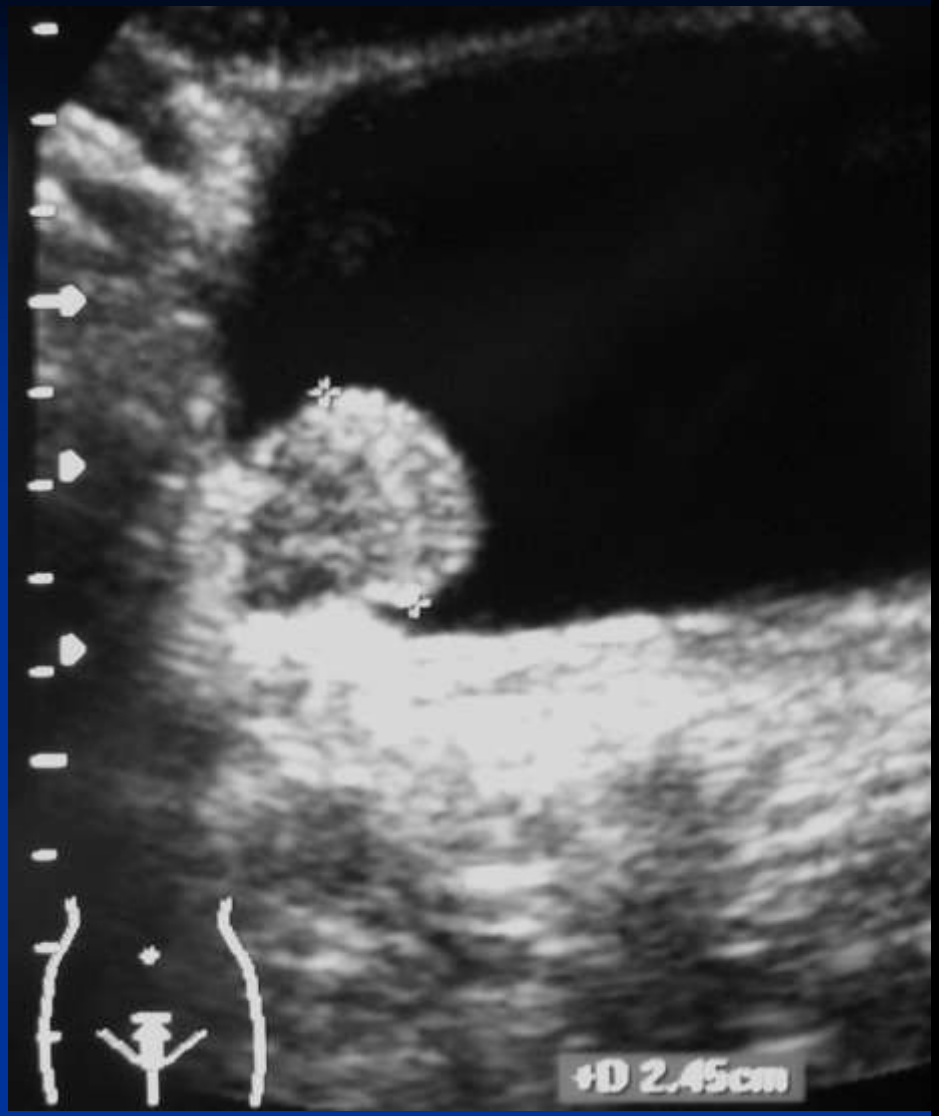
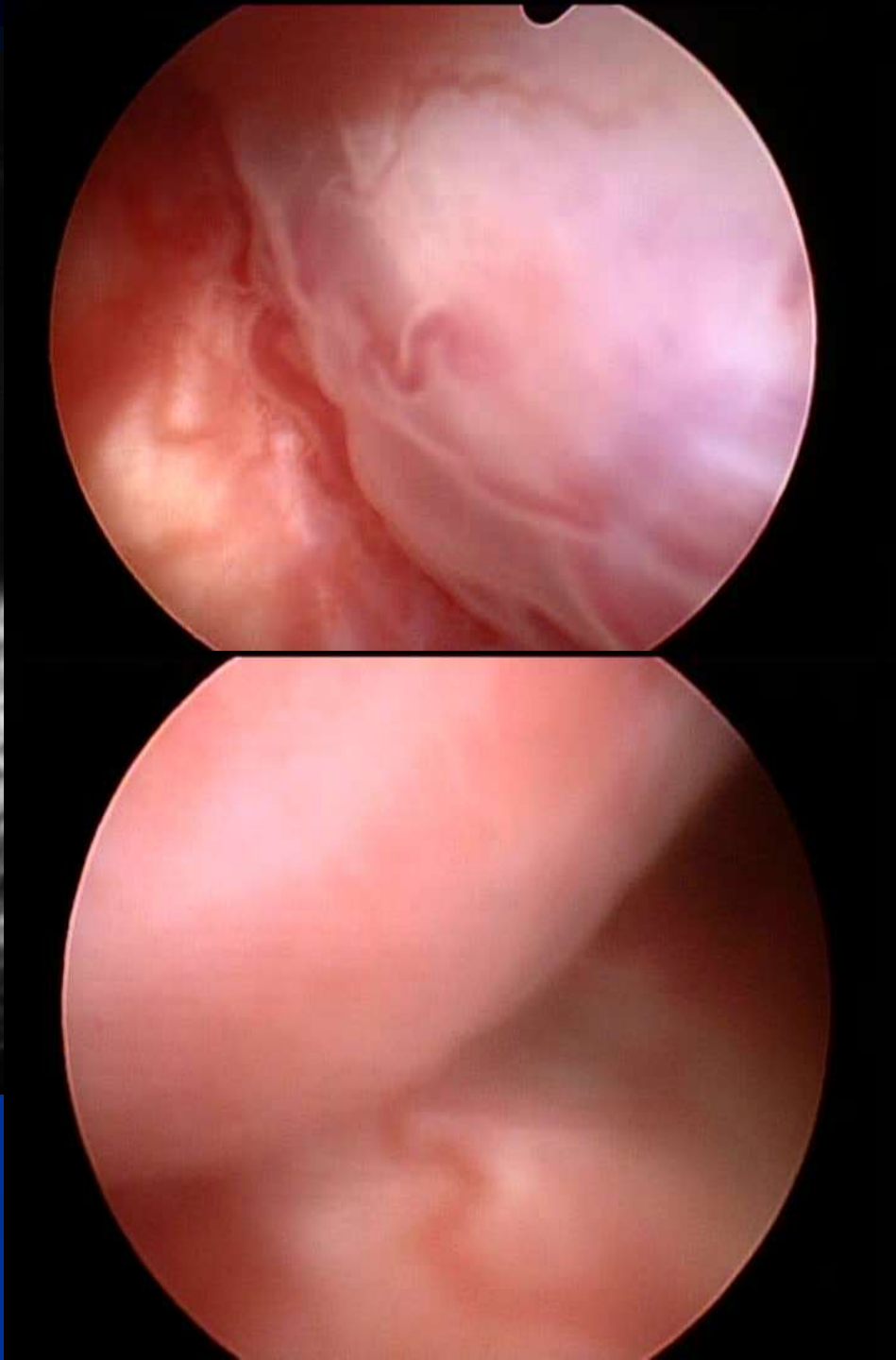
Sergio Sánchez Sosa- Puebla México

