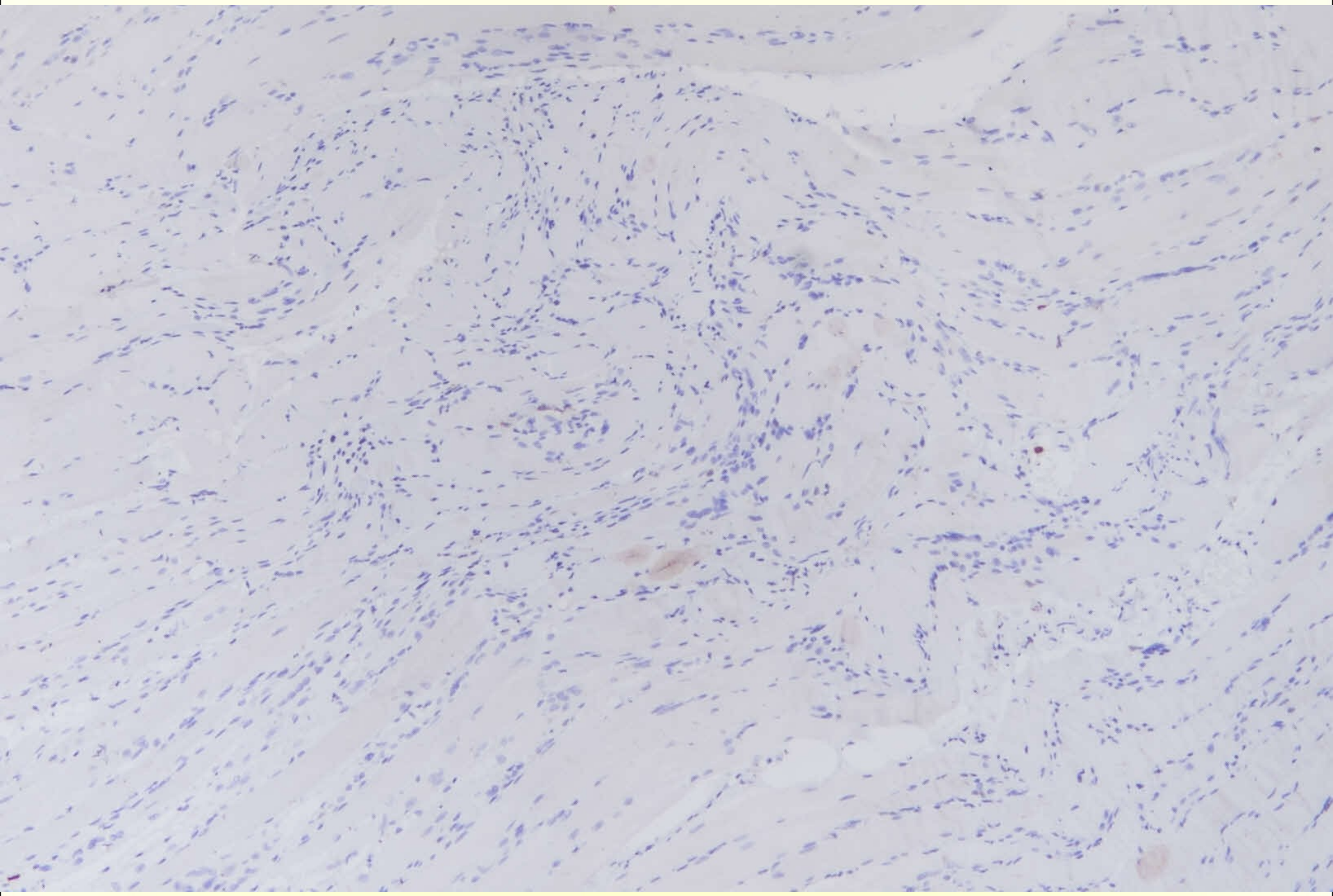
CD3(+)



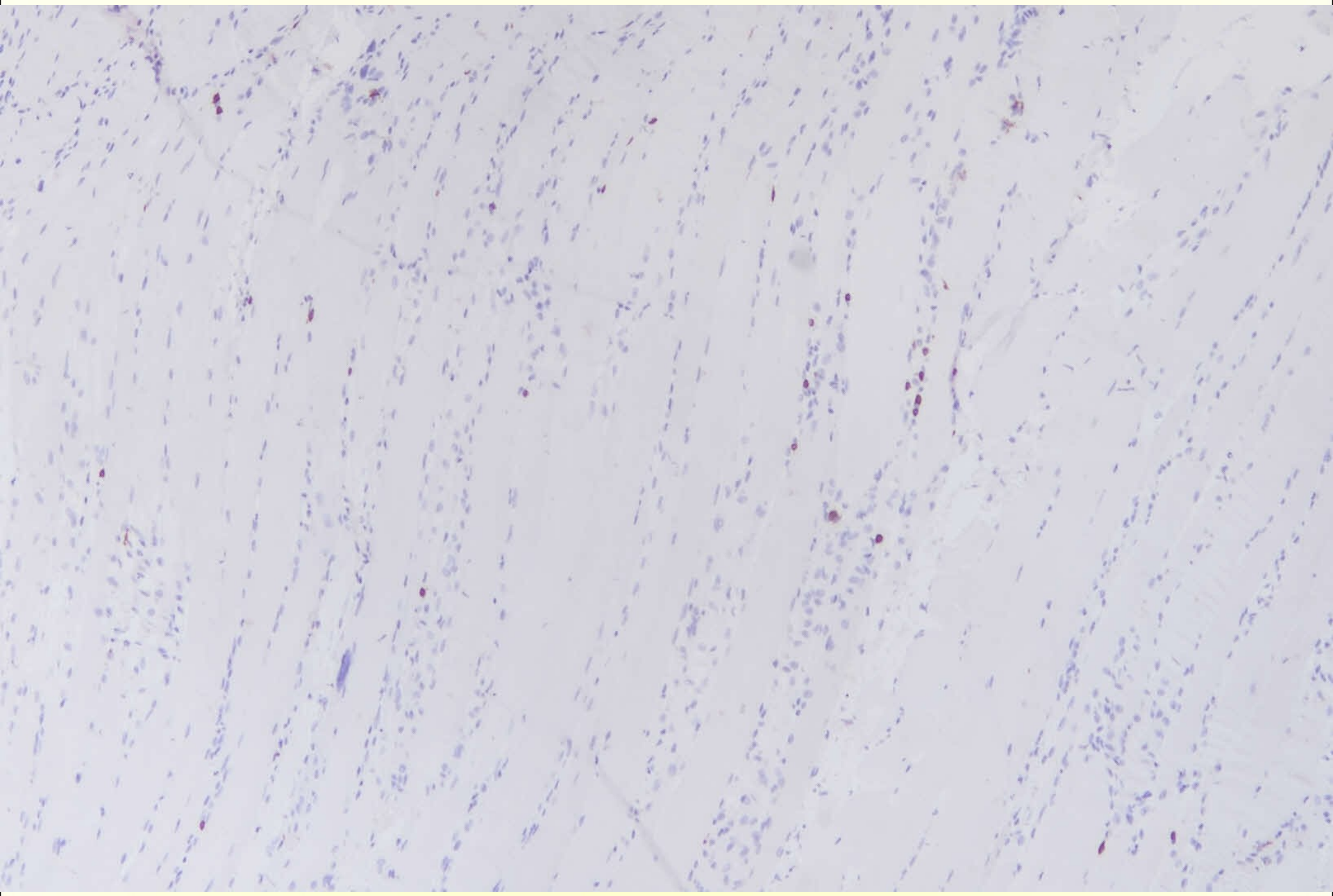
CD3(+)



