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par

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GLOMERULOPATHIES POST INFECTIEUSES A DEPOTS D'IGA : UNE ETUDE DE COHORTE MULTICENTRIQUE FRANCAISE

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RESUME

INTRODUCTION :

La glomérulonéphrite aiguë post-infectieuse, bien que rare chez l'adulte, est devenue de plus en plus fréquente ces dernières décennies en raison d'une augmentation de l'incidence des infections à staphylocoque. Différentes formes histologiques ont été décrites, la plus récente étant la glomérulonéphrite aiguë à dépôts d'IgA. À notre connaissance, aucune autre étude concernant l'épidémiologie, le pronostic et le suivi de cette forme de glomérulonéphrite aigue post infectieuse n'a été réalisée à ce jour en Europe. L'objectif de notre étude était d'analyser les données cliniques, histologiques et évolutives de patients ayant un diagnostic de glomérulonéphrite aiguë post-infectieuse à dépôts d'IgA.

MATERIELS ET METHODES:

Les données cliniques et biologiques d'une cohorte française multicentrique de 27 patients ont été collectées. Nous avons revu les données de microscopie optique et d'immunofluorescence des biopsies rénales et comparé l'expression immunohistochimique de C4d dans ces biopsies avec des biopsies rénales de patients ayant eu un diagnostic de glomérulonéphrite aigue post infectieuse sans dépôts d'IgA ou de néphropathie à IgA. Nous avons analysé la corrélation entre les caractéristiques cliniques, histologiques et le pronostic rénal et vital des patients.

RESULTATS:

Parmi les 27 patients (23 hommes, 4 femmes, âge moyen = 62 ± 15 ans) inclus, 84% avaient une infection à Staphylococcus Aureus, sensible à la méticilline dans 67% des cas et 44% des patients étaient diabétiques. Les infections étaient le plus fréquemment ostéo-articulaires (44%), cutanées (41%) ou liées à une bactériémie (41%). Tous les patients présentaient une protéinurie, de rang néphrotique dans 70 % des cas, associée à une hématurie chez 95 % des patients; 48 % des patients avaient une insuffisance rénale sévère de stade III de la classification KDIGO avec une créatininémie supérieure à 353,6 µmol/L au moment de la biopsie. Trente deux pourcents des patients avaient une hypocomplémentémie C3 et/ou C4.

La médiane du délai entre l'infection et la maladie rénale était de 20 jours, le premier quartile de patients étant à 12 jours et le troisième à 65 jours ; 7,4% des patients avaient un délai supérieur à 3 mois.

Sur le plan histologique, une glomérulonéphrite (GN) proliférative mésangiale était observée dans 89 % des cas (isolée dans 7 % des cas); une GN proliférative endocapillaire segmentaire ou globale dans 89 % des biopsies (exsudative dans 81% des cas); des croissants étaient présents dans 37 % des cas, et une nécrose fibrinoïde dans 11% des cas. Des dépôts extra-membraneux de type « humps » étaient présents dans 48% des cas et des dépôts endomembraneux dans 11% des cas. Une nécrose tubulaire aiguë et une fibrose interstitielle avec atrophie tubulaire étaient observées dans 85% des cas. Les dépôts d'IgA étaient dominants ou codominants dans 67 % des cas.

Le suivi était disponible pour 26 des 27 patients avec un suivi moyen de 18 mois : malgré le traitement utilisé (une antibiothérapie pour 100% des patients, et une corticothérapie pour 41% des patients), 46% des patients ont gardé une insuffisance rénale chronique terminale, stade IIIA pour 19% des patients, stade IIIB pour 19% des patients et stade IV pour 26% des patients. Une insuffisance rénale terminale a été retrouvé chez 15% des patients. Le mauvais pronostic rénal était corrélé à la présence d'une fibrose interstitielle avec atrophie tubulaire sévère.

CONCLUSION:

La glomérulonéphrite aiguë post-infectieuse à dépôts d'IgA est un diagnostic difficile et correspond à une entité à ne pas méconnaître en raison de la présentation clinique souvent atypique et un spectre lésionnel histologique étendu. Il s'agit d'une néphropathie de mauvais pronostic posant le problème du diagnostic différentiel avec des pathologies ayant un pronostic et une implication thérapeutique différents.

Mots clés: glomérulonéphrite, infections, IgA, staphylocoque aureus, étude multicentrique

ABSTRACT

INTRODUCTION: Infection-related glomerulonephritis (IRGN) is uncommon in adults. Among them, IRGN associated with IgA-dominant immune deposits (IRGN-IgA+) has specific characteristics. To our knowledge no series addressing epidemiology and outcome of IRGN-IgA+ in Europe has been reported. The aim of our study was to assess clinical, pathologic and outcome in patients with IRGN-IgA+.

PATIENTS AND METHODS: A multicentric cohort of patients from 11 French hospitals was studied during the 2007-2017 period. We reviewed clinical, biological and renal histology findings, and we compared expression of C4d in IRGN-IgA+ vs IRGN without IgA deposits (IRGN-IgA-) and IgA nephropathy (IgA-NP). We analyzed associations between renal outcome and clinical or histologic features.

RESULTS: Twenty-seven patients (23 men, 4 women; age: 62±15 years, diabetes: 44.4%) were included. *Staphylococcus Aureus* infection as present in 87.5% of patients (methicillin-sensitive: 66.7%) mostly in bone and joint (44.4%) or skin (40.7%) sites. All patients presented with proteinuria and 95.2% had hematuria. Serum creatinine was >353.6 µMol/l in 48.1%. Hypocomplementemia was detected in 16%. The median delay between infection and renal disease was 20 days (IQR: 12-65 days) but was >120 days in 7.4% of patients.

Mesangial proliferative glomerulonephritis (GN) (88.9%); segmental or global endocapillary proliferative GN (88.9%) with exudative pattern (81.4%); crescentic GN (37.0%); necrotizing GN (11.1%) were frequently found. Subepithelial deposits were present in 48.1% and deposits in capillary loop wall in 11.1% of biopsies. Acute tubular necrosis and interstitial fibrosis with tubular atrophy (IF/TA) were observed in 85.1%.

Acute/subacute histology pattern (vs resolving pattern) was associated with shorter delay to diagnosis (21.5 vs 44.5 days, p=0.0329), more frequent in diabetic patients (71.4% *vs* 36.8%,

p=0.1904) and skin infections (46.2% *vs* 15.6%, p=0.0535) and less frequent in males (28.6% vs 90%, p=0.0047).

C4d expression was observed in 65.2% of the IRGN-IgA+, 57% of the IRGN-IgA-, 83% of the IgA NP with 2+ staining in 18% of IRGN IgA+ and 0% in IRGN IgA- and IgA NP.

During a median follow-up of 13.2 months in 26/27 patients, 46% patients had persistent renal dysfunction (stage IIIA for 19%, IIIB for 19% and IV for 26% of patients) and 15% had end-stage renal disease, despite antibiotics in all patients and steroids in 37% of patients. The poor outcome was correlated to severity of IF/TA.

DISCUSSION: IgA associated-IRGN can be misleading because of atypical clinical presentation, various histologic pattern and differential diagnosis with distinct prognosis and treatment.

