

SÍNDROME NEFROTICO DESPUÉS DE APLICACIÓN DE

VACUNA CONTRA COVID-19



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Chagolla**
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Toluca, MX

Identificación



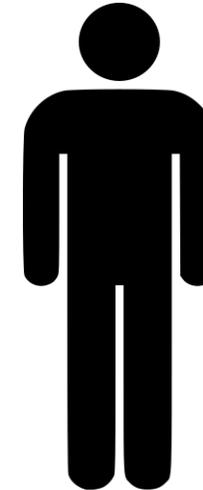
Masculino

69 años

Médico

Originario y Residente de Metepec, Estado México

Católico



Antecedentes
heredo familiares:

- Tío con Cancer renal, desconoce estirpe histológica.
- Abuela con diabetes mellitus tipo 2

Antecedentes Patológicos



Diabetes mellitus tipo 2 diagnosticado hace 7 años en tratamiento con Metformina cada 24 horas

Hipertensión arterial sistémica diagnosticado hace 6 años en tratamiento. Con losartan cada 24 horas

Enfermedad por SARS-CoV-2 en diciembre 2020

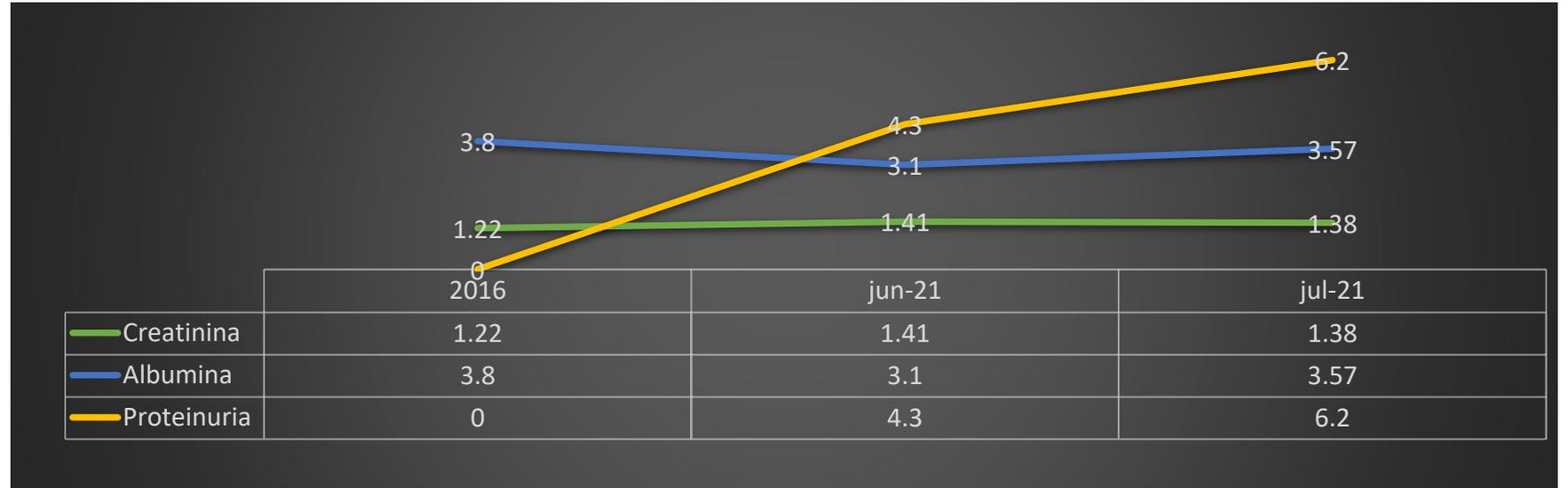
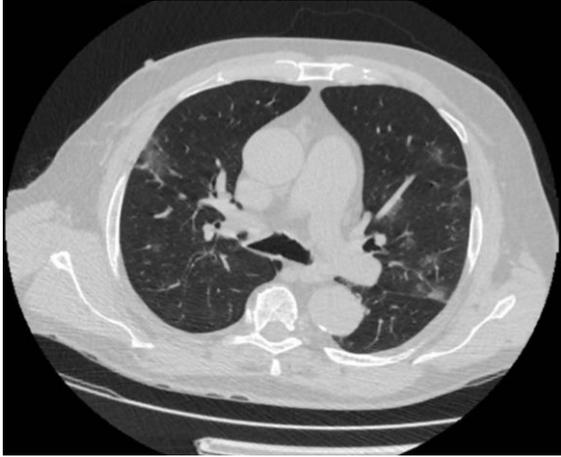
- Neumonía atípica diagnosticada el 11/12/2020, sin requerimiento de Oxígeno suplementario, tratamiento domiciliario
- Actualmente en rehabilitación pulmonar

Fibrilación auricular permanente diagnosticado en junio 2021, se inició tratamiento con apixaban cada 24 horas

Alergias / transfusiones : no refiere.

Quirúrgicos: osteosíntesis fractura de tobillo derecho en 2013

- **ENFERMEDAD ACTUAL:** Inicia en junio 2021, con edema de extremidades inferiores, astenia adinamia, de forma inicial relacionada a secuelas por neumonía por SARS COV2, sin embargo durante su revisión de seguimiento post-Covid se detecta aparición de Proteinuria en Examen general de orina, motivo por el que es enviado a consulta de Nefrología



Enero 2021:

Inicia rehabilitación pulmonar con seguimiento en consulta de Neumología.

18 de Marzo 2021 y

16 de Abril 2021:
Vacunación SINOVAC

Junio 2021: Aparición de edema + proteinuria. Se envía a Nefrología

Se aumenta Bloqueo del RAAS

Julio 2021:
Hospitalización

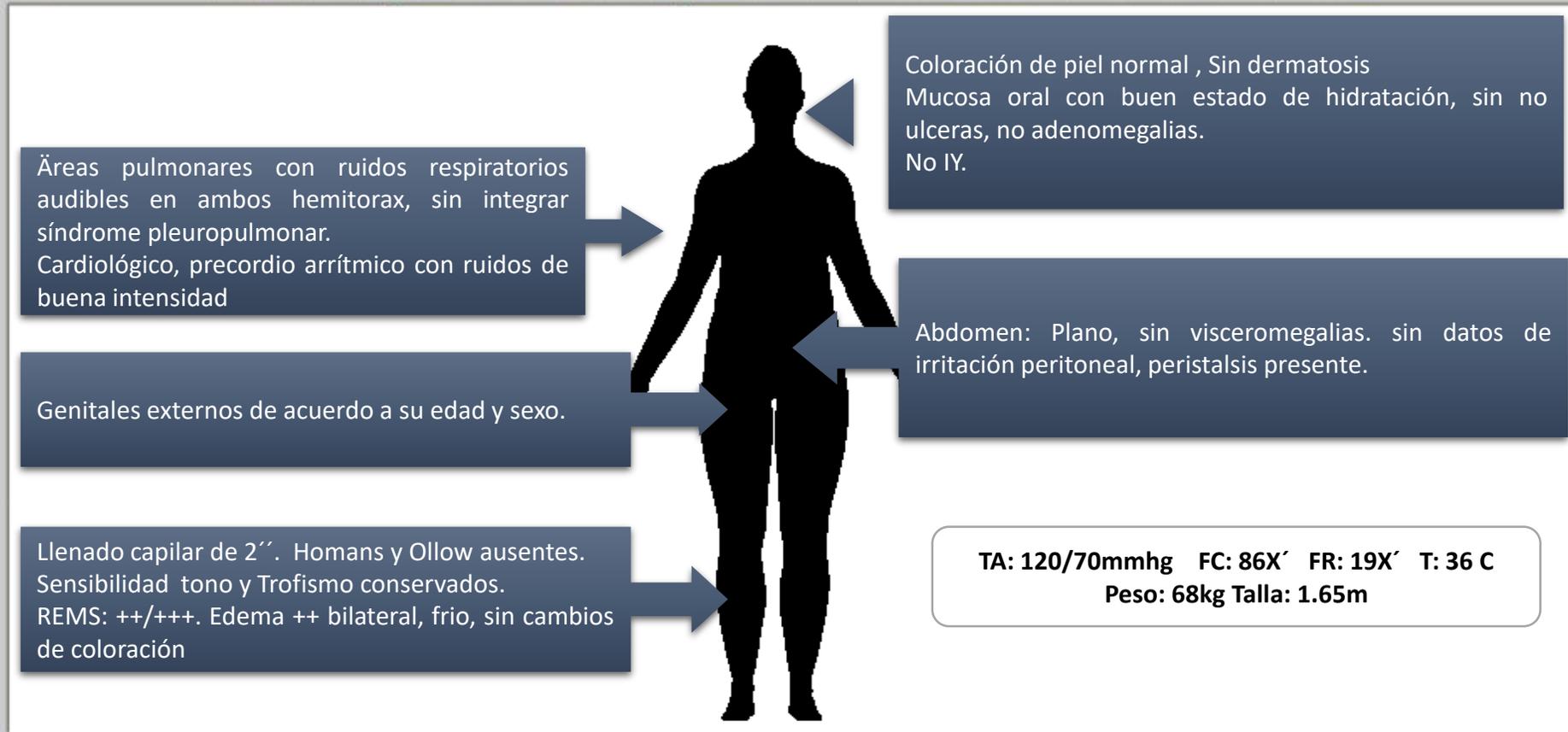
Síndrome Nefrótico



Diciembre 2020:
Neumonía por SARS COV2



Exploración Física



Idx: Síndrome Nefrótico en Estudio

15 Junio 2021

Sx Nefrótico

Ego: densidad 1.025, ph 6.5, nitritos negativo, **proteínas 4302**, eritros 63, leucos 0-2

Proteinuria en 24 horas: 5.67g / Albuminuria en 24 horas: 5.1g/dl

Glu 78, cre 1.4, Ac urico 9.05, col 213, alb 3.1

Sedimento Urinario

6 Julio: consulta de Nefrología e ingreso

Anticuerpos antinucleares / anti DNA: **NEGATIVO**

Complemento
c4 0.19 g/L (0.10-4.0)
c3: 1.01 g/L (0.9-1.8)

Panel viral hepatitis B, C y VIH: **negativo**

Urocultivo **negativo**

Marcadores tumorales: alfafetoproteína, ag carcinoembrionario, ca 19-9, **negativo**

Internamiento Julio 2021

ULTRASONIDO RENAL
RD: 114X69X58
RI: 118X 55X52



Anticuerpos Anti PLA2r: **NO CONTAMOS CON ESTUDIO**

ECOTT: Cardiopatía hipertensiva, Dilatación de aurícula izquierda. FEVI 57%, PSAP 47mmhg

