CASO CLÍNICO

NEFROLOGÍA PEDIÁTRICA-HIBA

HOSPITAL ITALIANO
de Buenos Aires

LAURA PINEDA GUIO - RESIDENTE I AÑO

Tabla de Contenido

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INTRODUCCIÓN

Paciente ingresa el 29/04 , derivada desde Formosa por presentar Insuficiencia Renal Aguda, para diagnóstico y tratamiento.

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ENFERMEDAD ACTUAL

EDAD: 8 años

GÉNERO: Femenino

ANT. PERS: CBO/ Tto ambulat.

ORIGEN: Formosa

Dolor articular con predominio en rodillas y tobillos asociado a registros febriles intermitentes

Enero/2020

Decaimiento, Inapetencia y Pérdida de peso

Vómitos, Palidez y disminución del ritmo diurético

Mayo/2020

ANTECEDENTES PERSONALES

- Embarazo controlado
- Nacida a término (38 sem)
- Cesárea electiva.
- Peso Al Nacer: 3500 gr

ANTECEDENTES FAMILIARES

MADRE	PADRE	ABUELOS
Sana	Sano	—
	—	Materno/parkinson
—		Paterno/DM

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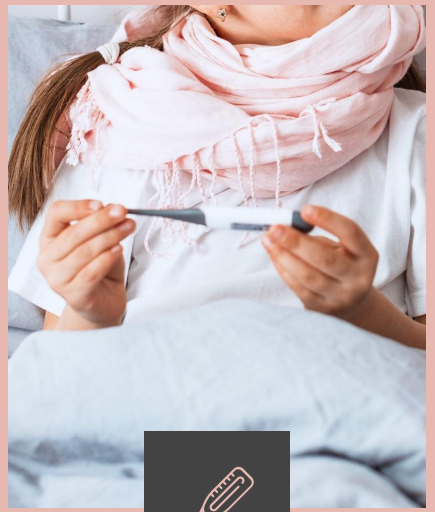
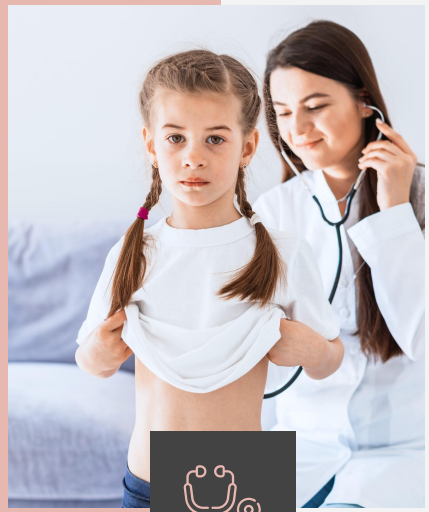
EXÁMEN FÍSICO



AFEBRIL

Palidez generalizada

Talla: 110 cm (P50-75)



CARDIOPULMONAR

Sin compromiso cardiopulmonar

Godet pretibial

ABDOMEN

Dolor en epigastrio
Catarsis positiva
Oliguria

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LABORATORIO DE INGRESO

Hto: 20% **Hb: 6.5** GB: 5643 Plaq: 258000	**Urea 170** **Cr: 6.5** Ionograma: 133/**6,1**/107 EAB: 7,35/28/**15**	**OC: Abundantes hematíes, hemoglobinuria** **Proteinuria: ++**
Serologias: HB-HC: Neg HIV: Neg ASTOS: Neg	GOT: 15 GPT:5 FAL:76 ALB:3,7 Colt: 96 LDH: 134	PT:76% KPTT:27 C3: 91 C4: 34 Ac AntiADN:Neg FAN: Neg Anti la: Neg Anti ro: Neg Anti sm: Neg ASTO: Neg
Ecocardio: Normal	Covid19:Neg	**Sideremia: <10** **Ferritina: 163**

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EVOLUCIÓN

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01-03

EVOLUCIÓN

- Hemodiálisis
- IC Reumatología
- Programación de Biopsia Renal
- 1° pulso de Metilprednisolona de 3 totales
- Se solicitan marcadores Inmunológicos

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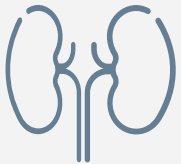
Sospecha de Vasculitis ANCA P (+)

Ic Reumato

ERS, FAN, anti ADN, C3, C4, dosaje de Inmunoglobulina G, A y M, ANCA P y C, anti PR3, anti MPO, Acs antifosfolipídos

ANCA P	1/640	**AntiMPO:>739**
ANCA C	✖	AntiPR3: <2,3
IGA-IGG-IGM	✖ 211 1320 37	ESD: 3 PCR:1,2
	Aumento de la ecogenicidad de ambos riñones RD 82 mm RI 84 mm ambos (P50)	Vit D: 33 **PTH: 387**

EVOLUCIÓN

04

- Bx Renal

TC

Engramiento mucoso
SMx
Ganglios mediast. no adenomegálicos
Atelectasia de decúbito.

Ic Oftalmo: Normal

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BIOPSIA RENAL

BIOPSIA BAJO GUIA RADIOLOGICA CON INMUNOFLUORESCENCIA

ORGANO: RIÑON
PROCEDIMIENTO: BIOPSIA

Hallazgos

MICROSCOPÍA ÓPTICA: cilindro de corteza y médula renal que incluye cortes de inclusión en parafina teñidos con hematoxilina y eosina , PAS, tricrómico de Masson y metenamina de plata
COMPARTIMIENTO GLOMERULAR:
Cantidad de glomérulos total: 14.
Cantidad de glomérulos globalmente esclerosados: 12.
Cantidad de glomérulos permeables: 2 en vías de esclerosis.
Cantidad de semilunas total: 1 celulares

