Autopsia: Incidentaloma suprarrenal izquierdo.

Residentes: Carlos Nicolás Triana-Pérez, Andreea Stănică, Francisco Vizcaino-Pastor
Adjuntos: Carlos Zac-Romero, Nuria Mancheño-Franch, Jaime Ferrer-Lozano, Mónica Elizabeth Bauza

La Fe Anatomía Patológica

La Fe Hospital Universitari i Politècnic

Caso clínico:

Varón de 56 años .

HTA recientemente diagnosticada en tratamiento y en seguimiento por dolor toracico.

Motivo de consulta: **Cefalea y dolor torácico.**

Sospecha inicial: Infarto agudo de miocardio vs angina inestable.

Otros diferenciales: Síndrome aórtico agudo.

Analitica: Marcadores cardiacos elevados, transaminitis, elevación de creatinina, lactato elevado.

TC vascular: Ausencia de SAA. Masa adrenal izquierda de 5,3 x 3,9 x 3,8 cm, con captación de contraste, sin presencia de grasa macroscópica.

Coronariografía y ECOTE: Arterias coronarias epicárdicas ligeramente ateromatosas, **sin lesiones.**
Depresión **moderada-grave de la FEVI**
Descartar miocarditis??*

Deterioro clínico persistente, por lo que se comenta para asistencia circulatoria.

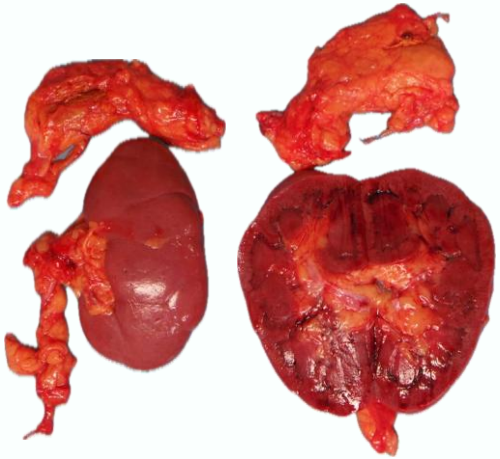
Continua hipotenso, taquicardico y con requerimientos crecientes de soporte vasoactivo, mecánico.

Midriasis arreactiva súbita.
TC cerebral: **Varios focos hemorrágicos intraparenquimatosos** en distinto estadio con apertura al sistema ventricular, **herniación subfalciana hacia la derecha, uncal izquierda, transtentorial descendente central y de amigdalas cerebelosas**

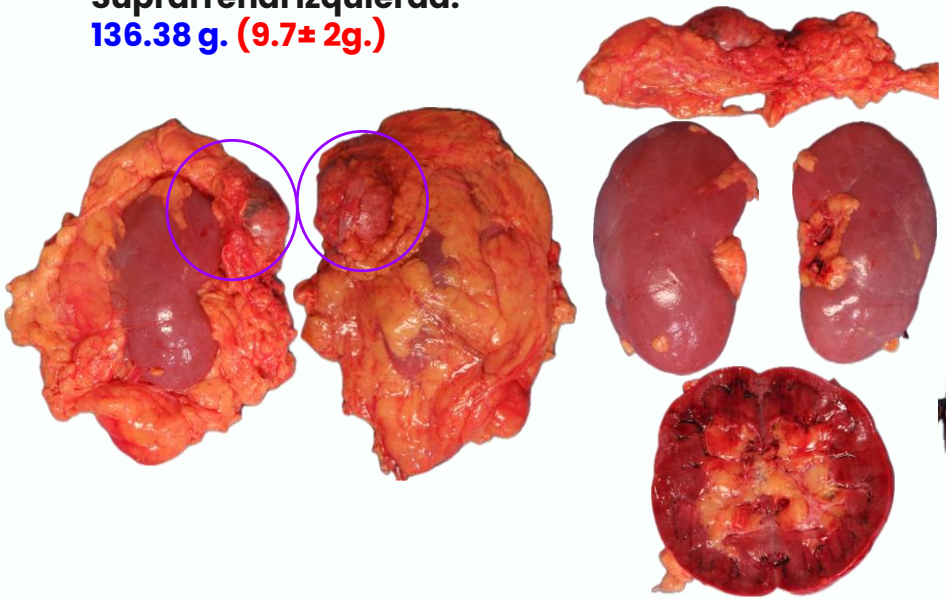
Hallazgos macroscópicos.

No se encuentra adherida a la superficie renal ni presenta infiltración aparente a ninguna otra estructura anatómica

Suprarrenal derecha:
41.83 g. (9.7± 2g.)



Suprarrenal izquierda:
136.38 g. (9.7± 2g.)

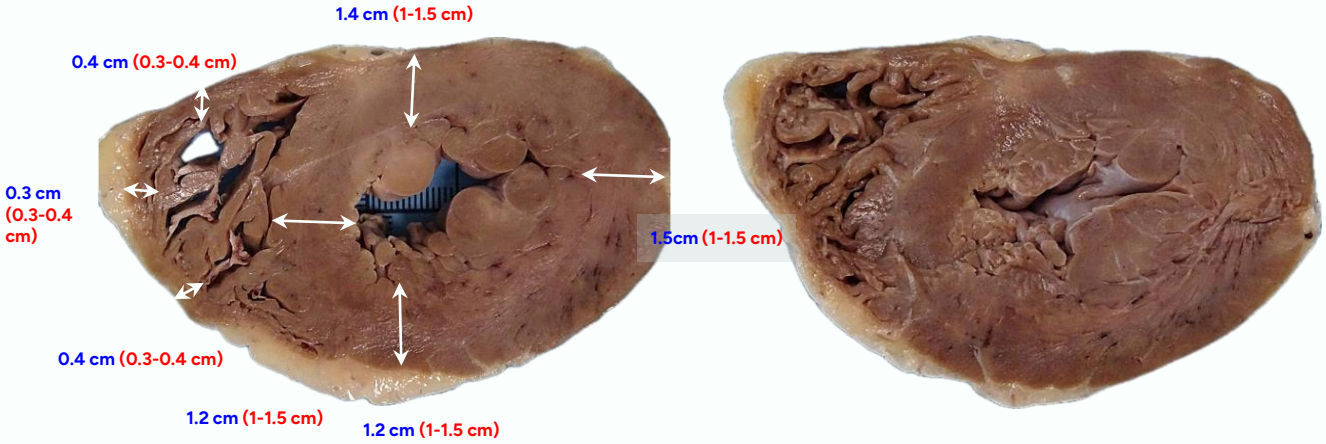


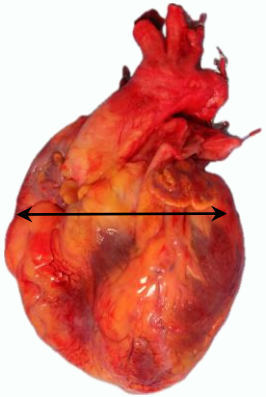
5x6x3 cm

Corazón

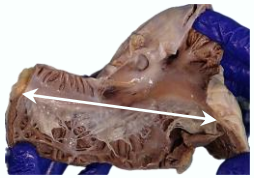
Dominancia derecha
10 cc de líquido pericárdico

358,43 g. (321± 30g.)

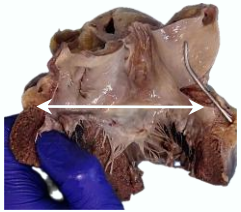




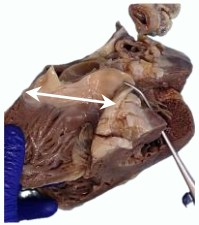
Válvula tricuspidea.
11.3 cm (hombres 11,2-11,8 cm)



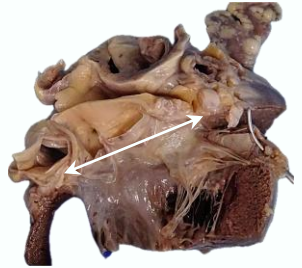
Válvula mitral.
9 cm (hombres 9,2-9,9 cm)



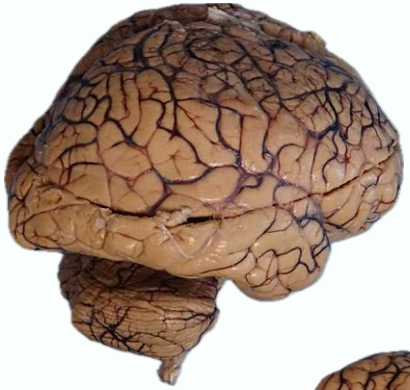
Válvula pulmonar.
7 cm (hombres 6,1-7,7 cm)

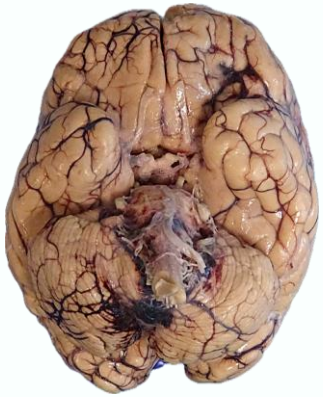


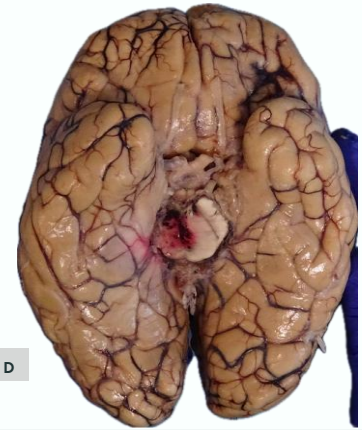
Válvula aórtica.
6.8 cm (hombres 6-8,5 cm)



SNC: 1395 g. (1378 ± 20 g.)