Ultrasonido / Sedimento



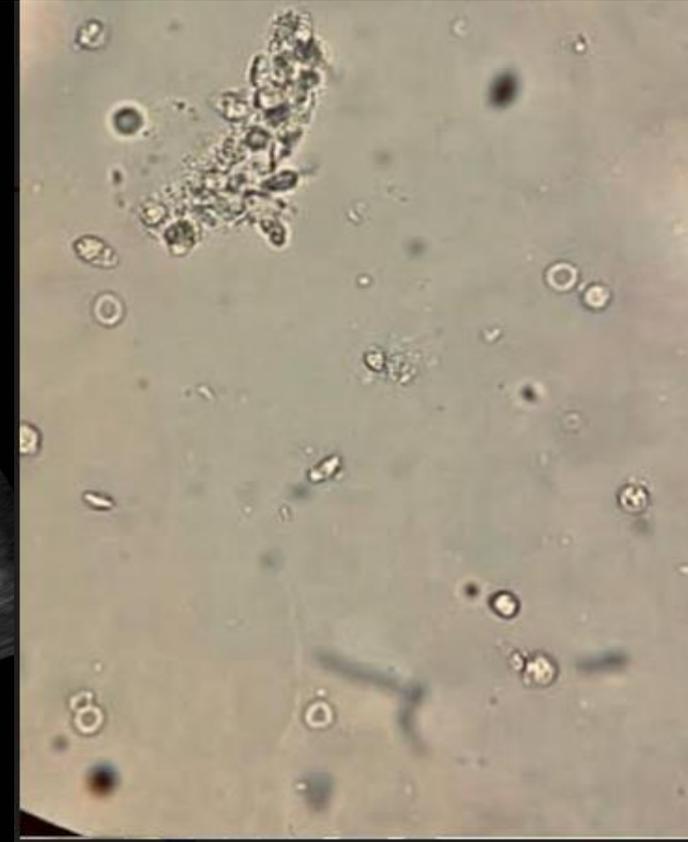
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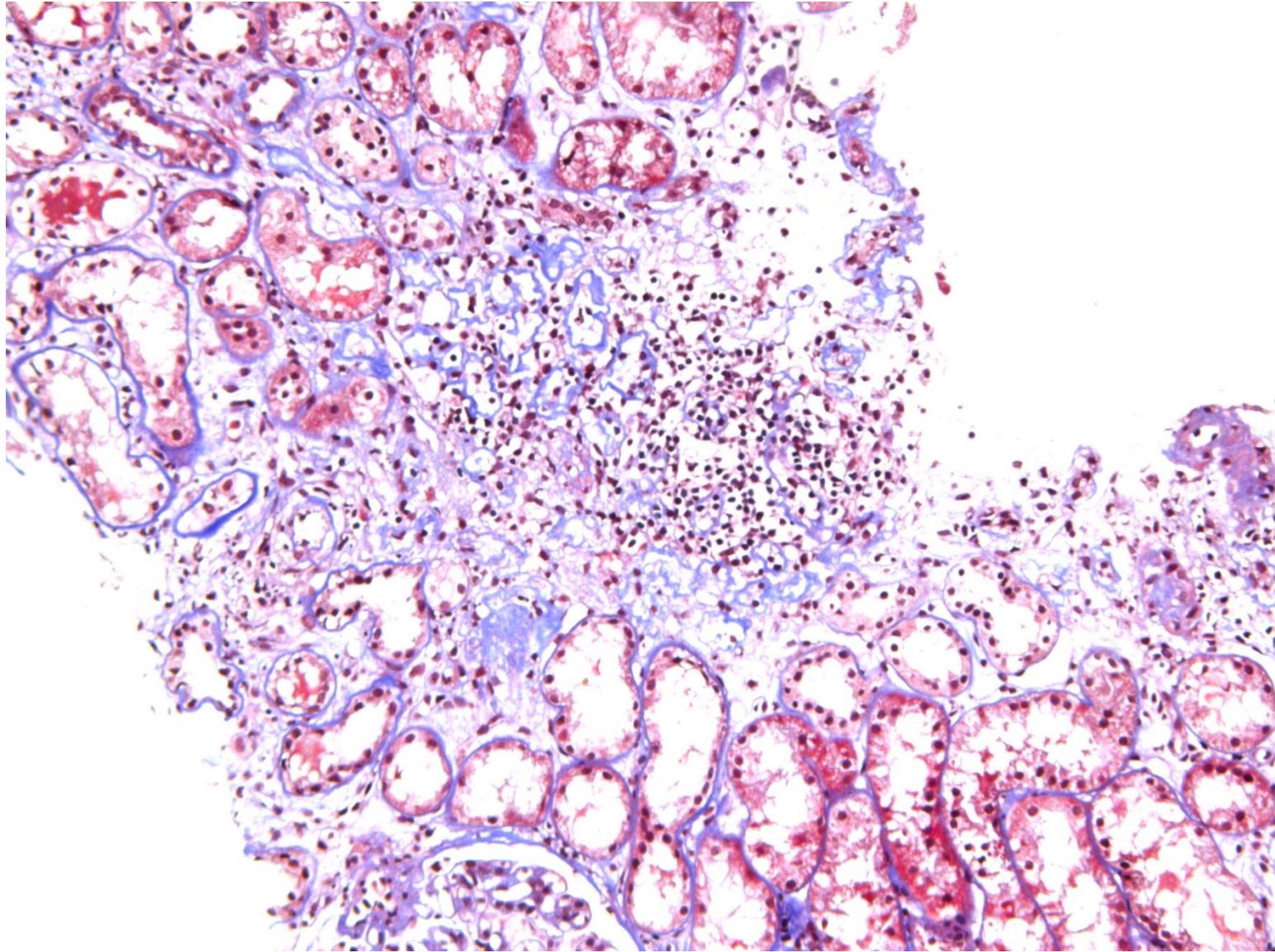
RIÑÓN DERECHO

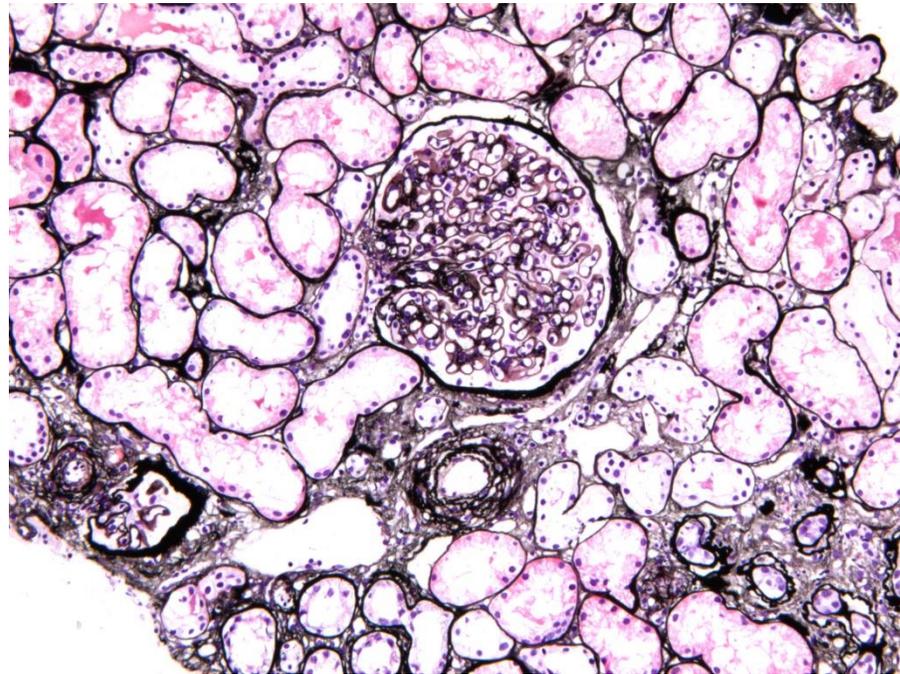
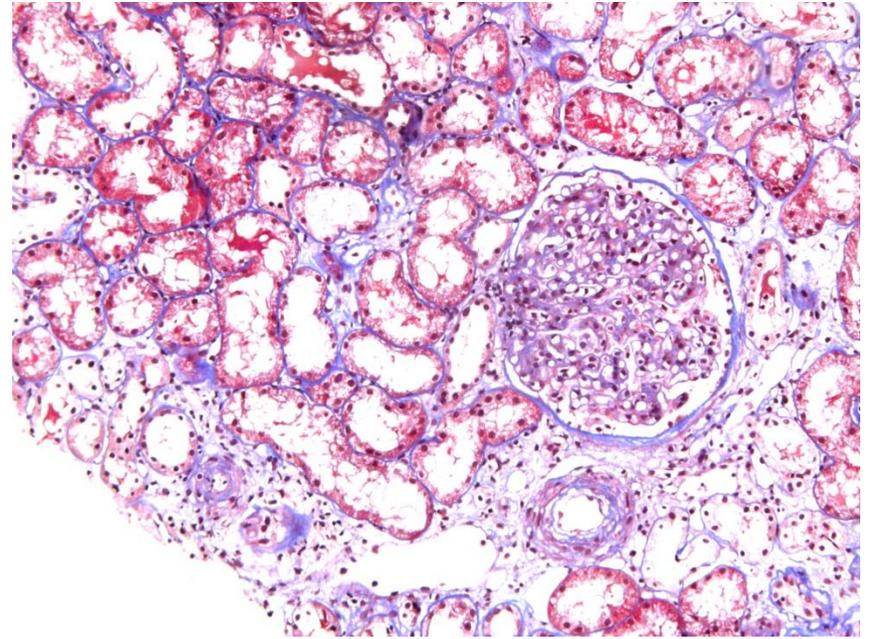
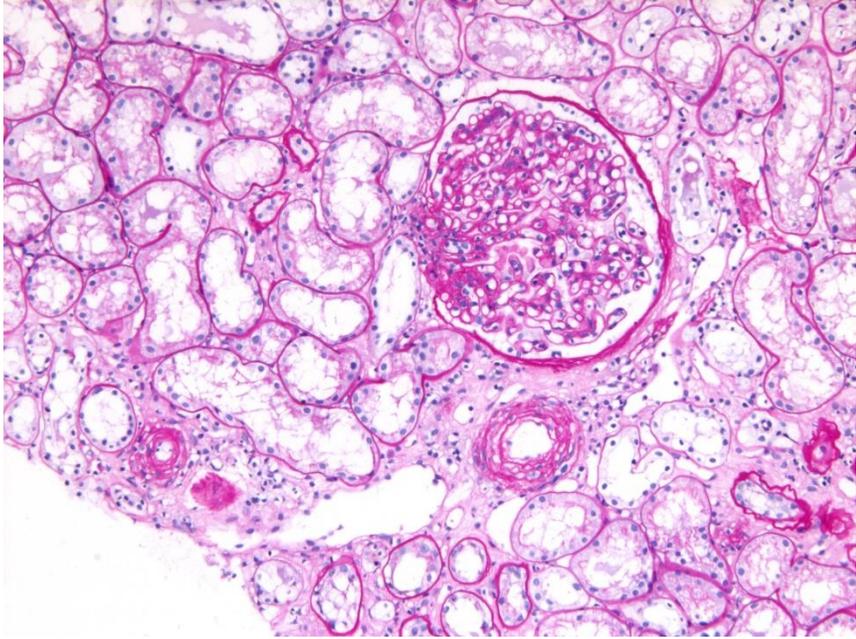
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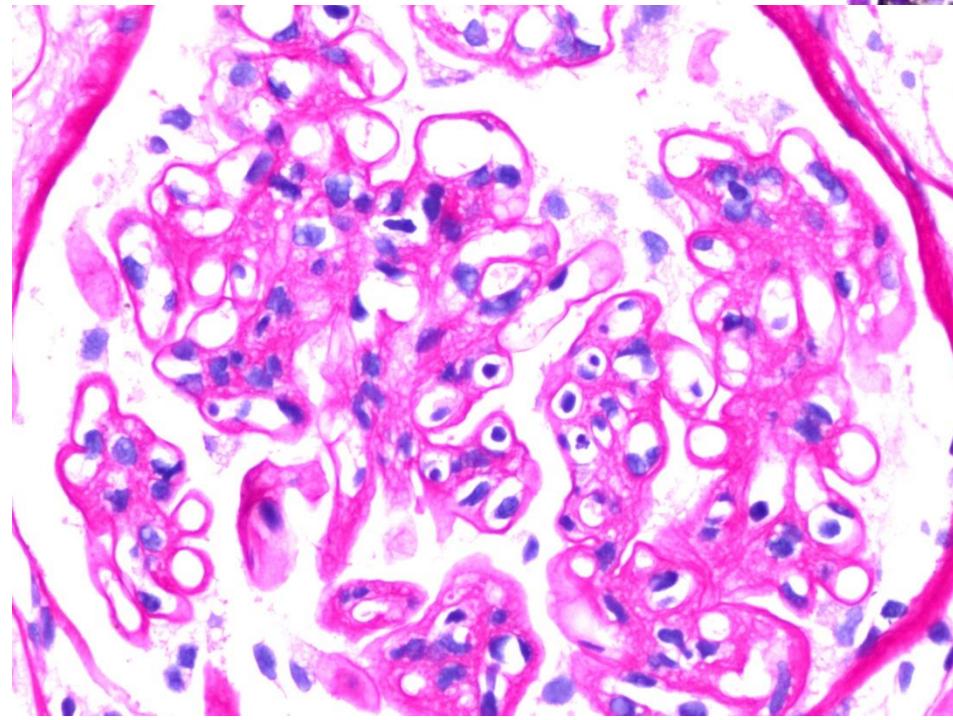
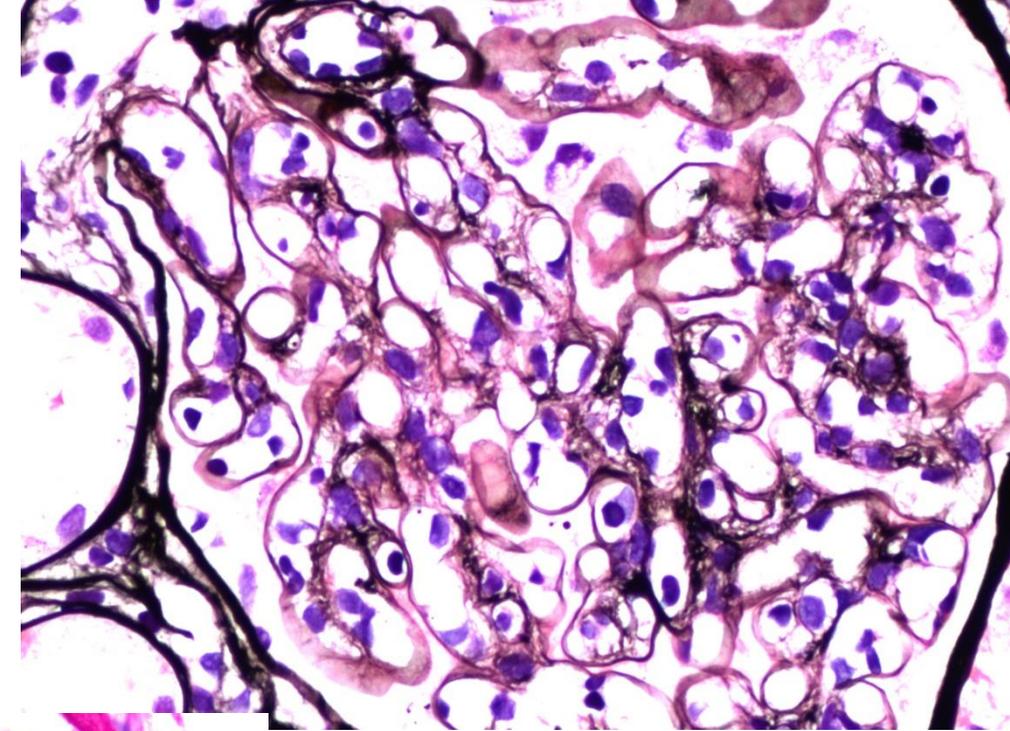
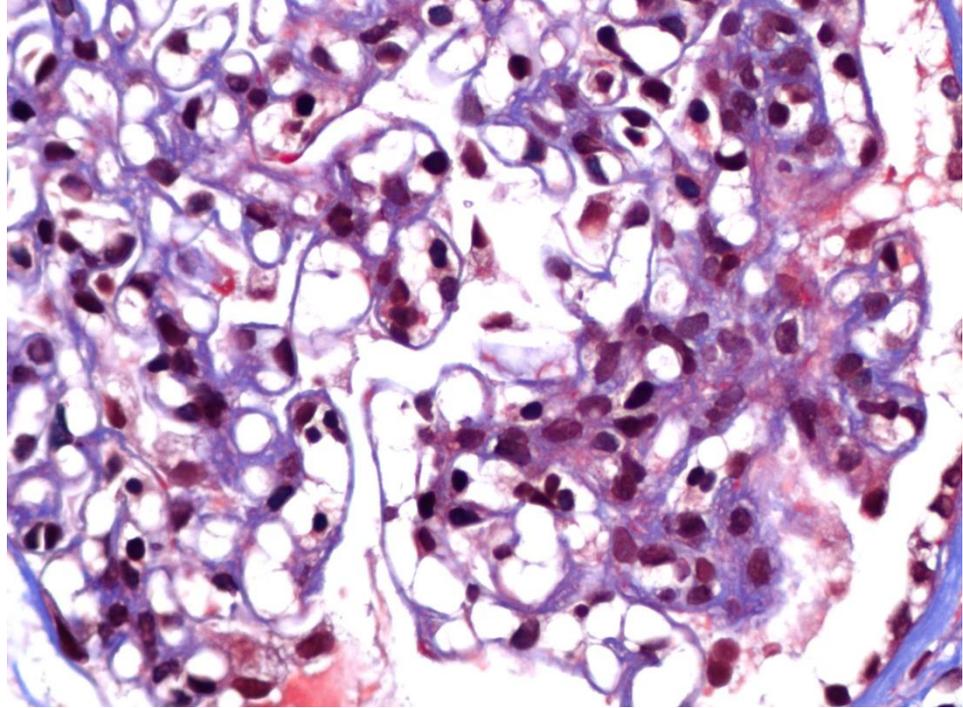