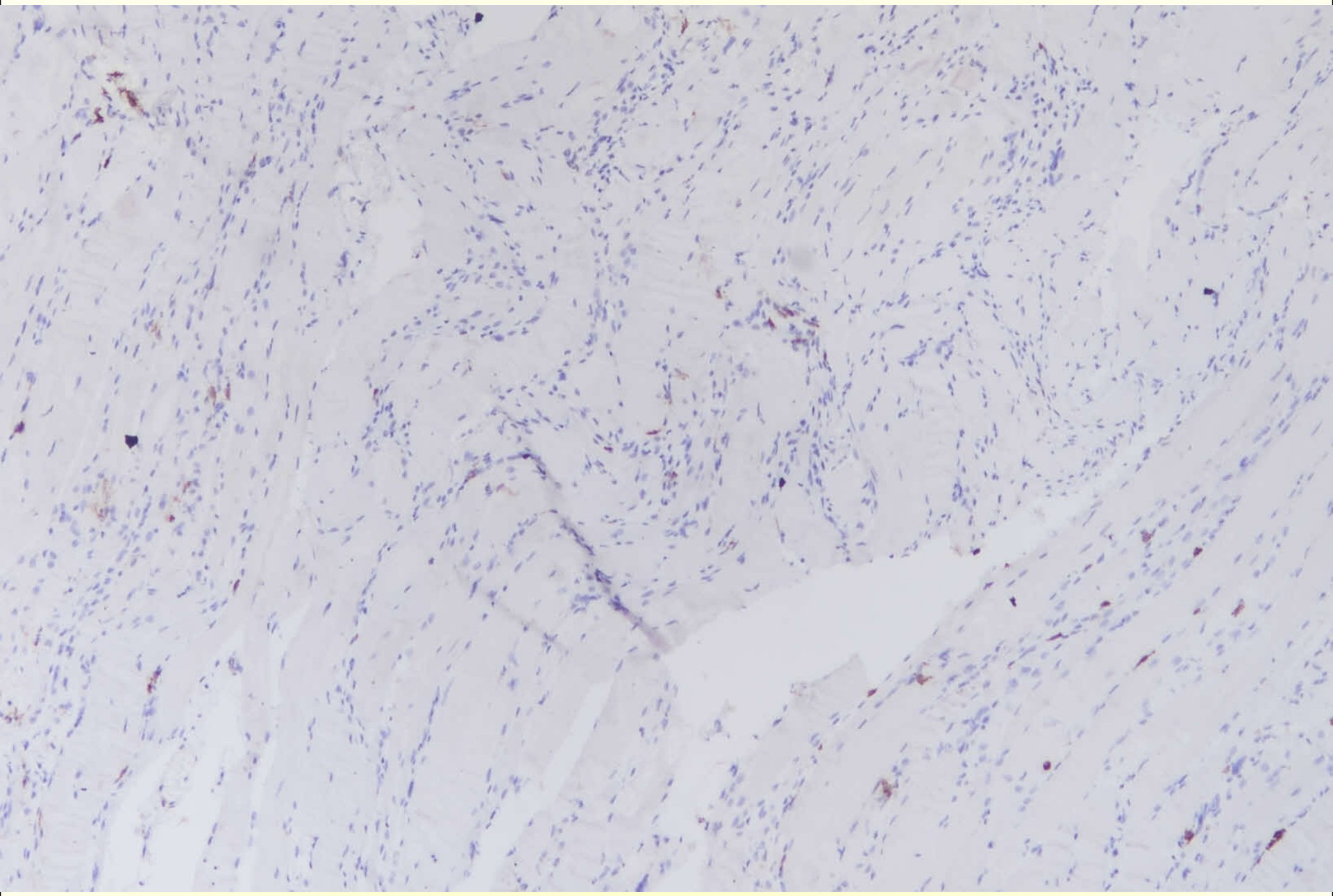
CD20(rare)