Key words : Glomerulonephritis, infections, IgA, staphylococcus aureus, multicentric study

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SERMENT D'HIPPOCRATE

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ABREVIATIONS:

APIGN : Acute postinfectious glomerulonephritis

IgA : Immunoglobulin A

APIGN with IgA deposits : APIGN IgA +

APIGN without IgA deposits : APIGN IgA –

IgA Nephropathy : IgA NP

KDIGO : Kidney Disease Improving Global Outcomes

IF/TA: Interstitial Fibrosis with Tubular Atrophy

GN : Glomerulonephritis

MPGN: membranoproliferative glomerulonephritis

IF : Immunofluorescence

IgG : Immunoglobulin G

IgM : Immunoglobulin M

ANCA: antineutrophil cytoplasmic antibody

eGFR : estimated glomerular filtration rate

CKD EPI : Chronic Kidney Disease Epidemiology Collaboration

ESRD : End-stage renal disease

MSSA: Staphylococcus Aureus

MRSA : Staphylococcus Aureus

ESBL : Extended Spectrum producting Beta Lactamase

TABLE DES MATIERES

INTRODUCTION

The epidemiology of infection-related glomerulonephritis (IRGN) has changed over the last two decades. IRGN was mainly constituted by poststreptococcal APIGN in children until recently [1,2]. However, more recent reports indicate that poststreptococcal APIGN still exists in developing countries and in Northern Australia [3,4]. However, in developed countries, IRGN due to *Staphylococcus* is observed with an increasing frequency in adults and in the elderly [5–8]. Poststaphylococcal GN histologically presented with two patterns: one resembling acute poststreptococcal glomerulonephritis (GN), mostly observed in patients with diabetes mellitus, neoplasia or those with chronic alcoholic consumption, infected with *Staphylococcus Aureus* infection; the other corresponding to membranoproliferative glomerulonephritis (MPGN) in *Staphylococcus epidermidis* infection of atrio-ventricular shunt [8,9]. A third form was reported in 1980 by Spector *et al*, and described in 2003 by Nasr *et al.* with 5 cases of type 2 diabetes patients with a *Staphylococcus Aureus* infection, presenting with acute renal failure and histologic proliferative exudative GN with predominant mesangial IgA deposits [10,11]. Since then, several American or Asiatic teams reported cases and cohorts of infection-related glomerulonephritis with IgA deposits (IRGN-IgA) dominant or codominant with C3 deposits. However, the epidemiology and pathologic findings of IRGN-IgA have not been described in Europe. The aim of the present French nationwide study was to assess clinical, pathologic and outcome of patients with IRGN-IgA.

PATIENTS AND METHODS

Inclusion criteria

Data from 27 patients with IRGN-IgA were retrospectively collected from 11 French hospitals from 2007 to 2017. The diagnostic of IRGN-IgA required following criteria: 1/ proliferative glomerulonephritis (endocapillary and/or mesangial proliferation); 2/ IgA deposits in immunofluorescence (IF); 3/ clinical diagnostic or laboratory evidence of infection preceding the renal biopsy. One patient (3.7%) was included without proliferative glomerulonephritis but only globally sclerotic glomeruli because of his typical clinical history.

Biopsy specimens

All renal biopsy samples were processed by standard techniques of light microscopy and immunofluorescence. They were centrally reviewed by a renal pathologist (E.M.S.) who was blinded from the clinical data. Slides obtained from fixed and paraffin-embedded samples were stained with hematoxylin eosin and saffron, periodic acid-Schiff, trichrome, and Jones or Marinozzi silver. Immunofluorescence was performed in frozen sections using fluorescein isothiocyanate-conjugated antibodies to IgG, IgM, IgA, C3, C1q, kappa, lambda, albumin following manufacturer instructions. Additional immunohistochemistry and electron microscopy analyses were assessed: immunohistochemistry was performed in 23 cases of IRGN IgA+ and 13 supplementary cases (7 IRGN without IgA deposits and 6 IgA nephropathy) in fixed and paraffin-embedded samples using C4d antibody (clone A24T, prediluted, DB Biotech, Kosice, Slovakia) in a BenchMark XT Platform (Ventana Medical Systems, Oro Valley, Arizona, USA) following manufacturer instructions.

Definition of histologic parameters from renal biopsies

The following parameters were noted: total glomeruli, globally sclerotic glomeruli, mesangial hypercellularity, segmental or global endocapillary proliferation, presence of more or less than 5 neutrophils per glomerulus, membranoproliferative pattern, crescentic proliferation,

fibrinoid necrosis, subepithelial (humps) or intramembranous deposits, interstitial fibrosis with tubular atrophy (IF/TA), interstitial inflammation, acute tubular injury, red blood cells within tubular lumens, chronic vascular lesions. Glomerular lesions were segmental when less than 50% of the flocculus was involved, global when more than 50% of the flocculus involved. Interstitial fibrosis with tubular atrophy, interstitial inflammation and acute tubular injury were defined as absent, mild (0-25% of cortical surface area), moderate (26-50%) or severe (>50%). Chronic vascular lesions were defined as absent, mild (vascular narrowing of up to 25% luminal area by fibrointimal thickening), moderate (26-50%), severe (>50%). To evaluate potential prognostic involvement, intensity of these four histologic features was converted into 0 (absent), 1 (mild), 2 (moderate) and 3 (severe).

We classified glomerulonephritis in three different histologic patterns, based on Haas *et al.* [12]: acute (exudative proliferative GN, more endocapillary than mesangial with 5 or more neutrophils per glomerulus), subacute (diffuse endocapillary and mesangial hypercellularity but less than 5 neutrophils per glomerulus), resolving (exclusively or mainly mesangial hypercellularity without crescents, necrosis or 5 or more neutrophils per glomerulus). Crescents and necrosis can be observed in both acute and subacute GN.

The intensity of IF staining was graded on a scale of 0 to 3 and localization of deposits was assessed. The C4d immunohistochemistry staining was graded as follow: 0 (absent), 1 (segmental and focal), 2 (global and diffuse).

Baseline clinical and biological data

Clinical data included age, sex, previous medical history, cause of infection, type of pathogen, clinical presentation. Renal parameters included serum creatinine, proteinuria, serum albumin levels and hematuria. Severe acute renal injury was defined as a stage 3 of Kidney Disease Improving Global Outcomes (KDIGO) classification, corresponding to a serum creatinine >353.6 µmol/L or need for dialysis.

Other parameters were recorded including serum IgA levels, C3 and C4 levels, presence of antineutrophil cytoplasmic antibody (ANCA) and specific treatments (including specific antibiotics, steroids and immunosuppressive drugs).

Follow-up data

Delay from disease to diagnosis was expressed in days and interquartile range (IQR range).

Follow-up parameters were recorded from biopsy date to last visit, dialysis or death. Persistent renal dysfunction was defined as an estimated glomerular filtration rate (eGFR using CKD-Epi) <60 mL/min/1.73m². End-stage renal disease (ESRD) was defined as a duration of dialysis >90 days.

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 5.0 (GraphPad Software, La Jolla, California, USA). Univariate analysis was performed using the Kruskal-Wallis test and Chi2 test as appropriate for variable type. Statistical significance was assumed at $p<0.05$. The study was approved by the Institutional Ethics Committee in Human Research (No. 2018 008).

RESULTS

Clinical and demographic features

Twenty-seven patients (23 men, 4 women) with mean age of 62 ± 15 years (range, 5-83) were included (**Table 1**). One patient was a 5-year old child. Forty-four percent (44.4%) of patients had type 2 diabetes, 69.2% had hypertension, 52.0% had cardiovascular history (including ischemic heart disease or heart failure). Forty-four percent (44.0%) were persistent or former smokers, 37.5% had active chronic alcoholic consumption and 9.1% had liver cirrhosis. Three patients had an immunocompromised background including pulmonary squamous cell carcinoma being treated for one patient, myelodysplasia for one patient, and immunosuppressive drug for Crohn disease for one patient.