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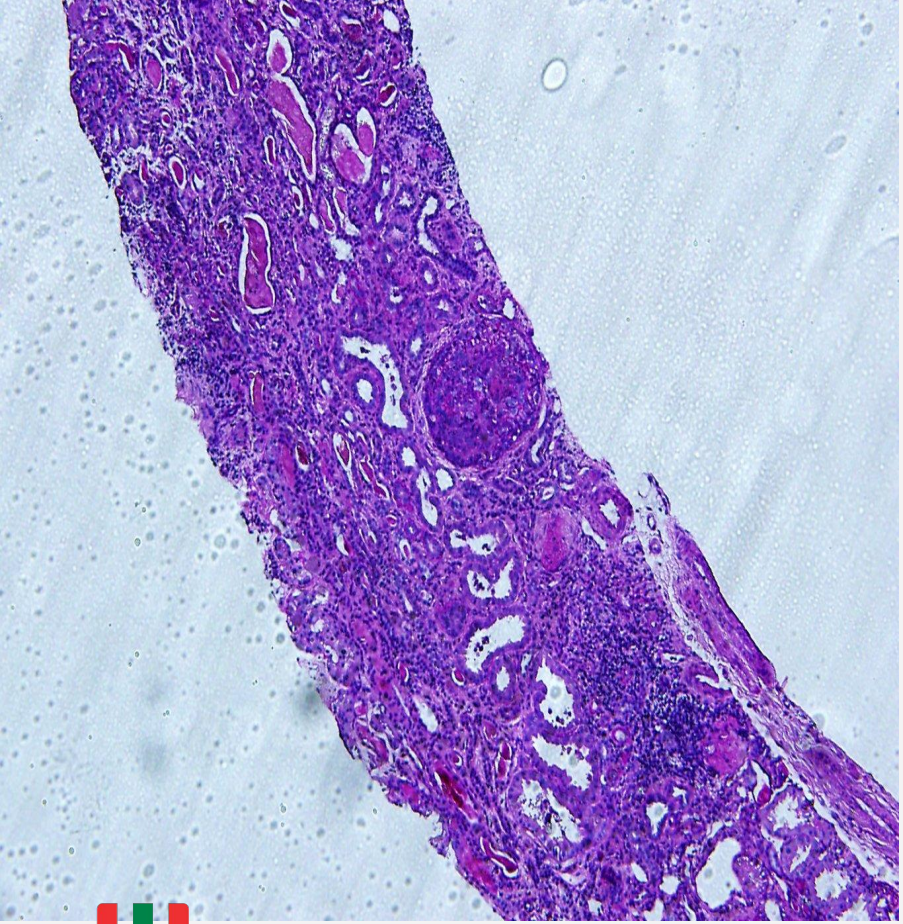