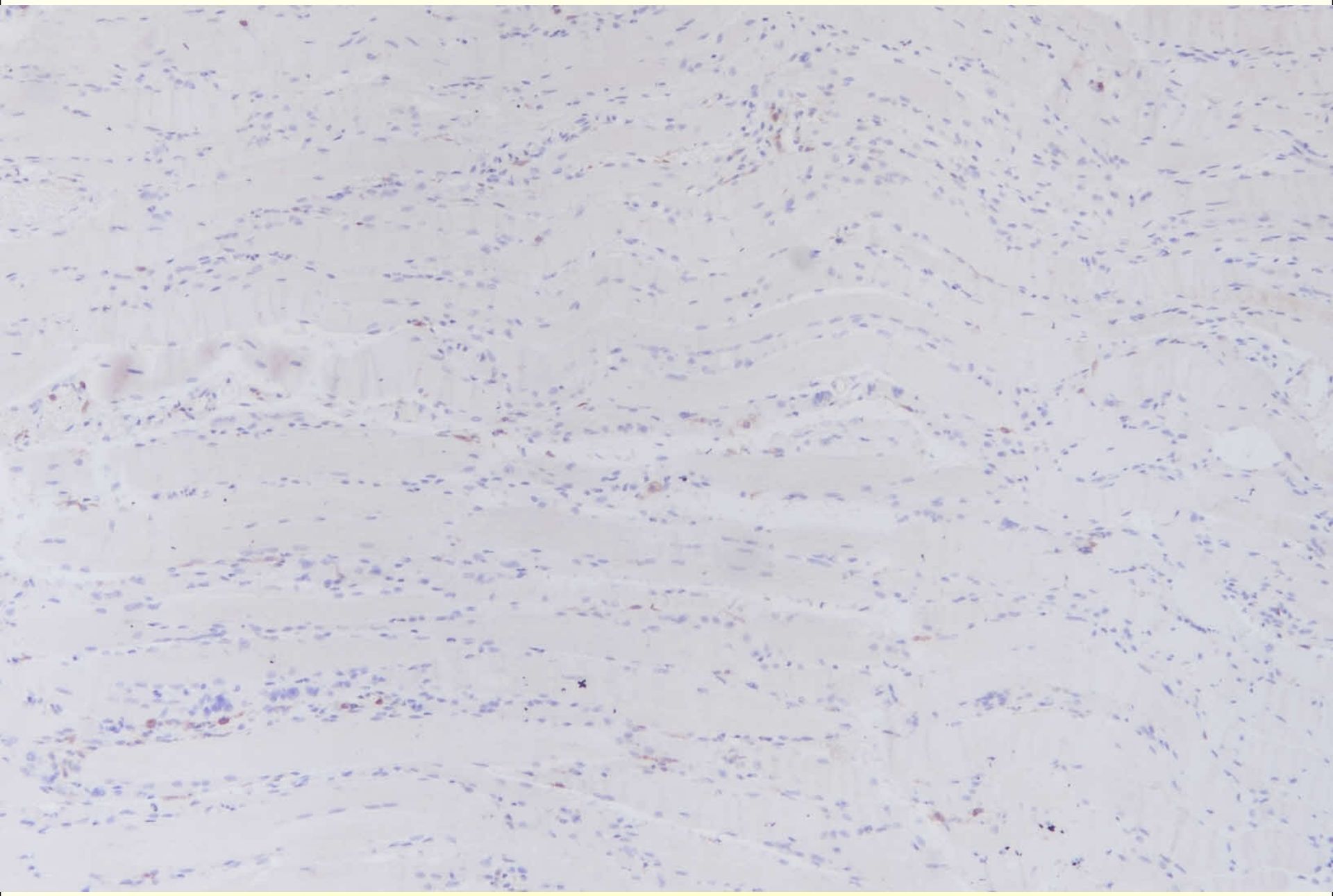
CD8(+)



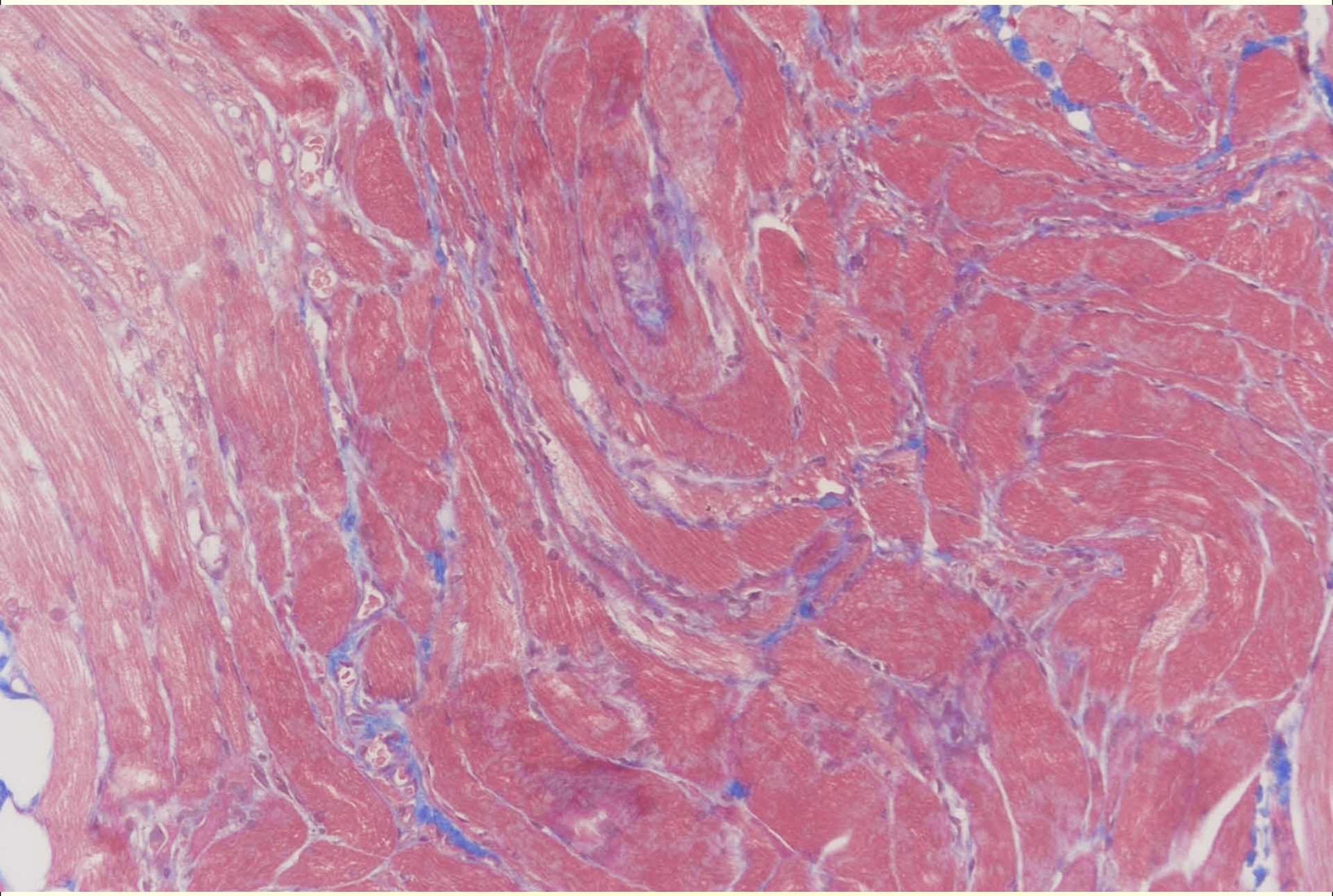
CD8(+)