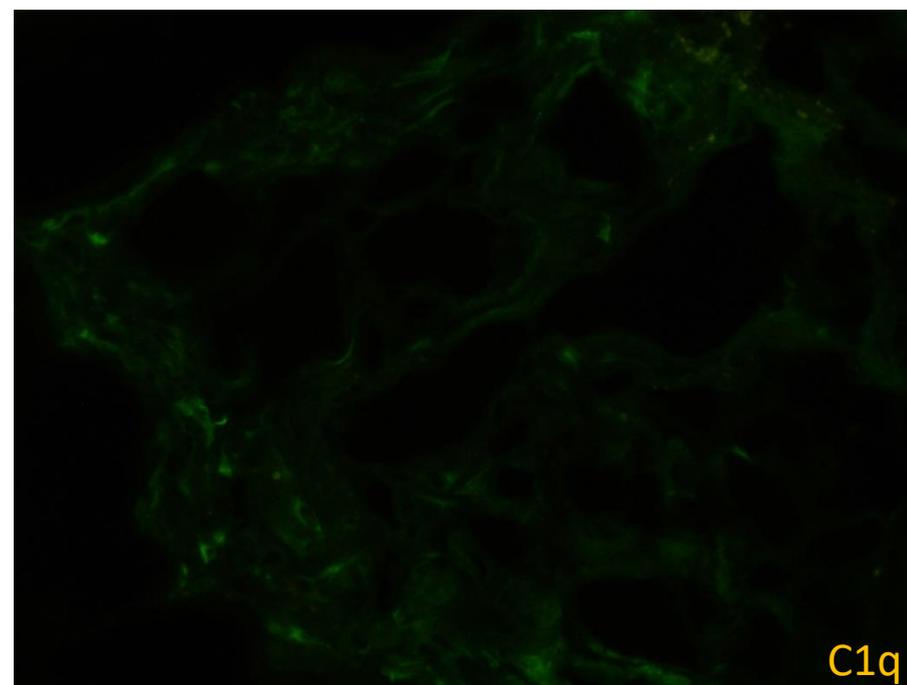
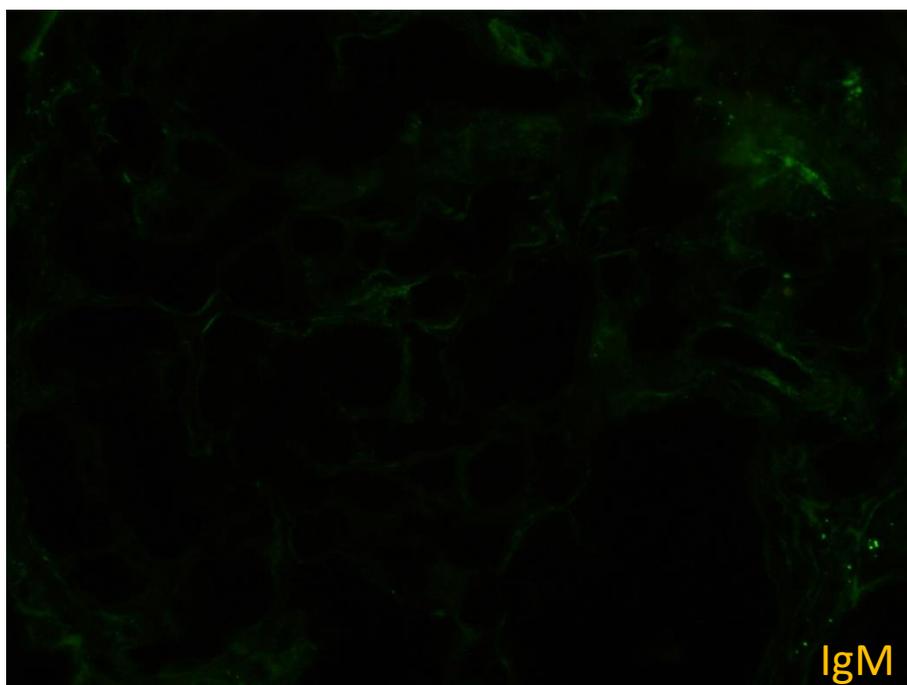
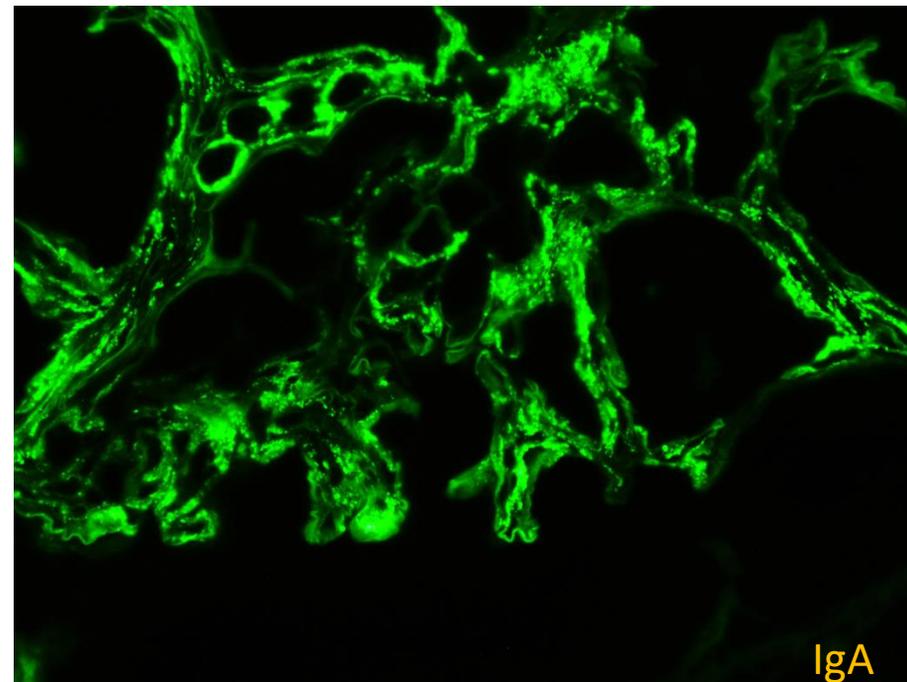
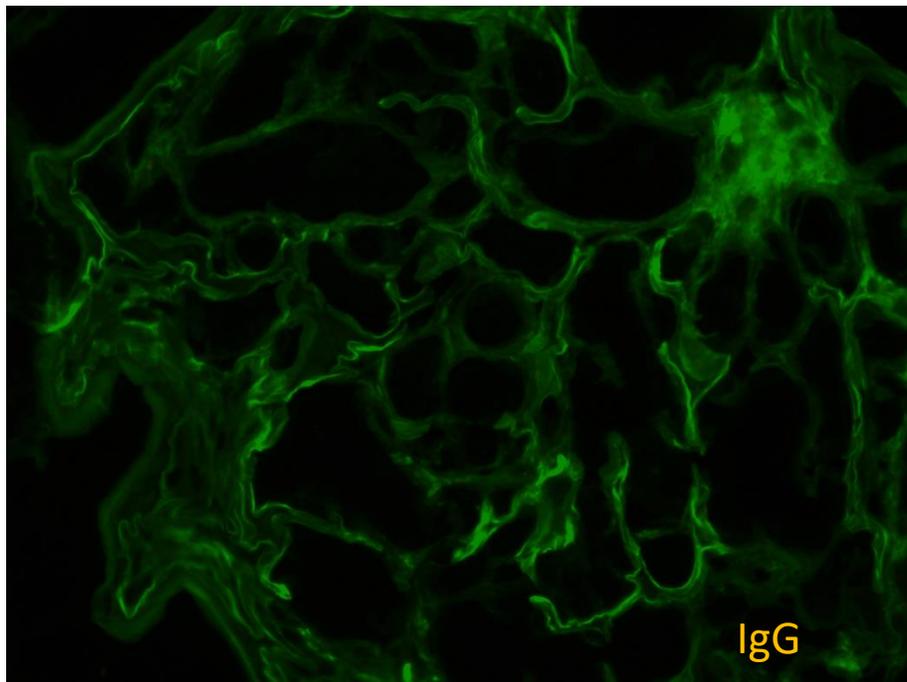
Biopsia Renal