D

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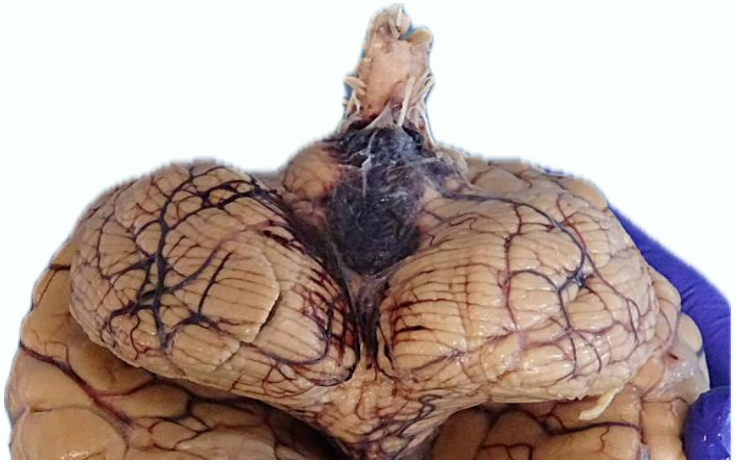
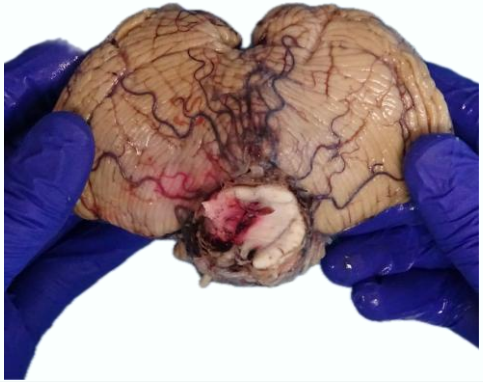
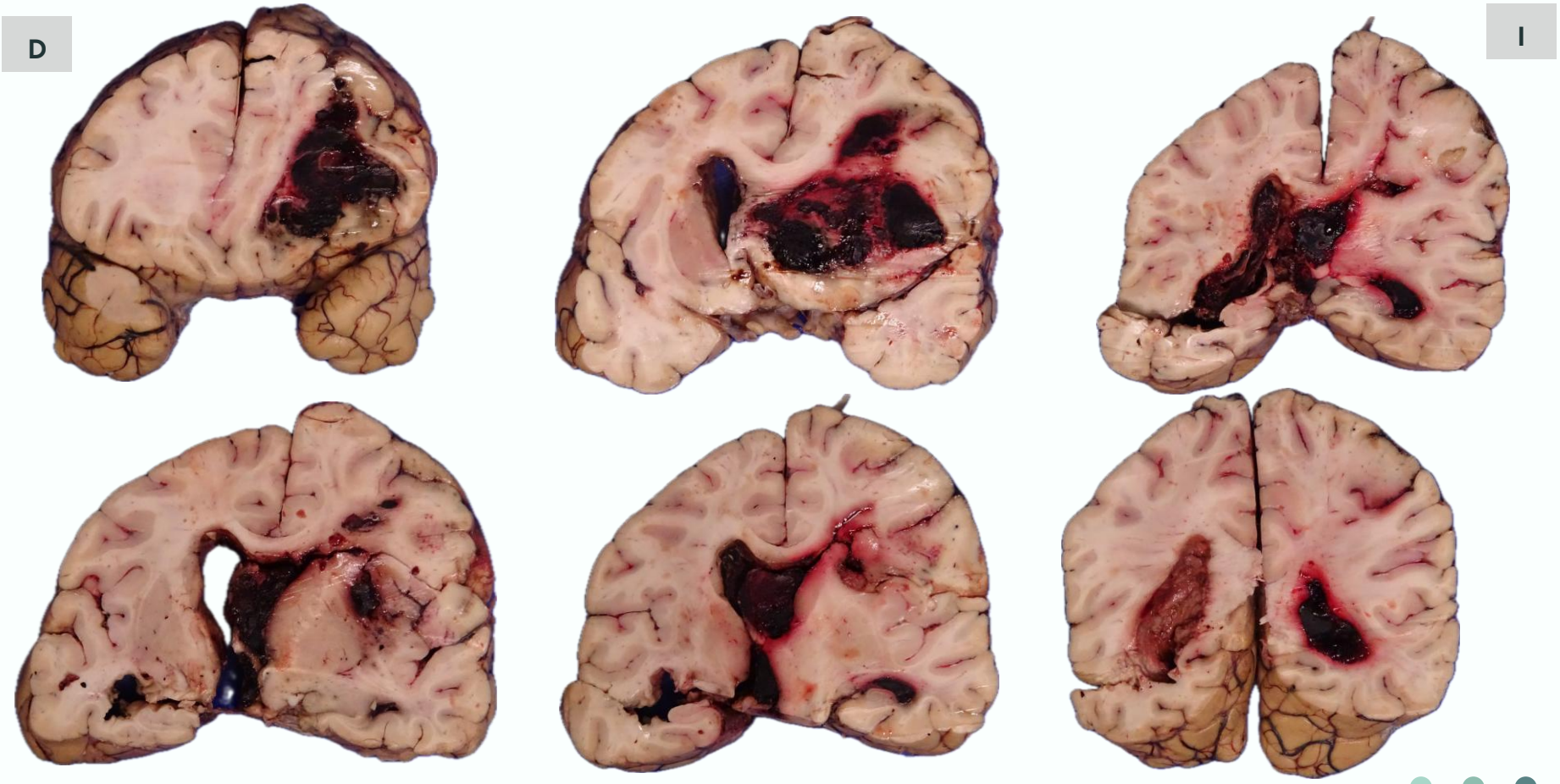
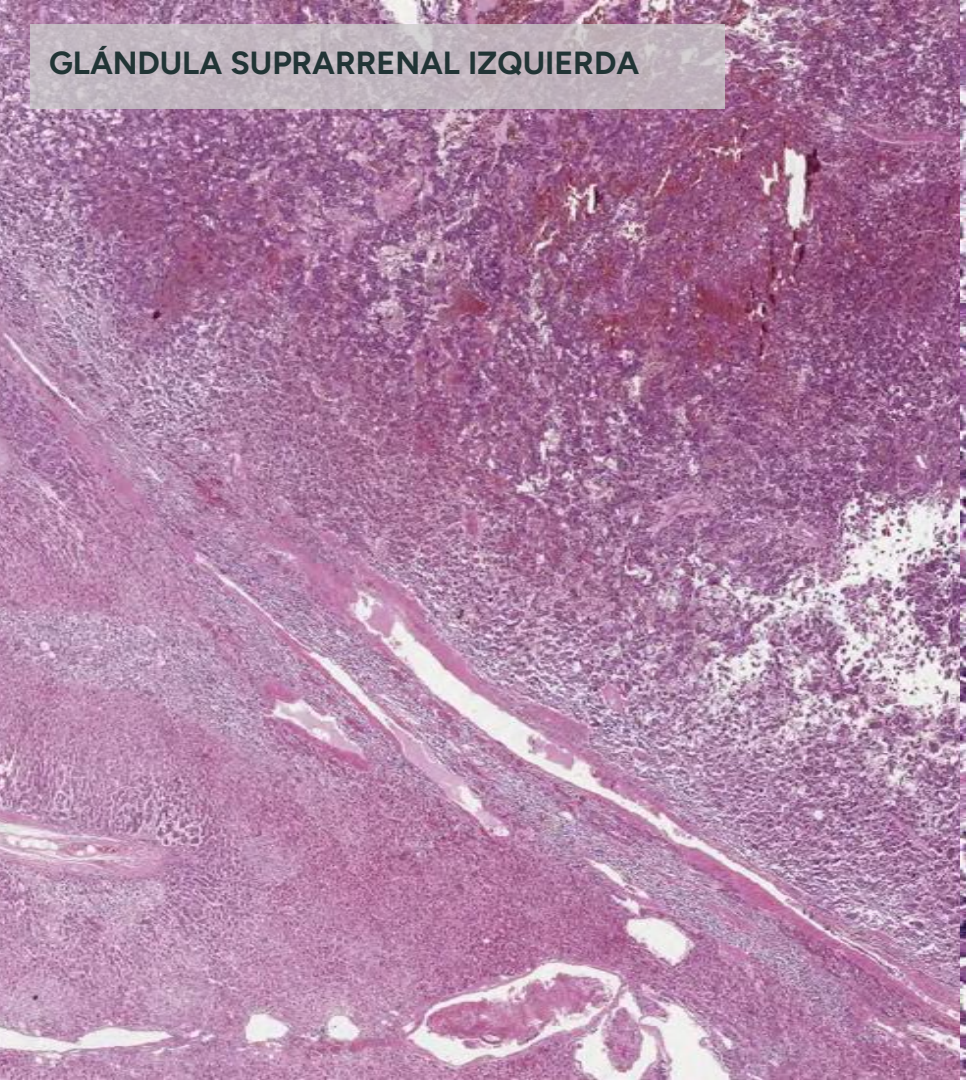
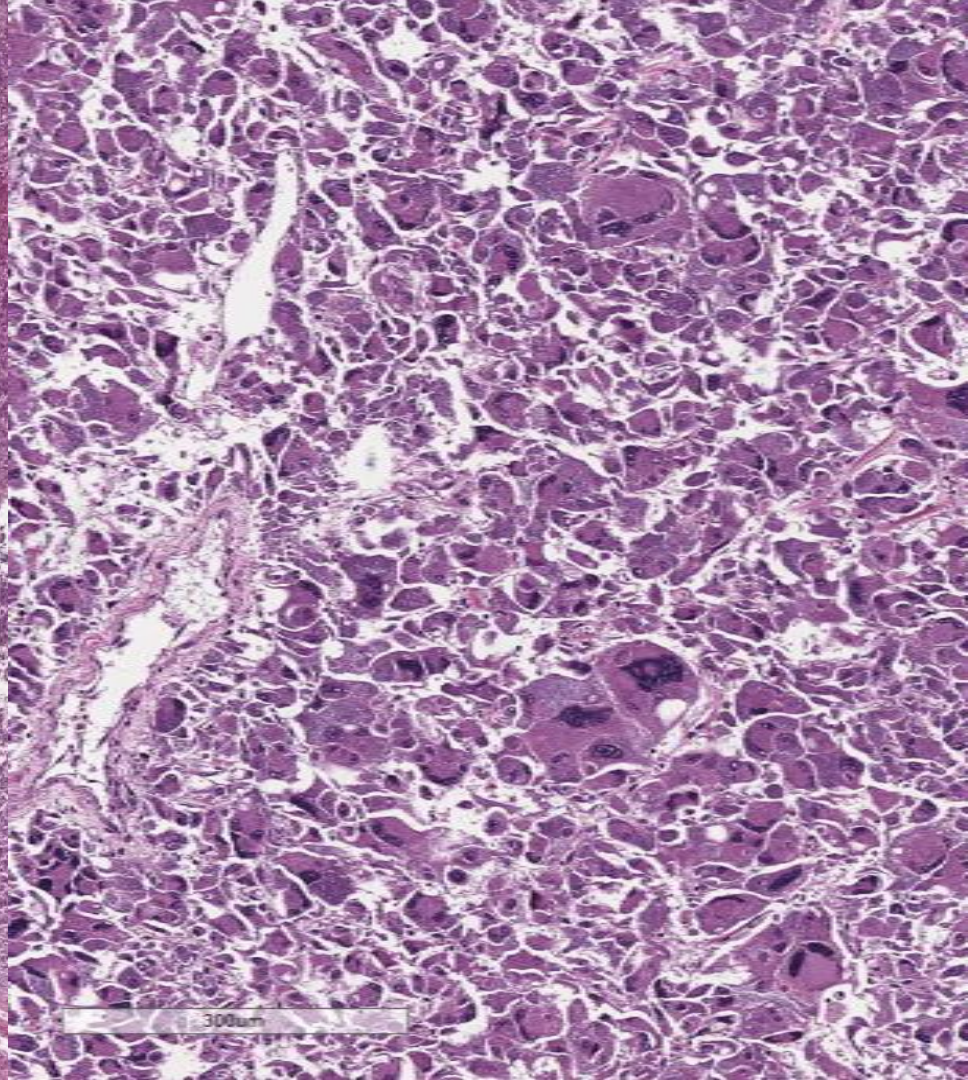