Hospital Angles Puebla

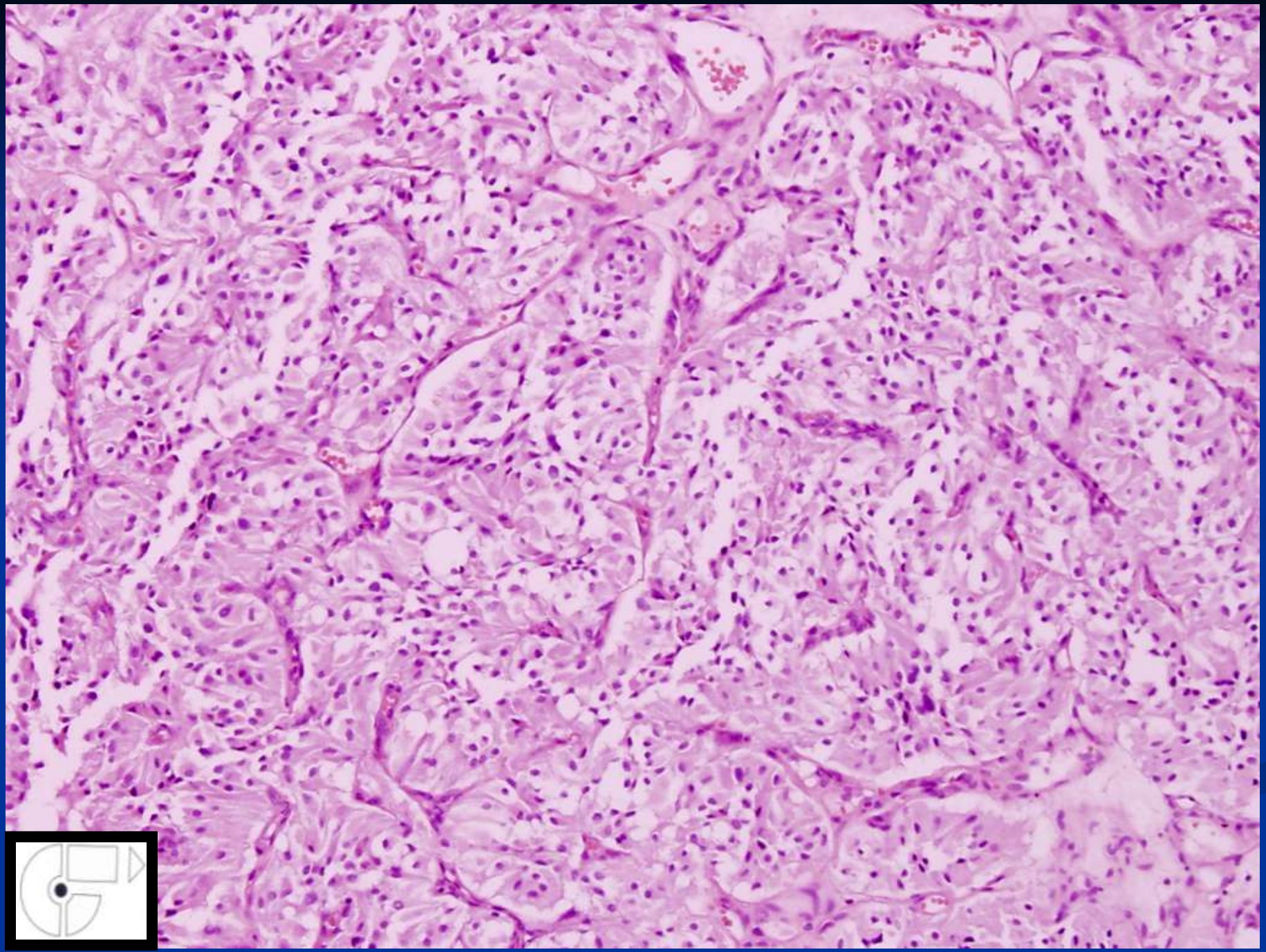
Resumen clínico

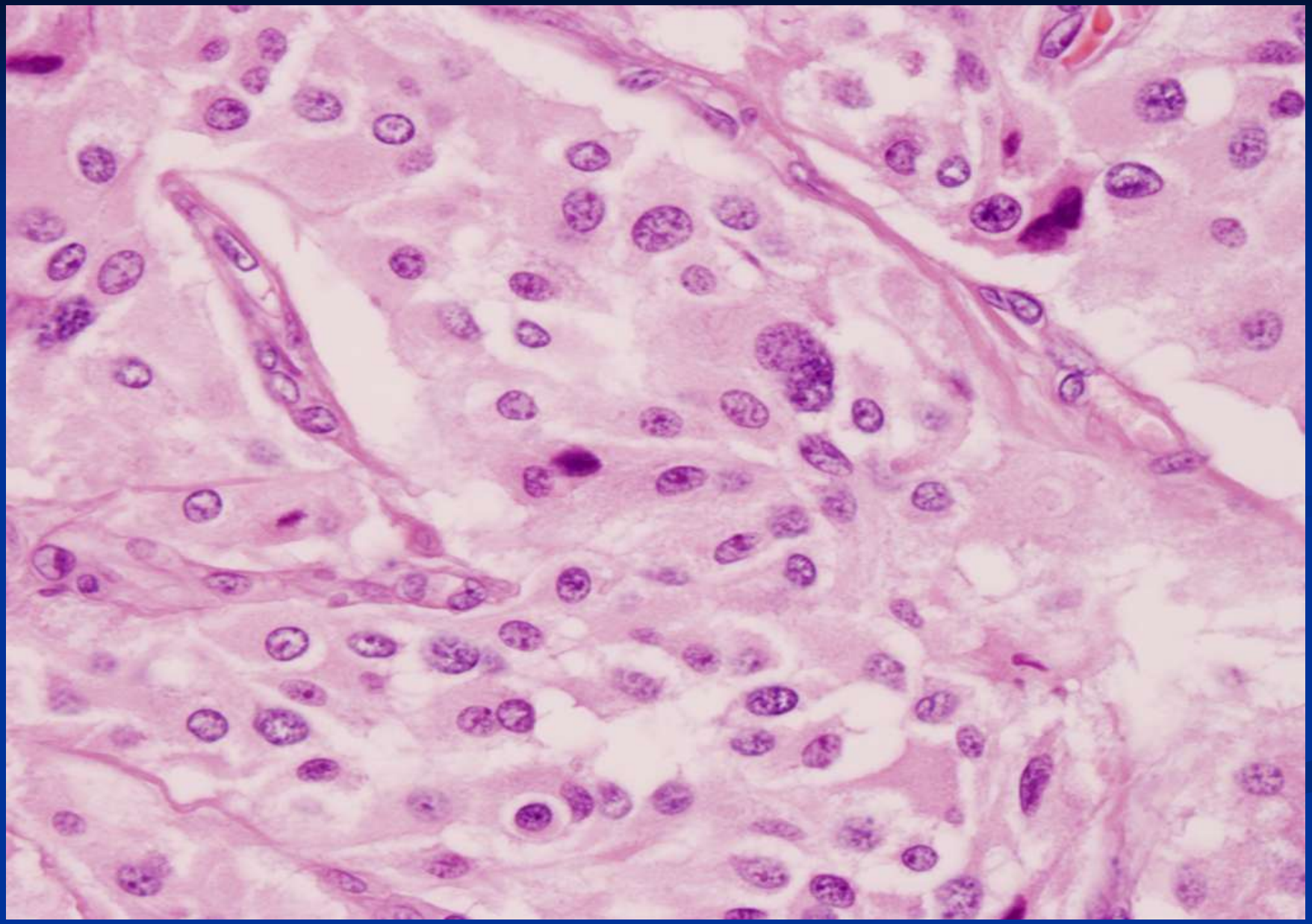
- Mujer de 16 años
- Hematuria macroscópica repentina, anemia normocítica normocrómica