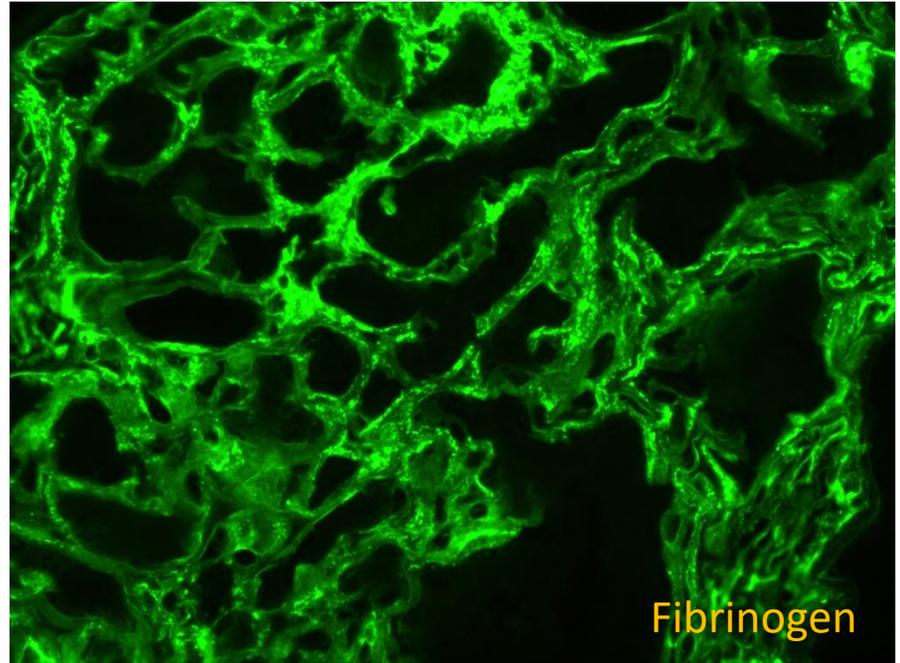
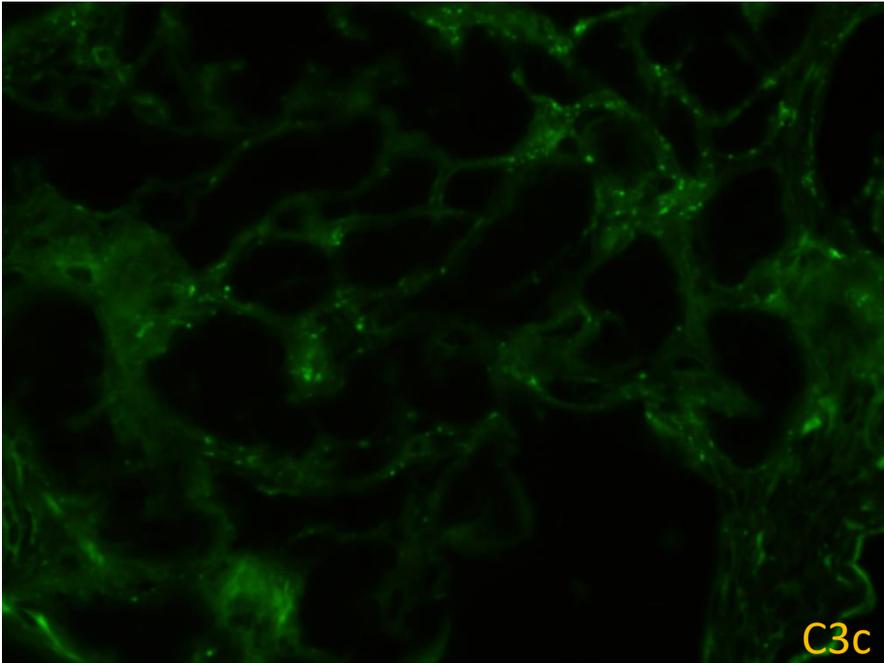
Dra. Yolotzin Valdespino
Dra. Isabel Mora Mendoza



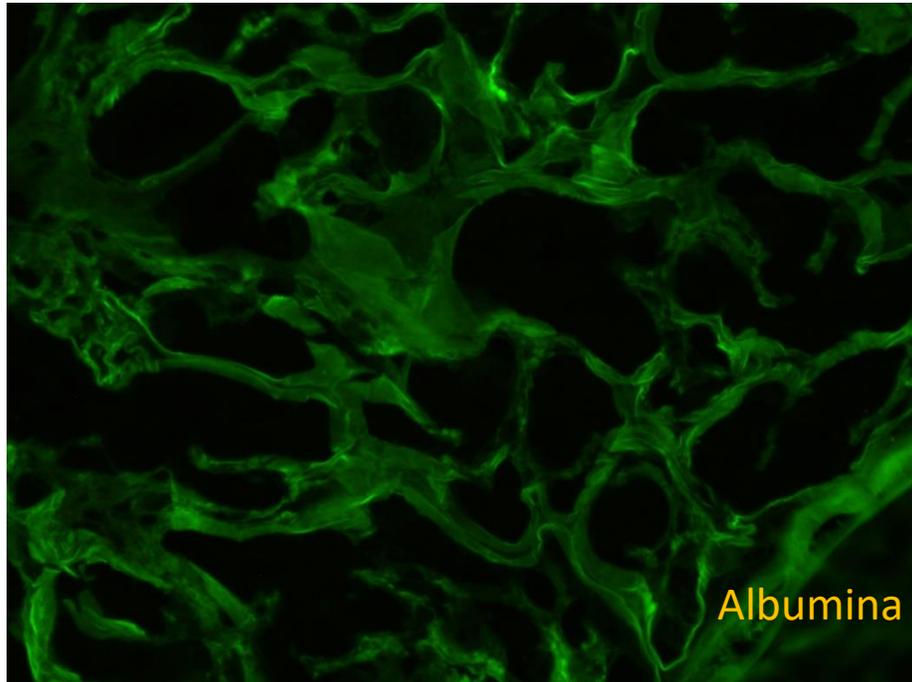


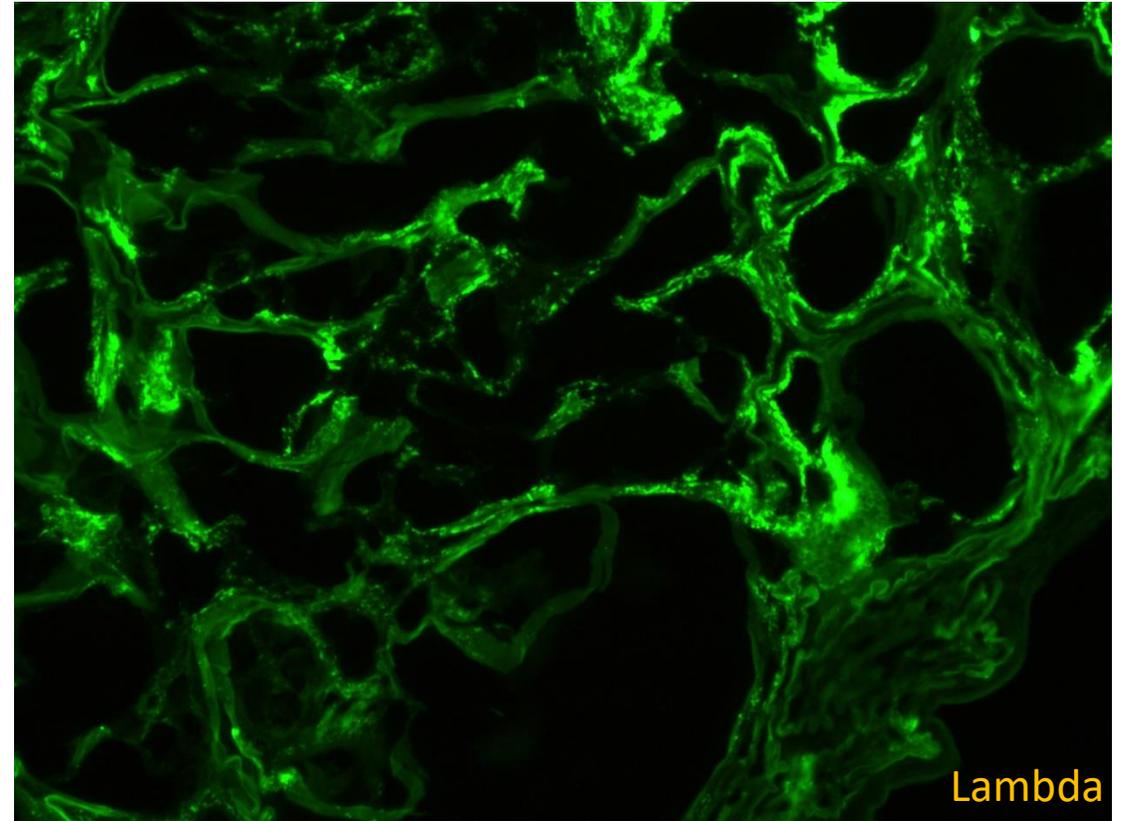
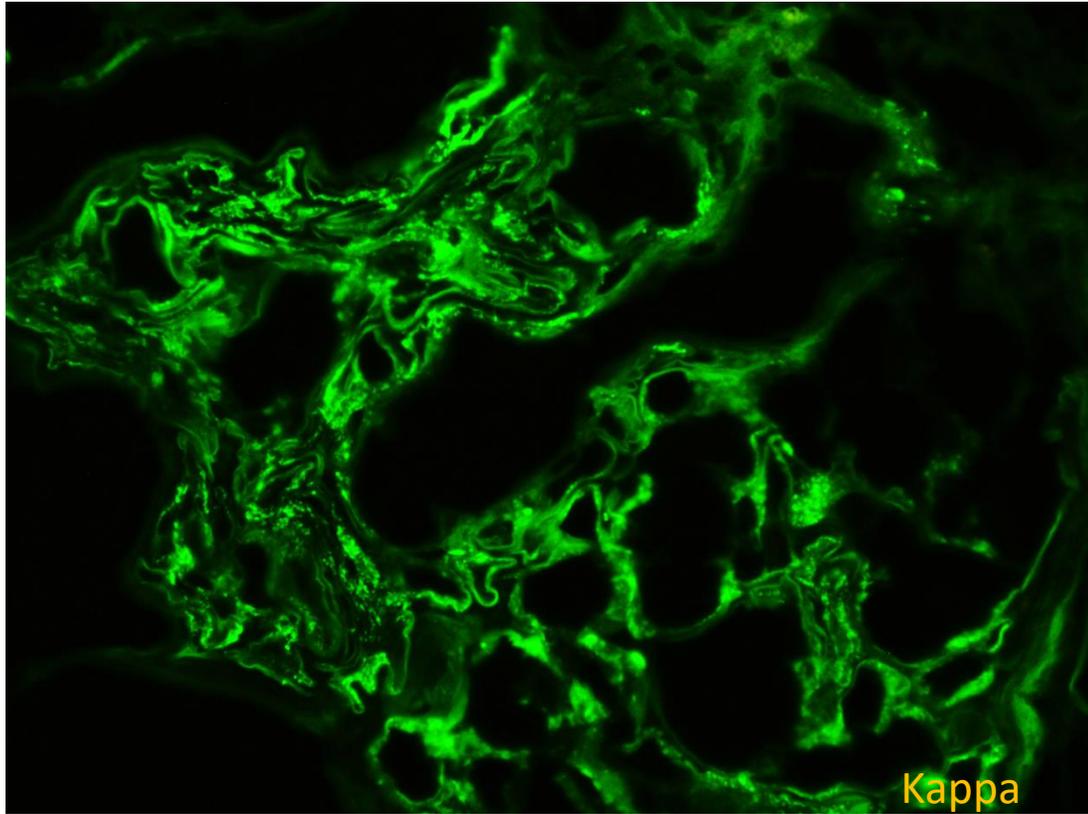