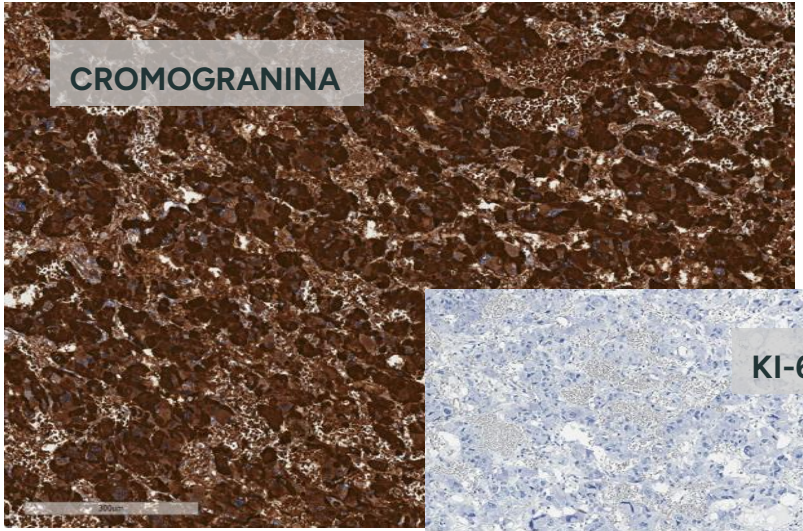


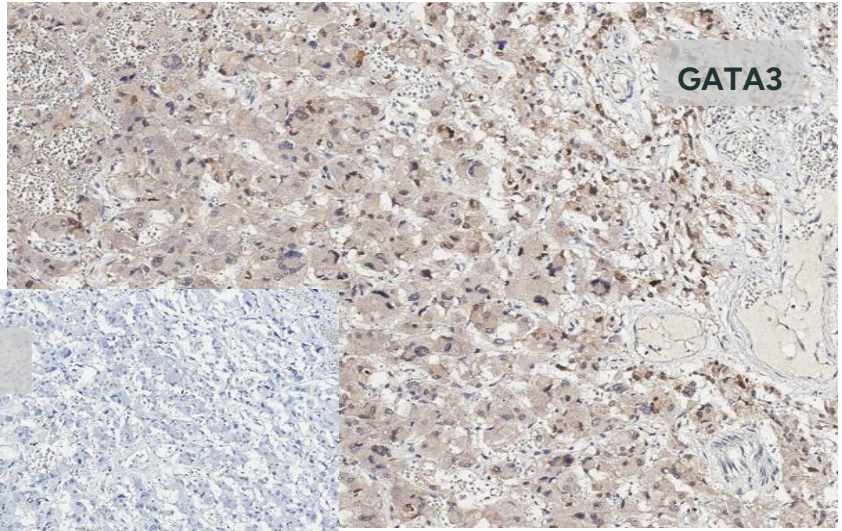

D
I

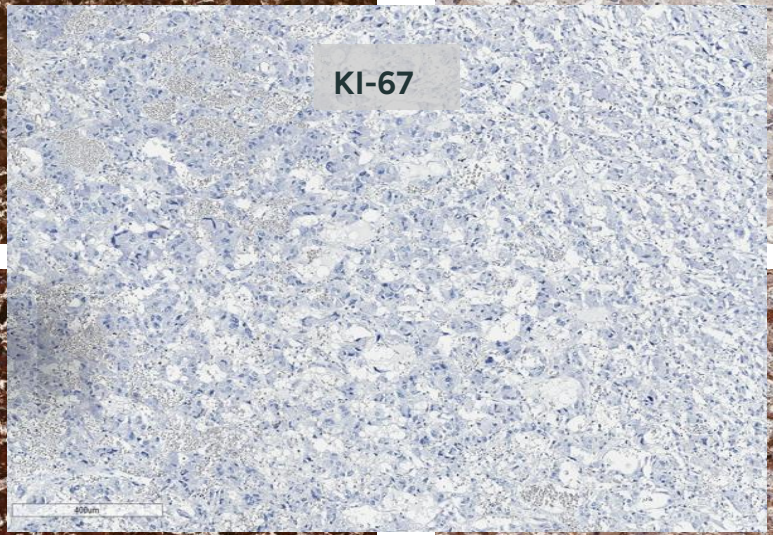
GLÁNDULA SUPRARRENAL IZQUIERDA

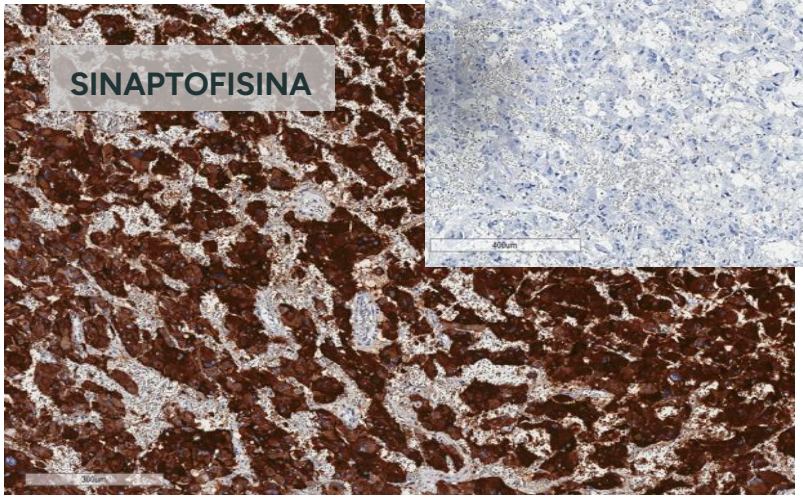


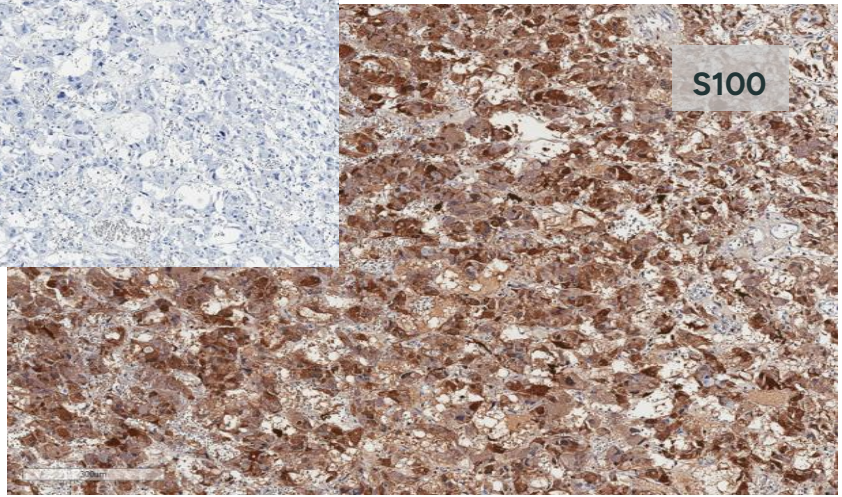



CROMOGRANINA


GATA3


KI-67


SINAPTOFISINA

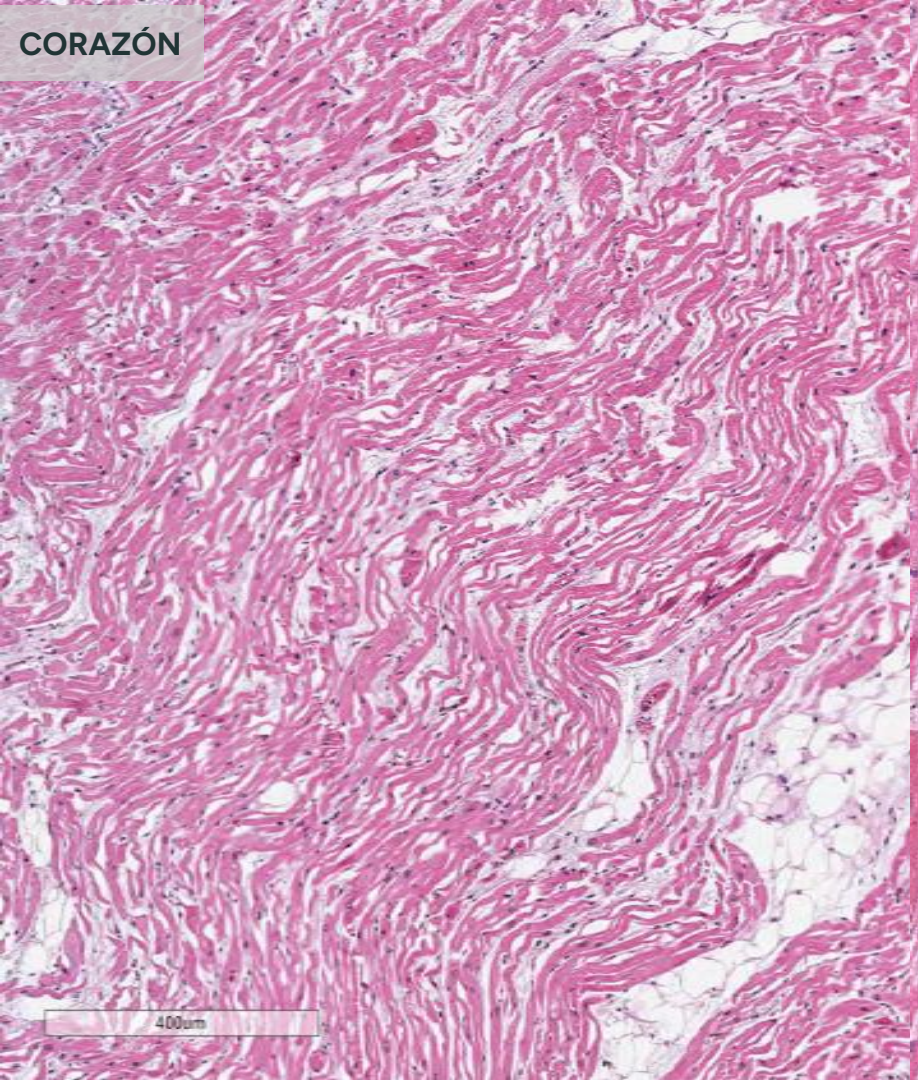

S100

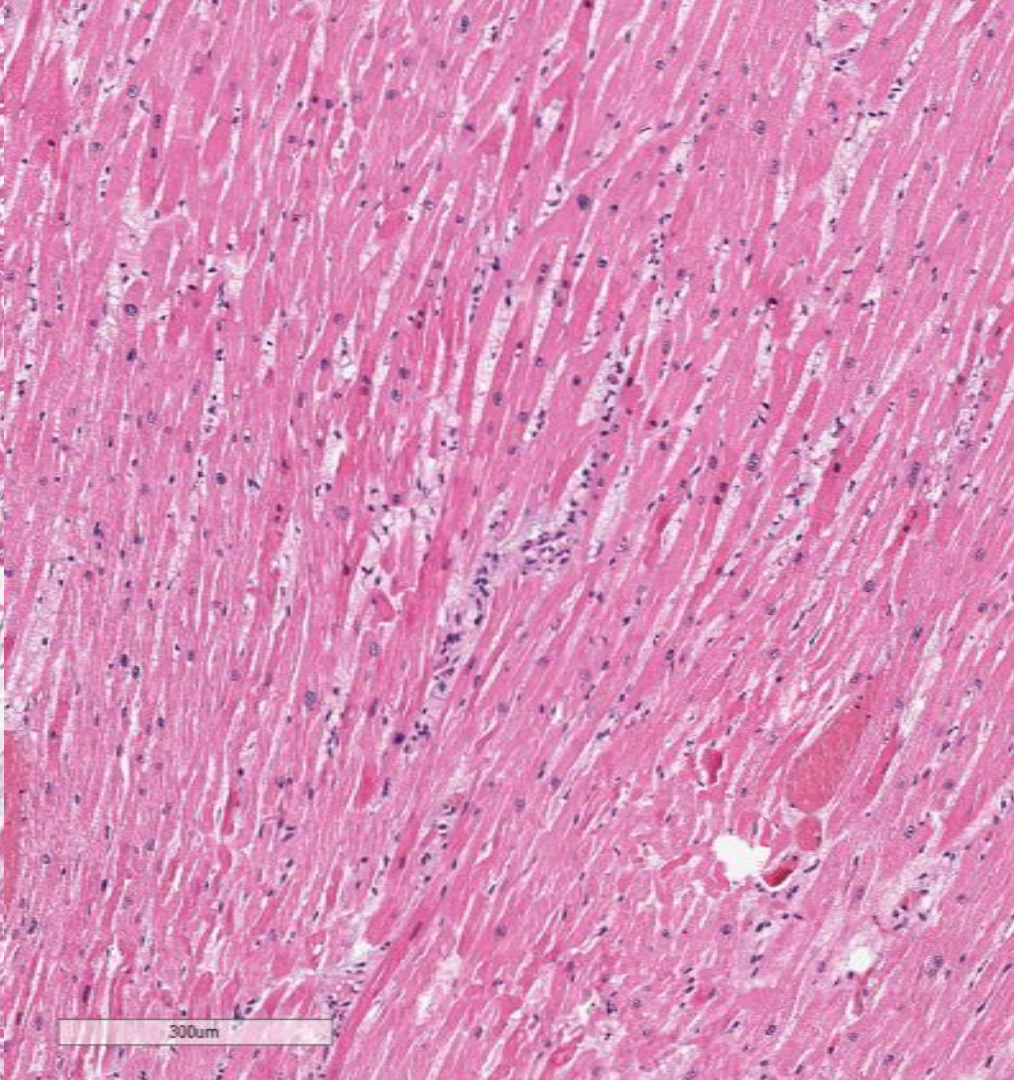
PASS SCORE. Pheochromocytoma of the adrenal gland scaled score (Am J Surg Pathol 2002;26:551)

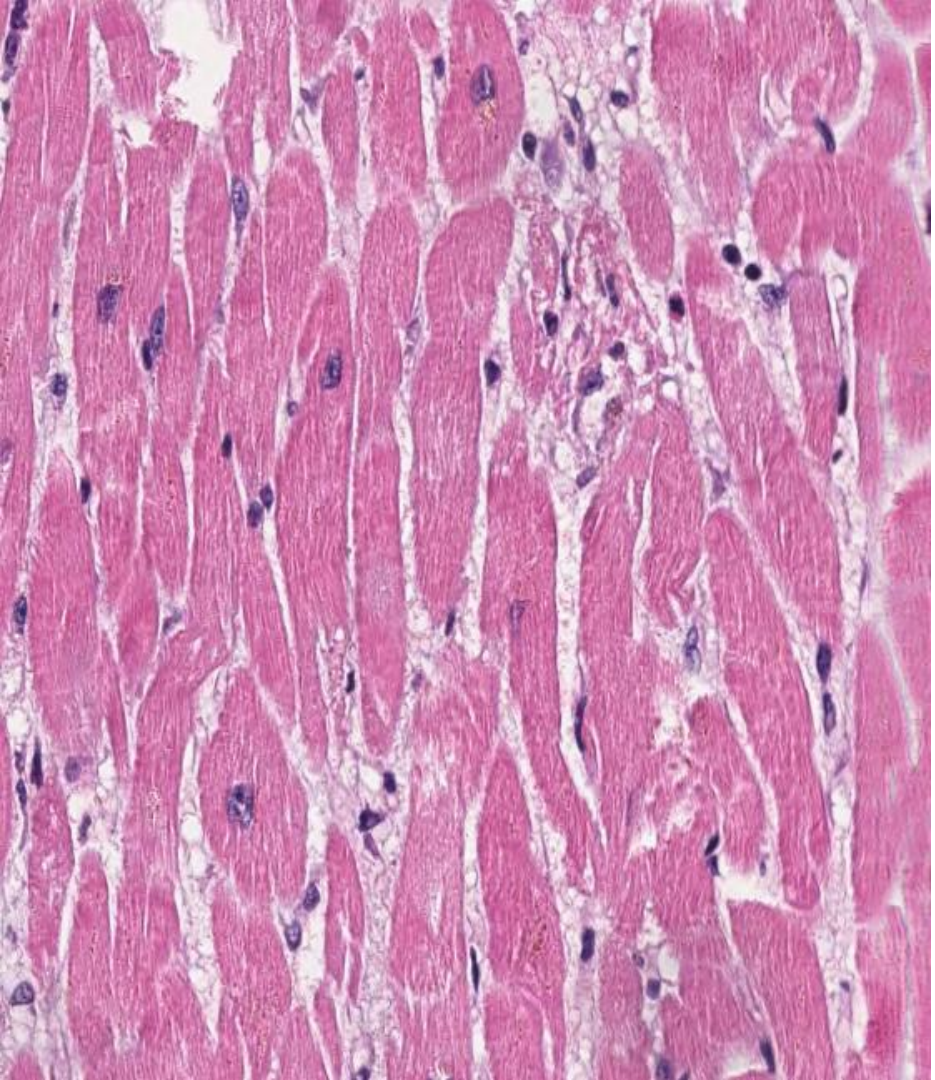
Histologic feature	Score (total ≥ 4 is concerning for malignancy)	Puntuación asignada
Periadrenal adipose invasion	+2	0
> 3 mitoses/10 high power fields	+2	0
Atypical mitoses	+2	0
Necrosis	+2	0
Cellular spindling	+2	0
Marked nuclear pleomorphism	+1	+1
Cellular monotony	+2	0
Large nests or diffuse growth	+2	+2
High cellularity	+2	0
Capsular invasion	+1	0
Vascular invasion	+1	0
Hyperchromasia	+1	+1