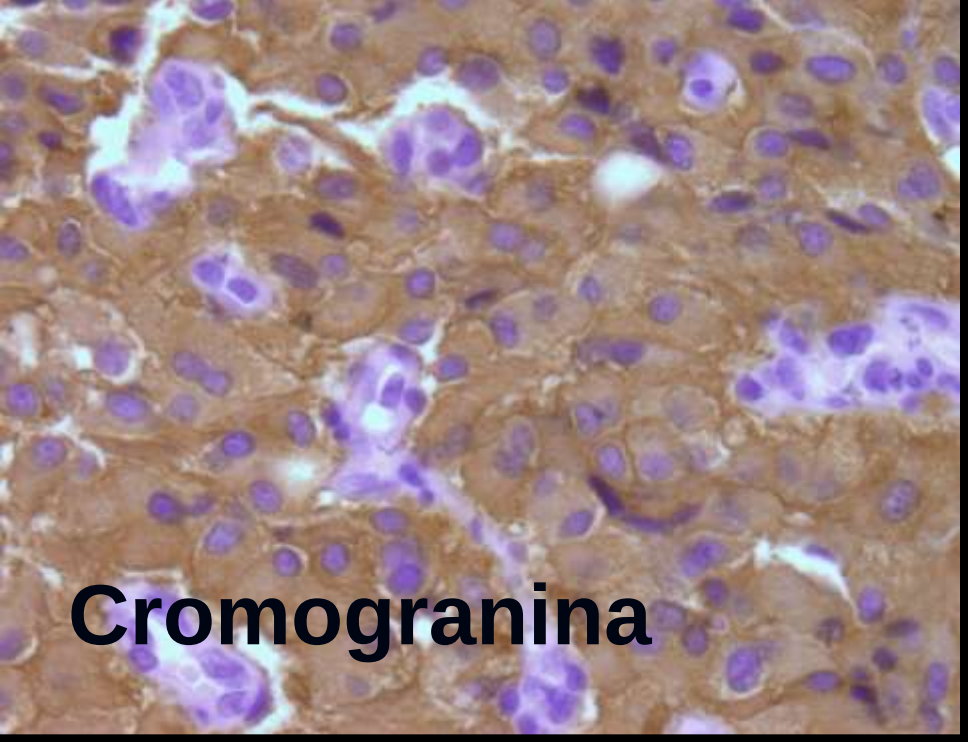


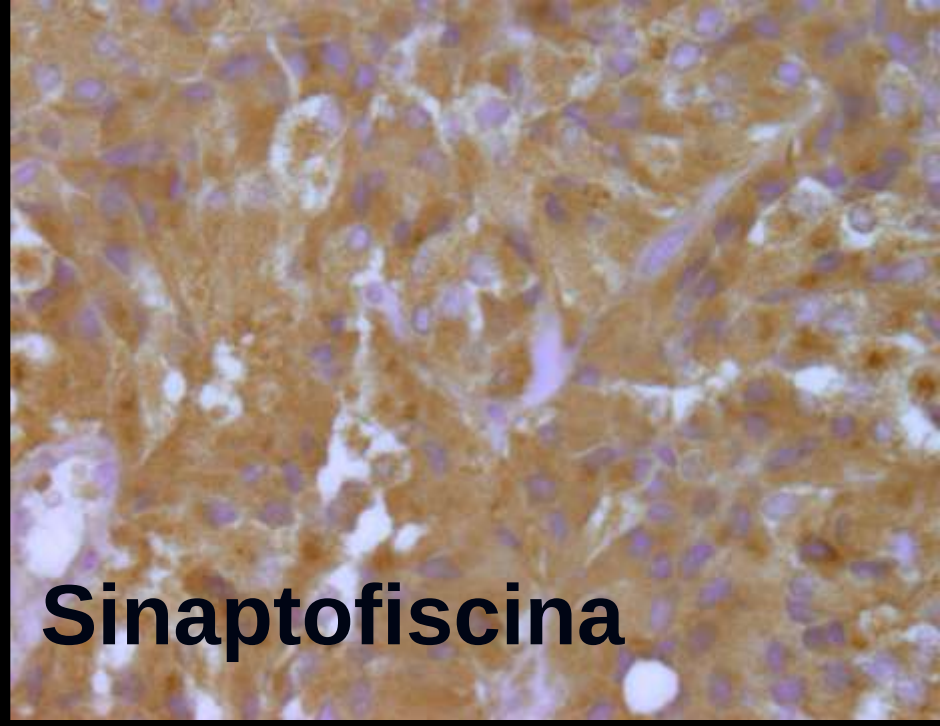


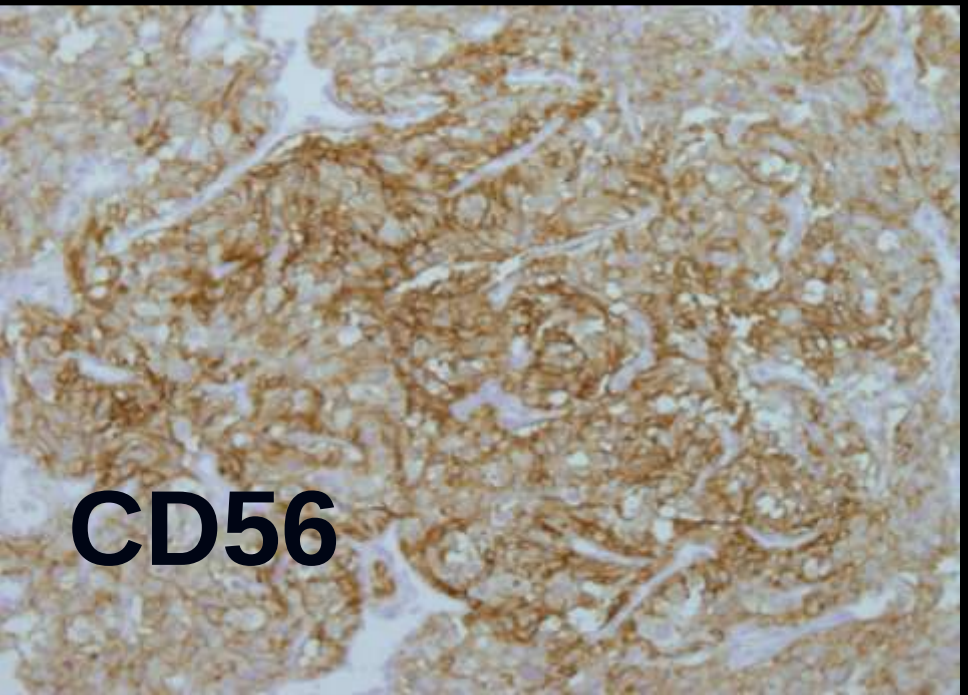
- **Lesión de polipoide, de 2.45 cm, ubicada en el piso de la vejiga urinaria.**