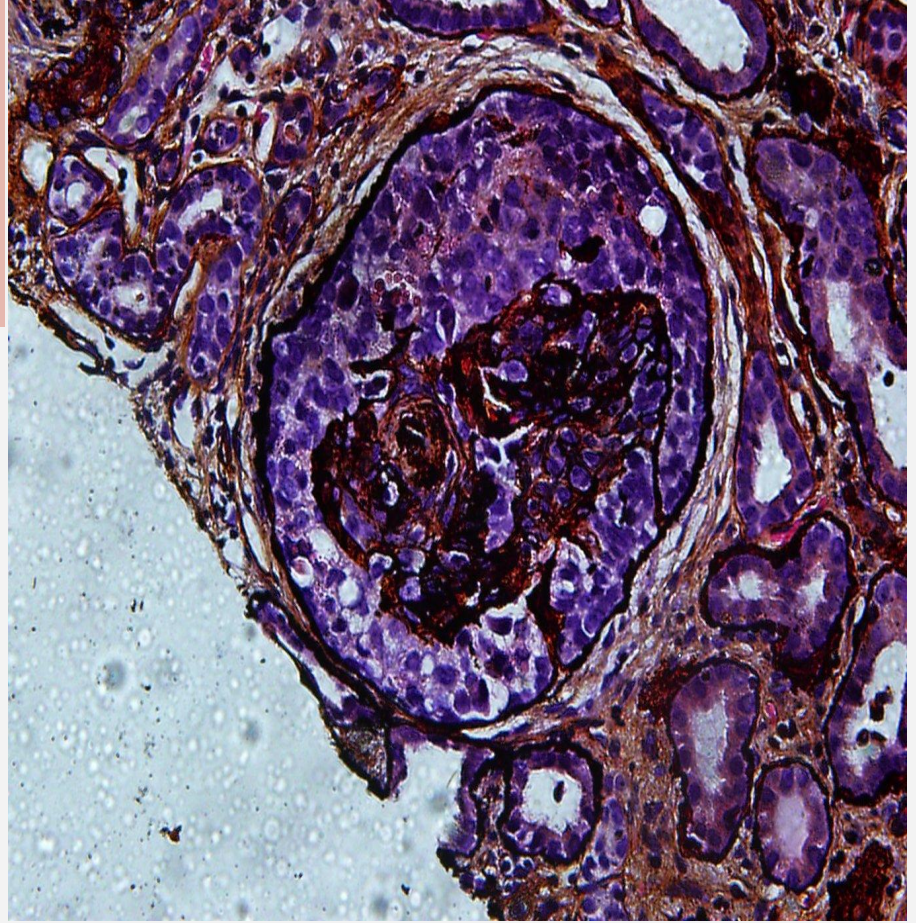

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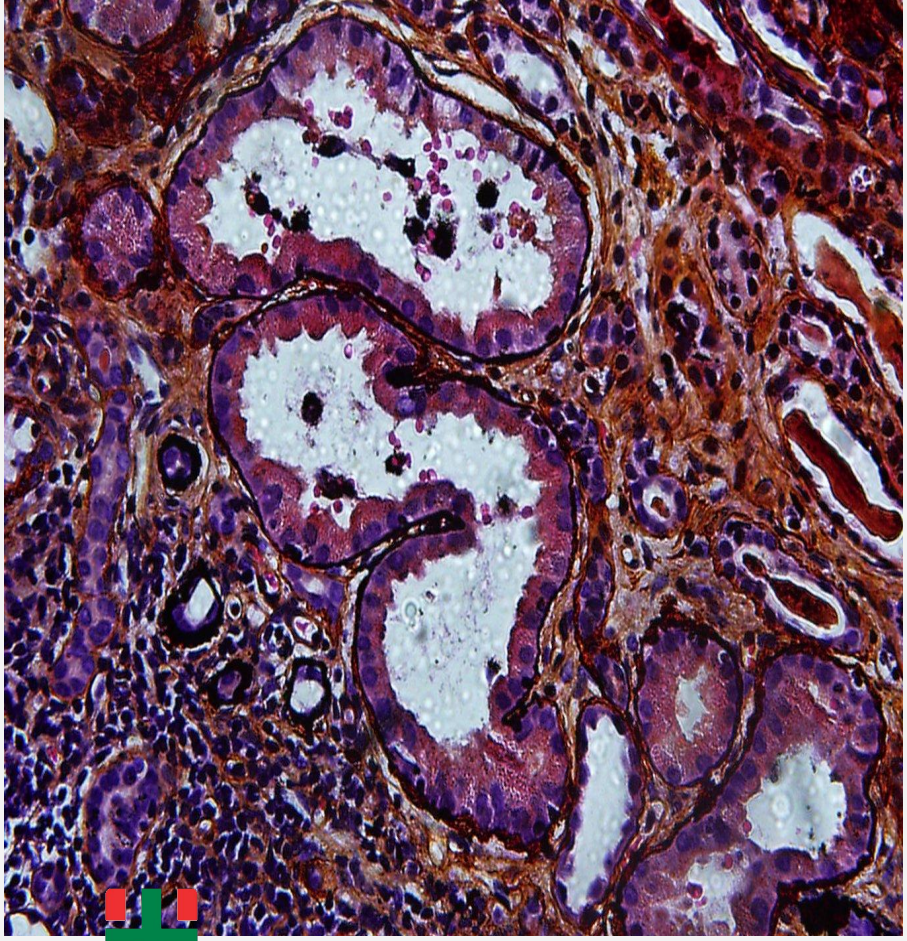

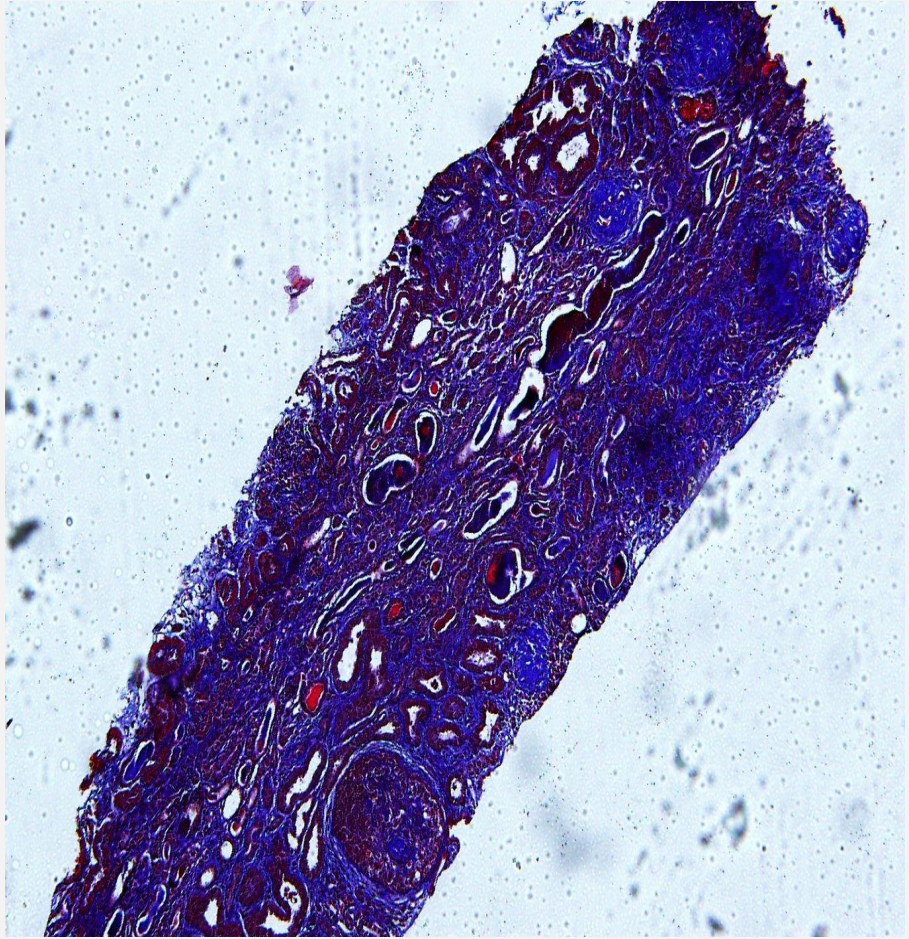

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BIOPSIA RENAL

DIAGNÓSTICO:

PROLIFERACION EXTRACAPILAR FOCAL Y GLOMERULOESCLEROSIS GLOBAL Y DIFUSA.
NEFROPATIA INTERTICIAL AGUDA DIFUSA.
NECROSIS TUBULAR AGUDA CON CILINDROS ERITROCITARIOS.

Comentarios: Teniendo en cuenta el antecedente clínico y serológico los hallazgos morfológicos podrían corresponder a una Glomerulopatia pauciinmune ANCA + en fase avanzada cicatrizal.

INMUNOFLUORESCENCIA.

Cantidad de glomérulos permeables: 6 glomerulos globalmente esclerosados.
IgG , IgA, C1q, Cadenas livianas Kappa y Cadenas livianas Lambda Negativo.
IgM , C3 y Fibrinogeno positivo inespecifico en áreas de esclerosis.