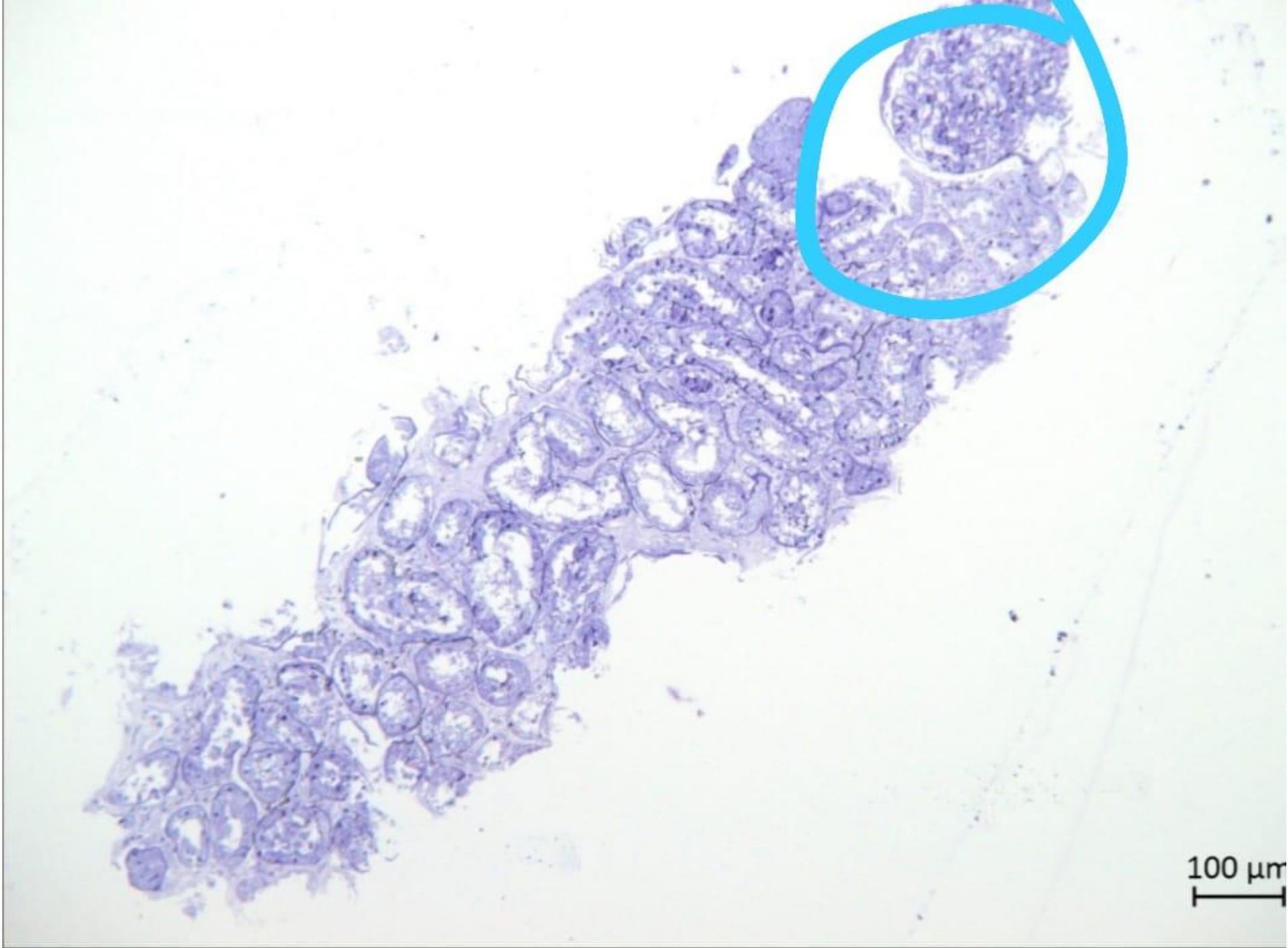
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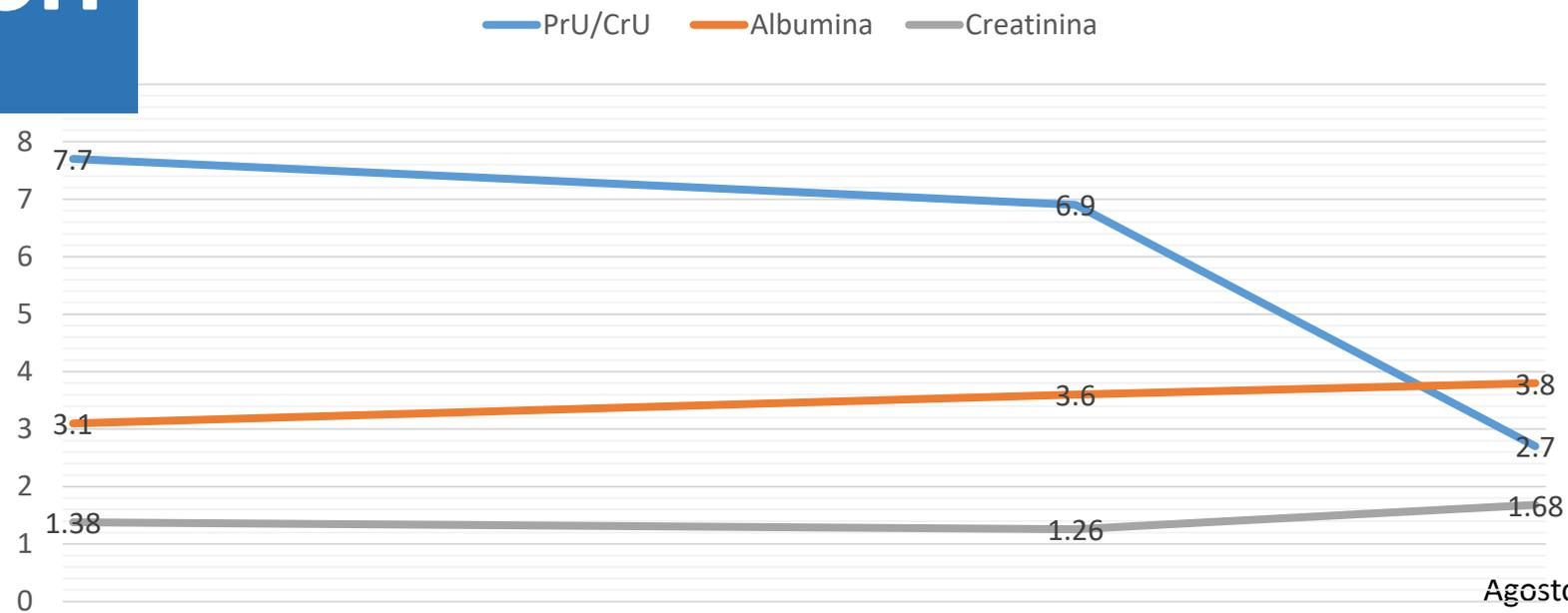
Diagnóstico:

- Nefropatía por IgA con hipertrofia podocitaria (M 1, E1, S0, T0, EX0).
- Fibrosis intersticial grado I



100 μm

Evolución



Julio 21: Diagnostico IgAN

Agosto 2021

- PDN 60mg
- Furosemide 20mg cada 12 h
- Losartan 50mg cada 12h
- Espironolacona 50mg cada 24 h
- Apixaban 5mg cada 12h (FA)

Inicio de Tratamiento julio2021

- PDN 1mg/kg/día
- Losartan
- Atorvastatina
- Tamsulosina
- Espironolactona



Review of Early Immune Response to SARS-CoV-2 Vaccination Among Patients With CKD

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Table 1. Summary of COVID-19 vaccine platforms and status

| Platform | Target | Examples | Status | Trials in dialysis or transplant? |
|-----------------------------|------------------------|---|--|-----------------------------------|
| mRNA | S protein | BNT162b2 (Tozinameran/Comirnaty, Pfizer/BioNTech), mRNA-1273 (Moderna), CVnCoV (Curevac), PTX-COVID19-B (Providence) | BNT162b and mRNA-1273 approved in many jurisdictions; others under development | No |
| Adenovirus vector | S protein | AZD1222 (Vaxzevria/CoviShield, AstraZeneca/Oxford), Ad26.COV2.S (Janssen), Sputnik V (Gamaleya), Convidecia (CanSino) | Approved in many jurisdictions | No |
| Inactivated protein subunit | S protein | NVX-CoV2372 (Novavax), Epivac Corona (Vector Institute), GSK/Sanofi candidate vaccine | Approved in some countries | No |
| Inactivated virion | Whole virus | CoronaVac (Sinovac), Covaxin (Bharat Biotech), Covivac (Chumakov Centre, Russia) | Approved in some countries | No |
| Others | Whole virus, S protein | DNA vaccines, live attenuated virion, other viral vectors | Under development | No |

Table 4. A summary of glomerulonephritis cases and relapses after vaccination

| Study | Vaccine | Timing | GN type | Clinical course |
|-------------------------------|-----------|-----------------------------------|--|--|
| Minimal change disease | | | | |
| Moas <i>et al.</i> | BNT162b2 | 7 days, first dose | New diagnosis, MCD | Steroid responsive |
| Lebedev <i>et al.</i> | BNT162b2 | 4 days, first dose | New diagnosis, MCD and AKI | AKI resolved, MCD improving with steroids |
| Agati <i>et al.</i> | BNT162b2 | 7 days, first dose | New diagnosis, MCD and AKI | AKI resolved, still proteinuric at 3 weeks on steroids |
| Kervella <i>et al.</i> | BNT162b2 | 10 days, second dose | MCD relapse | Steroid responsive |
| Schwotzer <i>et al.</i> | BNT162b2 | 3 days, first dose | MCD relapse | Responded to steroids + tacrolimus |
| Holzworth <i>et al.</i> | mRNA-1273 | 1 week, first dose | New diagnosis, MCD and AKI | On treatment |
| Komaba <i>et al.</i> | BNT162b2 | 8 days, first dose | MCD relapse | Steroid responsive |
| IgA nephropathy | | | | |
| Gul Rahim <i>et al.</i> | BNT162b2 | Hours, second dose | IgA nephropathy, gross hematuria | Spontaneous resolution |
| Negrea <i>et al.</i> | mRNA1273 | Hours, second dose | IgA nephropathy, gross hematuria and increased proteinuria | 2 patients, spontaneous resolution of hematuria |
| Perrin <i>et al.</i> | mRNA-1273 | Second day, first and second dose | IgA nephropathy, gross hematuria | 3 patients, 1 with transient proteinuria, spontaneous resolution |
| RPGN presentations | | | | |
| Tan <i>et al.</i> | BNT162b2 | 1 day, second dose | IgA nephropathy with fibrocellular crescents, mild IFTA | Underlying IgA, unmasked post vaccination with hematuria |
| Anderegg <i>et al.</i> | mRNA-1273 | Second dose | Crescentic IgA nephropathy | Steroid responsive |
| Sekar <i>et al.</i> | mRNA-1273 | 2 weeks, second dose | Crescentic GN, c-ANCA vasculitis | Dialysis dependent at 2 weeks |
| Anderegg <i>et al.</i> | mRNA-1273 | First dose | Crescentic GN, c-ANCA vasculitis | Responded to cyclophosphamide + steroids |
| Tan <i>et al.</i> | BNT 162b2 | 1 day, second dose | Crescentic GN, anti-GBM | RPGN presentation |
| Membranous nephropathy | | | | |
| Aydin <i>et al.</i> | Sinovac | 2 weeks, first dose | Membranous, relapse | PLA2R positive; remission at 3 months on CNI + steroids, ACEi |

ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; c-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies; CNI, calcineurin inhibitor; IFTA, interstitial fibrosis and tubular atrophy; MCD, minimal change disease; RPGN, rapidly proliferative glomerulonephritis.

Table 1. Patient clinical characteristics

| Patient | Age, yr | Sex | MH | Medications | Evidence of systemic IgA vasculitis before vaccination | Temporal relation of gross hematuria to Moderna SARS-CoV-2 mRNA vaccination | Baseline (hematuria / uPCR / SCr) | Presentation (hematuria / uPCR / SCr) | Evidence of systemic IgA vasculitis after vaccination | Biopsy | Treatment | Follow-up 1 mo post second dose (hematuria / uPCR / SCr) |
|---------|---------|-----|------|--|--|---|-----------------------------------|---------------------------------------|---|-------------|-----------|--|
| 1 | 22 | F | None | None since episodic steroids for IgA vasculitis at age 10 yr | Yes | 48 h after second dose | 4–10 / neg / 0.80 | >50 / 0.40 / 0.80 | No | No | None | 0–3 / 0.27 / 0.80 (hematuria returned to baseline) |
| 2 | 39 | F | None | None | No | 48 h after second dose | 0–3 / neg / no baseline | >50 / 0.90 / 0.80 | No | No | None | 0 / below detection / 0.80 (hematuria and proteinuria returned to baseline) |
| 3 | 50 | M | HTN | None | No | 24 h after second dose | 11–25 / 2.40 / 1.17 | >50 / 3.56 / 1.54 | No | Yes, kidney | RAASi | 11–25 / 2.20 / 1.24 (hematuria and proteinuria returned to baseline; SCr improving but above baseline) |
| 4 | 67 | M | HTN | RAASi | No | 1 mo after first dose | 0–3 / 0.05 / 1.20 | >50 / 2.10 / 2.90 | Yes, bilateral lower extremity maculopapular rash | Yes, skin | Steroid | 0–3 / 0.09 / 1.40 (hematuria and proteinuria returned to baseline; SCr improving but above baseline) |

F, female; HTN, hypertension; M, male; neg, negative; MH, medical history; RAASi, renin-angiotensin-aldosterone system inhibition; SCr, serum creatinine (in mg/dL); uPCR, urine protein-to-creatinine ratio.

Hematuria is expressed as number of red blood cells per high-powered field on urinalysis. None of the patients had episodes of gross hematuria before vaccination, and none were known to have been infected with SARS-CoV-2, although serologic testing before vaccination was not performed.