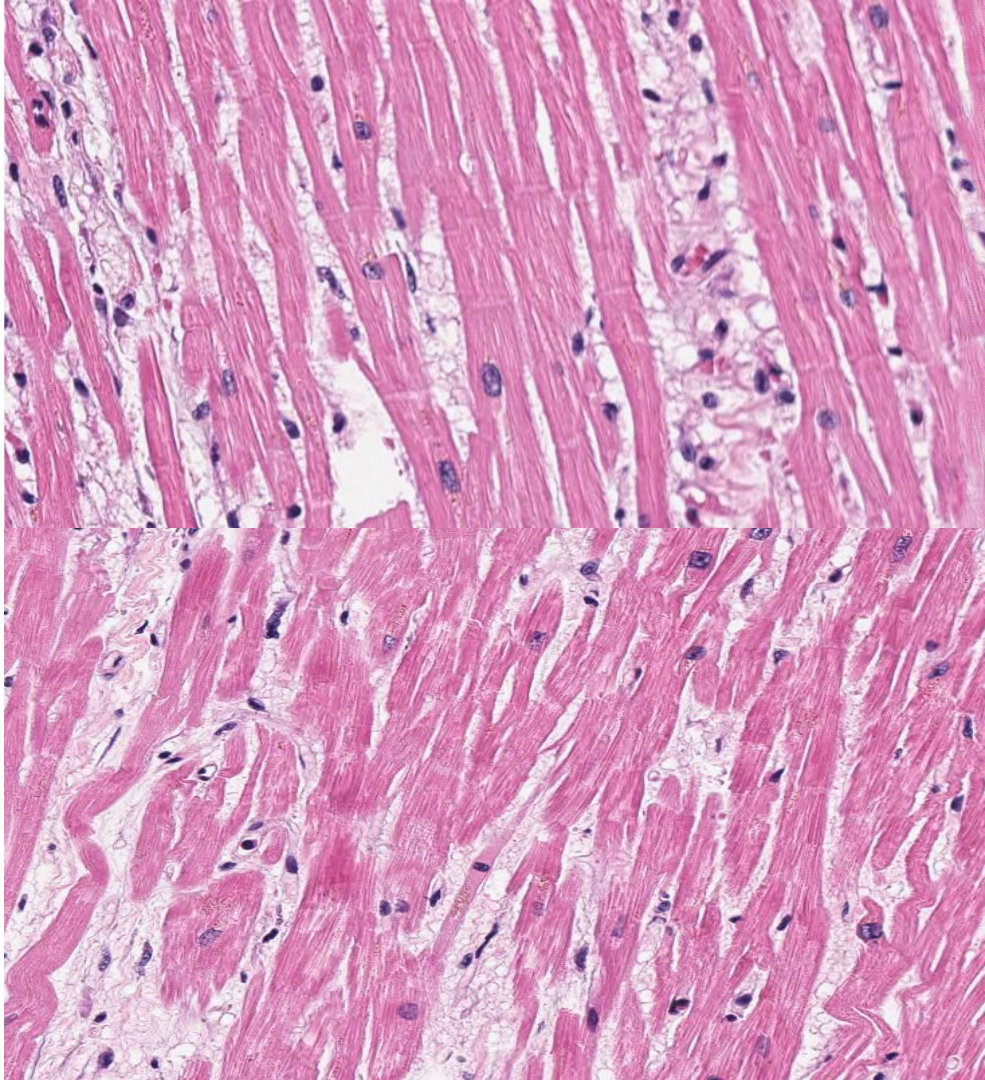
Puntuación total de 4 puntos, alto riesgo de metástasis