Type of infection and pathogens involved

The infectious agent was identified in 88.9% of patients (**Table 1**). *Staphylococcus* was the most frequent causative agent (87.5%) (methicillin-sensitive *Staphylococcus Aureus* (MSSA): 66.7%, methicillin-resistant *Staphylococcus Aureus* (MRSA): 16.7%, *Staphylococcus Haemolyticus*: 4.2%). A variety of other pathogens were identified including *Streptococcus Oralis*, *Chlamydia Pneumoniae* or *Escherichia Coli*. In 29.2% of cases, two or more pathogens were identified.

Sites of infection were identified in all patients with various locations. The bone and joint (44.4%) and skin (40.7%) were the most frequent sites. Other infections included prosthesis, plate osteosynthesis or implantable venous access port infections, endocarditis, pneumonia and urinary tract infection. Bacteremia was present in 40.7% of cases.

Biological presentation

Clinical renal presentation included nephrotic syndrome for 66.7% of patients with acute nephritic syndrome in 55.6% and rapidly progressing glomerulonephritis 55.6% of cases (**Table 2**). All patients had proteinuria, 95.2% had hematuria with macroscopic hematuria in 8 cases. The serum creatinine ranged from 87 to 1200 µmol/L (mean = 373 ± 258) and

estimated glomerular filtration rate (eGFR) varied from 3 to 82 mL/min/1.73m² (mean = 23.7 ± 19.9). Severe acute renal injury was present in 48.1% of patients and 33.0% required hemodialysis. Hypocomplementemia was detected in 16.0% of patients (both low C3 and C4 levels in 8.0%). Serum IgA level was increased in 84.6% of the 13 patients tested. Antineutrophil cytoplasmic antibodies (ANCA) were detected in 26.7% of 15 patients.

Pathology findings

The median delay between clinically apparent onset of infection and biopsy was 42 days (IQR range, 26-69). Pathology findings are summarized in **Table 3**. Endocapillary glomerulonephritis associated with mesangial proliferation was the most frequent pattern (81.5%) (**Figure 1A**). Mesangial proliferation was pure in 7.0% of cases. Endocapillary glomerulonephritis was most frequently exudative (81.4%) (**Figure 1B**). In one patient we observed only globally sclerotic glomeruli without proliferation. Membranoproliferative and crescentic glomerulonephritis were also observed (33.3% and 37.0% respectively) (**Figures 1C and 1D**). In almost all biopsies we observed *de novo* proliferation except in one case (4.0%) in which proliferation was superimposed on diabetic nephropathy. We identified subepithelial humps deposits in 48.1% of biopsies and prominent deposits in glomerular capillary wall of 11.1% of biopsies with hyaline thrombi resembling cryoglobulin in one (**Figures 1E and 1F**). Interstitial fibrosis and tubular atrophy (IF/TA) was observed in 85.1% of cases (44.4% mild, 18.5% moderate, ^{22}.2% severe). Classification according to pattern presentation revealed 25.9% of acute, 63.0% of subacute and 11.1% of resolving GN. The delay between infection and renal biopsy, available for 88.9% of patients, was significantly increased according to glomerulonephritis pattern from acute GN (median = 21.5 days, IQR range, 20.3-27.3) to subacute (median = 43.5 days, IQR range, 32.5-72.8) and resolving GN (median = 94.5 days, IQR range: 85.3-103.8) (p=0.0348) (**Figure 2**).

When we compare characteristics of acute, subacute and resolving combined groups, we noted that the percentage of diabetic patients tends to be higher in acute group compared to

combined subacute/resolving group, but this difference is not statistically significant (71.4% *vs* 36.8%, p=0.1904). Moreover, skin infections tend to be more frequent in acute group compared to combined subacute/resolving (46.2% *vs* 15.6%, p=0.0535) whereas bone and joint infections tend to be less frequent in acute group compared to acute/resolving group (7.7% *vs* 34.4%, p=0.1340) (**Table 4**).

Immunofluorescence and immunohistochemistry

Immunofluorescence features are summarized in **Table 5**. IgA granular deposits were observed all biopsies with various location: mesangium (34.6%), both mesangium and peripheral capillary loops (46.2%), capillary loops (19.2%). A "starry sky" pattern was noticed in 4 cases (15.0%). C3 staining was observed in 96.3% of biopsies. IgA deposits were most frequently codominant with C3 (55.5%). C1q deposits were not identified.

Immunohistochemistry with C4d antibody was performed in 23 biopsies of IRGN-IgA, 6 biopsies of IgA nephropathy (IgA NP) and 7 biopsies of IRGN without IgA deposits (IRGN-IgA-) (**Figure 3**). C4d 1+ staining was observed in most of the biopsies (47.8% of IRGN-IgA, 57.0% of IRGN-IgA- and 83.0% of IgA NP) and C4d 2+ staining was noticed only in 4 biopsies of IRGN-IgA (17.4%).

Therapeutic management and outcome

All patients received antibiotics according to the infectious agent and antibiotic resistance pattern (**supplemental data: Table s1**). The most frequent antibiotics used were penicillin (77.8%) and rifampicin (40.7%), and 88.9% of patients received two or more antibiotics. Other antibiotics included cephalosporin, aminoside, macrolide, quinolone, glycopeptides and penem. In addition to antibiotics, corticosteroids were used in 37.0% of patients.

Clinical follow-up was available in 26 patients (96.3%) with a median follow-up time of 13.2 days (IQR range, 4.0-22.2) (**Table 6**). The duration of follow-up was <3 months in 23.0% of patients and ≥3 months in 77.0%. At the last follow-up, poor outcome was observed in 84.6% of patients: 23.1% died, 46.1% had persistent renal dysfunction, 15.4% had ESRD. One

patient died because of the progression of a pulmonary carcinoma, one had aspiration pneumonia, one had a septic shock. For the 3 remaining patients, the etiology of death was not available.

Twenty-five patients (92.5%) could be classified according to their eGFR at follow-up (**Table 7**): 28.0% had eGFR>60 mL/min/1.73m², 56.0% had persistent renal disease (PRD) and 16.0% had end-stage renal disease (ESRD). One of the patients with ESRD had underlying diabetic glomerulosclerosis. In univariate analyses, there were no significant correlates between renal outcome and respectively age, eGFR or proteinuria at biopsy. At follow-up, we observed a significant correlate between interstitial fibrosis with tubular atrophy and renal outcome (p=0.0237): IF/TA score was significantly higher in PRD group (IF/TA score=1.6) and ESRD group (IF/TA score=2.5) compared to eGFR>60mL/min group (IF/TA score=0.9). We did not observe correlates between renal outcome and other pathologic features. Due to small sample size it was not possible to accurately assess the prognostic role of steroids (ESRD in 1/10 (10.0%) with steroids vs 3/16 (18.8%) patients, p=0.5474).

DISCUSSION

Infection-related glomerulonephritis with IgA deposits, rarely reported in Europe [13,14], correspond to a wide spectrum of both clinical presentations and histologic patterns. Clinically, patients usually present with nephrotic range proteinuria, hematuria and severe acute renal injury and/or rapidly progressive glomerulonephritis. Histologic pattern may vary from pure mesangial proliferation to exudative diffuse endocapillary proliferation and crescentic glomerulonephritis. Glomerular dominant or codominant IgA deposits, while unusual in classical postinfectious GN, are observed in this particular form. Improvement of socio-economic conditions and health induced a decrease of poststreptococcal GN in Western countries and led to a modification of microbiologic data with increasing in non-streptococcal GN, particularly poststaphylococcal GN [8,9]. This GN is uncommon but probably underdiagnosed because of various clinical and histologic presentations, sub-clinical or no documented infections and pathologic similarities with IgA nephropathy.