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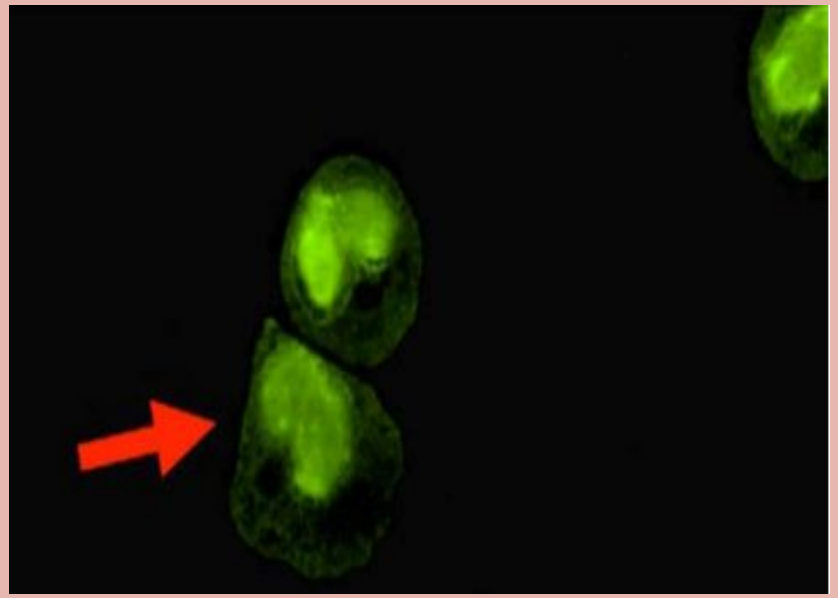
DIAGNÓSTICO

GLOMERULOPATIA PAUCIINMUNE (ANCAP+)

Vasculitis ANCA P+
Sin otro compromiso sistémico.



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EVOLUCIÓN Y TRATAMIENTO

07...

1. Continúa con Meprednisona 20 mg/día
2. Se agrega Azatioprina a TTO. (25 mg/dia)
3. Ingresa a programa de ERCT, Diálisis Peritoneal

14

Hto: 28% Hb: 9,4 GB: 11500 N73% Plaq: 254500	C3: 68 C4: 20 FAN: Neg **ANCA P: 1/640** PCR:0,8

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REINGRESO

Un día posterior al egreso, reconsulta a la Central de Emergencias por **hemorragia digestiva baja.**

Ingresa hemodinámicamente estable y en buen estado general.
Presentó en el laboratorio **caída del HTO de 4 puntos con respecto al día previo**.

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EVOLUCIÓN

ECO ABDOMINAL
NORMAL

RX DE ABDOMEN
NORMAL

2° EPISODIO DE PROCTORRAGIA

Caída de HTO <20 por lo que requiere TGR

ENDOSCOPIA DIGESTIVA ALTA Y BAJA

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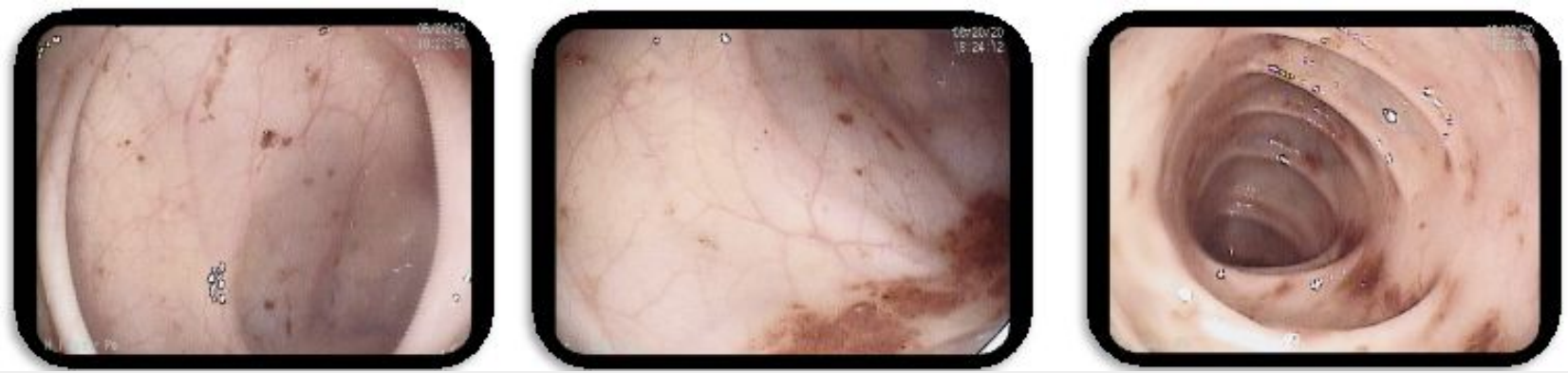
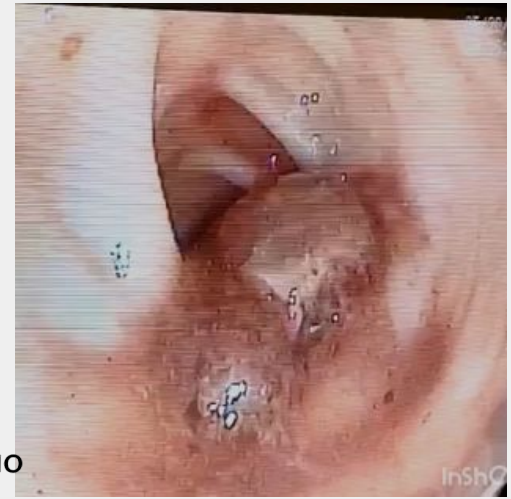
VIDEOENDOSCOPIA DIGESTIVA BAJA





Lesiones vasculares de 3-5 mm en forma parcheada en toda la mucosa evaluada

A 55 cm de margen anal hematoma que ocupa el 50% de la luz intestinal.