Cromogranina


Sinaptofiscina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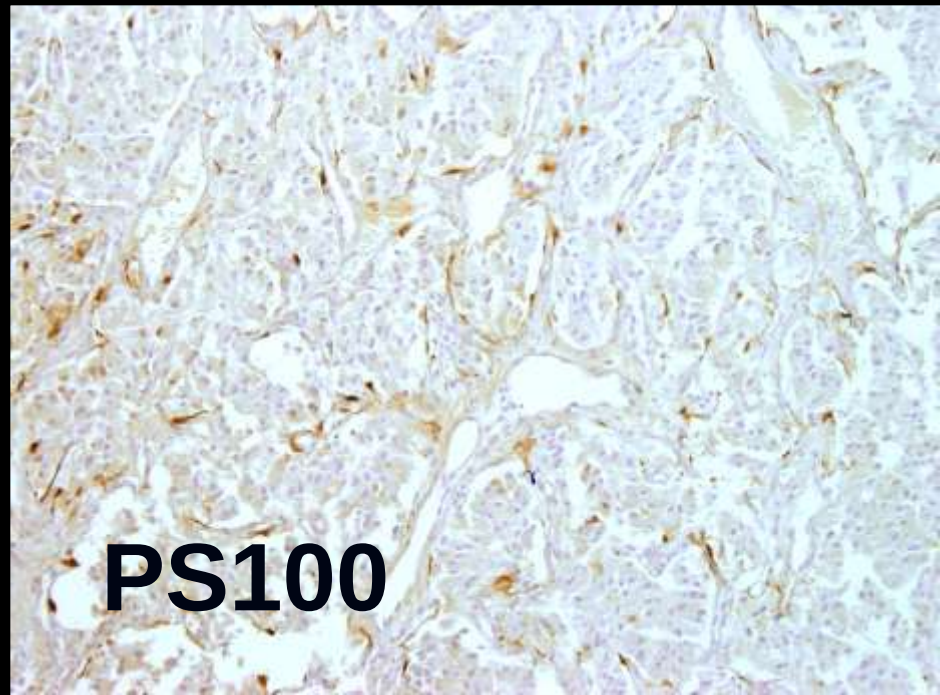
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