C3 glomerulonephritis accompanied with lupus nephritis

Lomerulonefritis C3 acompañada de nefritis lúpica

Dear Editor:

Complement 3 (C3) glomerulopathy is diagnosed when C3 dominant glomerulonephritis is seen in kidney biopsy with C3 only deposition without immunoglobulin (Ig), or dominant C3 with up to 1 + IgM, or dominant C3 of +2 orders of magnitude of intensity by immunoflourescent (IF) greater than any other immune reactant (using a scale of 0 to 3, including 0, trace, 1+, 2+, 3+).[1] Systemic lupus erythematosus (SLE) lead to renal damage through immune deposition such as IgG, IgA, IgM, C3, and C1q, with IgG dominance or codominance in a specific pattern known as full-house.[2]

A 49 year old male patient applied to our clinic due to high serum creatinine levels noticed at dermatology department during examination for discoid rash. He was well until his skin eruptions have erosen one month ago. Hydroxychloroquine and topical corticosteroid were prescribed to him for cutaneous lupus erythematosus diagnosed by skin biopsy. His blood pressure was 120/80 mmHg. Trace pretibial edema and hypopigmented lesions on forearms were detected. Biochemically, his serum creatinine (Cr) level was 1.28 mg/dL, estimated glomerular filtration rate (eGFR) Chronic Kidney Disease Epidemiology Collaboration equation (CKD–EPI-cre based): 66 mL/min/1.73 m^2, serum albumin level was 3.6 g/dL, proteinuria was 660 mg/day, his urine sediment was inactive at admission. Kidneys were ultrasonographically normal in size and echogenicity. Double-checked result of proteinuria level was 1.87 g/day, complement 3 (C3) and complement 4 (C4) levels were normal (104 mg/dL, normal range = 90–180; and 16 mg/dL, normal range = 10–40 respectively), antinuclear antibody (ANA) was detected positive at 1/1000–1/3200 titration by IFA (immunofluorescence assay), anti-double-stranded deoxyribonucleic acid (anti-dsDNA) antibody level was found as 176.2 IU/mL (negative titration = <100 IU/mL) by IFA, presence of perinuclear (myeloperoxidase) anti-neutrophil cytoplasmic antibodies (ANCA) was observed by IFA with a serum titration between 1/32 and 1/100 together with positive anti-SS-A, anti-Smith (anti-Sm), anti-histone, and anti-nucleosome antibodies tested by immunoblot analysis.

Renal biopsy revealed membranoproliferative glomerulonephritis with diffuse glomerular basal membrane thickening and global mesangial matrix expansion by light microscopy (Fig. 1). Six of the 17 glomeruli were globally sclerotic. No cellular/fibrous crescent and necrosis was noticed. Direct immunofluorescence microscopy displayed granular full-house staining with predominant intense C3 staining (severity degree of +3) (Fig. 2), followed by C1q (mild staining), and IgG (mild staining), in addition to lambda (moderate staining), kappa (mild staining) and fibrin (severe staining). C4d staining showed presence of C4d deposition. Autoantibody test results and findings of skin biopsy made us thought lupus nephritis at first. However kidney biopsy revealed findings associated with both lupus nephritis class IV-G (A/C) and C3 dominant glomerulopathy. The dominant C3 deposition made it necessary to research molecular genetic

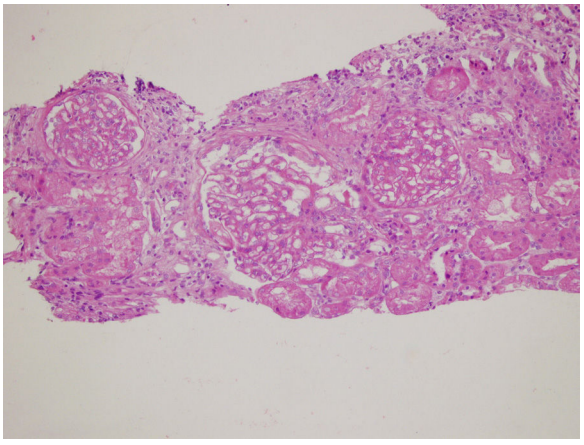

Fig. 1 – Renal biopsy which shows diffuse global basal membrane thickening, lymphocyte dominant tubulointerstitial inflammation, increased fibrosis, and tubular atrophy by light microscopy, H.E. 400×.