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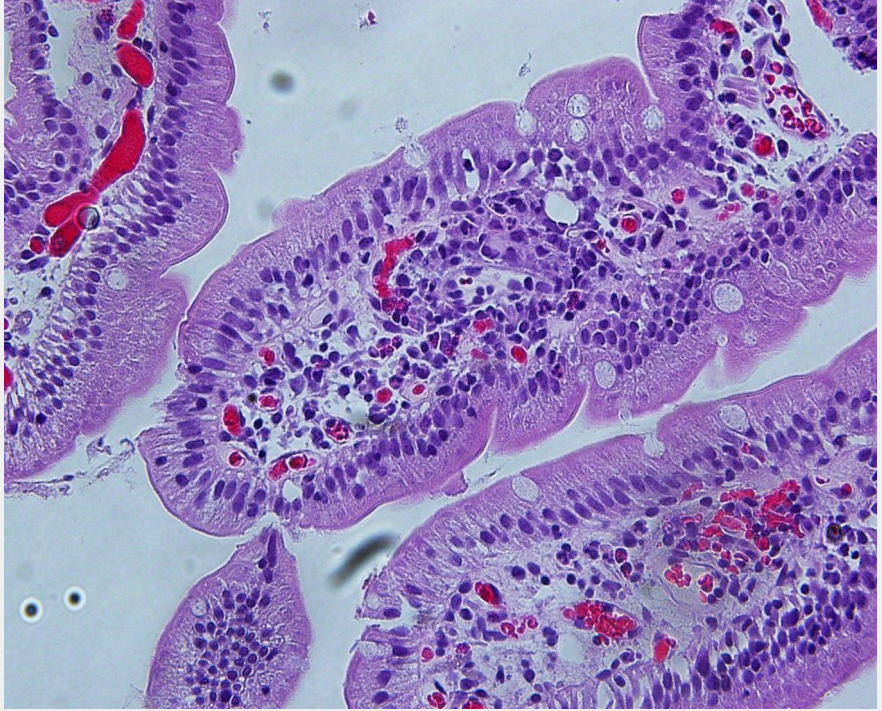
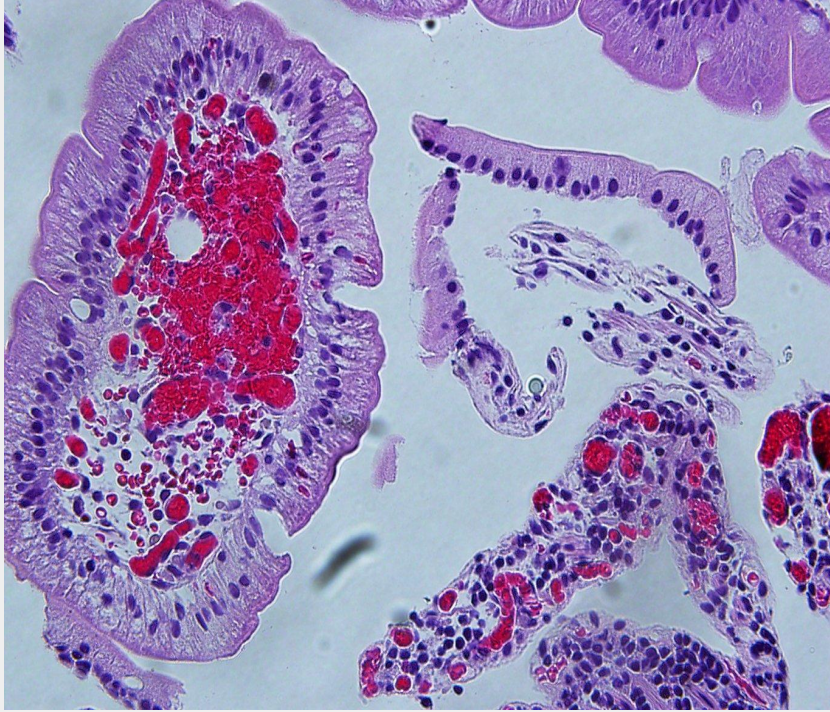
BIOPSIA INTESTINAL





Anatomía patológica de biopsia intestinal: *Vasculitis focal en vasos capilares de duodeno y hallazgo de un foco sospechoso de inflamación perivascular con eosinófilos en mucosa colónica*

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DIAGNÓSTICO

VASCULITIS ANCA P ACTIVA CON COMPROMISO EXTRARRENAL

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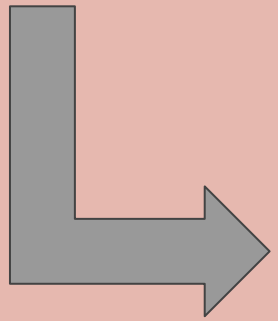
TRATAMIENTO

NUEVO PLAN TERAPEUTICO:

- ➔ 3 pulsos más de Metilprednisolona + Ciclofosfamida 6 ciclos
- ➔ Suspendió Azatioprina.



Disminución de los títulos:

(ANCA P) 1/20 (para previo de 1/640)
(ANTI MPO): 19.4 (para previo > 740)

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DISCUSIÓN

VASCULITIS

- Trastornos que tienen en común un proceso inflamatorio, eventualmente necrótico , que compromete la pared de los vasos (arterias, venas, capilares) de cualquier tamaño

- La inflamación conduce a daño de órgano blanco

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CLASIFICACIÒN EULAR/PRES 2008

EULAR/PRINTO/PRES 2008 classification scheme

Predominately large vessel
Takayasu arteritis
Predominately medium-sized vessel
Childhood polyarteritis nodosa
Cutaneous polyarteritis nodosa
Kawasaki disease
Predominately small vessel
Granulomatous
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)
Granulomatosis with polyangiitis (Wegener's)
Nongranulomatous
Microscopic polyangiitis
IgA vasculitis (Henoch-Schönlein purpura)
Isolated cutaneous leukocytoclastic vasculitis
Hypocomplementemic urticarial vasculitis

CLASIFICACIÒN EULAR/PRES 2008

Other vasculitides
Behçet syndrome
Secondary vasculitides due to infection, malignancy, or drugs, including hypersensitivity vasculitis
Isolated vasculitis of the central nervous system
Cogan's syndrome
Unclassified

EULAR: European League against Rheumatism; PRINTO: Paediatric Rheumatology International Trials Organisation; PRES: Paediatric Rheumatology European Society; IgA: immunoglobulin A.