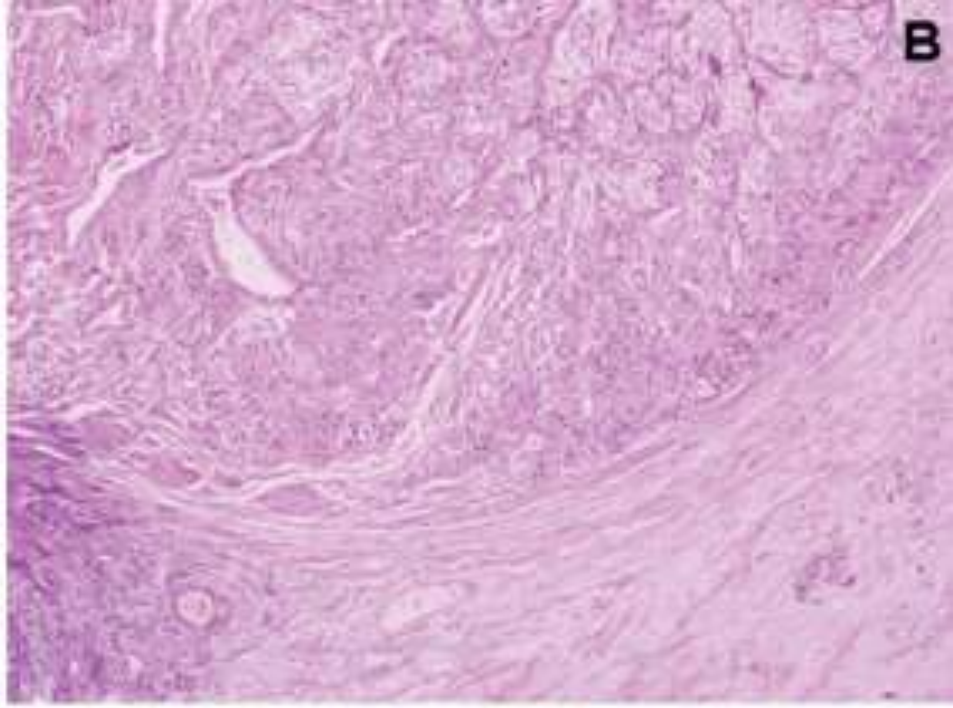
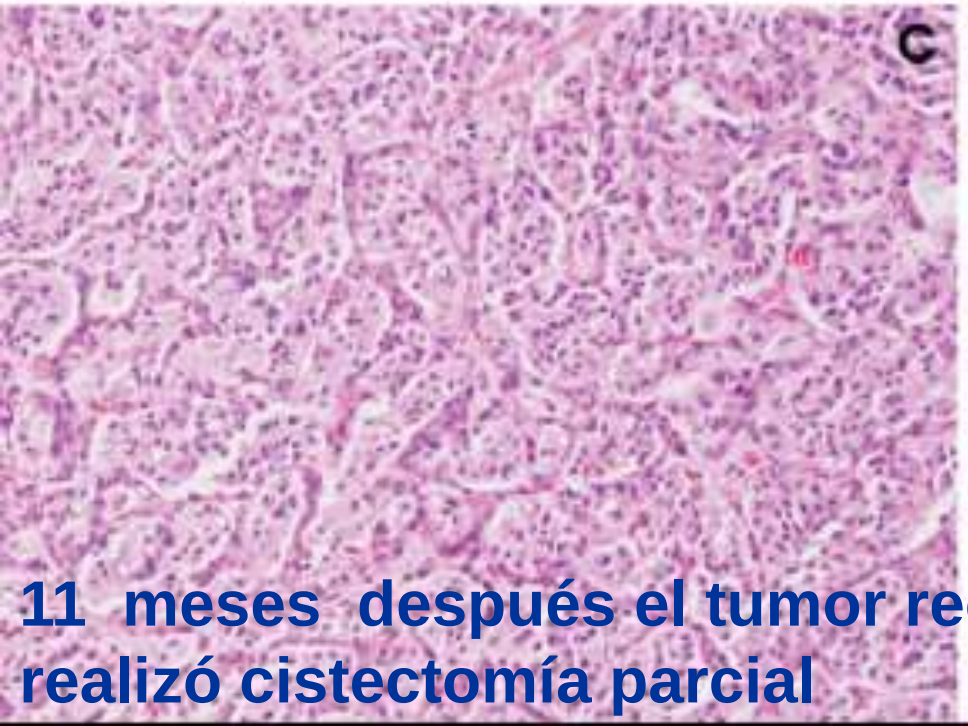
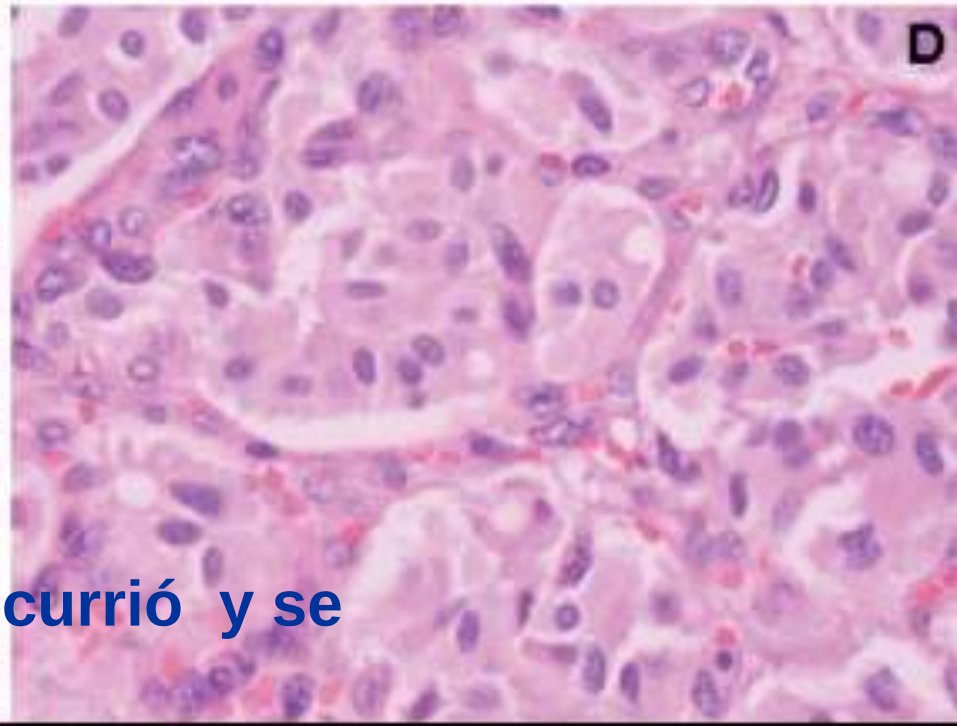
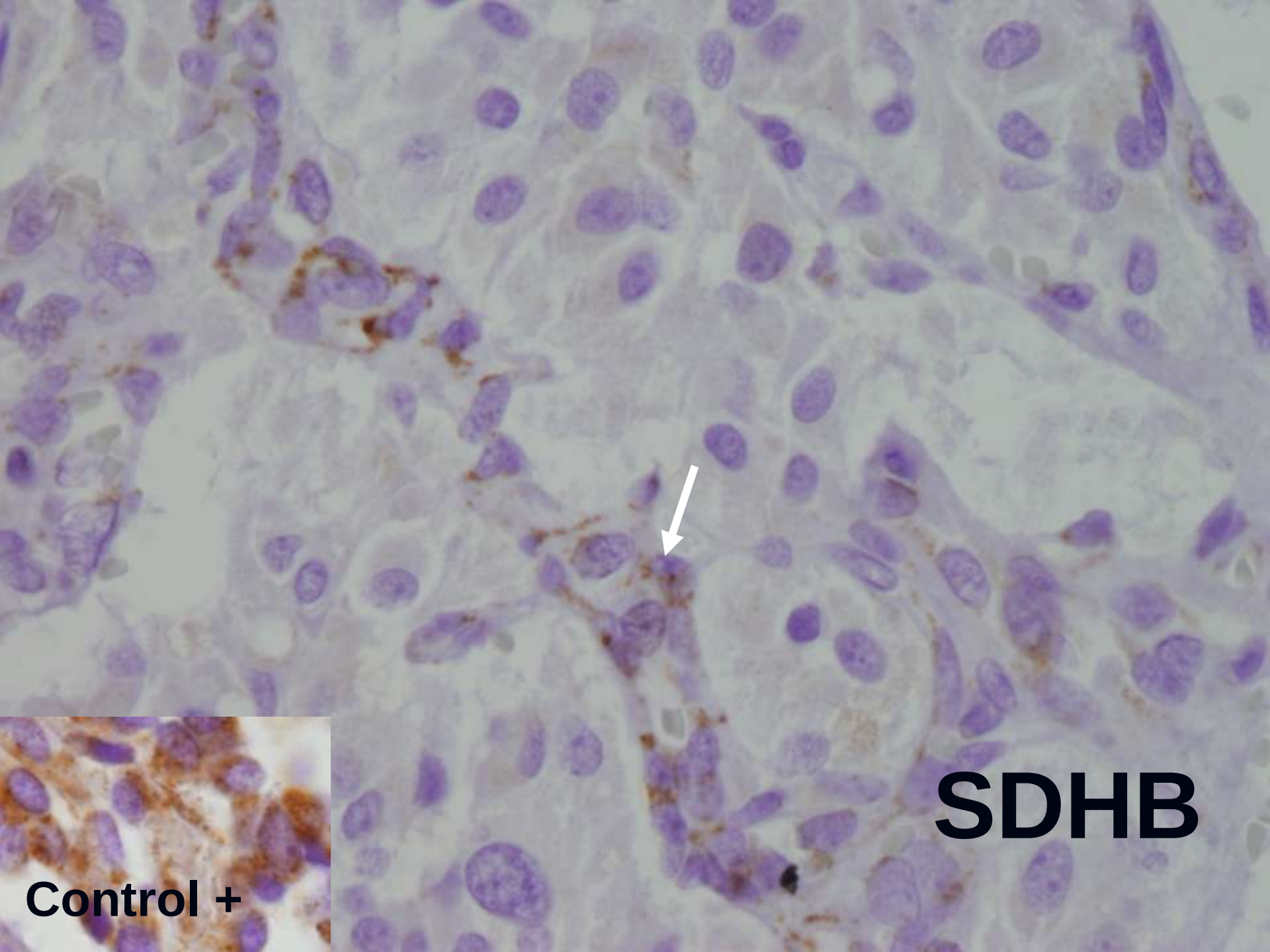