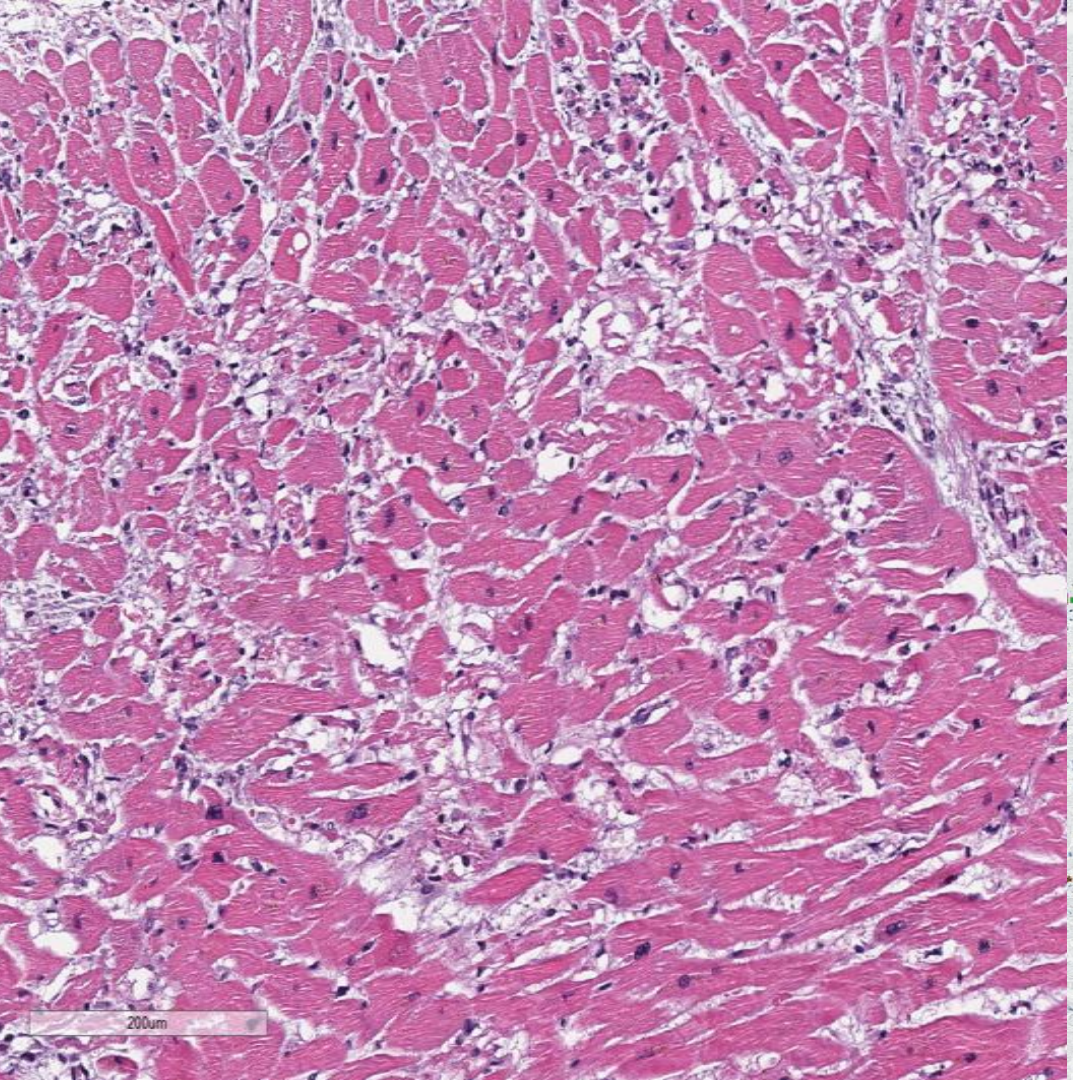
CORAZÓN



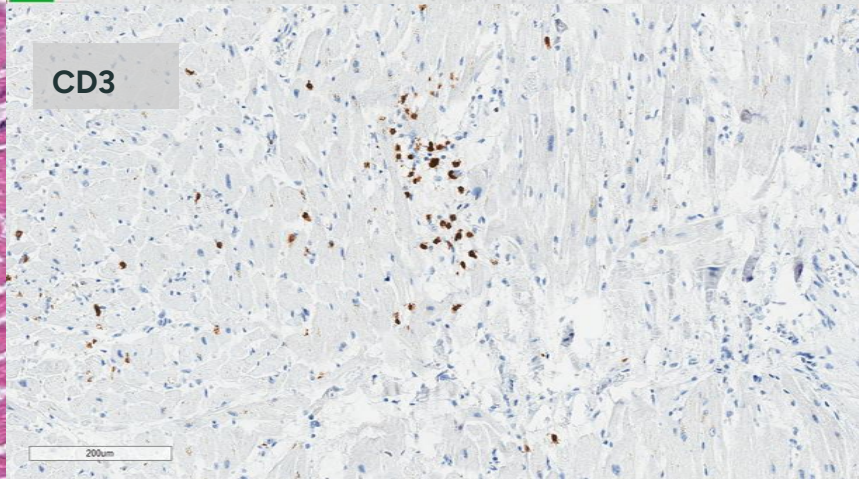


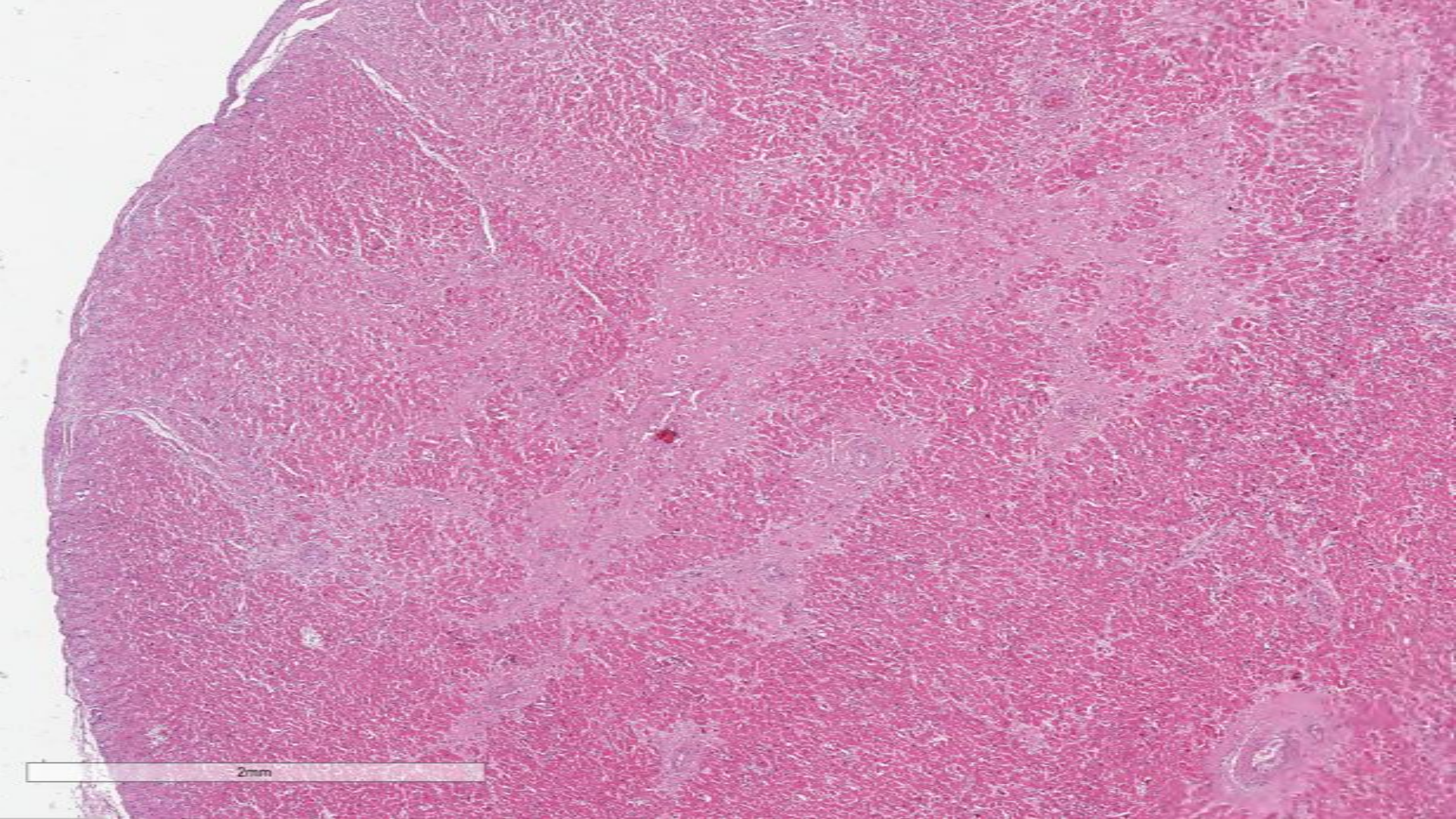


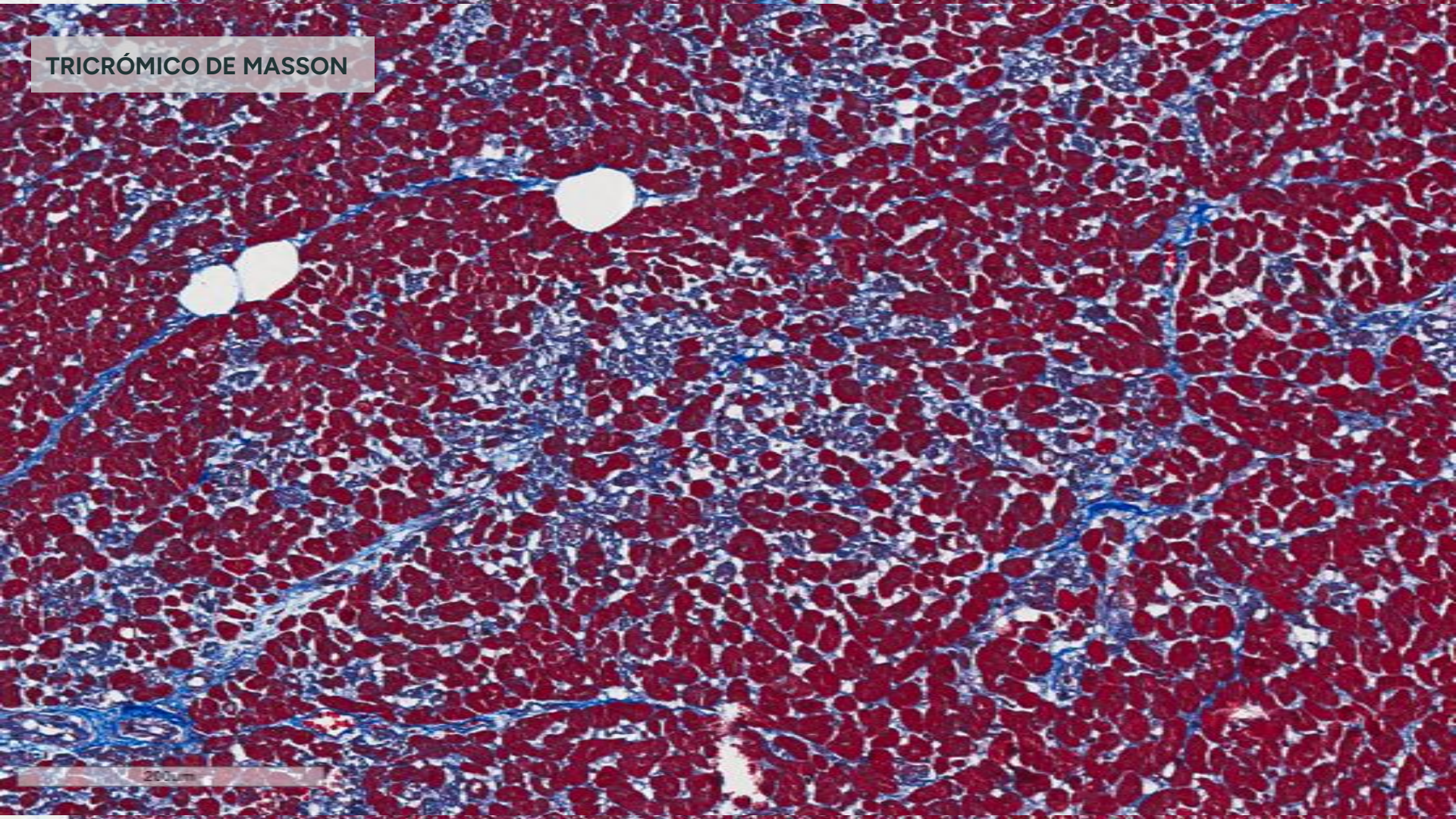



200um

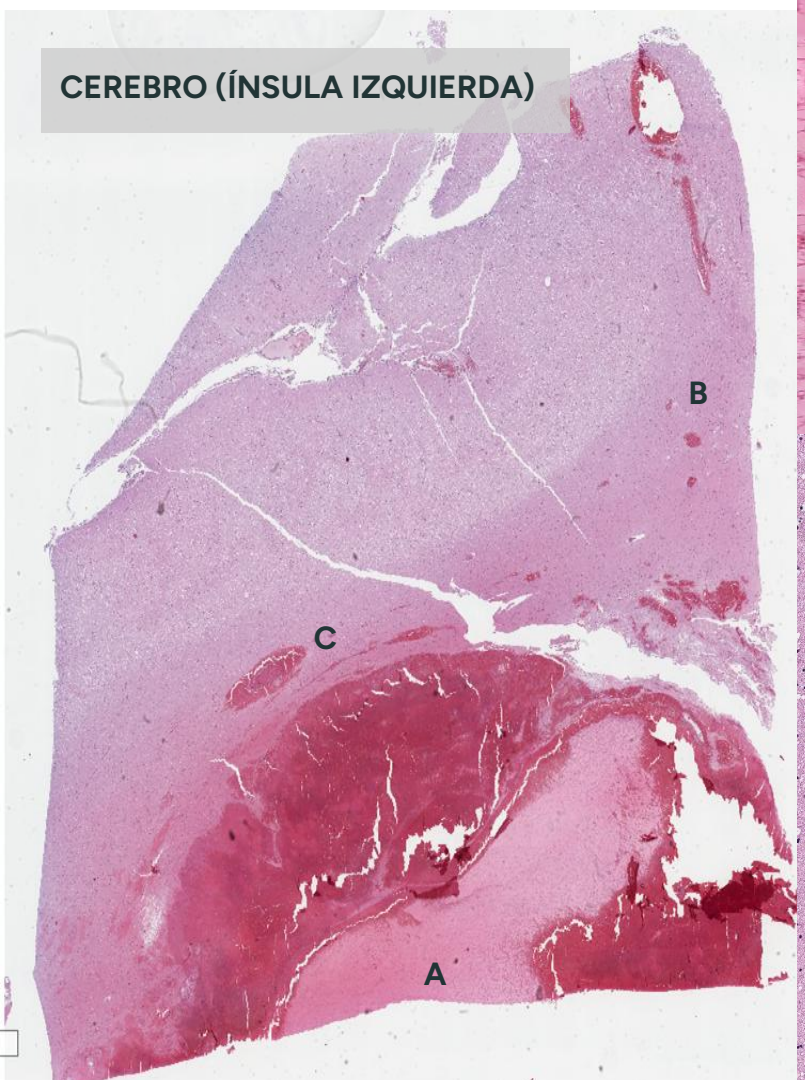

CD3
1mm

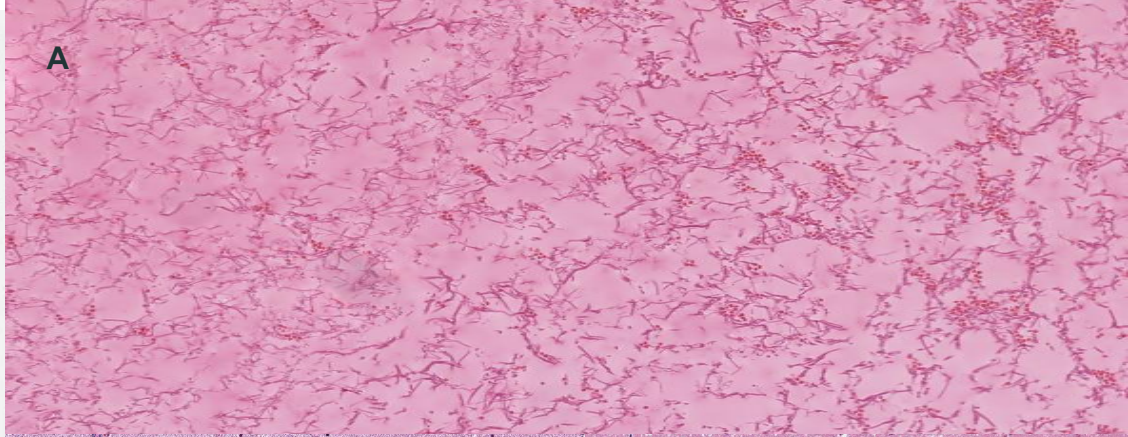

CD3
200um

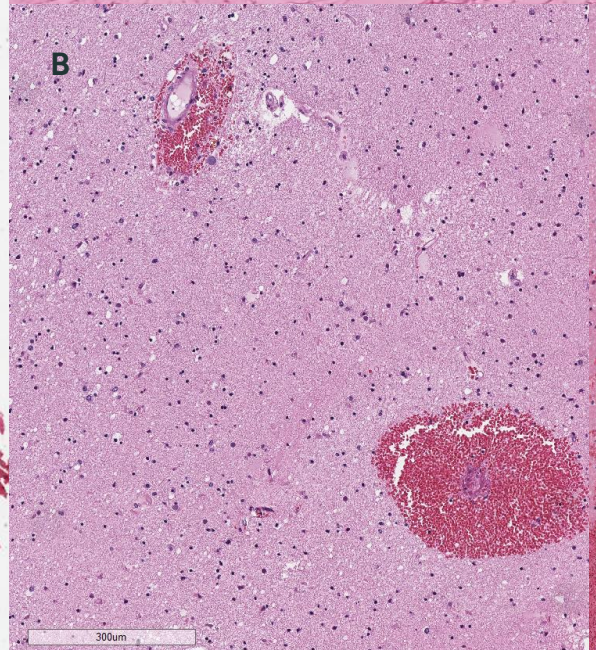

2mm

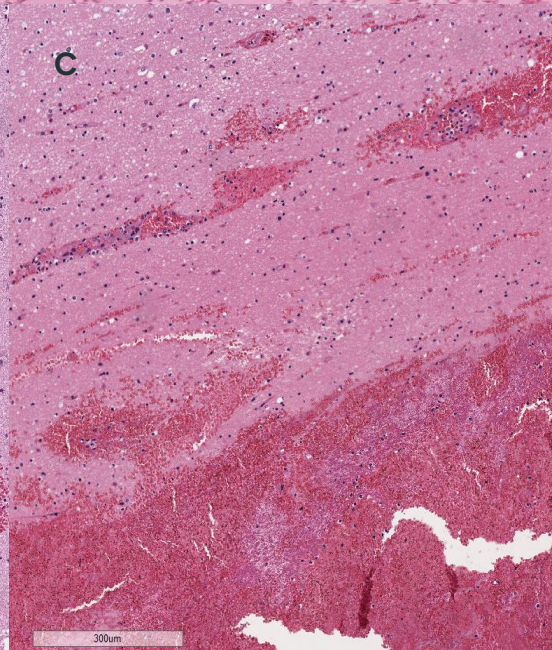

TRICRÓMICO DE MASSON
200µm

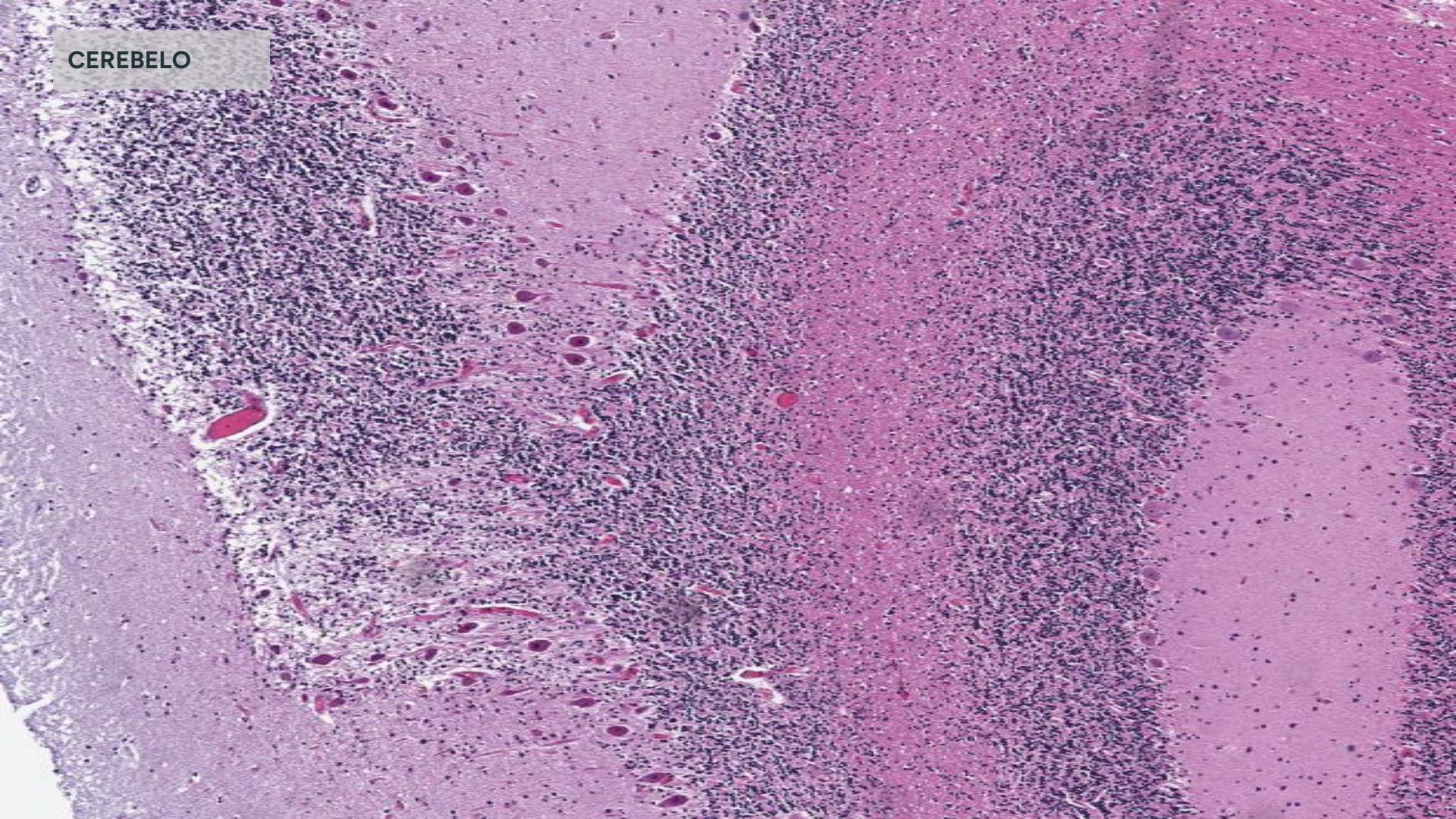
CEREBRO (ÍNSULA IZQUIERDA)










CEREBELO

Principales diagnósticos anatomopatológicos:

1. **Causa inmediata:** Hemorragia cerebral intraparenquimatosa multifocal, de distribución bilateral, supra e infratentorial, sin evidencia de infiltración tumoral.
    a. Edema cerebral difuso con herniación subfalcina hacia la derecha, uncal izquierda, transtentorial y de amígdalas cerebelosas.
2. **Causa intermedia:**