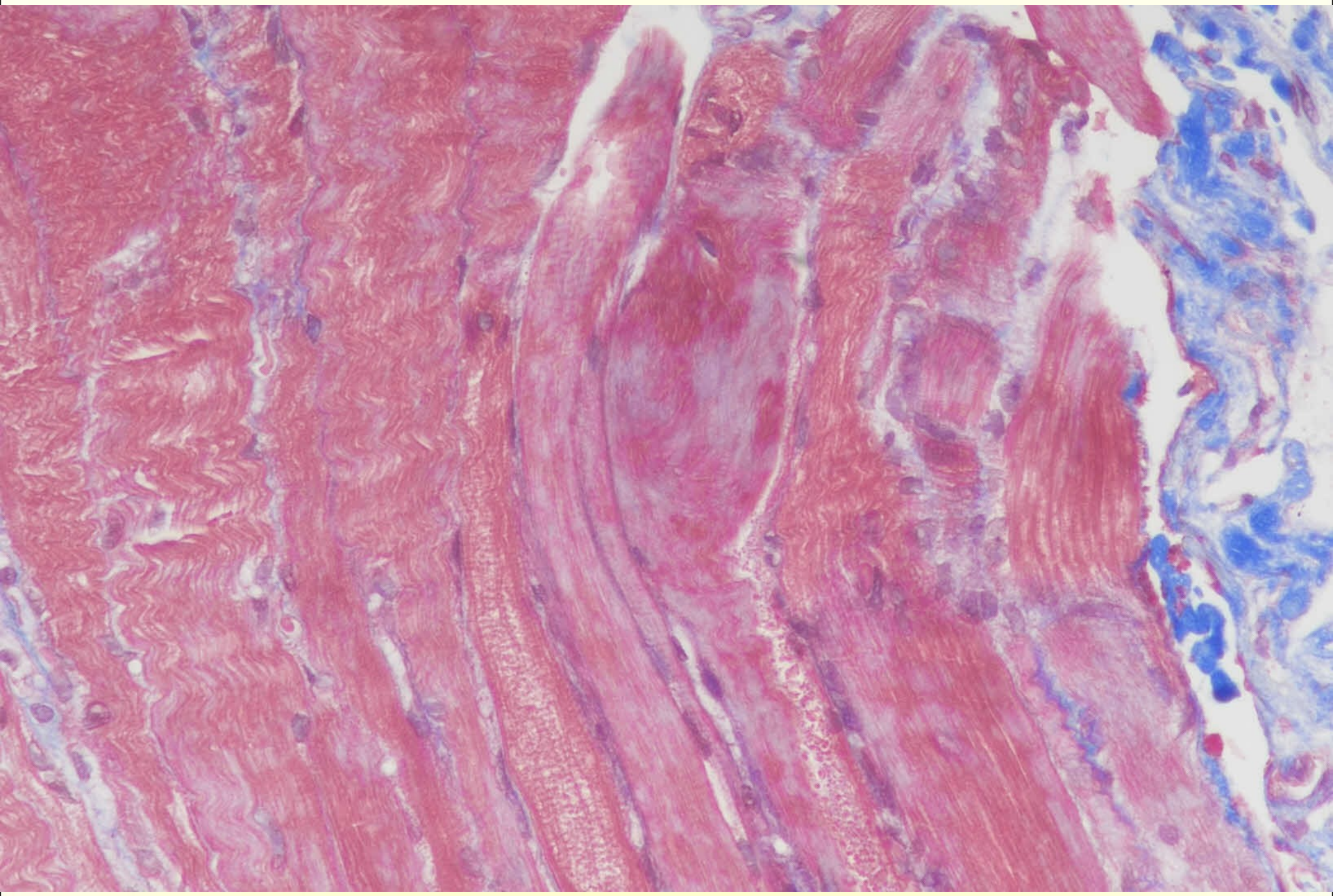
CD4 less than CD8 T lymphocytes



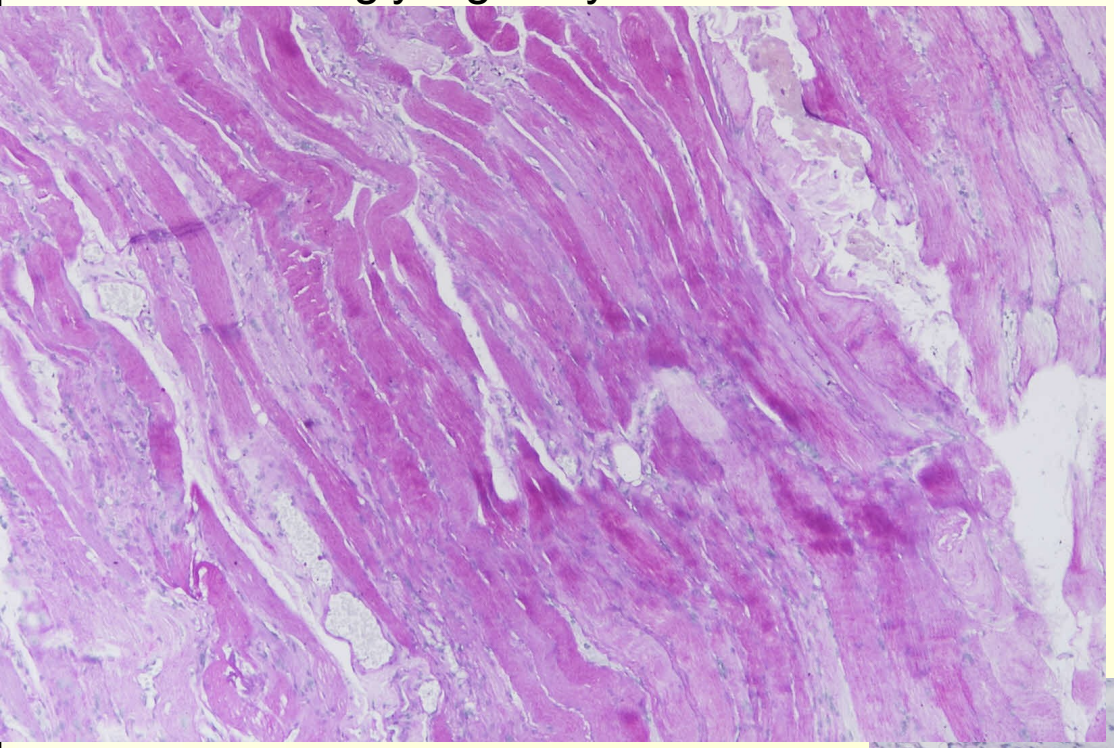
MassonTrichrome: Mild interstitial fibrosis