IgA Nephropathy After SARS-CoV-2 Vaccination

Matthew Abramson,* Samuel Mon-Wei Yu,* Kirk N. Campbell, Miriam Chung, and Fadi Salem

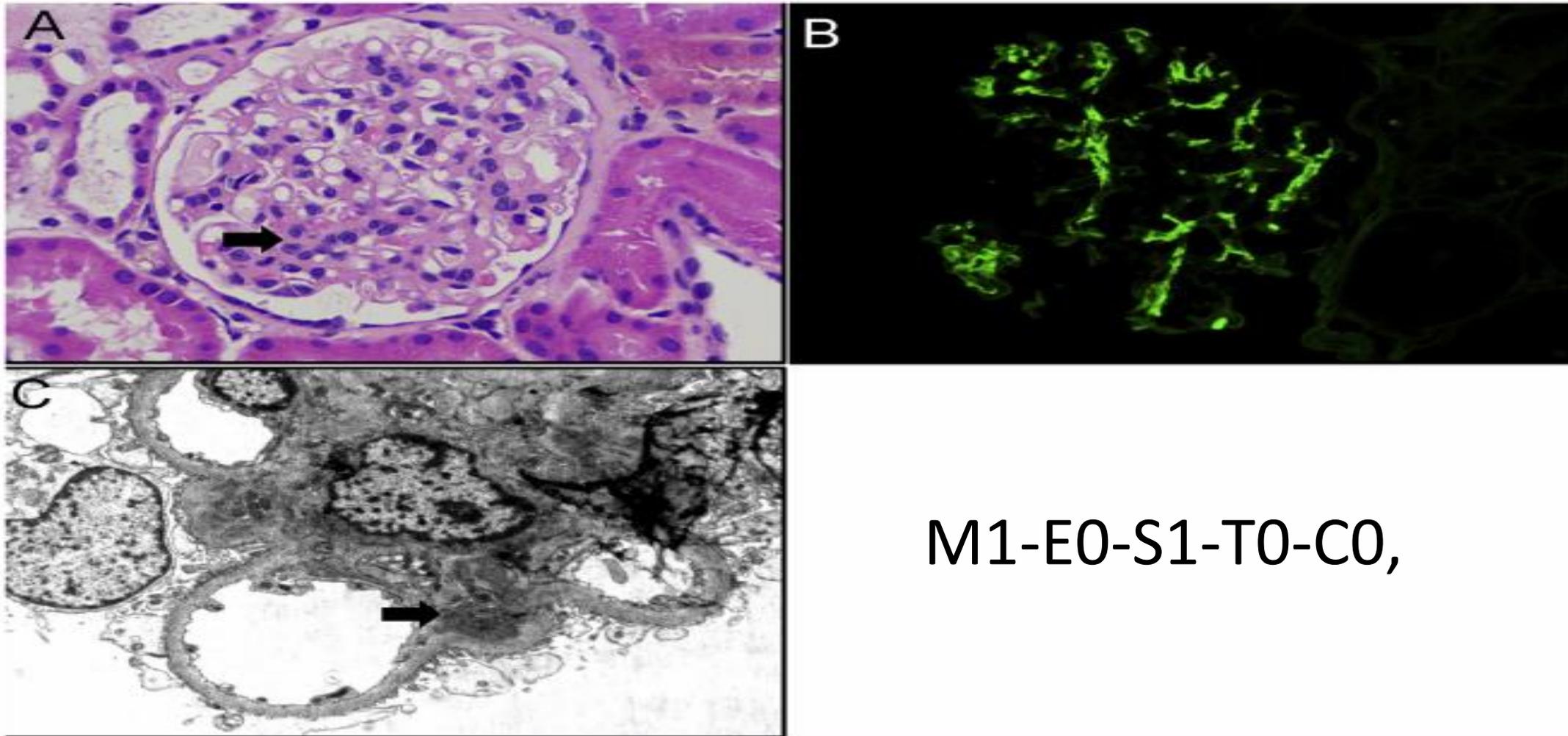
Here we present the first case of newly diagnosed IgA nephropathy (IgAN) after a SARS-CoV-2 vaccination. A 30-year-old man with no known past medical history presented with gross hematuria and subnephrotic proteinuria 24 hours after the second dose of the mRNA-1273 SARS-CoV-2 vaccine. A kidney biopsy showed IgAN. He was started on an angiotensin receptor blocker, resulting in proteinuria reduction. Similar to natural infection of SARS-CoV-2, persons who receive 2 mRNA-based vaccines demonstrate robust antibodies against the receptor-binding domain (RBD) of the S1 protein. Given the uniqueness of glycosylation of RBD and potent stimulation of immune response from mRNA-based vaccine compared to other vaccines, we hypothesize that our patient developed de novo antibodies, leading to IgA-containing immune-complex deposits. This case highlights the urgency of understanding the immunological responses to novel mRNA-based SARS-CoV-2 vaccines in more diverse populations. Despite the lack of clear causality, nephrologists should be alerted if any new-onset hematuria or proteinuria is observed.

Complete author and article information provided before references.

*M.A. and S.M.Y. contributed equally to this work.

Kidney Med. XX(XX):1-4.
Published online month xx, xxxx.

doi: 10.1016/j.xkme.2021.05.002



M1-E0-S1-T0-C0,

Figure 1. (A) Glomerular mesangial expansion and hypercellularity (black arrow) (hematoxylin-eosin, $\times 200$). (B) Strong glomerular mesangial deposits for IgA antisera (immunofluorescence study, $\times 200$). (C) Ultrastructural evaluation revealed immune-type electron-dense deposits involving the mesangium (black arrow) (transmission electron microscopy, $\times 4,000$).

Table 1 | Patient demographics and clinical characteristics

| | Patient 1 | Patient 2 | Reference range |
|---|--|--|--|
| Clinical presentation | | | |
| Age, yr/race/sex | 41/Chinese/female | 60/Malay/female | |
| Medical history | Gestational diabetes mellitus | Hyperlipidemia | |
| Date of vaccination | | | |
| First dose | March 3, 2021 | January 29, 2021 | |
| Second dose | March 26, 2021 | February 19, 2021 | |
| Date of hematuria | March 27, 2021 | February 20, 2021 | |
| Date of presentation to nephrology | March 28, 2021 | March 31, 2021 | |
| Blood pressure at presentation, mm Hg | 153/99 | 188/95 | |
| Significant laboratory results* | | | |
| Serum creatinine, $\mu\text{mol/L}$ | 153 | 541 | |
| Urine dysmorphic red blood cells/ μl | >200 | >200 | |
| Urine protein-to-creatinine ratio, g/g | 2.03 | 7.58 | |
| Serum Ig | | | |
| Serum IgG, g/L | 12.90 | 9.95 | 5.49–17.11 |
| Serum IgA, g/L | 6.40 | 1.62 | 0.47–3.59 |
| Serum IgM, g/L | 1.10 | 0.35 | 0.15–2.59 |
| Complement C3, g/L | 0.83 | 1.11 | 0.90–1.80 |
| Complement C4, g/L | 0.20 | 0.24 | 0.10–0.40 |
| Anti-nuclear antibody | 1:320; Homogeneous | Negative | |
| Anti-GBM antibody (ELISA) | <1.5 | 10.0 | <7 U/ml = negative; 7–10 U/ml = indeterminate; >10 U/ml = positive |
| Anti-GBM antibody (IF) | Not done | Positive | |
| Histopathology report | | | |
| Glomeruli | 36 Glomeruli; 5 globally sclerosed. Focal proliferative glomerulonephritis with focal segment glomerulosclerosis; 6% cellular and 8% fibrocellular crescents | 22 Glomeruli; 6 segmentally sclerosed. Diffuse crescentic glomerulonephritis with segmental sclerosis; 59% cellular, 14% fibrocellular, and 5% fibrous crescents | |
| Tubules and interstitium | Mild tubulointerstitial inflammation. Mild tubular atrophy and interstitial fibrosis | Acute tubular injury Mild tubular atrophy | |
| Vessels | Mild hyalinosis. No vasculitis or thrombotic microangiopathy | Mild intimal fibrosis | |
| IF | Dominant glomerular IgA staining | Trace to 1+ linear IgG staining of glomerular basement membrane | |
| Electron microscopy | Electron-dense deposits mostly in mesangial and paramesangial locations | No electron-dense deposits | |
| Treatment | Pulse methylprednisolone, followed by oral prednisolone; i.v. cyclophosphamide | Pulse methylprednisolone, followed by oral prednisolone; oral cyclophosphamide; plasma exchange | |

ELISA, enzyme-linked immunosorbent assay; GBM, glomerular basement membrane; IF, immunofluorescence.

*Other autoantibodies, such as anti-streptomyacin O titer (ASOT), anti-double-stranded DNA (anti-dsDNA), anti-neutrophil cytoplasmic antibody (ANCA) by IF, anti-myeloperoxidase, and anti-proteinase 3 antibodies, were not detected.

- 1) Complejos inmunes formados por IgA1 patógena e IgG o IgA específica
- 2) Una eliminación hepática deteriorada
- 3) Mayor afinidad por las células mesangiales. (1)

Mecanismos fisiopatológicos: IgAN



Multi Hit

- 1) Predisposición genética
- 2) Eventos desencadenantes: Infecciones, toxico ambientales (2)

¿Vacunas? (3)

Table 1. Vaccine-associated kidney diseases (Original).

| Vaccine | Kidney disease/pathology reported in the literature | References |
|----------------------------------|---|------------|
| Influenza | <ul style="list-style-type: none"> • Nephrotic syndrome: MCD, MN • Rhabdomyolysis with ATN, AIN • Pauci-immune GN/ Renal vasculitis • HSP • Kidney graft rejection | 5-30 |
| Hepatitis B | <ul style="list-style-type: none"> • Nephrotic syndrome: MCD • Lupus nephritis: Class IV | 31-34 |
| Pneumococcal | <ul style="list-style-type: none"> • Crescentic GN due to anti-GBM disease • Nephrotic syndrome: MCD | 35,36 |
| Pertussis | <ul style="list-style-type: none"> • Renal vasculitis | 37 |
| Diphtheria pertussis tetanus | <ul style="list-style-type: none"> • Cryoglobulinemia and proliferative GN | 38 |
| Tetanus diphtheria poliomyelitis | <ul style="list-style-type: none"> • Nephrotic syndrome: MCD | 39 |
| Smallpox | <ul style="list-style-type: none"> • Nephrotic syndrome: MN | 40 |
| Measles | <ul style="list-style-type: none"> • Nephrotic syndrome: MCD | 41 |
| Rabies | <ul style="list-style-type: none"> • Nephrotic syndrome | 42 |
| Meningococcal | <ul style="list-style-type: none"> • Relapse of nephrotic syndrome | 43 |
| BCG | <ul style="list-style-type: none"> • Renal granulomas • AIN with or without granulomas • HSP • Nephrotic syndrome: MN | 45 |

MCD: Minimal change disease, MN: Membranous nephropathy, ATN: Acute tubular necrosis, AIN: Acute interstitial nephritis, HSP: Henoch-Schoenlein Purpura, GN: Glomerulonephritis, GBM: Glomerular basement membrane, BCG: Bacillus Calmette-Guerin.

1. Novak J, Julian BA, Tomana M, Mestecky J. IgA glycosylation and IgA immune complexes in the pathogenesis of IgA nephropathy. Semin Nephrol. 2008;28(1):78-8
2. Lai KN. Pathogenesis of IgA nephropathy. Nat Rev Nephrol. 2012;8(5):275-283.
3. Patel C, Shah HH. Vaccine-associated kidney diseases: a narrative review of the literature. Saudi J Kidney Dis Transpl. 2019;30(5):1002-1009

Humoral immune response to influenza vaccination in patients with primary immunoglobulin A nephropathy. An analysis of isotype distribution and size of the influenza-specific antibodies.

A W van den Wall Bake, ... , N Masurel, L A van Es

J Clin Invest. 1989;**84**(4):1070-1075. <https://doi.org/10.1172/JCI114269>.

Research Article

Primary IgA nephropathy (IgAN) is characterized by mesangial deposits of IgA1, increased serum IgA1 levels, and circulating immune complexes containing predominantly IgA1. It has previously been found that patients with IgAN have a higher than normal IgA response to vaccination, but the IgA subclasses have not been studied. To investigate whether the IgA hyperresponsiveness is limited to the subclass IgA1, which is involved in the pathogenesis of IgAN, we compared the immune responses of 18 patients with 22 healthy controls after intramuscular vaccination with inactivated influenza virus. Antibody titers were significantly higher (P less than 0.0001) for the IgA1 subclass in patients versus controls, but not for the other isotypes. A substantial portion of the IgA and IgA1 antiinfluenza immune response comprised polymers in both patients and controls. There was no preferential response to the polymer form in patients. There were more monomeric IgA1 antibodies than controls. These results indicate that the hyperresponsiveness is limited to the subclass IgA1 and mainly expressed by polymers.