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MANIFESTACIONES CLÍNICAS

TIPO DE LESIÓN HISTOLÓGICA

LOCALIZACIÓN

EXTENSIÓN DEL PROCESO VASCULITICO

COMPROMISO

PIEL
ÓRGANOS INTERNOS
MULSTISISTÉMICO

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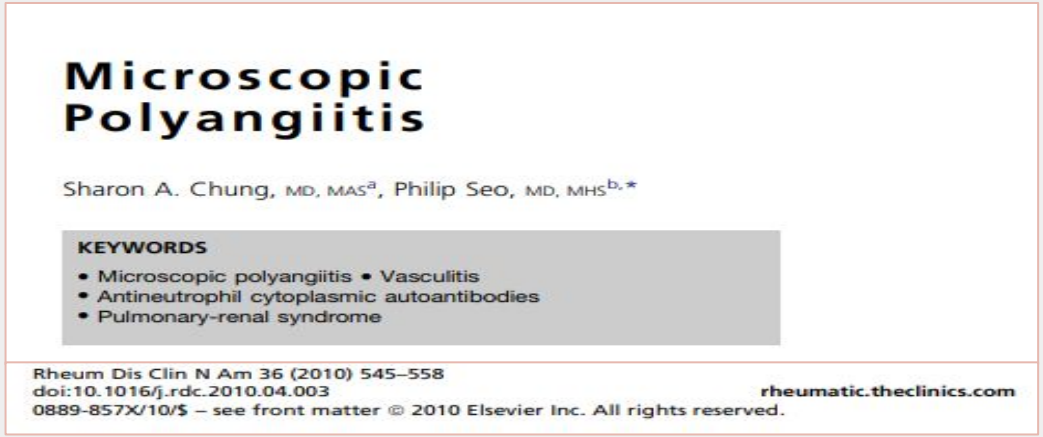
Table 1 Features in pediatric patients with Wegener granulomatosis, microscopic polyangiitis and Churg–Strauss angiitis

Feature	Wegener granulomatosis	Microscopic polyangiitis	Chrurg-Straus angiitis
IgG/ANCA positivity	90%	70%	≤50%
Antigen	Proteinase 3[a]	Myeloperoxidase > proteinase 3	Myeloperoxidase > proteinase 3
Peripheral eosinophilia	Rather rare (and mild)	-	Very often (and severe)
Histology	Necrotizing vasculitis–granulomatous inflammation	Necrotizing vasculitis–no granulomatous inflammation	Necrotizing vasculitis–granulomatous inflammation–tissue eosinophilia
Fever, weight loss	Very often	Very often	Very often
Ear, nose, throat	Sinusitis, saddle nose, epistaxis, oral or nasal ulcers, otitis, conductive hearing loss, subglottic stenosis	Absent or mild	Nasal polyps, allergic rhinitis, conductive hearing loss
Lung	Nodules, infiltrates, cavitary lesions, rarely alveolar hemorrhage	Alveolar hemorrhage	Asthma, nonfixed infiltrates, rarely alveolar hemorrhage
Kidney	Segmental necrotizing glomerulonephritis (granulomatous inflammation rarely seen in biopsy specimens)	Segmental necrotizing glomerulonephritis	Segmental necrotizing glomerulonephritis
Eye	Conjunctivitis, (epi)scleritis, orbital inflammatory disease, uveitis	Occasionally (epi)scleritis, uveitis	Occasionally (epi)scleritis, uveitis
Peripheral	Occasionally vasculitic neuropathy	Often vasculitic neuropathy	Often vasculitic neuropathy
Heart	Occasionally valvular lesions	Rare	Often cardiomyopathy, pericardial

DISCUSIÓN



Microscopic Polyangiitis

Sharon A. Chung, MD, MAS[a], Philip Seo, MD, MHS[b,*]

KEYWORDS
- Microscopic polyangiitis • Vasculitis
- Antineutrophil cytoplasmic autoantibodies
- Pulmonary-renal syndrome

Rheum Dis Clin N Am 36 (2010) 545–558
doi:10.1016/j.rdc.2010.04.003
rheumatic.theclinics.com
0889-857X/10/$ – see front matter

RENAL	RPGN/80-100%	Biopsia: GFS 100% Semilunas glomerualres 90%
PULMONAR	25-55%	Hemoptisis y hemorragia alveolar, pleuritis y fibrosis intestinal
PIEL	30-60% y 15-30% como presentación inicial	Purpura palpable, livedo reticularis, uritcaria y ulceras con necrosis
GASTROINTESTINAL	30-58% 21-29% Rara	dolor abdominal sangrado Hemorragia Masiva Ulceras colonicas, perforación intestinal

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DISCUSIÓN

Table 2. Summary of patients with PAN or MPA with massive gastrointestinal bleeding

Patient no.	Author	Age (years) /Sex	Diagnosis[a]	Site of gastrointestinal bleeding	Other manifestations in the clinical course	Outcome	Findings of abdominal angiogram	
							Multiple aneurysms	Extravasation of contrast medium
1	Cabal and Holz[17]	43/M	Periarteritis nodosa	Duodenum	Retroperitoneal hemorrhage; rupture of the left kidney	Died	Hepatic artery (a.) Pancreaticoduodenal a. Splenic a. Superior mesenteric a.	Detected
2	Painter[16]	70/F	Polyarteritis nodosa	Ileum		Alive	Not performed	
3	Han et al.[18]	50/F	Polyarteritis nodosa	Colon	Intraabdominal and retroperitoneal bleeding; jaundice, prominent transaminase elevation	Died	Hepatic a.; superior and inferior mesenteric a.	Detected
4	Shin and Ho[19]	41/M	Necrotizing angiitis	Colon	Hypertension; renal insufficiency	Died	Superior mesenteric a.	Not detected
5	Roikjaer[20]	23/M	Polyarteritis nodosa	Colon	Renal insufficiency; peritonitis due to perforation of the cecum; colon necrosis; sepsis, positive for ANCA	Died	Not performed	
6	Kotiloglu et al.[21]	13/F	Microscopic PAN	Stomach	Intractable diarrhea; *Salmonella* infection; necrotizing glomerulonephritis	Died	Not performed	
7	Yazici et al.[22]	16/M	Polyarteritis nodosa	Jejunum	Hemobilia	Alive	Hepatic a.; superior mesenteric a.	Detected
8	Inaguma et al.[23]	54/M	ANCA-related vasculitis	Ileum	Pulmonary hemorrhage; duodenal ulcer; rapidly progressive glomerulonephritis; perforation of the gastrointestinal tract	Alive	Not detected	Detected
9	Mocan et al.[24]	10/M	Polyarteritis nodosa	Not described	Perforation of the cecum; uncontrollable hypertension; intraabdominal hematoma; perforation of the gastrointestinal tract	Died	Not performed	
10	Our patient	74/M	MPA	Ileum	Pulmonary hemorrhage; renal insufficiency; positive for ANCA	Died	Not detected	Detected