11 meses después el tumor recurrió y se realizó cistectomía parcial


SDHB
Control +

Tumores vesicales en niños

- Rabdomiosarcoma
- Neuroblastoma
- Neurofibroma
- Paraganglioma
- Metástasis

Paragangliomas vesicales

- La serie mayor (AFIP con 77 casos).
- Actualmente 220 casos informados en la literatura mundial en idioma inglés (pubmed-2010)
- Se han informado solo 11 casos en pacientes menores de 20 años de edad.

Paragangliomas vesicales

- Cefalea – Hipertensión - Palpitación
- Crisis hipertensiva con micturia, defecación, actividad sexual, eyaculación o instrumentación vesical.
- Hematuria
- Hipertensión paroxística 65%
- Actividad hormonal: 83% metanefrinas en orina elevadas
- 170 casos informados: 17 son malignos.
- Niños: 2% son malignos.

Case Journal 2009;2:8585

URINARY BLADDER PARAGANGLIOMA IN THE CHILDHOOD: A case report and review of the literature.

Olga L. Bohn[1,2*], Edgar Pardo-Castillo[2], Mariana Fuertes-Camilo[2], Nina P Rios-Luna[2], Andres Martinez[3], Sergio Sanchez-Sosa[2].

Table 1. Urinary Bladder Paraganglioma in the childhood reported in the literature

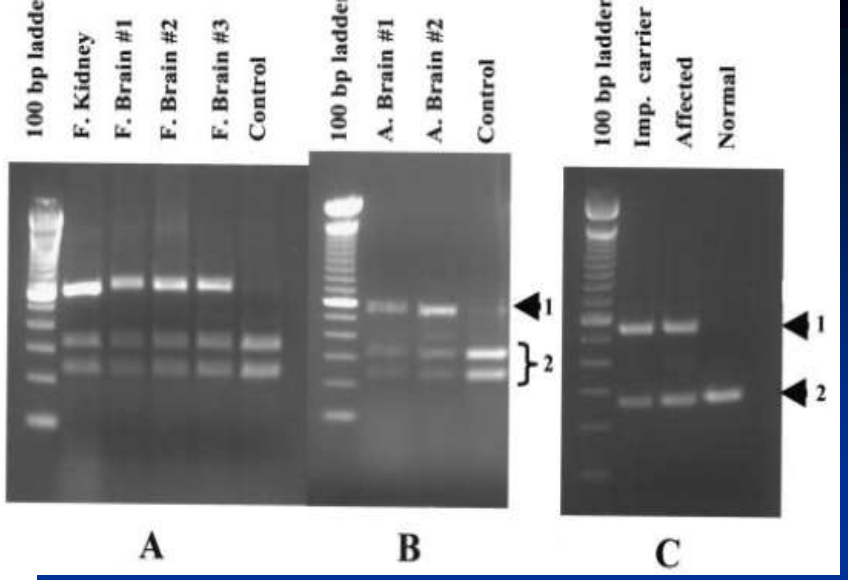
Author	Age	Gender	Location	EM/IHC	Treatment	Prognosis
Pinto et al [2]	10	Female	Trigone	Dense membrane bound granules in the cytoplasm, abundant mitochondria and rough endoplasmic reticulum. IHC: ND	Open resection and bladder reconstruction	Normal VMA, norepinephrine and dopamine levels after 6 months postoperatory
Scott et al [6]	14	Male	Left ureterovesical junction	ND	Total cystectomy, prostatectomy and lymphadenectomy	Recurrence
Higgins et al [7]	14	Male	Anterior wall	ND	Partial cystectomy, lymphadenectomy and radiotherapy	NA
Mou et al [8]	14	Female	Left posterior wall	ND	Partial cystectomy	Asymptomatic after three-month follow-up
Bissada et al [9]***	NA	NA	Bladder	ND	Partial cystectomy	Unknown
Tan et al [10]	11	NA	Bladder	ND	Partial cystectomy	Unknown
Bonacruz-Kazzi [11]	7	Male	Right ureterovesical junction	ND	Partial cystectomy, reimplation of right ureter, excision perivesical tissue and lymphadenectomy	Full recovery
Meyer et al [12]	12	Female	Anterior wall Metastasis to a lymph node	ND	Partial cystectomy, lymphadenectomy	No recurrence, two-years follow-up
Fournier et al [13]	11	Male	Anteroinferior wall	EM: Neurosecretory granules IHC: ND	Partial cystectomy	No recurrence, eighteen months follow-up
Yang FC et al [14]	16	Female	Anteroinferior wall	ND	Partial cystectomy	No recurrence
Present case	16	Female	Floor	Synaptophysin, Chromogranin and CD56, S100 (+) AE1/AE3, CK7, CK20, SDHB (-)	Transurethral resection Partial cystectomy	No recurrence, eight month follow-up.

IHC indicates immunohistochemistry; EM, electron microscopy; ND, not done; NA, not available.

PEDIAT DEV PATHOL MARZO 2011 On line

Mutations in *SDHD*, a Mitochondrial Complex II Gene, in Hereditary Paraganglioma

Bora E. Baysal,[1]* Robert E. Ferrell,[2] Joan E. Willett-Brozick,[1] Elizabeth C. Lawrence,[2] David Myssiorek,[5] Anne Bosch,[6] Andel van der Mey,[7] Peter E. M. Taschner,[6] Wendy S. Rubinstein,[3] Eugene N. Myers,[4] Charles W. Richard III,[1] Cees J. Cornelisse,[8] Peter Devilee,[6] B. Devlin[1]



Hereditary paraganglioma (PGL) is characterized by the development of benign, vascularized tumors in the head and neck. The most common tumor site is the carotid body (CB), a chemoreceptive organ that senses oxygen levels in the blood. Analysis of families carrying the *PGL1* gene, described here, revealed germ line mutations in the *SDHD* gene on chromosome 11q23. *SDHD* encodes a mitochondrial respiratory chain protein—the small subunit of cytochrome b

SCIENCE VOL 287 4 FEBRUARY 2000

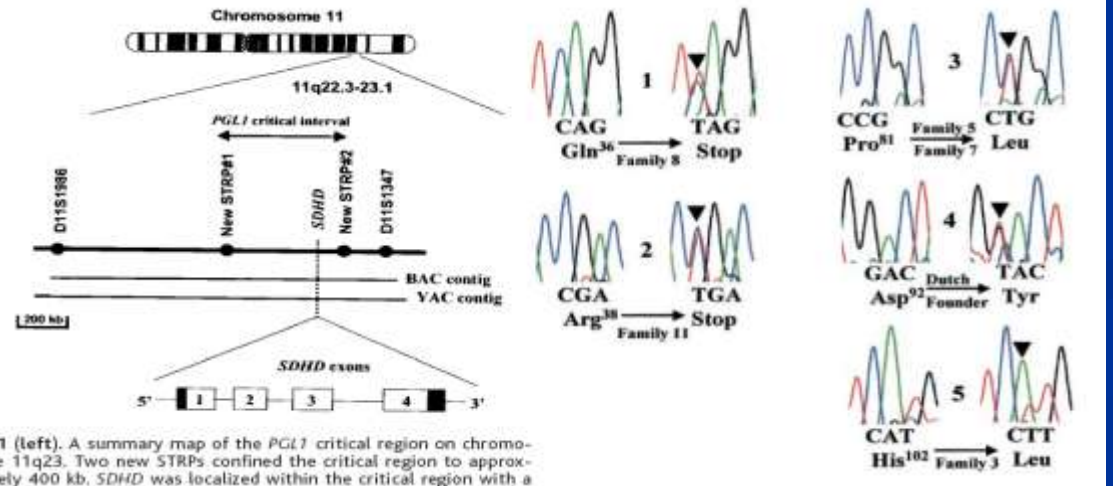


Fig. 1 (left). A summary map of the *PGL1* critical region on chromosome 11q23. Two new STRPs confined the critical region to approximately 400 kb. *SDHD* was localized within the critical region with a

