IgG4-related disease: a wide spectrum of disease of nephrological interest

Quaglia M, Bozzola C, Musetti C, Izzo C, Nappo A, Merlotti G, Boldorini RL, Stratta P
Nephrology and Kidney Transplant, Univ. Piemonte Orientale, Novara, Italy
Unit of Pathology , Department of Health Science, Novara, Italy

claudio.musetti@med.uniupo.it

BACKGROUND

IgG4-related disease (IgG4-RD) is a recently defined disease with an extremely wide clinical presentation; it is characterized by the inflammatory involvement of one or more organs. Also renal manifestations may vary widely, including inflammatory pseudo-tumors, acute or chronic tubule-interstitial nephritis (TIN), membranous nephropathy (MN), pulmonary-renal syndrome (PRS) and obstructive nephropathy due to retroperitoneal fibrosis (RPF).

As this disease has been defined only recently, we looked for histological or laboratory signs of IgG4-related disease in patients with compatible renal manifestations.

METHODS

	Circulating IgG4 (normal < 135 mg/dL)	Immunostaining for IgG4
Idiop. Membranous Nephrop.	30 pts	Done + antiPLA2R staining
Chronic Tubulo-Interstitial Neph.	9 pts	Done
Retroperitoneal Fibrosis	16 pts	Only one pt
Pulmonary-renal syndrome	1 pt	-
Renal Mass (not growing)	1 pt	-
Total	57 pts	39 pts

IgG4-RD DIAGNOSIS

Histology: plasmacell rich TIN (>10 IgG4+ pc/hpf); tubular basement membrane IC deposits (IF, IHC or EM); interstitial focal fibrosis with or without lympho-plasmacytic infiltrate

Imaging: small peripheral low-attenuation cortical nodules, round or wedge shaped lesions, or diffuse pathcy involvement or diffuse enlargement

Serology: High circulating IgG4 or total IgG

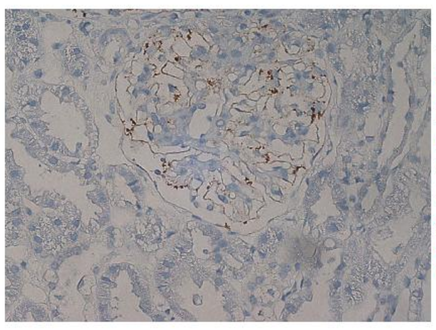
Other organs: AI pancreatinis, sclerosig cholangitis, inflammatory masses, sialoadenitis, inflammatory aortic aneurysm, lung involvement (UIP, NSIP, AIP, LIP, other ILD, pleurisy), retrop. fibrosis.

RESULTS

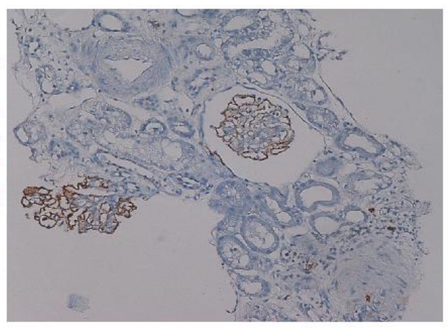
	High serum IgG4 (>135 mg/dL)	IgG4 levels	IHC-IgG4	Concordance
I. Membr. N.	3/30 (10%)	360	3/30	Yes
cTIN	1/9 (11.1%)	576	1/9	Yes
RPerit. Fibros.	2/16 (12.5%)	3740	1/1	Yes
PulmRen S	1/1	495	n/a	n/a
Renal Mass	1/1	1735	n/a	n/a

IgG4-related membranous nephropathies

Pt (sex/age)	U-Prot (g/day)	CrCl (ml/min)	IgG4 (mg/dL)	Anti PLA-2R (cserum/tissue)	Extra-Renal?	Therapy	U-Prot (g/day)
L.C. (M/60)	2,5	66	450	Neg/Neg	Prostatitis, sialodenitis, atopy	ACE-i	1.0
Q.P. (M/69)	4	60	340	Neg/Neg	Sclerosing cholangitis	St + CPx (6 mo)	0.5
S.B. (M/47)	4,5	110	290	Neg/Neg	Riedel thyroiditis	St + CPx (6 mo)	<0.3