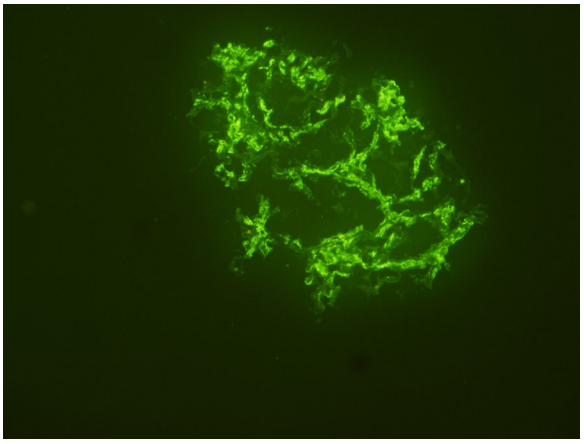

Fig. 2 – Renal biopsy which shows peripheral and mesangial granular pattern severe (+3) C3 deposition in glomerulus by immunoflourescence microscopy, 400×.

complement disorders.[3,4] In our patient, further examinations in order to enlighten C3 glomerulopathy, yielded homozygous p.His402Tyr mutation due to c.1204C>T change in the complement factor H (CFH) gene and homozygous p.Val306fs mutation due to c.914_915insA insertion in the complement 3 (C3) gene and heterozygous p.Lys565Glu mutation due to c.1693A<G change in the complement factor B (CFB) gene by new generation DNA sequencing analysis. In the meantime, proteinuria level of the patient was increased to 5.7 g/day. Methylprednisolone and mycophenolate mofetil were given to the patient because he developed hypersensitivity to cyclophosphamide. Proteinuria level decreased to 2.56 g/day, serum creatinine level decreased to 1 mg/dL, and serum albumin level increased to 3.9 g/dL after 1 year of follow-up.

Our patient was diagnosed as SLE by fulfillment of either the 1997 American Collage of Rheumatology (ACR) criteria and by the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria.[5] The signature of lupus nephritis in renal pathology is polyclonal staining of IgG, IgA, IgM, C3 and C1q with dominant or codominant IgG.[2] There was no dominant IgG deposits, even no uniform involvement of IgG and C3 deposits in our case.[6] Instead, C3 dominance fulfilled the criterion necessary to diagnose C3 glomerulopathy defined by consensus report of International Society of Nephrology.[1] Dysregulation of complement system due to mutations or antibodies lead to C3 glomerulopathy. Only ≅25% of cases diagnosed as C3 glomerulopathy were reported to have genetic mutations in genes of C3 (encoding complement factor 3), CFB (encoding complement factor B), CFH (encoding complement factor H, the regulatory protein of compleman activation), CFI (encoding complement factor I, inactivator of C3b), and CFHR5 (encoding complement factor H-related protein 5, enhancer of complement activation).[7] The c.1204c>T; p.His402Tyr variant in the CFH gene has been reported to be highly associated with dense deposit disease and favorable outcomes in age-related macular degeneration.[8,9] This variant of CFH put our patient at an increased risk for liability to complement-mediated diseases which emerge in adulthood. The second variant in genetic sequence of complement factor B gene was probably pathogenic for complement mediated disorders like thrombotic microangiopathy as reported previously.[10] It remains to be determined whether the third genetical variant in complement 3 gene is capable of causing complement mediated disease. The data about mutation in the complement factor B gene of our patient and its clinical importance for enhanced formation and delay in inactivation of C3bBb convertase needs to be searched.

In conclusion, as far as we know this is the first case showing the togetherness of C3 glomerulopathy and lupus nephritis. After one year of treatment with methylprednisolone and mycophenolate mofetil, renal improvement was achieved. Further studies will enlighten the best therapeutic approach for this new entity in the future.

Authorship contributions

Concept: Kubra Kaynar. *Design*: Kubra Kaynar, Beyhan Güvercin. *Control*: Kubra Kaynar, Beyhan Güvercin, Sahile Safarlı, Sevdegül Mungan, Mustafa Şahin. *Data Collection*: Sahile Safarlı, Sevdegül Mungan, Mustafa Şahin. *Literature review*: Kubra Kaynar. *Writing the manuscript*: Kubra Kaynar.

Compliance with ethical standards

All authors declare that there are no conflicts of interests related to the study and no fund was taken. Informed consent was obtained from patient.