18 pacientes (14 hombres y 4 mujeres con una edad media de 36,0 años; rango, 24-78 años) con IgAN comprobada por biopsia.

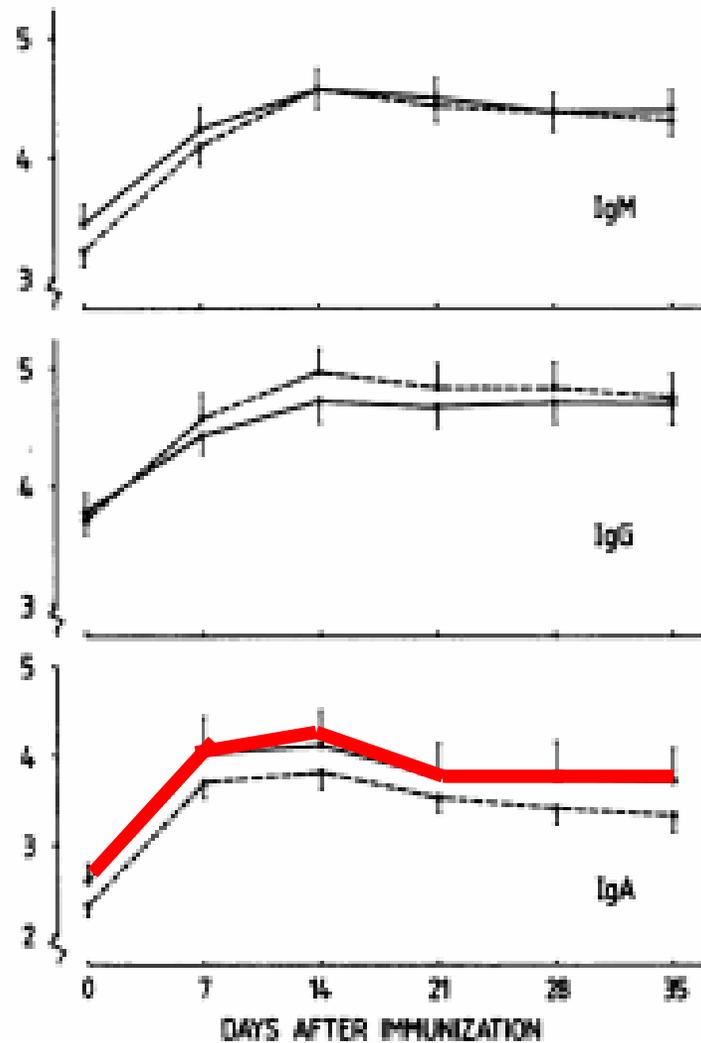


Figure 1. Plot of the IgM, IgG, and IgA anti-influenza titers, transformed to their natural logarithms, versus time after immunization. *Solid line*, mean response in patients ($n = 18$); *dashed line*, controls ($n = 22$); *vertical bars*, SEM. (Top) IgM immune response; (middle) IgG response; (bottom) IgA response. Patients were not significantly different from controls for IgM ($P = 0.36$) or IgG ($P = 0.31$). The difference between patients and controls was marginally significant for IgA ($P = 0.058$).

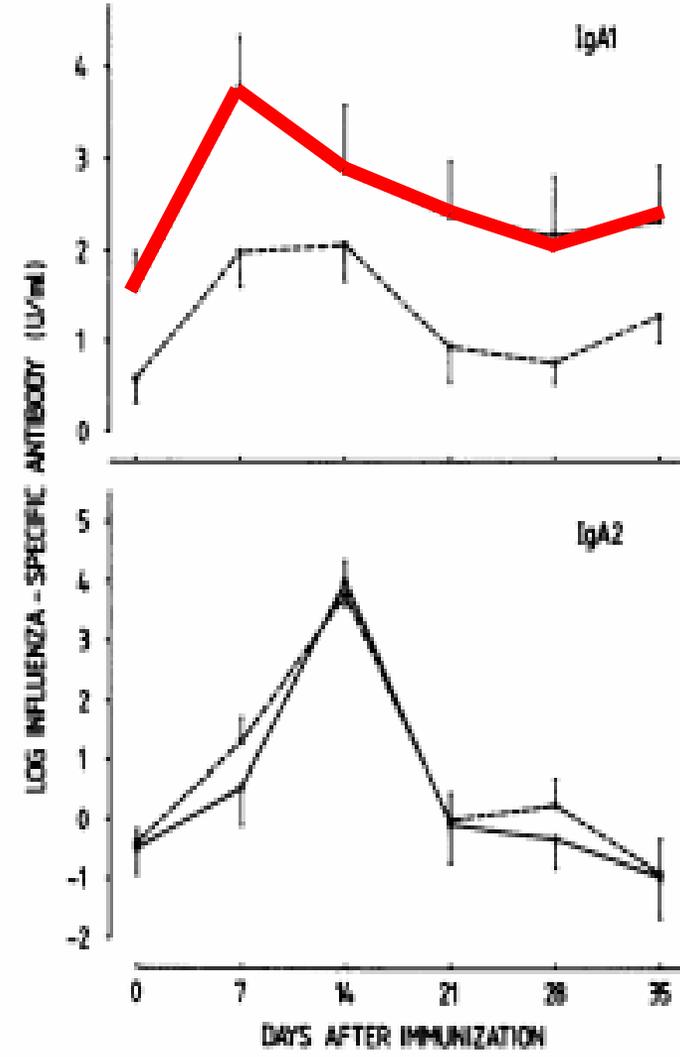


Figure 2. Plot of the IgA1 and IgA2 anti-influenza titers, transformed to their natural logarithms, versus time after immunization. *Solid line*, mean response in patients ($n = 18$); *dashed line*, controls ($n = 22$); *vertical bars*, SEM. (Top) IgA1 immune response; (bottom) IgA2 response. Patients had a significantly higher IgA1 anti-influenza response than controls ($P < 0.0001$). The IgA2 response was not significantly different from controls ($P = 0.44$).

Immune response to oral polio vaccine in patients with IgA glomerulonephritis

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(Accepted for publication 22 October 1986)

SUMMARY

Oral poliovirus vaccine was used to immunize 51 patients with IgA glomerulonephritis and 44 healthy controls. The patients showed an enhanced antibody response compared to controls. This was apparent in a higher frequency of strong increases in neutralizing antibody titres during the course of immunization as well as higher levels of virus-specific IgA-class antibodies. IgG-class antibodies showed similar activity in both groups. In patients the neutralizing antibodies correlated with the virus-specific IgA-class antibodies, suggesting that the IgA-antibodies synthesized by the patients are functionally competent antibodies

| Sample | Test | Mean values (EIU) | | Statistical significance* |
|--------|-----------|-------------------|----------|---------------------------|
| | | IgA-GN | Controls | |
| I | ELISA IgG | 90.5 | 90.8 | NS |
| | ELISA IgA | 62.3 | 31.6 | $P < 0.001$ |
| | NT | 220 | 150 | NS |
| II | ELISA IgG | 99.4 | 99.3 | NS |
| | ELISA IgA | 67.5 | 32.6 | $P < 0.001$ |
| | NT | 454 | 276 | NS |
| III | ELISA IgG | 101.6 | 103.7 | NS |
| | ELISA IgA | 68.6 | 39.5 | $P < 0.001$ |
| | NT | 651 | 552 | NS |

ELISA, enzyme-linked immunosorbent assay; NT, neutralization test.

* Tested by Mann-Whitney test.

Exceptional Case

Influenza virus vaccination and kidney graft rejection: causality or coincidence

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Table 1. Comparison of the three cases

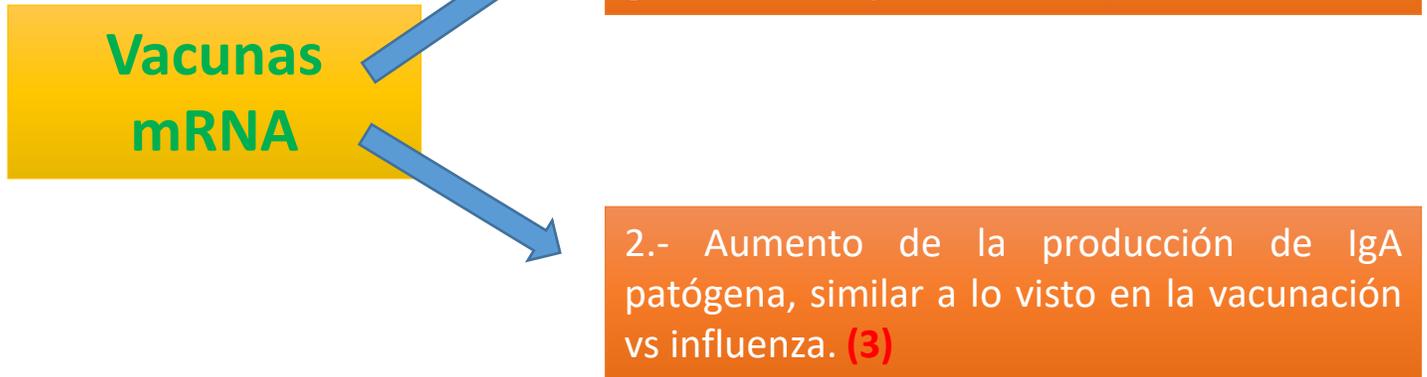
| | Case 1 | Case 2 | Case 3 |
|--|---|--|---|
| Time from vaccination until hospitalization (days) | 58 | 53 | 34 |
| Kidney biopsy | Acute and chronic humoral rejection, C4d positive | Acute cellular rejection (Banff-type IA), C4d negative | Recurrent IgA nephropathy, C4d negative |
| Urine protein prior to vaccination (g/L) | 0.418 | Undetectable | Undetectable |
| Urine protein after vaccination (g/L) | 0.732 (5 months after admission) | 0.2 (2 months after) | 4.98 (3½ months after) |

- 1) Complejos inmunes formados por IgA1 patógena e IgG o IgA específica
- 2) Una eliminación hepática deteriorada
- 3) Mayor afinidad por las células mesangiales. (1)

Mecanismos fisiopatológicos:

Multi Hit

Vacunas mRNA



1.- Formación de Acs anti glicanos que reaccionan de forma cruzada vs IgA1 sub galactosidada pre formada. (3)

2.- Aumento de la producción de IgA patógena, similar a lo visto en la vacunación vs influenza. (3)

- 1) Predisposición genética
- 2) Eventos desencadenantes: Infecciones, toxico ambientales (2)

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2. Lai KN. Pathogenesis of IgA nephropathy. Nat Rev Nephrol. 2012;8(5):275-283.
3. Abramson M, Mon-Wei Yu S, Campbell KN, Chung M, Salem F. IgA Nephropathy After SARS-CoV-2 Vaccination [published online ahead of print, 2021 Jul 14]. Kidney M 2021;10.1016/j.xkme.2021.05.002. doi:10.1016/j.xkme.2021.05.002

Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine



Larissa Lebedev, Marina Sapojnikov, Alexander Wechsler, Ronen Varadi-Levi, Doron Zamir, Ana Tobar, Nomy Levin-Iaina, MD, Shlomo Fytlovich, and Yoram Yagil

We report on the development of minimal change disease (MCD) with nephrotic syndrome and acute kidney injury (AKI), shortly after first injection of the BNT162b2 COVID-19 vaccine (Pfizer-BioNTech). A 50-year-old previously healthy man was admitted to our hospital following the appearance of peripheral edema. Ten days earlier, he had received the first injection of the vaccine. Four days after injection, he developed lower leg edema, which rapidly progressed to anasarca. On admission, serum creatinine was 2.31 mg/dL and 24-hour urinary protein excretion was 6.9 grams. As kidney function continued to decline over the next days, empirical treatment was initiated with prednisone 80 mg/d. A kidney biopsy was performed and the findings were consistent with MCD. Ten days later, kidney function began to improve, gradually returning to normal. The clinical triad of MCD, nephrotic syndrome, and AKI has been previously described under a variety of circumstances, but not following the Pfizer-BioNTech COVID-19 vaccine. The association between the vaccination and MCD is at this time temporal and by exclusion, and by no means firmly established. We await further reports of similar cases to evaluate the true incidence of this possible vaccine side effect.