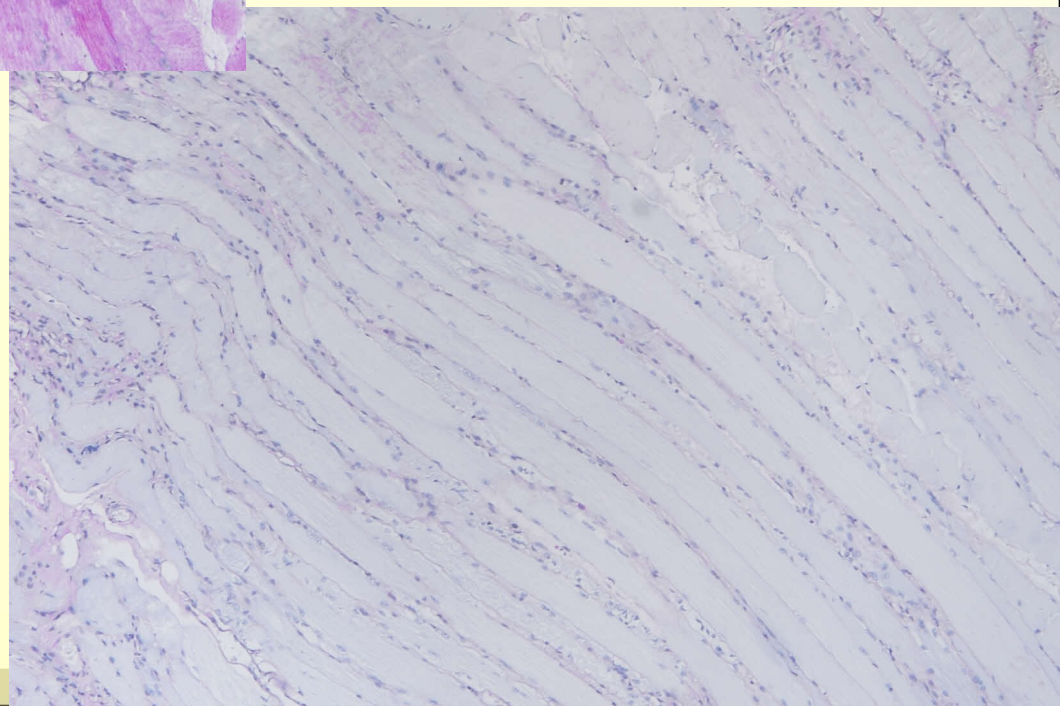


MassonTrichrome: greyish in areas loss of myofibrils

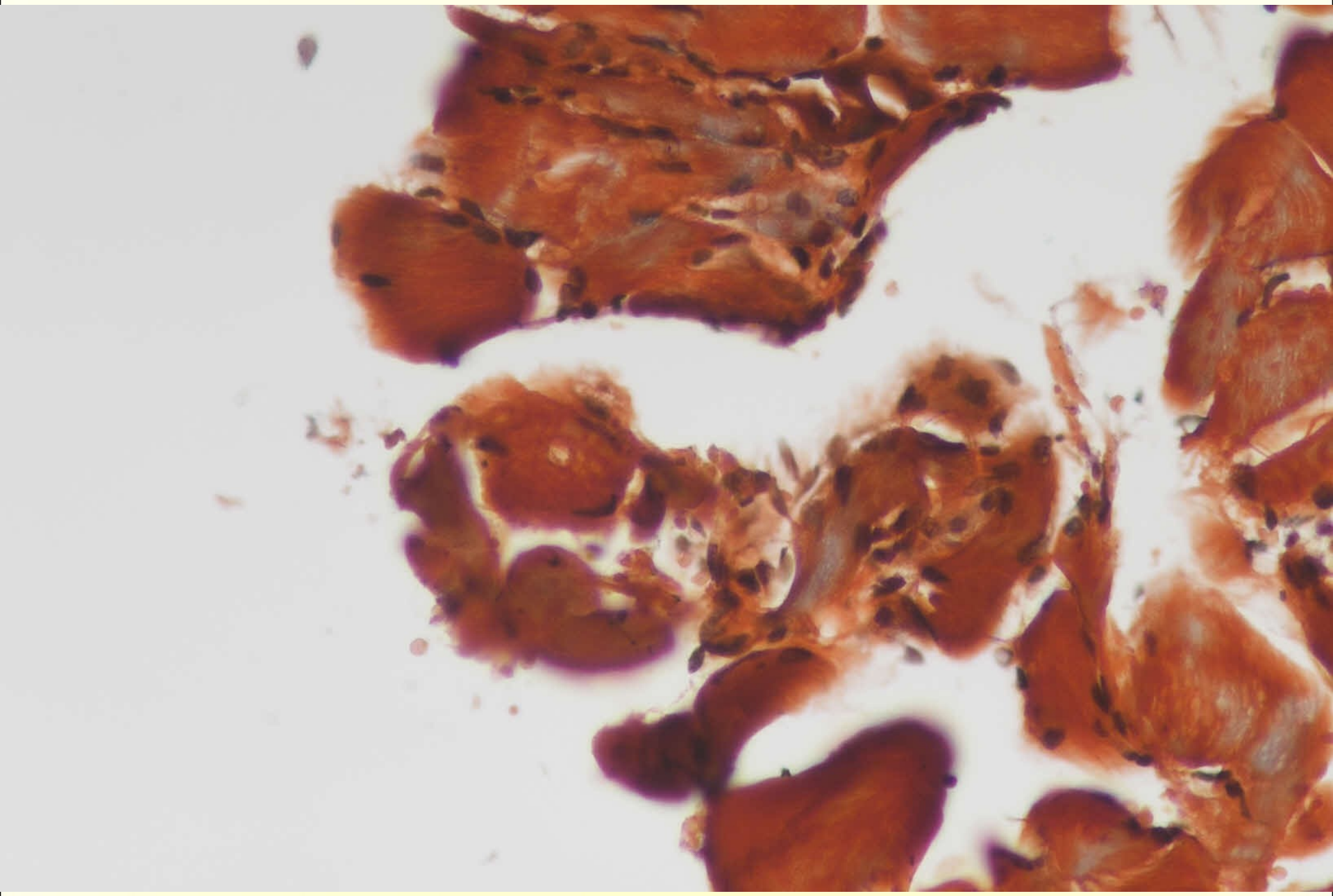


No decrease in glycogen by PAS and diastase stains.





Congo red: No inclusion



Skeletal muscle biopsy findings:

Mild mononuclear inflammatory infiltrate:
Mildly increased number of CD8(+) T cells
Rare CD20(+) B cells.
Phagocytosis of the degenerative/necrotic cells by CD68(+) macrophages.

Scattered individual myocytes with atrophic change, segmental necrosis, loss of cross striation, and vacuolar degeneration.
Randomly distributed, without peri-fascicular pattern.

No evidence of inclusion body by HE stain and Congo red stain.
No conspicuous decrease in glycogen by PAS and diastase.

Compatible with inflammatory myopathy, favor polymyositis due to absence of inclusion, and rare B cell infiltration

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Pathological differential diagnoses of inflammatory myopathy: polymyositis, inclusion body myositis, dermatomyositis.