    a. Daño miocárdico secundario a estrés, asociado a infiltrado linfocitario en el contexto de toxicidad por catecolaminas.
3. **Causa básica:** Feocromocitoma de glándula suprarrenal izquierda, con riesgo aumentado de metástasis (PASS score 4 puntos)

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THE PRESENT AND FUTURE

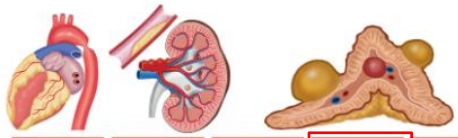
JACC STATE-OF-THE-ART REVIEW

Cardiac Phenotypes in Secondary Hypertension

JACC State-of-the-Art Review

Andrzej Januszewicz, MD, PhD,[a,*] Paolo Mulatero, MD,[b,*] Piotr Dobrowolski, MD, PhD,[a] Silvia Monticone, MD, PhD,[b] Patricia Van der Niepen, MD, PhD,[c] Pantelis Sanafidis, MD, MSc, PhD,[d] Martin Reincke, MD,[e] Emrush Rexhaj, MD,[f] Graeme Eisenhofer, PhD,[g] Magdalena Januszewicz, MD, PhD,[a,h] Alexandros Kasiakogias, MD, PhD,[i,j] Reinhold Kreutz, MD, PhD,[k] Jacques W.M. Lenders, MD, PhD,[g,l] Maria Lorenza Muiesan, MD, PhD,[m] Alexandre Persu, MD, PhD,[n] Enrico