Complete author and article information provided before references.

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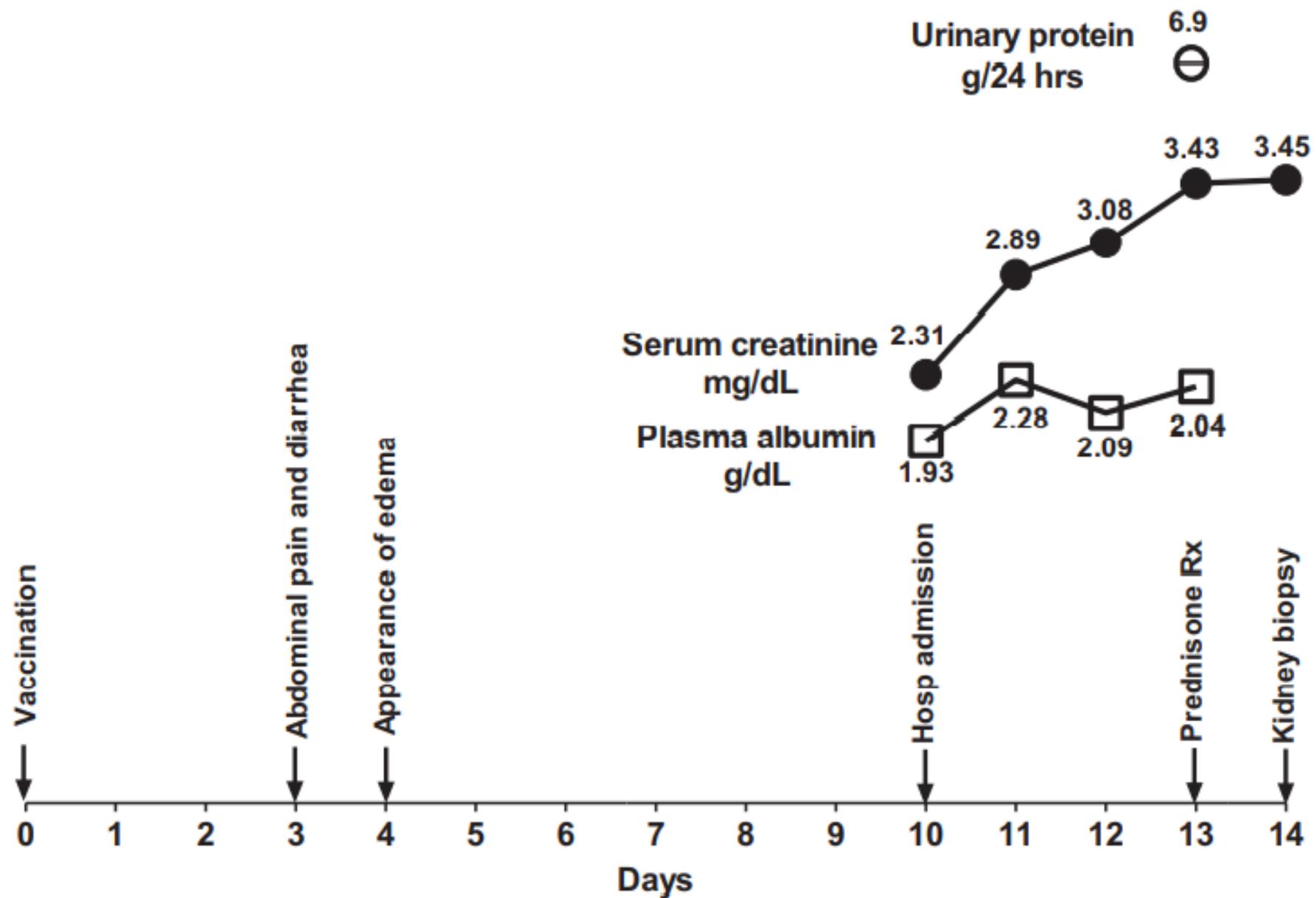


Figure 1. Timeline of clinical events from time of vaccination and until the kidney biopsy was performed.

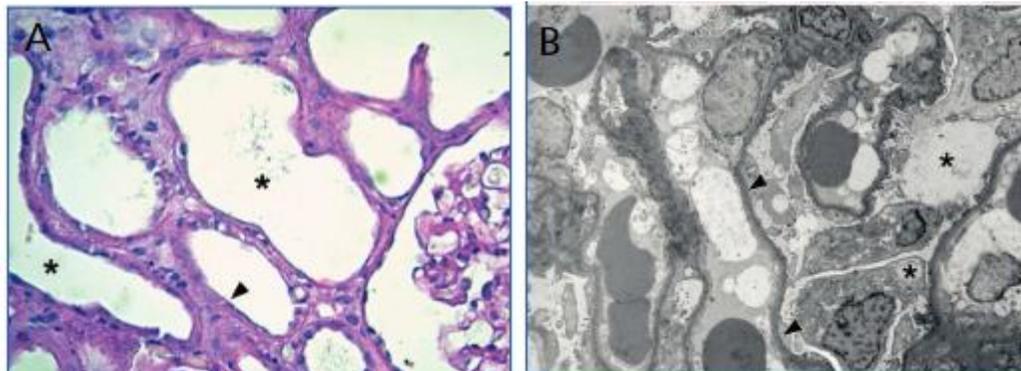
Minimal change disease following influenza vaccination and acute renal failure: just a coincidence?

Nefrologia 2012;32(3):414-5

doi:10.3265/Nefrologia.pre2012.Feb.11370

Hombre de 44 años ingresó en con edema en cara y piernas y linfadenopatía cervical que se presentó 18 días después de la vacunación contra la influenza (Agrippal®, Novartis).

- 1) Disfunción de las células T con producción de un factor de permeabilidad.
- 2) "intercomunicación" entre células dendríticas y linfocitos con la consiguiente producción de citocinas intrarrenales.
- 3) La modulación del citoesqueleto de actina a nivel del diafragma de filtración
- 4) Desestabilización de la proteína sinaptopodina 5



Case report

Open Access

Minimal change nephrotic syndrome in an 82 year old patient following a tetanus-diphtheria-poliomyelitis-vaccination

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Table 1: Summary of MCNS following vaccination in literature

| Vaccination against | Tetanus-diphtheria-poliomyelitis-vaccination | Pneumococcus [6] | Influenza [7] | Hepatitis B [3] | Hepatitis B [4] | Hepatitis B [5] |
|----------------------------------|---|---|-------------------------------------|---------------------------|-----------------------------------|---------------------------|
| Age [years] | 82 | 67 | 65 | 3 | 40 | 4 |
| Gender | female | female | female | male | female | male |
| Baseline creatinine | 76 $\mu\text{mol/l}$ | no data | normal | 44 $\mu\text{mol/l}$ | normal | no data |
| Peak creatinine | 138 $\mu\text{mol/l}$ | 274 $\mu\text{mol/l}$ | 158 $\mu\text{mol/l}$ | no data | no data | no data |
| Baseline proteinuria | negative in dipstick | past history unremarkable | no data | past history unremarkable | past history unremarkable | past history unremarkable |
| Peak proteinuria | 12 g/day | 10.4 g/day | 13.2 g/day | 24.8 g/day | 8 g/day | 1.25 g/day |
| Vaccination to onset of symptoms | 4 weeks | 4 months | 4 days | 17 days | after 2 nd inoculation | 8 days |
| Biopsy | typical minimal change lesion (MCL) | MCL and mild interstitial nephritis | typical minimal change lesion (MCL) | not indicated | minimal change nephropathy | not indicated |
| Treatment | Steroids 1 mg/kg bw ACE-inhibitor | 750 mg Steroids for 3 days; followed by 40 mg/day | None specific | Steroids 2 mg/kg bw | Steroids (12 mg every other day) | Steroids 2 mg/kg bw |
| Renal function/ follow up | 80 $\mu\text{mol/l}$ 6 months after diagnosis | Urinary protein neg. after one year; 15 mg Steroids/day | Clearance 95 ml/min after one year | no data | no data | Complete remission |



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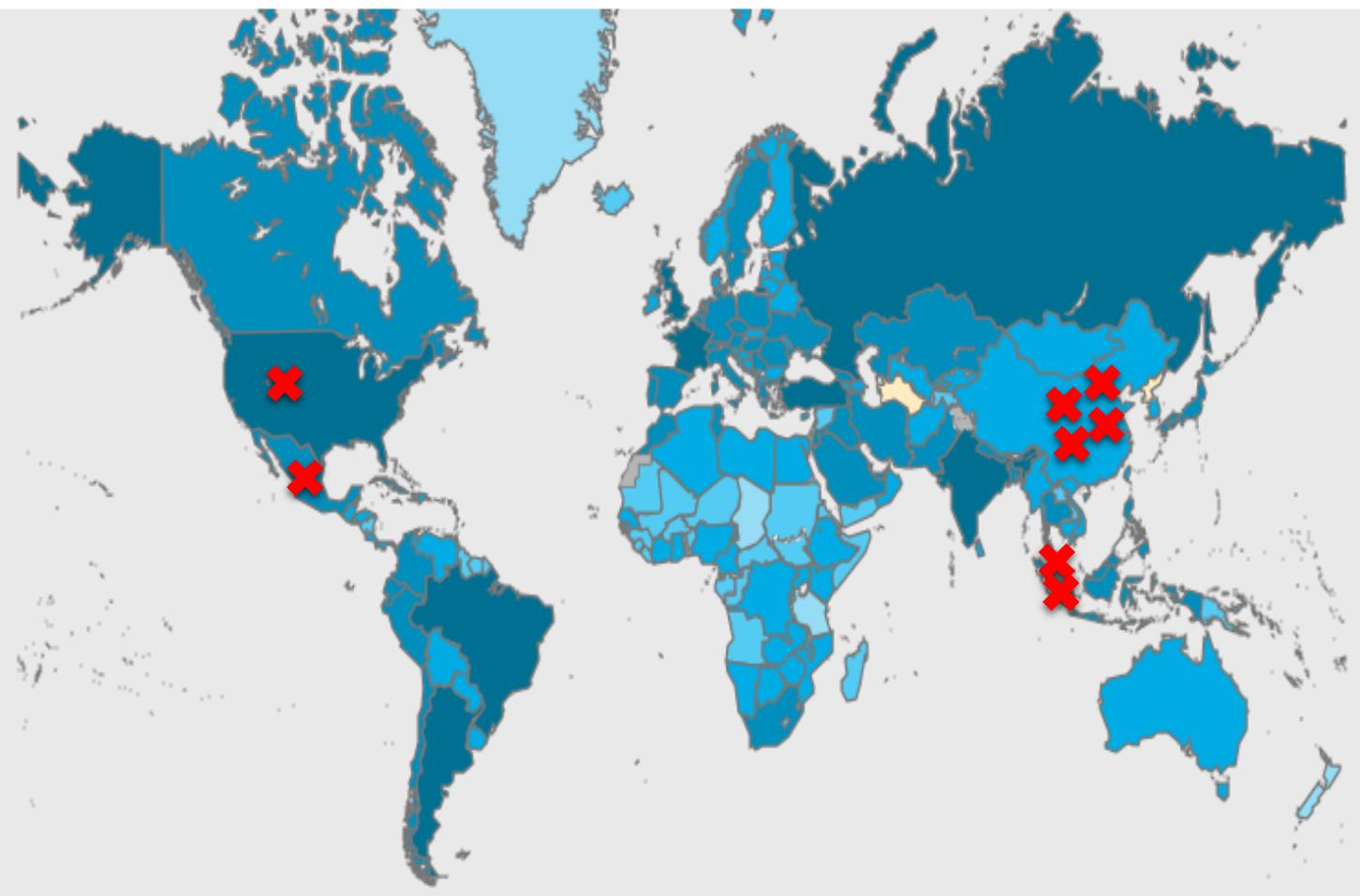
Cases
Total

521,035
new cases

216,867,420
confirmed cases

4,507,837
deaths

5,019,907,027
vaccine doses administered



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Conclusiones:

- No existen elementos suficientes para establecer causalidad.
- ¿Coincidencia?.
- Incidencia **“extremadamente baja”**.
- Los pacientes con IgAN tienen una respuesta inmune más alta de lo normal a la vacuna contra antígenos virales (influenza, polio) limitada al isotipo IgA1.
- Necesidad de farmacovigilancia.
- **¿Tratamiento?**, basado en recomendaciones de GN de base.
- Valorar **“riesgo – beneficio”** de esquemas de inmunosupresión en pandemia.
- Las vacunas son por mucho **“la mejor alternativa”**