Non-neoplastic skeletal muscle diseases:

- Neurogenic atrophy
- Neuromuscular junction disorder
- Primary myopathic diseases

Non-neoplastic skeletal muscle diseases:

- Neurogenic atrophy
  - Often angular small muscle fibers, grouped atrophic fibers, decreased glycogen
- Neuromuscular junction disorder
  (rarely biopsied such as myasthenia gravis: unremarkable muscle ~ muscular atrophy +/- neurogenic change +/- lymphocytic inflammation)
- Primary myopathic diseases

Non-neoplastic skeletal muscle diseases:

- Neurogenic atrophy
- Neuromuscular junction disorder
- Primary myopathic diseases:
  - Characterized by marked variation of individu al fiber size and endomysial fibrosis, with or w ithout necrotic and regenerative fibers.
  - Often minimal morphological change: clinical information, EMG findings, serum crea tine kinase (CK) levels are essential

This patient:

- Clinical:
  - Symmetric proximal weakness and dysphagia
- EMG and SNCV:
  - Myopathy considered
- Serum creatine kinase (CK)
  - Elevated CK

日期	CK
單位	U/L
2020-09-17	134
2020-07-16	*270
2020-06-18	
2020-06-10	
2020-06-08	*283
2020-06-05	*297
2020-06-03	*381
2020-06-01	*666
2020-05-30	*1308
2020-05-28	*1590
2020-05-27	*1475

參考值:,CK(M:27-168;

Primary myopathic diseases

- Inflammatory myopathies:
  - Commonly encountered in biopsies: Polymyositis, dermatomyositis, and inclusion body myositis
- Non-inflammatory myopathies
  - Muscular dystrophies, developmental disorders of the muscle, myofibrillary myopathies, metabolic myopathies, and toxic and drug-induced myopathies

Inflammatory myopathies

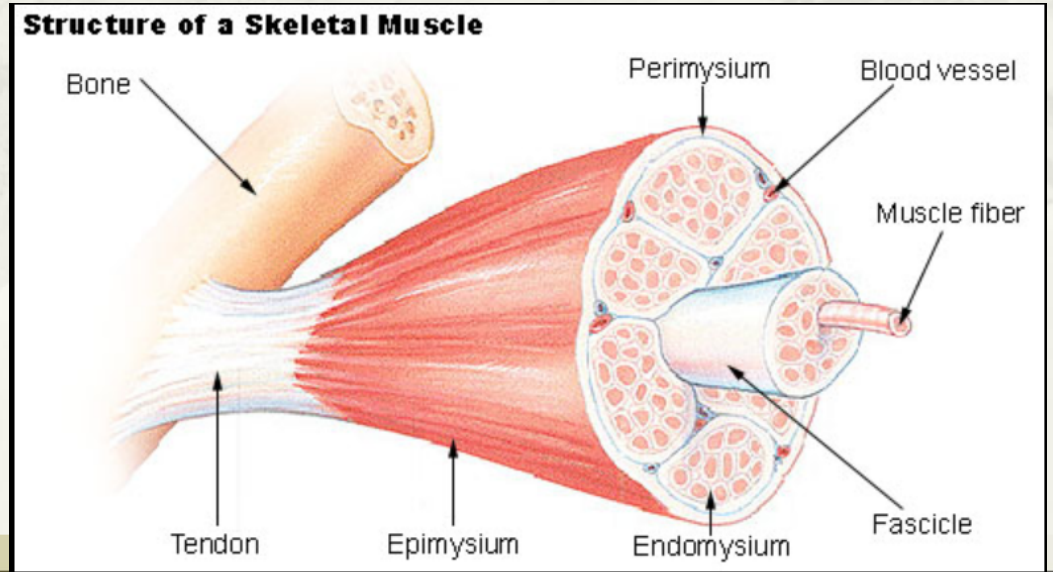
- Polymyositis
- Dermatomyositis
- Inclusion body myositis

Polymyositis

- Clinical:
  - A subacute or chronic course
  - Insidious onset without a precipitating event
  - Symmetric weakness involving proximal muscles; later dysphagia
- Pathology:

Polymyositis

- Pathology: Nonspecific (diagnosis of exclusion)
  - Mononuclear inflammatory infiltrate mostly T cells esp activated CD8(+) cells, intra-fascicular (endomysial) surrounding or invading individual non-necrotic muscle fibers.
  - Few or no B cells
  - Necrotic and regenerating fibers scattered within the fascicle.



https://en.wikipedia.org/wiki/Endomysium#/media/File:Illu_muscle_structure.jpg

Polymyositis

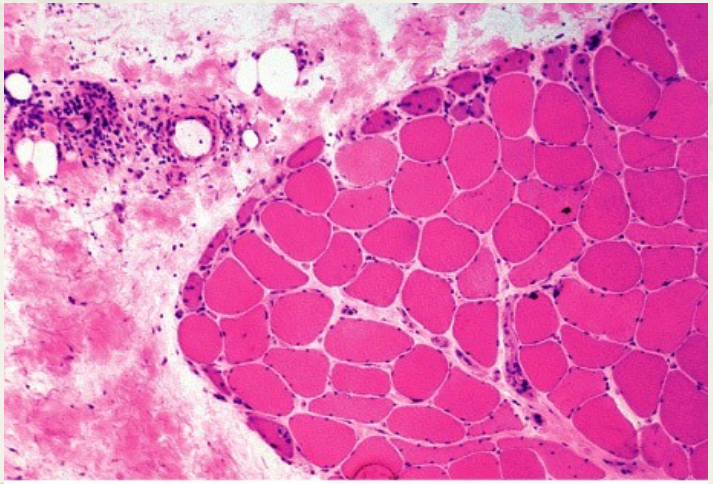
- Pathology: Nonspecific (diagnosis of exclusion)
  - Early, sarcoplasm of necrotic fibers appears hypereosinophilic and granular with nuclear pyknosis and karyorrhexis.
  - Later, the fibers become pale and vacuolated and undergo phagocytosis (myophagia)

Dermatomyositis

- Clinical:
  - A distinct clinical entity characterized by skin r ash heralding the onset of muscle weakness.
  - May occur alone or can be associated with mi xed connective tissue diseases or malignancy.
- Pathology:

Dermatomyositis

- Pathology:
  - Inflammatory infiltrate consists of mainly lymphocytes.
  - The lymphocytes: High percentage of B cells; T cells are mostly CD4 lymphocytes.
  - The inflammation is predominantly perivascular, focally in the perimy sium and less commonly in the endomysial compartment.
  - Atrophic fibers at the periphery of fascicles, perifasicular atrophy: Hig hly suggestive of dermatomyositis, absent in polymyositis and inclus ion body myositis