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Hipernatremia grave tras el empleo de cloruro sódico hipertónico en cirugía de hidatidosis hepática

Severe hypernatremia after hypertonic saline use as treatment of hepatic hydatidosis surgery

Sr. Director:

La hipernatremia secundaria al empleo de suero salino hipertónico (SSH) como escolicida en la cirugía del quiste hidatídico es una complicación muy infrecuente, pero de extrema gravedad ya que puede causar complicaciones neurológicas irreversibles[1].

Presentamos el caso de una hipernatremia aguda y grave tras la cirugía de un quiste hidatídico. La paciente tenía 60 años, sin ningún antecedente personal de interés, y residía en medio urbano. Consultó por molestias abdominales en hipocondrio derecho de un año de evolución. En la ecografía abdominal se objetivó una imagen quística compatible con un quiste hidatídico que medía 20 cm de diámetro, categoría CE1-CE2 según la clasificación de la Organización Mundial de la Salud[2]; además, la serología del *Echinococcus granulosus* fue positiva. Tras el diagnóstico de hidatidosis hepática se decidió tratamiento con albendazol durante 4 semanas y se realizó una quisto-periquistectomía parcial.

Se llevó a cabo una laparotomía con apertura local del quiste, y protección de la pared abdominal y del peritoneo con material plástico, se aspiraron un total de 2.500 cc de contenido quístico. Durante la punción del quiste la paciente presentó hipotensión arterial brusca y bradicardia que respondió a adrenalina, metilprednisolona y dexclorfeniramina. Posteriormente se llevaron a cabo 2 instilaciones consecutivas de SSH al 3% en la cavidad quística hasta su repleción completa, con una permanencia, cada una de ellas, de 15 min tras lo cual se aspiraron un total de 5 l de contenido. Se estimó un sangrado de 1.000 cc. Durante la cirugía se administraron un total de 1.000 cc de suero salino al 0,9% y 600 cc de concentrados de hematíes. Posteriormente presentó tendencia a la hipotensión arterial precisando noradrenalina en perfusión continua. Al finalizar el procedimiento se evidenció una marcada hipernatremia con Na^+ 182 mmol/l (osmolaridad plasmática de 378 mosm/kg).

En las primeras 24 h se administraron 2.000 cc de suero glucosado al 5% (SG5). Además, presentó fracaso hepático agudo, anemización, hiperfibrinólisis y coagulopatía de consumo con un débito hemático por drenaje de 1.500 cc precisando transfusión de hematíes, de plaquetas y de plasma fresco congelado, constituyendo un volumen total de 1.650 cc. Presentó una diuresis de 680 cc. Se realizó una TC craneal sin alteraciones agudas.

Tras 24 h, el sodio descendió a 171 mOsm/l (osmolaridad plasmática de 361 mOsm/kg), una glucemia de 445 mg/dl y se objetivó un fracaso renal agudo (FRA) con creatinina de 2,22 mg/dl con una diuresis de 180 cc. Se administraron 1.800 cc de SG5, se inició perfusión de furosemida a 20 mg/h durante 24 h y perfusión de insulina.

A las 72 h se había corregido la hipernatremia por lo que la perfusión de SG5 se suspendió y se inició nutrición parenteral. Persistía una mala situación hemodinámica, dependiente de ventilación mecánica invasiva y perfusión de noradrenalina; además estaba en oligoanuria con creatinina de 4,45 mg/dl. Precisó hemodiafiltración intravenosa continua (HDFVVC) durante 2 semanas, posteriormente se consiguieron balances negativos con diurético, y tras ello se obtuvo ritmo espontáneo de la diuresis recuperando función renal plena. Al alta hospitalaria no presentaba ninguna secuela neurológica ni de otro tipo. En la tabla 1 se adjuntan los datos analíticos de interés.

La quistoperiquistectomía total abierta o parcial requiere el empleo de agentes escolicidas que tienen como finalidad la muerte del parásito e impedir su diseminación intraperitoneal. Se han utilizado varios, entre ellos: nitrato de plata, formaldehído, agua oxigenada, alcohol, povidona yodada y SSH. En el año 1950 se empleó por primera vez el SSH[1].

La complicación más grave del uso del SSH en la cirugía del quiste hidatídico es la hipernatremia aguda hipervolémica, el primer caso recogido fue en el año 1982[3]. La hipernatremia puede producirse porque el SSH se administre de forma accidental en un vaso sanguíneo hepático, por su derrame en el peritoneo, por su absorción a través de la pared quística o