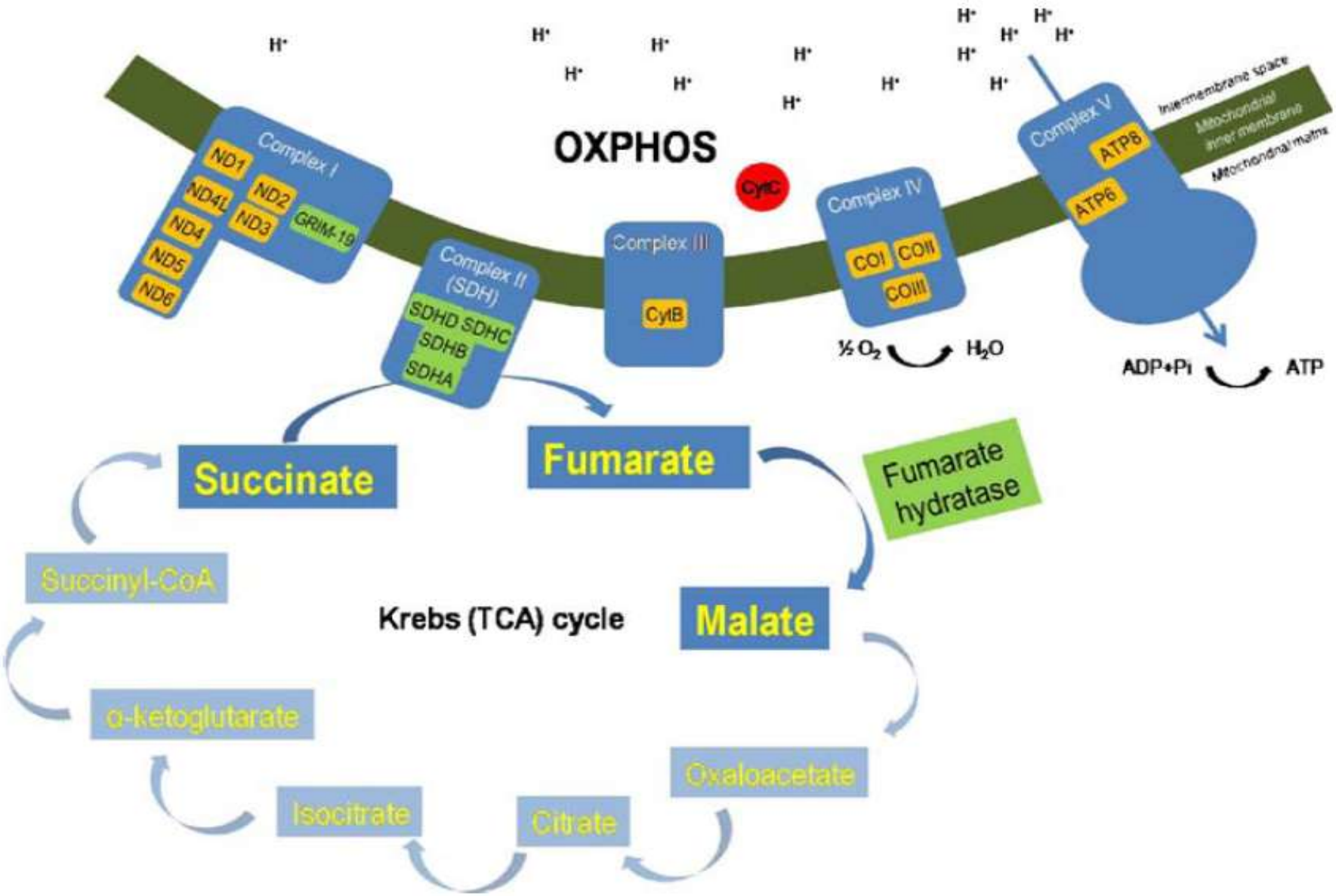
Condiciones hereditarias asociadas con Feocromocitomas y Paragangliomas

Enfermedad	Cromosoma	FEO	PGL	Génética mutación
MEN 2A&2B	10q11.2	+		RET
Von Hippel Lindau	3p26-29	+		VHL
Neurofibromatosis	17q11.2	+		NF1
S PGL 1	11q23	+/-	+	SDHD
S PGL 3	1q2		+	SDHC
S PGL 4	1p36	+/-	+	SDHB

S. Fam PGL-Feocromocitoma

Genes: SDHB, SDHC y SDHD

- Codifican 3-4 subunidades del complejo mitocondrial II; enzima succinato ubiquinona oxido-reductasa (Succinato deshidrogenasa)
- Localización: crestas mitocondriales entre la cadena de transporte de electrones aeróbica y el ciclo de ácido tricarboxilico



Ciclo de Krebs en la mitocondria y el sistema de fosforilación oxidativa
En naranja genes ADN mitocondrial que codifican proteínas OXPHOS y en verde Proteínas mitocondriales codificas en núcleo.

Nuclear genes
(GRIM-19, SDH, FH, …)

Oncocytic features

Positive feedback mechanism &
mitochondrial proliferation

Lactic acidosis,
decreased apoptosis,
activation of HIF-1α,
angiogenesis, …

Tumourigenesis

Mitochondrial genes
(Complex I, III, IV, V)

TUMOUR CELLS

Imbalance of mitochondrial electron transport
Increased ROS-production
Decreased mitochondrial ATP formation

HYPOXIA

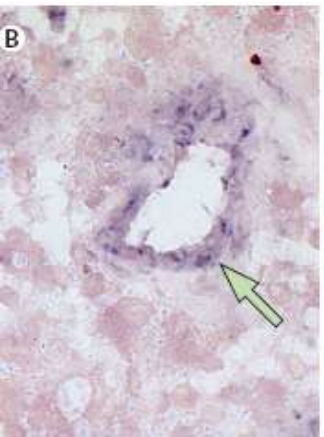
Decreased prolyl-hydroxylase activity

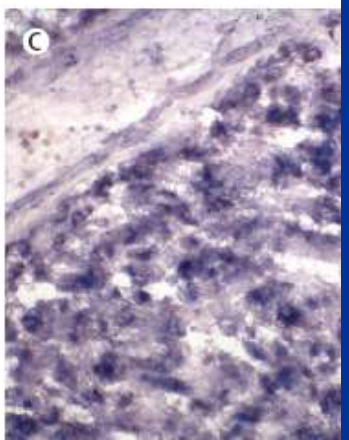
Increased HIF1α

Virchows Arch (2009) 454:481–495

An immunohistochemical procedure to detect patients with paraganglioma and phaeochromocytoma with germline *SDHB*, *SDHC*, or *SDHD* gene mutations: a retrospective and prospective analysis

Francien H van Nederveen*, José Gaal*, Judith Favier*, Esther Korpershoek, Rogier A Oldenburg, Elly M C A de Bruyn, Hein F B M Sleddens, Pieter Derkx, Julie Rivière, Hilde Dannenberg, Bart-Jeroen Petri, Paul Komminoth, Karel Pacak, Wim C J Hop, Patrick J Pollard, Massimo Mannelli, Jean-Pierre Bayley, Aurel Perren, Stephan Niemann, Albert A Verhofstad†, Adriaan P de Bruïne, Eamonn R Maher, Frédérique Tissier, Tchao Méatchi, Cécile Badoual, Jérôme Bertherat, Laurence Amar, Despoina Alataki, Eric Van Marck, Francesco Ferrau, Jerney François, Wouter W de Herder, Mark-Paul F M Vrancken Peeters, Anne van Linge, Jacques W M Lenders, Anne-Paule Gimenez-Roqueplo, Ronald R de Krijger‡, Winand N M Dinjens‡





Lancet Oncol 2009; 10: 764–71

Published Online
July 2, 2009
DOI:10.1016/S1470-2045(09)70164-0

	Number	Gene mutated	Sex (male/female)	Age range (years; mean)	Phaeochromocytoma	Paraganglioma	SDHB immunohistochemistry positive	SDHB immunohistochemistry negative
NF1	12	NF1	3/9	29–67 (44·2)	12	0	12	0
MEN2	24	*RET*	8/16	18–76 (35·6)	24	0	24	0
VHL	29	*VHL*	12/13 (4 U)	7–62 (25·6)	21 (3U)	5	29	0
Phaeochromocytoma-paraganglioma	36	*SDHB*	13/12 (11 U)	10–63 (34·6)	11 (7U)	18	0	36
Phaeochromocytoma-paraganglioma	5	*SDHC*	2/3	15–47 (30·6)	0	5	0	5
Phaeochromocytoma-paraganglioma	61	*SDHD*	25/35 (1 U)	16–72 (40·9)	5 (3U)	53	0	61
Sporadic	53	None	17/34 (2 U)	12–79 (49·3)	34 (1U)	18	47	6

NF1=neurofibromatosis type 1. MEN2=multiple endocrine neoplasia type 2. VHL=von Hippel-Lindau disease. U=unknown.