Since we report the first large cohort of patients with IRGN IgA+ in Europe, we compared these results with those of Asian and American studies to search for potential differences. Our results showed that most of the patients affected are male (85%) of mean age 62 years. This is comparable to previous results reporting that 75% to 86% of the patients are male and that mean age is 55 to 65 years [9,10,15–20]. It must be noticed that the youngest of our patients is a 5-year-old boy, meaning that IRGN IgA+, even if rarely reported, can raise in pediatric patients. In our case and in other pediatric cases reported, children with *Staphylococcus*-related GN have the same presentation than the adults, namely proteinuria and renal function impairment [21]. Underlying diabetes or immunocompromised background are common features reported, however incidence of diabetes varies according to studies from 8 to 100% of the patients (44% in our series). As noticed since the first report, *Staphylococcus* represents the most frequent germ (83% in our study, 60 to 100% in other studies) with a higher frequency of MRSA in previous Asian and American studies (50 to 60%) compared to our observation

(17%). This observation is consistent with the low incidence of MRSA observed in France, even if this germ previously associated with healthcare institution is now also encountered in community conditions [22]. Moreover, this incidence seems to decrease in some Asian countries like Japan, as reported by Usui *et al.*, responsible for a parallel decrease of glomerulonephritis [23]. Concerning germs reported, it is to note that proportion of no documented infections represents 0 to 31% of the cases in the previous studies and 12.5% in our study. Regarding sites of infection, our data are comparable to previous data with cutaneous infections representing up to 50% of the cases (41% in our study). This observation may be a corollary of the frequency of diabetes in these patients which increases risks of infections, particularly with *Staphylococcus*, and may consequently represent a risk factor for IRGN IgA+. All patients with IRGN IgA+ in our study presented with proteinuria (nephrotic range proteinuria in 70% and nephrotic syndrome in 67% of the cases), 95% of them had hematuria, 48% had an acute renal injury stage 3 of the KDIGO classification at the time of the biopsy and about half of them presented with rapidly progressing glomerulonephritis. This is comparable to American and Asian data reporting frequent acute kidney injury (serum creatinine varying from 3.69mg/dl to >10mg/dl), hematuria in 90 to 100% of the cases. Nephrotic range proteinuria was less frequent in these studies compared to our, observed in 40 to 60 % of the cases [9,10,15,17–20].

Infection-related GN is a serious pathology sometimes threatening life or kidney survival with risk of hemodialysis evaluated between 8 and 100% of patients, risk of end-stage renal disease between 20 and 80% of patients, and risk of death up to 30% according to different studies [5,11,15,18,20]. Even though our patients presented more acute histological pattern, we did not observe important differences in renal or vital outcome. In our study, 33% of the patients required hemodialysis during acute phase of GN, 15% of the patients progressed to an end-stage renal disease, and 23% died. Poststaphylococcal GN can occur in various immunocompromised background and poor prognosis is mainly linked to age and

comorbidities [5,6]. The initial description of Nasr *et al.* reported diabetic nephropathy in all biopsies. Nevertheless, the association between diabetes and IRGN IgA+ is inconstant, reported in 8 to 55 % of the patients in other previous studies and in 44 % of the patients in our study [10,15–18,24–26]. Previous studies did not show correlation between histologic pattern and renal prognosis, even if some authors observed that patients with renal recovery had less frequent acute tubular injury, interstitial inflammation or IF/TA [5,18]. Our results showed an association between severity of IF/TA and renal prognosis, but no correlation between other histological features and renal outcome.

Reference treatment of this form of GN is antibiotics therapy with adaptation according to the germ and its potential resistances. In addition to antibiotics, 10 patients (37%) in our study received corticosteroids without significant improvement of renal outcome: 2 patients died, one patient had ESRD, the last 7 had persistent renal dysfunction, and none of the 10 patients had renal recovery. The use of corticosteroids in poststaphylococcal GN, which has not always been declared in previous studies, seems to be lower in these reports (12.5 to 22%) compared to our study [9,18]. This use remains controversial. For some authors [27], steroids may have a place in the treatment of patients who fail to respond to antibiotic therapy or patients with crescentic GN, whereas for other authors [28] it can be deleterious in this form of GN in which infection is often ongoing. Moreover, for these latter authors the term “postinfectious” to designate a GN related to *Staphylococcus* infection is unappropriated because it is assimilated to poststreptococcal GN in which infection is resolved. It should be noted that, among 6 patients who died in our study, 2 received corticosteroids, and one of them died of a septic shock. Three of the ten patients who were treated with corticosteroids had a crescentic glomerulonephritis, and two additional had a diagnosis of IgA nephropathy on the renal biopsy.

The various clinical presentations of IRGN IgA+ require more frequent renal biopsies compared to classical poststreptococcal GN. As observed in previous studies, renal biopsies

displayed frequent mesangial and exudative endocapillary proliferative glomerulonephritis, associated in a less frequent proportion with crescentic and necrotizing GN. However, we noticed some variations compared to Asian and American studies. Most of them, but not all, reported crescentic or necrotizing glomerulonephritis in the same proportion than observed in our study (about 30% and 15% of the biopsies respectively). Mesangial proliferation was frequent and also represented in comparable proportion (89% of our biopsies, 58 to 100% of previous cases). However, endocapillary proliferation was more frequent in French patients (89% *vs* 23% to 63% in previous series) as well as exudative pattern (81% *vs* 15 to 63% of the biopsies) [9,10,15,17,18,20]. If endocapillary and mesangial proliferations are frequently associated (81.5% of our cases), pure mesangial proliferation may be observed in some cases. This aspect was less frequently noted in our series (7% of the biopsies) compared to the previous (up to 67%) [9,15,17,20]. We noticed similar variations when we compared histological patterns as classified in acute, subacute and resolving GN by Haas *et al.* in 2008 [15]. They reported more resolving GN and less acute or subacute GN compared to our cohort with 15% of acute, 23% of subacute and 62% of resolving GN *versus* 41%, 52% and 7% respectively in our cohort. Since we observed that the mean time from clinical onset of infection to renal biopsy increased with histological pattern from acute to resolving GN, one explanation of the fact that we reported more acute and subacute (exudative) GN, could be a shorter delay between infection and renal biopsy in French centers (mean of 54 days for our patients, no data for other studies). This can be related to economic factors or even to clinical presentation since nephrotic syndrome appears to be most frequent in our cohort (70% *vs* 40-60%). Moreover, the relation between the infection-to-biopsy delay and histological pattern supports the concept that these patterns represent different evolving aspects of the same disease. Only one patient, presenting with acute pattern even though the biopsy was performed 134 days after a documented infection, did not follow this rule. For this patient who had a clinical history of endocarditis and plantar neuropathic ulcer without microbiologic documentation at the time of

biopsy, we can hypothesize that a more recent unnoticed infection was responsible for the present pattern.

Acute tubular injury is frequently observed *Staphylococcus*-related GN (86% in our study, 60 to 100% in other previous studies), as well as intratubular red blood cells which are presents in 67% of our biopsies and in 77% of previous biopsies [6,8,15,16,18,20]. These tubular lesions were also present in our pediatric case and is to notice because it remains unusual in classical poststreptococcal GN.

Contrary to subepithelial "humps" deposits which are commonly described in IRGN IgA+ (31 to 75% according to studies, 81% in our cohort), we also observed large subendothelial deposits with hyaline thrombi in 19% of the biopsies. These deposits are rarely encountered but were previously reported by Satoskar *et al.* in one biopsy [18].