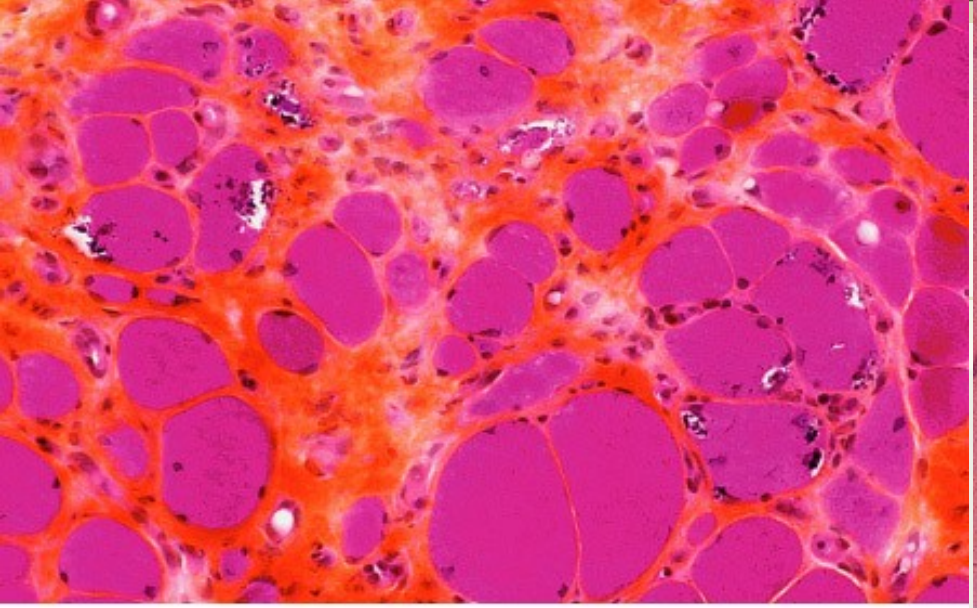
Perifascicular fiber atrophy is typical of dermatomyositis.

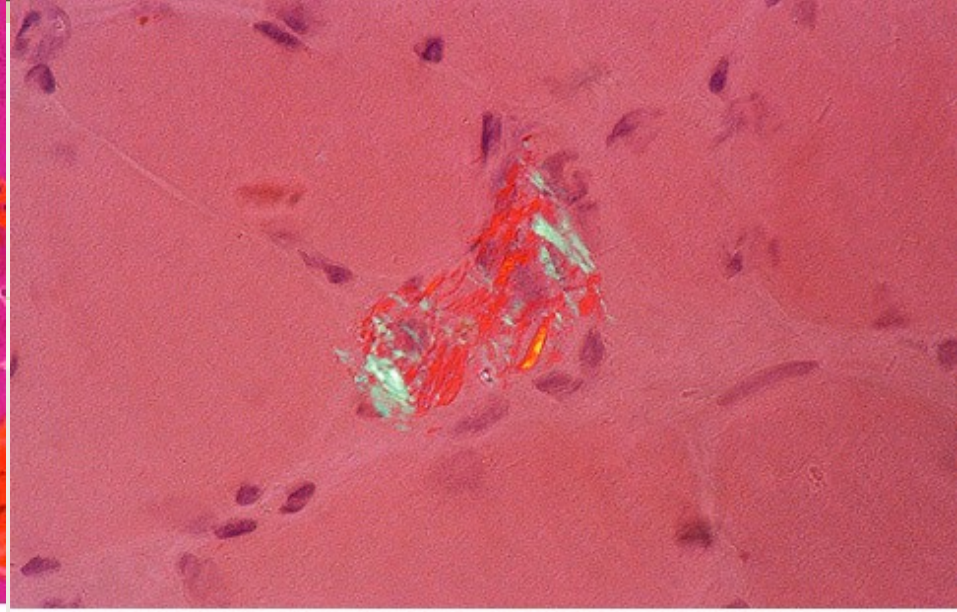
Inclusion body myositis

- Clinical:
  - Commonly asymmetric weakness of foot and hand muscles
- Pathology:

Inclusion body myositis

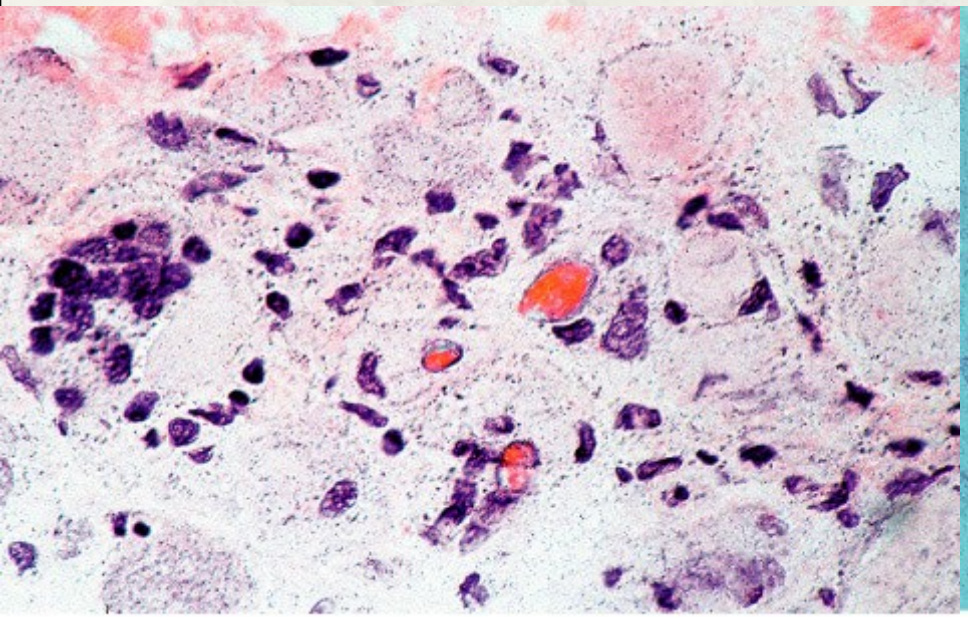
- Pathology:
  - Diagnostic feature: Slit-like vacuoles in the sar coplasm containing hematoxyphilic granules o r eosinophilic inclusions, Congo red(+)
  - Endomysial chronic inflammatory infiltrate simi lar to polymyositis, with lymphocytic mainly T cells
  - Small group atrophy of fibers