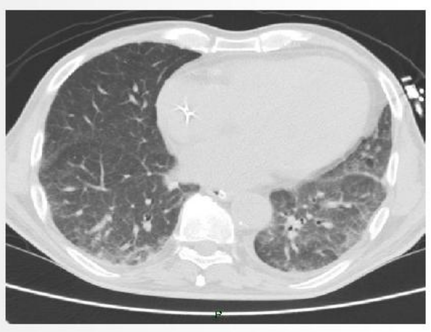
IgG staining in MN: mainly granular positivity on glomerular basement membranes



IgG staining in MN: Intense positivity of both linear and granular aspect along glomerular basement membranes (L.C.)

Pulmonary-Renal Syndrome (acute on chronic)

- Male, 70 yrs
- At 69, diagnosed with UIP with ground glass lesions. BAL: macrophages and eosinophils (10%); mediastinic lymphoadenopathy.
- Chronic hyper IgG (about 2500 mg/dL)
- Since then, unintentional loss of > 20 Kg
- Hospital admission for ARDS with AKI : transbronchial biopsy: *AIP with lympho-plasmacytic infiltrates.*
- Need of invasive ventilation.
- Microbiology/Culture tests: negative
- ANCA: negative; IgG4 = 495 mg/dL



- Therapy: "Low-dose" steroid pulses (total: MP 500 mg)
- Outcome: resolution of lung infiltrates; Creat 5-> 1.3 mg/dL; IgG4 = 220 mg/dL
- Maintenance on oral steroids

IgG4+ Retroperitoneal fibrosis

Pt (sex/age)	Presentation	Other sites of disease?	IgG4 (mg/dL)	Follow up
C.U. (M/76)	AKI: Creat up to 3.4 mg/dL	Lung (Interst. L. Disease w/ ground glass focal fibrosis; lymphocytic alveolitis) Stenosis of choledocus	1320	Therapy: Steroids + Tamoxifen Outcome: Creat = 1,2 mg/dL Indwelling Biliar prosthesis No ureteral stents
A.A. (M/45)	CKD (Creat 2.5 mg/dL) from bilateral hydronephrosis Bialteral ureteral stents. CT and MRI: neoformed tissue PET: positive (retroperitoneal) Biopsy (laparos, Oct 2007): aboundant fibrotic tissue, with eosinophilic nests and intense lympho-plasmacytic infiltrates; Dx: idiopathic Retro-Perit Fibr	Atopy (rhinitis) Lymphadenopathy (mediastinum; lateral cervical) Sialoadenitis (Parothitis)	6160 (at relapse)	2007 Ther: Steroids + Tamoxifen Complete response; no stents, Creat = 2 mg/dL. Steroid tapering during 2010 (still on Tamoxifen): relapse three months after steroid withdrawal (Jul 2010). PET: positive retrop, lymphoadenopathy, parothid gland. IHC for IgG4 on previous biopsy: positive (>40% PC are IgG4+) 2010 Therapy: steroids Complete response; no stents, Creat = 2 mg/dL. Drop of IgG4 levels (563 mg/dL)

DISCUSSION

Renal manifestations of IgG4-related disease may mimic several kidney diseases, including glomerulonephritis, TIN, PRS, RPF and pyelonephritis.

Among "idiopathic" nephropathies, *IgG4-RD manifestations are relatively common, particularly in PLA2R-negative membranous nephropathy, TIN and RPF*.

The diagnosis of IgG4-RD renal involvement may be challenging in atypical cases (ie: renal masses or PRS), but defining this diagnosis has major therapeutic and prognostic implications, as it usually recovers completely after steroid therapy. Given the dramatic response to steroids, *the "ex adiuvantibus" criteria might be used to confirm the diagnosis of IgG4-RD.*

DOI: 10.3252/pso.eu.52era.2015
ePosters supported by F. Hoffmann- La Roche Ltd.