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DISCUSIÒN

Pediatric Nephrology (2019) 34:1425–1433
https://doi.org/10.1007/s00467-019-04228-4

ORIGINAL ARTICLE

Epidemiology and clinical features of child
cytoplasmic antibody–associated vasculitis
analysis

Daishi Hirano[1] · Tomoaki Ishikawa[2] · Aya Inaba[3] · Mai Sato[4] ·

Variables	MPA ($n=38$)	GPA ($n=9$)	Others ($n=2$)	Total ($n=49$)
Gender				
Male	8 (21%)	4 (44%)	1 (50%)	13 (27%)
Female	30 (79%)	5 (56%)	1 (50%)	36 (73%)
Age at diagnosis (median in years)	10.0 (7.7–12.0)	12.8 (11.7–13.7)	10.5 (10.0–11.0)	10.7 (8.3–12.4)
Time from initial symptom to diagnosis (median in months)	2.0 (1.0–4.0)	2.0 (2.0–5.0)	1.0 (1.0)	2.0 (1.0–4.0)
Detected by school urinary screening program	27 (71%)	0 (0%)	0 (0%)	27 (55%)
Organ involvements				
General symptom	13 (34%)	7 (78%)	2 (100%)	22 (45%)
Fever	10	7	2	19
Weight loss	3	3	0	6
Renal involvement	31 (82%)	3 (33%)	1 (50%)	35 (71%)
Proteinuria	31	3	1	35
Nephrotic range proteinuria	13	0	0	13
Hematuria	15	2	1	18
Macroscopic hematuria	15	2	0	17
Oliguria	2	0	0	2
Renal insufficiency	5	0	0	5
Pulmonary involvement	10 (26%)	4 (44%)	0 (0%)	14 (29%)
Alveolar hemorrhage	7	1	–	8
Pleural effusion	1	0	–	1
Abnormal chest imaging	2	2	–	4
Dyspnea	1	2	–	3
Cardiovascular involvement	3 (8%)	0 (0%)	1 (50%)	4 (8%)
Otolaryngology involvement	1 (3%)	7 (78%)	1 (50%)	9 (18%)
Eyes involvement	4 (11%)	5 (56%)	1 (50%)	10 (20%)
Mucocutaneous involvement	8 (21%)	2 (22%)	1 (50%)	11 (22%)
Joint involvement	3 (8%)	1 (11%)	0 (0%)	4 (8%)
Gastrointestinal involvement	5 (13%)	1 (11%)	2 (100%)	8 (16%)
Central nervous system involvement	0 (0%)	2 (22%)	1 (50%)	3 (6%)

Estudio Restrospectivo - Multice

49 casos con AAGNV (38 Polan

88% presentaron Falla Renal Ag

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DISCUSIÒN

Nephrol Dial
doi: 10.1093/
Advance Acc

Origi

Clini
ANC

Anne-Sy
Stéphan

	GPA (*n* = 28)	MPA (*n* = 38)	Total (*n* = 66)
Girls, *n* (%)	21 (75)	34 (89)	55 (83)
Caucasian origin, *n* (%)	21 (75)	26 (68)	47 (71)
Median age at diagnosis in years (IQR)	12.8 (10.1–14.6)	11.2 (8.9–12.3)	11.5 (9.6–13.1)
Median interval from initial symptoms to diagnosis in months (IQR)	1.8 (0.8–5.0)	1.0 (0.6–8.1)	1.0 (0.6–7.9)
Clinical features, *n* (%)			
Fever (*n* = 64)	19 (68%)	18 (50%)	37 (56%)
Malaise/fatigue (*n* = 65)	23 (82%)	29 (78%)	52 (79%)
Renal impairment	22 (78%)	36 (95%)	58 (88%)
Proteinuria	18	22	40
Elevated proteinuria	12	13	25
Heavy proteinuria	3	5	8
Haematuria	15	33	48
Macroscopic haematuria	2	8	10
Arterial hypertension	5	20	25
Acute kidney injury	14	30	44
Maximum serum creatinine in µmol/L, median (IQR)	120 (70–317)	263 (94–584)	
Pulmonary impairment	19 (68%)	11 (29%)	30 (45%)
Alveolar haemorrhage	12	9	21
Pleural effusion/thickening	1	1	2
Abnormal chest imaging			
Nodules	7	0	7
Fixed infiltrates	16	0	16
Transient interstitial infiltrates	0	10	10
Abnormal lung function tests	7/13	4/5	
Upper airway impairment	21 (75%)	0 (0%)	21 (32%)
Recurrent epistaxis	12	0	12
Chronic or recurrent sinusitis	10	0	10
Chronic purulent or bloody nasal discharge/crusts	2	0	2
Subglottic stenosis	1	0	1
Mucocutaneous impairment	15 (54%)	13 (34%)	28 (42%)
Purpura	12	7	19
Skin rash	6	4	10
Enanthema	2	1	3
Joint impairment	16 (57%)	11 (29%)	27 (41%)
Arthralgia	16	10	26
Arthritis	5	3	8
Musculoskeletal impairment	1 (4%)	1 (3%)	2 (3%)
Gastrointestinal impairment	5 (18%)	4 (11%)	9 (14%)
Eyes impairment	6 (21%)	3 (8%)	9 (14%)
Central nervous system impairment	1 (4%)	2 (5%)	3 (5%)