Table 1: Clinical data and SDHB immunohistochemistry related to various syndromes

Lancet Oncol 2009; 10: 764–71
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Diagnóstico de feocromocitoma paraganglioma

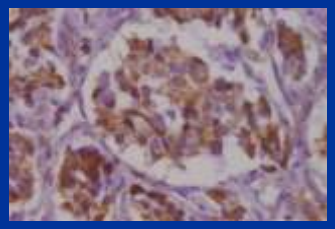
Investigar historia familiar de VHL, NIF1, MEA2 y S Feocromocitoma-Paraganglioma

Positivo

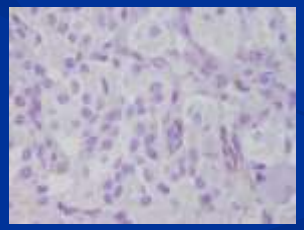
Estudio dirigido

Negativo

Estudio de Inmunohistoquímica SDHB



Investigar RET- VHL



Investigar SDHB- SDHC SDHC

PGL simpático

SDHD

PGL Parasimpático SDHB

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DOI:10.1016/S1470-2045(09)70164-0

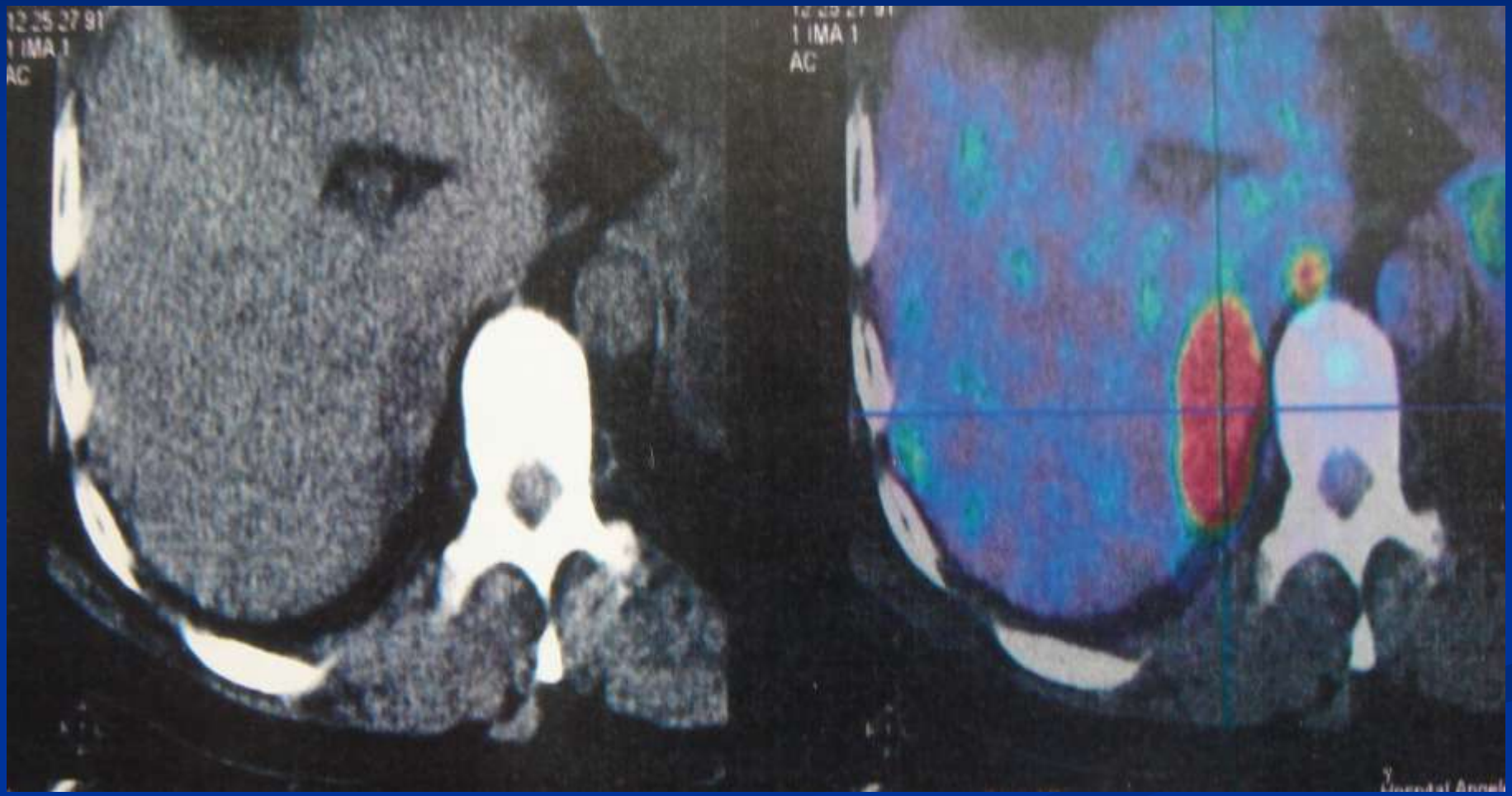
Feocromocitomas-paragangliomas con mutaciones SDH

Mutación	PGL	Cambios
SDHD	PGL1	Multifocal, enf. extra-adrenal, < 35 años, paragangliomas o feocromocitomas
SDHB	PGL4	Más común en paraganglioma simpáticos asociados con malignidad
SDHC	PGL3	Son más comunes en cabeza y cuello, generalmente benignos. Raro en adrenal.

Síndrome de feocromocitoma-paraganglioma familiar estudiados con SDHB por IHQ. Hosp. Angeles Puebla

Caso	Edad	Sexo	Localización	Dx	SDHB IHQ
1	16	fem	Vejiga	Paraganglioma	negativo
2	49	masc	Adrenal	Feocromocitoma maligno	negativo
3	29	masc	Vejiga O. Zuckerkandl	Paragangliomas (2)	negativo
4	16	masc	Para-aórtico	Paraganglioma maligno	negativo
5	68	fem	Cuerpo carotídeo	Paraganglioma	Positivo
6	60	mas	Cuerpo carotídeo	Paraganglioma	Positivo

Caso2 : Dos meses más tarde



Conclusiones

- Paraganlgiomas vesicales son poco comunes y en menores de 20 años raros
- 3 de 11 casos publicados son malignos
- 17% hormonalmente inactivos
- SDHB IHQ permite identificar casos familiares que requieren estudio genético dirigido e identificar los que tienen riesgo de comportarse en forma maligna

Gracias