IgA deposits observed in this particular form of GN are classically absent in postinfectious GN. Pathogenesis of these particular form of GN remains poorly understood. Koyama *et al.* studies showed that a colocalization of IgA and *Staphylococcus Aureus* antigen was observed in 75% of the patients with post-MRSA GN [29]. Their results also suggested that GN is induced by a Staphylococcal enterotoxin which act as a superantigen. Superantigens are able to directly bind to major histocompatibility complex class II molecules at the surface of antigen presenting cells and to variable region of the β chain of the T cell receptor. This binding induces T cells and B cells activation responsible for polyclonal IgG and IgA secretion [30]. However, IRGN IgA+ also develops after infections with other infections agents that do not produce enterotoxin, leading us to mention a potential role of other antigens [15,20,31].

C4d deposits, never previously analyzed in this particular glomerulonephritis, were observed in 66% of our biopsies. Several hypothesizes have been proposed by Sethi *et al.* to explain C4d deposits in infection-related GN [32]. These deposits could be observed after the activation of the classical pathway of complement by the bacterial antigen-IgA immune complex or even after the activation of the lectin pathway of complement. However, in a significant

number of cases (34% in our study, 46% in their study), no C4d deposits are observed. Two mechanisms can be proposed: the first would concern a small number of patients, in which the alternative pathway of complement could be abnormally activated; the second could correspond to the long delay between the onset of infection and the renal biopsy assessment. When this delay is the longest, we can assume that the infection is no more active at the time of diagnosis, that immune complexes are no more formed and then the complement is no activated. This hypothesis is highlighted by the longest delay that we observed in patients with no or segmental and focal deposits compared to patients with diffuse and global C4d staining.

Clinical and histological similarities between IgA NP and IRGN IgA+ can be misleading, particularly in subclinical infections, in no documented infection history or when renal biopsy displays resolving pattern. Actually, contrary to immunoglobulin deposits of other postinfectious GN which disappear within 6 weeks after the infection, IgA can be observed even in resolving IRGN IgA+, as observed in our biopsies [15]. Some features reported by Wen *et al.* may help to distinguish these two entities. Patients are usually older in IRGN IgA+ group compared to IgA NP group (62.3 ± 16.9 years *vs* 37.9 ± 16.3 years), proteinuria is more often of nephrotic range and low complement is more frequent (58.3 % *vs* 5.3%) as well as acute renal failure at the time of diagnosis (83.3% *vs* 10.4% of the patients) [8]. However, in our study 8 patients were less than 60 years old and one case occurred in a child. Clinical infection history is one key point of the diagnosis but remains absent in up to 31% of the cases. Satoskar *et al.* reported histological features that may help to distinguish these two diagnosis: endocapillary proliferation (60% in IRGN IgA *vs* 10% in IgA NP) and crescentic GN (35% *vs* 20% respectively) are more frequent whereas focal segmental glomerulosclerosis is less frequent in IRGN IgA+ compared to IgA NP (2.5% *vs* 49% respectively). They observed subepithelial humps deposits in 31% of IRGN IgA+ whereas they were absent in IgA NP [19]. In other studies, prominent deposits in both mesangium and capillary loops are

observed in IRGN IgA+ whereas these deposits are smaller and localized to the mesangium in IgA NP, and lambda staining is usually predominant compared to kappa in IgA NP [10,15]. In their review, Nasr *et al.* noticed that C3 staining was usually more intense than IgA and that kappa was stronger or equal to lambda in APIGN. Nevertheless, these observations are inconstant and none of these histological features is pathognomonic for IRGN IgA+. We believe that diffuse and global C4d staining, even if rarely observed in our renal biopsies (18% of them) can be an argument in favor of IRGN IgA+ since it was not observed in IgA NP biopsies. The difficulty in distinguishing these two pathologies is not only clinicopathologic since they seem to share also pathophysiological features. Koyama *et al.* showed that the presence of Staphylococcal antigen was detected in 75% of post-MRSA GN as well as in 68.1% of IgA NP and 60% of Henoch-Schönlein purpura nephritis. This suggests a role of *Staphylococcus Aureus* antigens in the pathogenesis of both IgA NP and Henoch-Schönlein purpura nephritis [29]. It is yet unknow if IgA glycosylation mechanisms are different between IRGN and IgA NP, however Arakowa *et al.* observed a serum increase in both IgA1 and IgA2 subclasses in post-MRSA GN whereas only IgA1 was increased in IgA NP [33]. Another feature that remains unclear is that a significant number of patients with IRGN IgA+ (38% in our study) have chronic alcohol consumption with or without chronic liver disease. This raises the question of a more incidental observation than real deposits.

CONCLUSION:

IgA immune deposits-associated glomerulonephritis is a particular form of postinfectious GN that mostly presents in patients older than 60 years with nephrotic range proteinuria, hematuria and/or rapidly progressive glomerulonephritis. Histologically, various pattern from acute exudative endocapillary glomerulonephritis to resolving pure mesangial glomerulonephritis with IgA dominant or codominant deposits are observed. Global and diffuse capillary loop C4d staining may help to distinguish this entity from IgA nephropathy. However, the difference can sometimes be complex and remains a pitfall for pathologists.

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Table 1: Demographics, predisposing factors to infection and infectious history (27 patients).

Sex	
Male (n, %)	23 (85.2%)
Age, year (mean ± SD)	62 ± 15
Comorbid conditions	
Diabetes mellitus (n, %)	12/27 (44.4%)
Hypertension (n, %)	18/26 (69.2%)
Cardiovascular disease (n, %)	13/25 (52.0%)
Active or former smokers (n, %)	11/25 (44.0%)
Alcoholism (n, %)	9/24 (37.5%)
Liver cirrhosis (n, %)	2/22 (9.1%)
Immunosuppressive drug (n, %)	1/27 (3.7%)
Infectious agent	
Staphylococcus (n, %)	21/24 (87.5%)
MRSA (n, %)	4/24 (16.7%)
MSSA (n, %)	16/24 (66.7%)
Staphylococcus Haemolyticus (n, %)	1/24 (4.2%)
Morganella Morganii (n, %)	2/24 (8.3%)
Streptococcus Oralis (n, %)	1/24 (4.2%)
ESBL-producing Escherichia Coli (n, %)	1/24 (4.2%)
Enterococcus faecalis (n, %)	1/24 (4.2%)
EnterobacterAerogenes (n, %)	1/24 (4.2%)
Chlamydia Pneumoniae (n, %)	1/24 (4.2%)
Corynebacterium Amycolatum (n, %)	1/24 (4.2%)
Dermatobacter Hominis (n, %)	1/24 (4.2%)
More than one pathogen (n, %)	7/24 (29.2%)
Unknown (n, %)	3/27 (11.1%)
Sites of infection	
Bone and joint infection (n, %)	12/27 (44.4%)
Cutaneous infection (n, %)	11/27 (40.7%)
Bacteremia (n, %)	11/27 (40.7%)
Other sites	
Prosthesis, plate osteosynthesis or implantable venous access port (n, %)	5/27 (18.5%)
Endocarditis (n, %)	4/27 (14.8%)
Pneumonia (n, %)	4/27 (14.8%)
Urinary tract infection (n, %)	3/27 (11.1%)

ESBL: extended-spectrum beta-lactamases, MRSA: methicillin-resistant *Staphylococcus aureus*, MSSA: methicillin-sensitive *Staphylococcus aureus*, SD: standard deviation.

Table 2: Clinical presentation and laboratory findings.