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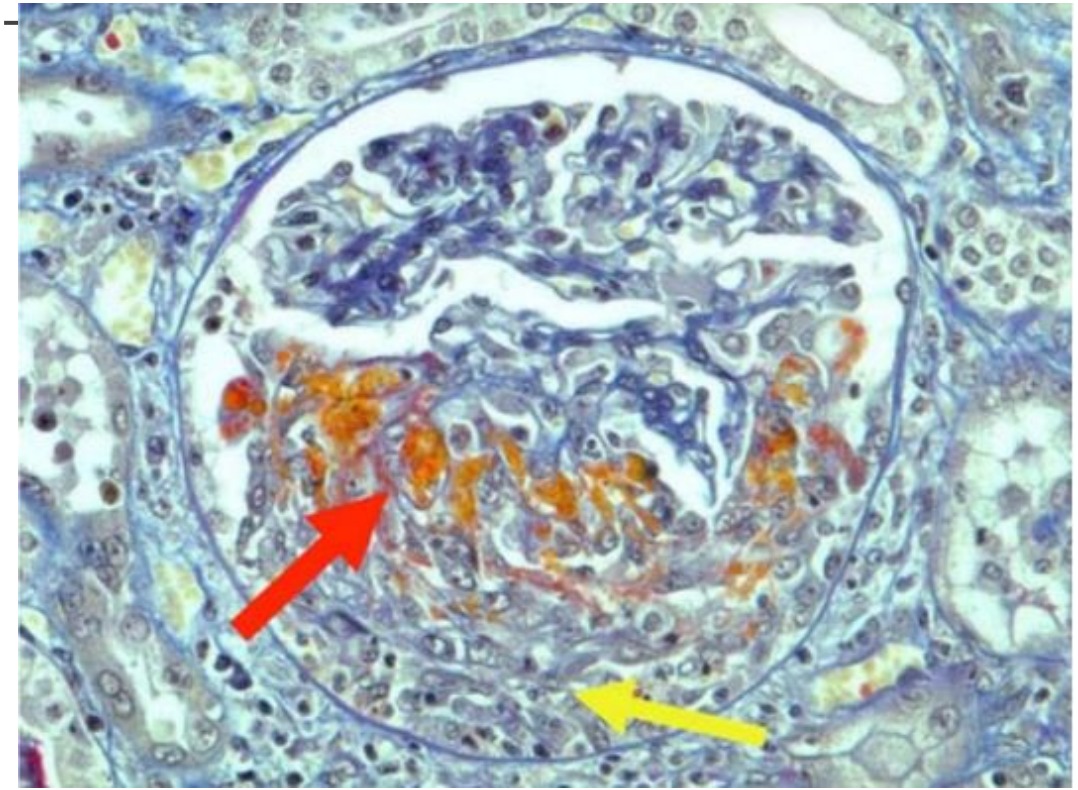
Glomerulonefritis ANCA +

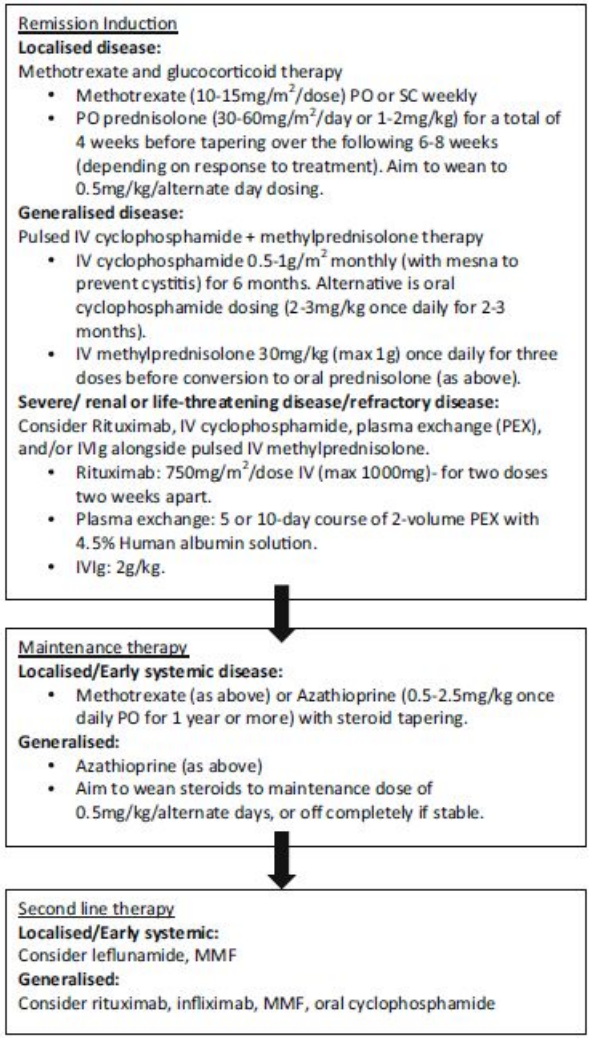


De los pacientes pediátricos que desarrollan la clásica glomerulonefritis pauciinmune necrotizante, el 30-40% progresa a enfermedad renal crónica y hasta un 34% a estadios terminales

Tratamiento

Corticoide + Ciclofosfamida

Mantenimiento: Azatioprina



Remission Induction

Localised disease:

Methotrexate and glucocorticoid therapy

- Methotrexate (10-15mg/m^2/dose) PO or SC weekly
- PO prednisolone (30-60mg/m^2/day or 1-2mg/kg) for a total of 4 weeks before tapering over the following 6-8 weeks (depending on response to treatment). Aim to wean to 0.5mg/kg/alternate day dosing.

Generalised disease:

Pulsed IV cyclophosphamide + methylprednisolone therapy

- IV cyclophosphamide 0.5-1g/m^2 monthly (with mesna to prevent cystitis) for 6 months. Alternative is oral cyclophosphamide dosing (2-3mg/kg once daily for 2-3 months).
- IV methylprednisolone 30mg/kg (max 1g) once daily for three doses before conversion to oral prednisolone (as above).

Severe/ renal or life-threatening disease/refractory disease:

Consider Rituximab, IV cyclophosphamide, plasma exchange (PEX), and/or IVIg alongside pulsed IV methylprednisolone.

- Rituximab: 750mg/m^2/dose IV (max 1000mg)- for two doses two weeks apart.
- Plasma exchange: 5 or 10-day course of 2-volume PEX with 4.5% Human albumin solution.
- IVIg: 2g/kg.

Maintenance therapy

Localised/Early systemic disease:

- Methotrexate (as above) or Azathioprine (0.5-2.5mg/kg once daily PO for 1 year or more) with steroid tapering.

Generalised:

- Azathioprine (as above)
- Aim to wean steroids to maintenance dose of 0.5mg/kg/alternate days, or off completely if stable.

Second line therapy

Localised/Early systemic:

Consider leflunamide, MMF

Generalised:

Consider rituximab, infliximab, MMF, oral cyclophosphamide

2da línea: Rituximab, Infliximab, MMF

MUCHAS GRACIAS!

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de Buenos Aires