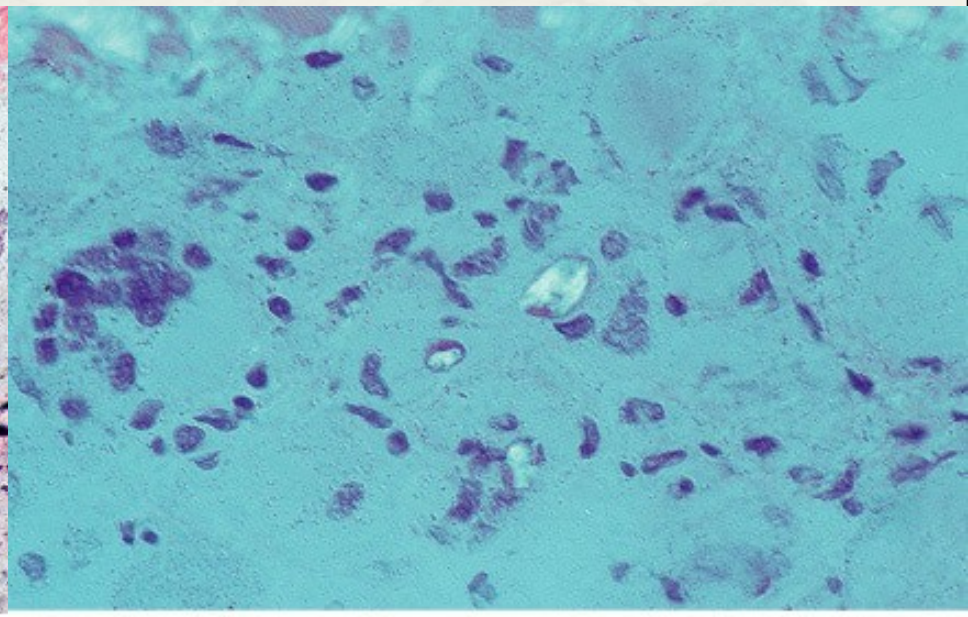




H&E: hematoxyphilic granules in sarcoplasmic vacuoles

Congo red(+) inclusions: intra-sarcoplasmic and/or intranuclear





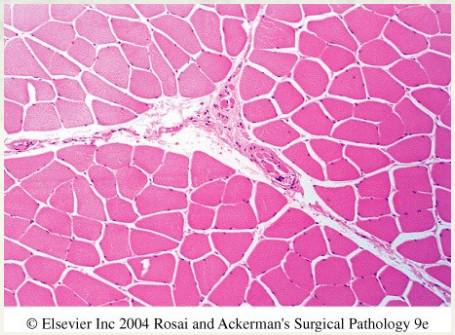
Pathologic Diagnosis:

Compatible with inflammatory myopathy, favor polymyositis due to absence of inclusion, and rare B cell infiltration.

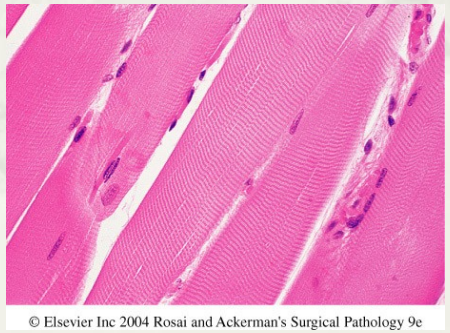
Discussion

Skeletal muscle biopsy

- When interpreting a muscle biopsy, the pathologist must have knowledge of the patient's clinical and family history, PE findings, and EMG, nerve conduction tests, and lab data such as serum creatinine phosphokinase.
- Biopsy site should be selected from a muscle that is moderately involved by the disease process. Not from a severely affected site having only fat and fibrous tissue; and not from minimally involved muscle which shows no diagnostic changes; and not from previously tramatized, for instance by EMG needles.
- Better biopsy from the belly of the muscle.
- (1) Cryostat: transverse oriented, frozen in liquid nitrogen-isopentane
- (2) Formalin and (3) Glutaldehye: transverse and longitudinal



transverse



longitudinal

Polymyositis
Signs and symptoms:

- The hallmark of polymyositis is weakness and/or loss of muscle mass in the proximal musculature, as well as flexion of the neck and torso.
- Dysphagia or other esophageal motility problems occur in as many as 1/3 of patients.

Polymyositis Causes:

- Polymyositis is an inflammatory myopathy mediated by cytotoxic [CD8(+)] T cells with an as yet unknown autoantigen,
  - Compare: dermatomyositis is a humorally mediated (B cells) resulting in myositis and a typical dermatitis.
- The cause of polymyositis is unknown and may involve viruses and autoimmune factors.
- Cancer may trigger polymyositis and dermatomyositis, possibly through an immune reaction against cancer that also attacks a component of muscles.

Polymyositis Diagnosis:

- History and physical examination,
- Elevation of creatine kinase,
- EMG(electromyograph) alteration, and
- Positive muscle biopsy

Polymyositis Treatment:

- The first line treatment for polymyositis is c orticosteroids.
- Specialized exercise therapy may supplem ent treatment to enhance quality of life.
- Polymyositis tends to respond well to treat ment, at least initially

2020/09/17 OPD

nonfunctional tumor
4. Gastric ulcer, Duodenal ulc

O： NE: clear consciousness, intact cranial nerve
MP 4-5/4-5
DTR ++/++
2020/06/18 CREA:0.74
2020/06/08 CK:283
Gallium tumor scane:Certain lesion in right scrotum can't be ruled out.
2020/09/17 GPT:20, CK:134, CREA:1.01

A+P:
◆IMP: 1. Myopathy,cause? , improved
-20200618, s/s improved. f/u CK
-20200716, CK 270(more low),
muscle power improved.
Mild Paresthesia between abdomen to bil.thigh
r/o T8-L2/3 dermatone -> Imipramine, OBS
-20200813, Imipramine: some effect+
Imipramine qd -> bid, f/u CK,liver function
-20200917, Seborrhic dermatitis improved after Megest Oral sup. ??. No weakness. CK 134.
Paresthesia over low abdomen+.

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2020-05-30	*1308
2020-05-28	*1590
2020-05-27	*1475

Biopsy

參考值:CK(M:27-168;F

ICD碼：G73.7 Myopathy in diseases classified elsewhere
G62.9 Polyneuropathy, unspecified
G40.001 Localization-related (focal) (partial) idiopathic epilepsy and epilept

References:

- Rosai and Ackerman's Surgical Pathology. 9th edi, vol 2, pp. 2663-2669
- HANS OOSTERHUIS AND JAAP BETHLEM. Neurogenic muscle involvement in myasthenia gravis: A clinical and histopathological study. Journal of Neurology, Neurosurgery, and Psychiatry, 1973, 36, 244-254
- https://en.wikipedia.org/wiki/Polymyositis
- https://neuromuscular.wustl.edu/lab/mbiopsy.htm

Thanks for your attention !!