Agabiti-Rosei, MD, PhD,[o] Rodrigo Soria, MD,[f] Mateusz Śpiewak, MD, PhD,[p] Aleksander Prejbisz, MD, PhD,[a,†] Franz H. Messerli, MD[f,†]

CENTRAL ILLUSTRATION Cardiac Phenotypes in Secondary Hypertension

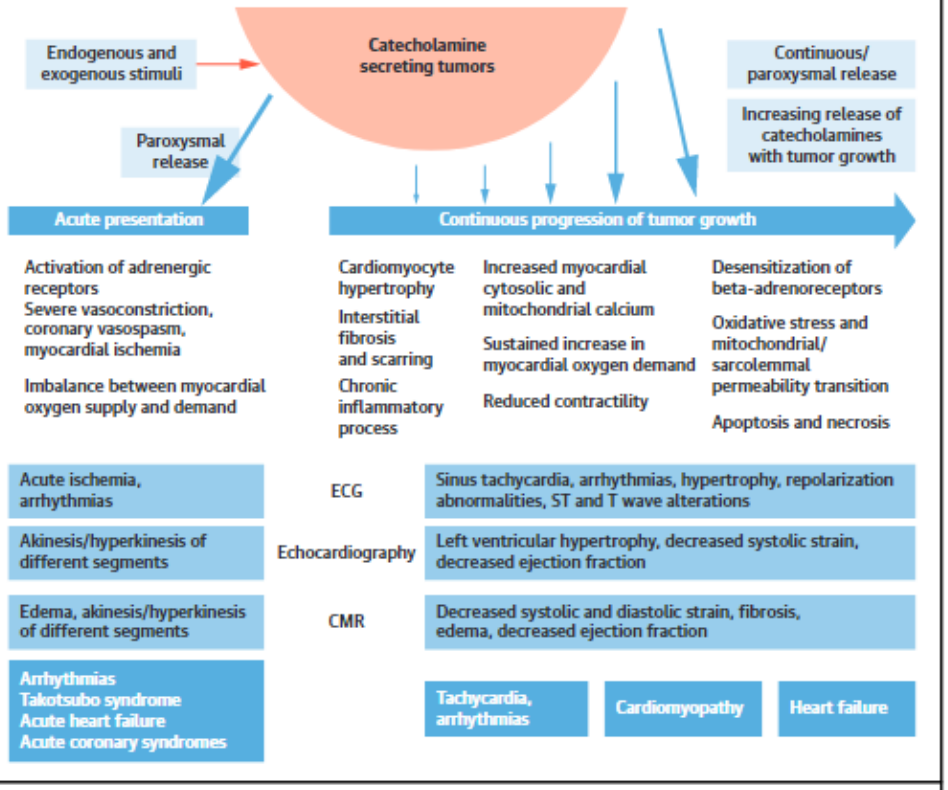


	Coartation of Aorta	Renovascular Hypertension	Primary Aldosteronism	Pheochromocytoma /Paraganglioma	Cushing Syndrome
	• Vasculopathy • Sympathetic activity	• Angiotensin II • Aldosterone • Sodium/volume retention	• Aldosterone • Sodium retention	• Catecholamines	• Cortisol
LVH	↑↑	↑ARAS ↔FMD	↑↑	↑	↑
Diastolic Function	↓	↓ARAS ↔FMD	↓↓	↔	↓
Systolic Function	↓(advanced)	-	↓↓ strain	↓↓ strain	↓
In CMR	LVH, aortic dilatation	-	LVH, fibrosis, edema	fibrosis, edema	↔fibrosis
Cardiac Events	CAD, HF	ARAS: CAD, AHF FMD: SCAD	CAD, HF, AF	TTS, hypertrophic/dilated cardiomyopathy, arrhythmias, ACS, AHF	CAD

Januszewicz A, et al. J Am Coll Cardiol. 2022;80(15):1480-1497.