Renal parameters	
Nephrotic syndrome (n, %)	18/27 (66.7%)
Acute nephritic syndrome (n, %)	15/27 (55.6%)
Rapidly progressive glomerulonephritis (n, %)	15/27 (55.6%)
Hematuria (n, %) (microscopic/macroscopic)	20/21 (95.2%) (11/8)
Serum creatinine, µmol/L (mean ± SD (range))	373 ± 258 (87-1200)
Creatinine >353.6 µmol/L (n, %)	13/27 (48.1%)
eGFR, mL/min/1.73m² (mean ± SD (range))	23.7 ± 19.9 (3-82)
Albumin, g/L (mean ± SD (range))	24.7 ± 7.4 (15-42)
Proteinuria, g/day (mean ± SD)	5 ± 3.4 (0.4-16.4)
Other biological parameters	
Low C4 levels (n, %)	2/26 (7.7%)
Low C3 levels (n, %)	4/25 (16.0%)
Both C3 and C4 low levels (n, %)	2/25 (8.0%)
High serum IgA levels (n, %)	11/13 (84.6%)
ANCA (n, %)	4/15 (26.7%)

ANCA: antineutrophil cytoplasmic antibodies, eGFR: estimated glomerular filtration rate, SD: standard deviation.

Table 3: Light microscopy findings (27 renal biopsies).

Light microscopy	
No. of glomeruli (mean ± SD (range))	15 ± 9 (3-46)
Globally sclerotic glomeruli (mean ± SD (range))	2 ± 2 (0-8)
Diabetic nephropathy (n, %)	1 (3.7%)
Mesangial proliferative GN (n, %)	24 (88.9%)
Endocapillary proliferative GN (n, %)	24 (88.9%)
Segmental (n, %) / Global (n, %)	9 (33.3%) / 11 (40.7%)
Exudative GN (n, %)	22 (81.4%)
<5 neutrophils per glomerulus (n, %) / >5 neutrophils per glomerulus (n, %)	15 (55.5%) / 7 (25.9%)
Membranoproliferative GN (n, %)	9 (33.3%)
Crescents (n, %)	10 (37.0%)
Fibrinoid necrosis (n, %)	3 (11.1%)
Deposits (n, %)	16 (59.2%)
Subepithelial humps (n, %) / Intramembranous (n, %)	13 (48.1%) / 3 (11.1%)
Interstitial fibrosis and tubular atrophy (n, %)	23 (85.1%)
Mild (n, %) / Moderate (n, %) / Severe (n, %)	12 (44.4%) / 5 (18.5%) / 6 (22.2%)
Interstitial inflammation (n, %)	21 (77.8%)
Mild (n, %) / Moderate (n, %) / Severe (n, %)	16 (59.3%) / 5 (18.5%) / 0
Acute tubular injury (n, %)	23 (85.1%)
Mild (n, %) / Moderate (n, %) / Severe (n, %)	8 (29.6%) / 8 (29.6%) / 7 (25.9%)
Intratubular red blood cells (n, %)	18 (66.7%)
Chronic vascular lesions (n, %)	24 (88.9%)
Mild (n, %) / Moderate (n, %) / Severe (n, %)	4 (14.8%) / 16 (59.3%) / 4 (14.8%)
Histological pattern	
Acute GN (n, %)	7 (25.9%)
Subacute GN (n, %)	17 (63.0%)
Resolving GN (n, %)	3 (11.1%)

GN: glomerulonephritis, SD: standard deviation.

Table 4: Histologic pattern according to clinical, biological, therapeutic features.

	Acute GN	Subacute/Resolving GN	p values
N	7	20	
Age, mean	66	61	0.8681
Male, % of patients	28.6	90.0	**0.0047**
Diabetes, % of patients	71.4	36.8	0.1904
Alcohol consumption, % of patients	28.6	41.2	0.6687
Staphylococcus infection, % of patients	83.3	83.3	1
Rapidly progressive GN, % of patients	42.9	60.0	0.6618
Nephrotic syndrome, % of patients	57.1	70.0	0.6527
Acute nephritic syndrome, % of patients	71.4	50.0	0.4082
Hematuria, % of patients	100	92.9	1
eGFR at diagnosis, mean	25.6	23.1	0.3058
Proteinuria at diagnosis, mean	4.5	5.1	0.9779
eGFR at follow-up, mean	51.6	53.7	1
Median infection-renal biopsy delay, days (IQR range)	21.5 (19.8-34.8)	44.5 (32.5-97)	**0.0329**
Site of infection			
Bone and joint, % of patients	7.7	34.4	0.1340
Skin, % of patients	46.2	15.6	0.0535
Bacteremia, % of patients	30.8	21.9	0.7036
Other, % of patients	15.4	28.1	0.4666

Table 5: Immunofluorescence and immunohistochemistry findings.

Immunofluorescence	
IgA	27/27 (100%)
+/ ++ / +++ (n, %)	8 (29.6%) / 9 (33.3%) / 10 (37.1%)
Mesangial / Capillary loop / Both (n, %)	9 (34.6%) / 5 (19.2%) / 12 (46.2%)
C3	27/27 (100%)
+/ ++ / +++ (n, %)	5 (19.2%) / 6 (23.1%) / 15 (57.7%)
Mesangial / Capillary loop / Both (n, %)	9 (36.0%) / 2 (8.0%) / 14 (56.0%)
IgA and C3 codominant (n, %)	15 (55.5%)
IgA dominant (n, %)	3 (11.1%)
IgG staining (n, %)	4/27 (14.8%)
IgM (n, %)	6/27 (22.2%)
C1q (n, %)	0
Kappa (n, %)	9/24 (37.5%)
Lambda (n, %)	14/24 (58.3%)
C4d Immunohistochemistry	23/27 (85.2%)
+ / ++ (n, %)	11 (47.8%) / 4 (17.4%)

Table 6: Follow-up and renal outcome.

At 3 months	
Serum creatinine, µmol/L (mean ± SD)	242 ± 215 (44-700)
Proteinuria, g/day (mean ± SD)	2.2 ± 2.8 (0.4-11)
eGFR, mL/min/1.73m² (mean ± SD (range))	42.3 ± 27.6 (5-108)
At 12 months	
Serum creatinine, µmol/L (mean ± SD)	163 ± 116 (62-500)
Proteinuria, g/day (mean ± SD)	1.7 ± 2 (0.1-5.4)
eGFR, mL/min/1.73m² (mean ± SD (range))	51.7 ± 27 (6-94)
Last visit	26/27 (96.3%)
Follow-up time, months (median (IQR range))	13.2 (4.0-22.2)
Persistent renal dysfunction (n, %)	12/26 (46.2%)
End-stage renal disease (n, %)	4/26 (15.4%)
Death (n, %)	6/26 (23.1%)

eGFR: estimated glomerular filtration rate, IQR: interquartile ranges, SD: standard deviation

Table 7: Outcome and prognostic factors (25 patients).

	eGFR>60 mL/min/1.73m² ¥	PRD ǂ	ESRD †	p values
No of patients	7	14	4	
% of patients	28	56	16	
Age, year	61	64	68	0.8971
Median follow-up, months	8.3	16.5	21.6	0.3485
Mean eGFR, ml/min/1.73m²				
At biopsy	28.9	20.9	17.5	0.6953
Follow-up	84.6	37.5	-	**0.0001**
Mean proteinuria, g/day				
At biopsy	3.5	5.5	6.5	0.2088
Corticosteroids, % of patients	0	64	25	**0.01439**
Median infection-renal injury delay, days (IQR range)	13 (8.5-36)	23 (17.8-69)	13 (10-47.3)	0.3308
Global glomerulosclerosis, % of glomeruli	13	18	44	0.2661
Crescentic GN, % of glomeruli	4	6	5	0.9752
Interstitial inflammation score, mean	0.9	0.9	1.5	0.2329
Acute tubular injury score, mean	1.6	1.8	1.75	0.8905
IF/TA score, mean	0.9	1.6	2.5	**0.0237**
Chronic vascular lesion score, mean	2	1.8	2	0.6606

¥One patient with eGFR>60 died; ǂOne patient with PRD died; †Two patients with ESRD died.
eGFR: estimated glomerular filtration rate, ESRD: end-stage renal disease, IF/TA: interstitial fibrosis with tubular atrophy, IQR: interquartile, PRD: persistent renal disease (eGFR<60ml/min/1.73m²)

Figure 1: Light microscopy.
A: mesangial and endocapillary proliferation was the most frequent pattern (Masson's trichrome stain x300; B: exudative proliferation (Masson's trichrome stain x200); C: membranoproliferative glomerulonephritis (Jones silver stain x200); D: crescentic glomerulonephritis with fibrinoid necrosis (Jones silver stain x300); E: subepithelial humps deposit (arrow) (Masson's trichrome stain x1000); F: intramembranous deposits with hyaline thrombus resembling cryoglobulin (arrow) (Masson's trichrome stain x1000).

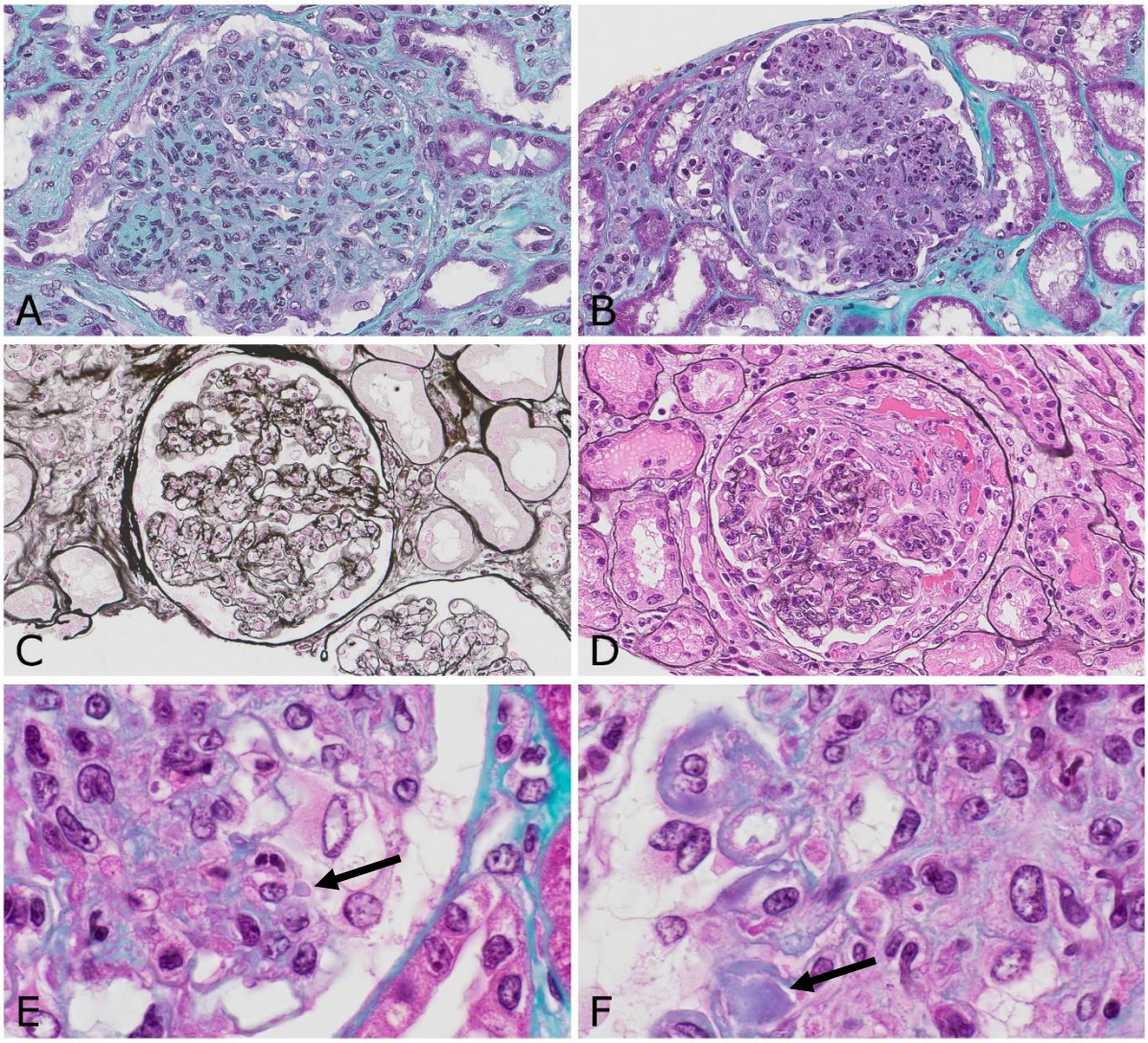


Figure 2: Glomerulonephritis pattern according to delay in days between documentation of infection and renal biopsy.
GN: glomerulonephritis

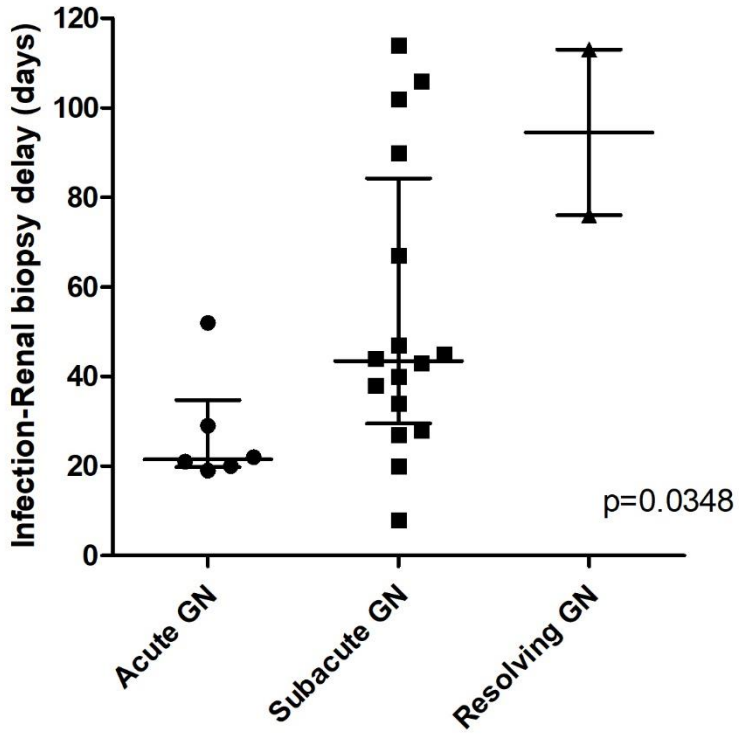
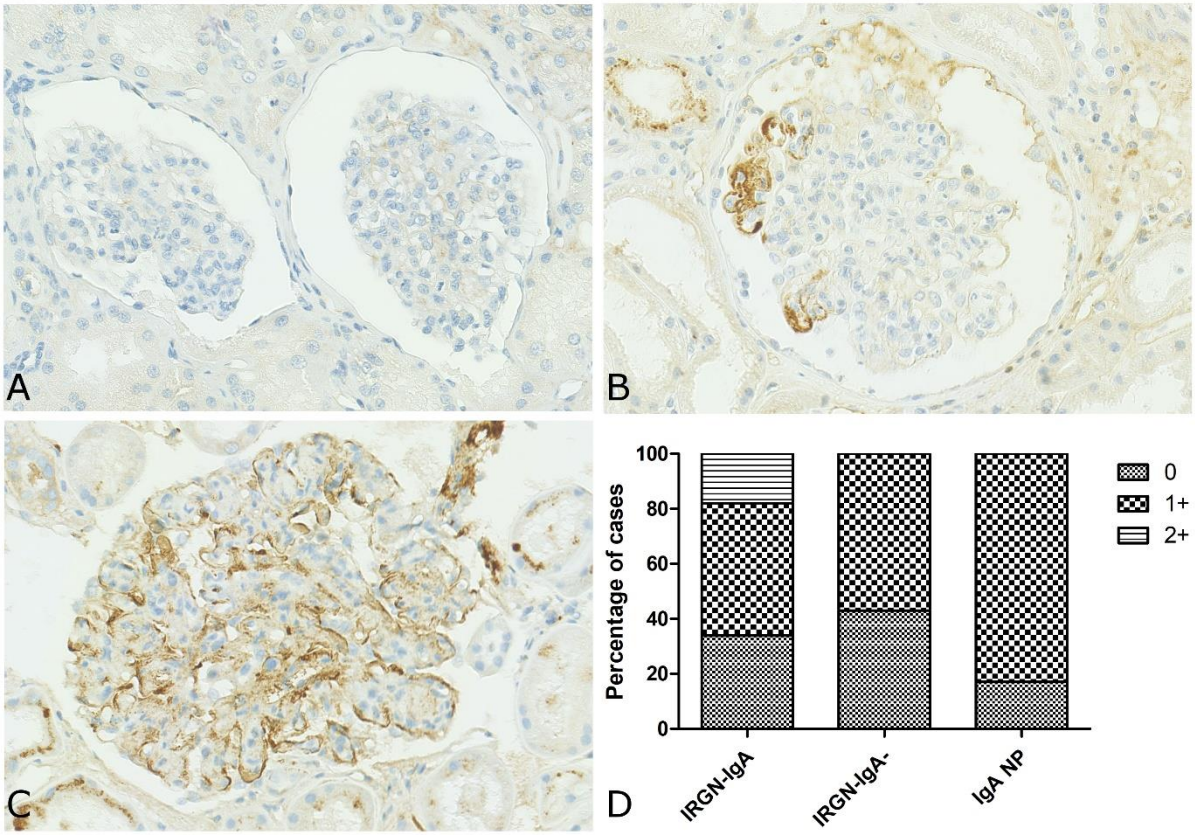