For any given blood pressure elevation, patients with secondary forms of hypertension such as primary aldosteronism (PA), renovascular hypertension, pheochromocytoma/paraganglioma (PPGL), Cushing syndrome (CS), and coarctation of the aorta (CoA) display a higher prevalence of structural and functional heart damage than patients with primary hypertension. Structural changes are not limited to an increase in left ventricular mass alone, but may include inflammation, fibrosis, and necrosis/apoptosis. Interestingly, these effects are largely independent of blood pressure (BP) levels and most likely represent the direct actions of biochemical substances excessively produced in each condition. ACS = acute coronary syndrome; AF = atrial fibrillation; AHF = acute heart failure; ARAS = atherosclerotic renal artery stenosis; CAD = coronary artery disease; CMR = cardiac magnetic resonance; FMD = fibromuscular dysplasia; HF = heart failure; LVH = left ventricular hypertrophy; SCAD = spontaneous coronary artery dissection; TTS = takotsubo syndrome.

FIGURE 3 Effects of Catecholamines on the Heart in Pheochromocytoma/Paraganglioma Patients



Pheochromocytomas and paragangliomas may have severe and even fatal cardiac consequences. Acute and chronic adverse effects of catecholamines on cardiac structure and function were proposed. Various acute and chronic pathophysiological mechanisms translate into diverse cardiac presentations. In addition, individual patients may be characterized by the presence of coexisting different cardiac alterations. CMR = cardiac magnetic resonance; ECG = electrocardiography.

Síndrome de Takotsubo

Sindrome coronario agudo

Falla cardiaca aguda

Miocardiopatía por estrés

Arritmias

JOURNAL ARTICLE

Life-threatening events in patients with pheochromocytoma

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Anna Riester, Dirk Weismann, Marcus Quinkler, Urs D Lichtenauer, Sandra Sommerey Roland Halbritter, Randolph Penning, Christine Spitzweg, Jochen Schopohl, Felix Beuschlein ... Show more

European Journal of Endocrinology, Volume 173, Issue 6, Dec 2015, Pages 757–764,
https://doi.org/10.1530/EJE-15-0483
Published: 01 December 2015 **Article history** ▾

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Abstract

Objective

Pheochromocytomas are rare chromaffin cell-derived tumors causing paroxysmal episodes of headache, palpitation, sweating and hypertension. Life-threatening complications have been described in case reports and small series. Systematic analyses are not available. We took an opportunity of a large series to make a survey.

Design and methods

We analyzed records of patients diagnosed with pheochromocytomas in three geographically spread German referral centers between 2003 and 2012 (n=135).

Results

Eleven percent of the patients (ten women, five men) required in-hospital treatment on intensive care units (ICUs) due to complications caused by unsuspected pheochromocytomas. The main reasons for ICU admission were acute catecholamine induced Tako-Tsubo cardiomyopathy (n=4), myocardial infarction (n=2), acute pulmonary edema (n=2), cerebrovascular stroke (n=2), ischemic ileus (n=1), acute renal failure (n=2), and multi organ failure (n=1). One patient required extracorporeal membrane oxygenation due to a hypertensive crisis with lung edema occurring during delivery (n=1). Two patients died of refractory shock and pheochromocytomas were found postmortem. Two patients were treated by emergency surgery. Compared to pheochromocytoma patients without life-threatening events (n=120), patients with complications had a significant larger maximal tumor diameter (7.0 vs 4.5 cm, P<0.01), higher levels of catecholamines (20- vs ninefold upper limit of normal, P<0.01), and tended to be younger (42 vs 51 years, P=0.05).

Conclusion

Although pheochromocytomas are rare, they are likely to be associated with a life-threatening situation. Clinicians have to be aware of these situations and perform a timely diagnosis.

> Horm Metab Res. 2012 May;44(5):379-84. doi: 10.1055/s-0032-1306294. Epub 2012 Apr 19.

High incidence of cardiovascular complications in pheochromocytoma

T Zelinka [1], O Petrák, H Turková, R Holaj, B Strauch, M Kršek, A B Vránková, Z Musil, J Dušková, J Kubinyi, D Michalský, K Novák, J Widimský

Affiliations + expand

PMID: 22517556 DOI: 10.1055/s-0032-1306294

Table 2 Cardiovascular complications in subjects with pheochromocytoma.

Type of cardiovascular complication	Number of subjects
Arrhythmia	15*
Atrial fibrillation (paroxysmal; permanent)	9 (7;2)
Supraventricular tachycardia	3
Junctional bradycardia (pacemaker insertion)	2 (1)
Mobitz type II second degree AV block	1
Ventricular tachycardia (torsade de pointes)	2 (1)
Myocardial involvement	6
Heart failure (takotsubo-like cardiomyopathy)	5 (2)
Hypertrophic obstructive cardiomyopathy	1
Myocardial ischemia and atherosclerosis of peripheral vessels	12
NSTEMI	7
STEMI	2
Coronary artery bypass grafting	1
Significant peripheral atherosclerosis	2
Cerebrovascular complications	7
Stroke with persistent hemiparesis	1
Stroke with spontaneous recovery with preceding TIA	1
TIA	3
Subarachnoidal bleeding	1
Ischemic white matter lesions with neurological symptoms	1

AV: atrioventricular; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; TIA: transient ischemic attack
*In 2 subjects, 2 types of arrhythmia were noted

Abstract

Excess of catecholamines in pheochromocytoma is usually accompanied with classical symptoms and signs. In some cases, severe cardiovascular complications (e. g., heart failure, myocardial infarction) may occur. We performed a retrospective analysis focused on the incidence of cardiovascular complications (classified as follows: arrhythmias, myocardial involvement or ischemia and atherosclerosis, cerebrovascular impairment) before the establishment of diagnosis of pheochromocytoma among 145 subjects treated in our hospital. Cardiovascular complications occurred in 28 subjects, but these subjects did not differ significantly from subjects without complications in age, gender, body mass index, paroxysmal symptoms, symptom duration, tumor dimension, catecholamine secretory phenotype, and incidence of hypertension or diabetes mellitus. Arrhythmias occurred in 15 subjects (2 arrhythmia types in 2 subjects): atrial fibrillation in 9 subjects, supraventricular tachycardia in 3 cases, and ventricular tachycardia in 2 patients. Significant bradycardia was noted in 3 cases. Five subjects presented with heart failure with decreased systolic function (takotsubo-like cardiomyopathy found in 2 cases). One subject suffered from hypertrophic obstructive cardiomyopathy. Seven subjects presented with non-ST-segment elevation myocardial infarction, 2 patients with ST-segment myocardial infarction, and 1 subject underwent coronary artery bypass grafting. Two subjects suffered from significant peripheral atherosclerosis. Among cerebrovascular complications, transient ischemic attack was found in 3 cases, 2 subjects suffered from stroke, and subarachnoidal bleeding occurred in 1 patient. One subject suffered from diffuse neurological impairment due to multiple ischemic white matter lesions. These data show relatively high incidence of cardiovascular complications (19.3%) in subjects with pheochromocytoma. Early diagnosis is mandatory to prevent severe complications in pheochromocytoma.

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CONSENSUS PAPER

International Expert Consensus Document on Takotsubo Syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology

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Table I International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)

1. Patients show transient[a] left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).[b]
2. An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
3. Neurologic disorders (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
4. New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
5. Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
6. Significant coronary artery disease is not a contradiction in takotsubo syndrome.
7. Patients have no evidence of infectious myocarditis.[b]
8. Postmenopausal women are predominantly affected.

[a]Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.
[b]Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

Catecholamine toxicity on cardiomyocytes

Transient LV dysfunction in TTS could also result from direct effects of catecholamines on cardiomyocytes. Endomyocardial biopsies revealed occasional contraction band necrosis, which is generally observed in clinical settings of extreme catecholamine production such as pheochromocytoma or subarachnoid haemorrhage, associated with hypercontracted sarcomeres, dense eosinophilic transverse bands, and interstitial mononuclear inflammation as a reflection of myocyte injury.[38] Catecholamines can decrease myocyte viability

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Stress Cardiomyopathy Diagnosis and Treatment:

***JACC* State-of-the-Art Review**

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CARDIOMYOPATHY ASSOCIATED WITH PHEOCHROMOCYTOMA.

Pheochromocytoma is a neuroendocrine catecholamine-secreting tumor, originating from chromaffin cells within the adrenal medulla or extra-adrenal paraganglia associated with paroxysmal elevation in blood pressure, headache, sweating, palpitations, chest pain, and panic attack. Several catecholamine-induced cardiovascular complications have been described, including a cardiomyopathy with global dysfunction. Symptoms in patients with pheochromocytoma are generally chronic or subacute. Stress cardiomyopathy and pheochromocytoma may coexist, and it is easy to imagine that chronically elevated circulating catecholamines may be a risk factor for stress cardiomyopathy (85,86). To further complicate the picture, occasionally patients with pheochromocytoma may present with acute lymphocytic myocarditis and small area of focal myocardial fibrosis with DGE detected by CMR (87).

Resumen de los hallazgos microscópicos

Resumen de hallazgos microscópicos a nivel cardiaco:

- Signos de **degeneración miocitaria**
  - Ondulación y adelgazamiento de fibra miocárdica
  - Vacuolización miocitaria
  - Hipereosinofilia
  - Picnosis nuclear
- **Fibrosis** subendocárdica, periarteriolar e intersticial difuso
- Focos de **infiltrados** linfocíticos Cd3 + y macrofagos difusos.
- **Ausencia** de enfermedad coronaria significativa.
- **Ausencia** de bandas de contracción

Gracias