Figure 3: C4d immunohistochemistry.
A: no C4d staining, B: segmental and focal staining (1+), C: diffuse and global staining (2+), D: percentage of cases with 0, 1+ and 2+ staining in 23 biopsies of IRGN with IgA (IRGN-IgA), 7 biopsies of IRGN without IgA (RIGN-IgA-), 6 biopsies of IgA nephropathy (IgA NP).



SUPPLEMENTAL DATA

Table s1: Treatments.

Antibiotics	27/27 (100%)
Penicillin (n, %)	21/27 (77.8%)
Rifampicin (n, %)	11/27 (40.7%)
Cephalosporin (n, %)	9/27 (33.3%)
Aminoside (n, %)	9/27 (33.3%)
Macrolide (n, %)	9/27 (33.3%)
Quinolone (n, %)	8/27 (29.6%)
Glycopeptides (n, %)	5/27 (18.5%)
Penem (n, %)	3/27 (11.1%)
≥ 2 antibiotics (n, %)	24/27 (88.9%)
Corticosteroids (n, %) (oral/pulse)	10 (37.0%) (10/1)
Acute dialysis (n, %)	9 (33.3%)

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RESUME

INTRODUCTION : La glomérulonéphrite aiguë post-infectieuse, bien que rare chez l'adulte, est devenue de plus en plus fréquente ces dernières décennies en raison d'une augmentation de l'incidence des infections à staphylocoque. Différentes formes histologiques ont été décrites, la plus récente étant la glomérulonéphrite aiguë à dépôts d'IgA. À notre connaissance, aucune autre étude concernant l'épidémiologie, le pronostic et le suivi de cette forme de glomérulonéphrite aigue post infectieuse n'a été réalisée à ce jour en Europe. L'objectif de notre étude était d'analyser les données cliniques, histologiques et évolutives de patients ayant un diagnostic de glomérulonéphrite aiguë post-infectieuse à dépôts d'IgA.

MATERIELS ET METHODES: Les données cliniques et biologiques d'une cohorte française multicentrique de 27 patients ont été collectées. Nous avons revu les données de microscopie optique et d'immunofluorescence des biopsies rénales et comparé l'expression immunohistochimique de C4d dans ces biopsies avec des biopsies rénales de patients ayant eu un diagnostic de glomérulonéphrite aigue post infectieuse sans dépôts d'IgA ou de néphropathie à IgA. Nous avons analysé la corrélation entre les caractéristiques cliniques, histologiques et le pronostic rénal et vital des patients.

RESULTATS: Parmi les 27 patients (23 hommes, 4 femmes, âge moyen = 62 ± 15 ans) inclus, 84% avaient une infection à Staphylococcus Aureus, sensible à la méticilline dans 67% des cas et 44% des patients étaient diabétiques. Les infections étaient le plus fréquemment ostéo-articulaires (44%), cutanées (41%) ou liées à une bactériémie (41%).

Tous les patients présentaient une protéinurie, de rang néphrotique dans 70 % des cas, associée à une hématurie chez 95 % des patients; 48 % des patients avaient une insuffisance rénale sévère de stade III de la classification KDIGO avec une créatininémie supérieure à 353,6 µmol/L au moment de la biopsie. Trente deux pourcents des patients avaient une hypocomplémentémie C3 et/ou C4. La médiane du délai entre l'infection et la maladie rénale était de 20 jours, le premier quartile de patients étant à 12 jours et le troisième à 65 jours ; 7,4% des patients avaient un délai supérieur à 3 mois.

Sur le plan histologique, une glomérulonéphrite (GN) proliférative mésangiale était observée dans 89 % des cas (isolée dans 7 % des cas); une GN proliférative endocapillaire segmentaire ou globale dans 89 % des biopsies (exsudative dans 81% des cas); des croissants étaient présents dans 37 % des cas, et une nécrose fibrinoïde dans 11% des cas. Des dépôts extra-membraneux de type « humps » étaient présents dans 48% des cas et des dépôts endomembraneux dans 11% des cas. Une nécrose tubulaire aiguë et une fibrose interstitielle avec atrophie tubulaire étaient observées dans 85% des cas. Les dépôts d'IgA étaient dominants ou codominants dans 67 % des cas.

Le suivi était disponible pour 26 des 27 patients avec un suivi moyen de 18 mois : malgré le traitement utilisé (une antibiothérapie pour 100% des patients, et une corticothérapie pour 41% des patients), 46% des patients ont gardé une insuffisance rénale chronique terminale, stade IIIA pour 19% des patients, stade IIIB pour 19% des patients et stade IV pour 26% des patients. Une insuffisance rénale terminale a été retrouvé chez 15% des patients. Le mauvais pronostic rénal était corrélé à la présence d'une fibrose interstitielle avec atrophie tubulaire sévère.

CONCLUSION: La glomérulonéphrite aiguë post-infectieuse à dépôts d'IgA est un diagnostic difficile et correspond à une entité à ne pas méconnaître en raison de la présentation clinique souvent atypique et un spectre lésionnel histologique étendu. Il s'agit d'une néphropathie de mauvais pronostic posant le problème du diagnostic différentiel avec

des pathologies ayant un pronostic et une implication thérapeutique différents.

Mots clés: glomérulonéphrite, infections, IgA, staphylocoque aureus, étude multicentrique

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