The "double positive" disease: a particularly severe form of systemic vasculitis.

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Introduction

The **rapidly progressive glomerulonephritis (RPGN) syndrome** is characterized by an acute renal failure with glomerular proteinuria and hematuria. Extra-renal symptoms are frequent, depending on etiology.

On renal pathology, RPGN is characterized by the presence of extracapillary proliferation, forming glomerular crescents. Immunofluorescence results are specific of the etiology.

Classicaly, there are three types of RPGN :

- Immune-complex deposit-driven GN, such as in systemic lupus erythematosus, post-infective glomerulonephritis or IgA nephropathy
- Goodpasture syndrome with linear deposits of anti-glomerular basement membrane (anti-GBM) antibody.
- Pauci-immune vasculitis associated with ANCA antibody. No immune deposits are detected.

The **"double positive"** disease is characterized by the presence of both **ANCA** and **anti-GBM**. This type of vasculitis is rare, not well described and there is no consensual treatment.

Objectives

The aim of this study was to describe the clinical presentation and the renal prognosis of the "double positive disease".

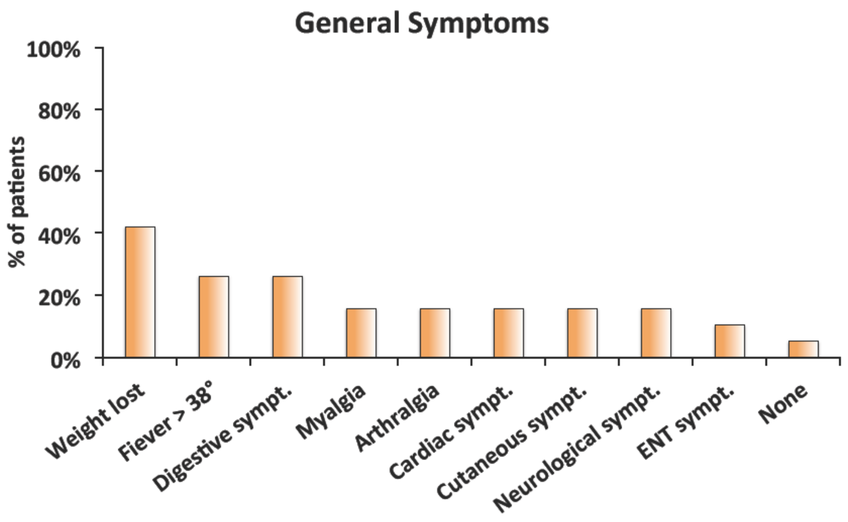
Method

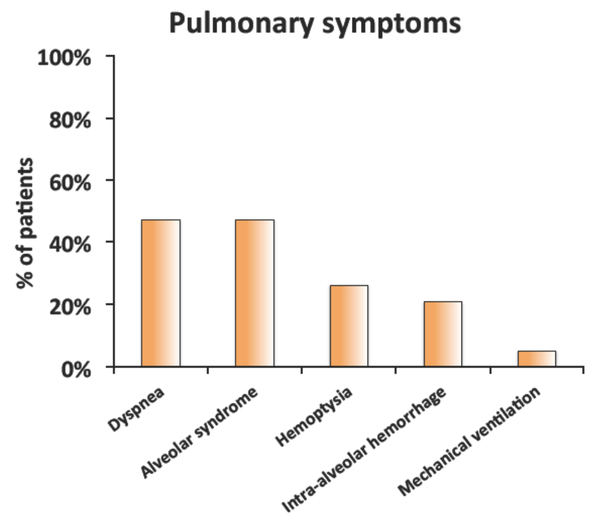
We conducted a retrospective study among 14 different nephrology centers in France and Belgium. Data on demographics, clinical presentation, renal pathology and treatment were obtained by chart review.
Inclusion criteria were ANCA positivity with anti-MPO or PR3 specificity, together with linear IgG deposition along GBM on renal biopsy.

Results

Clinical presentation

Nineteen patients have been included to date. The sex ratio (M/F) was 10/9. The average age at diagnosis was 67±21 years. All patients had a marked inflammatory syndrome (mean CRP 109±90 mg/L) and anemia was constant (mean Hb level 8,7±1,5 g/dl). Extrarenal involvement was frequent, as detailed below.

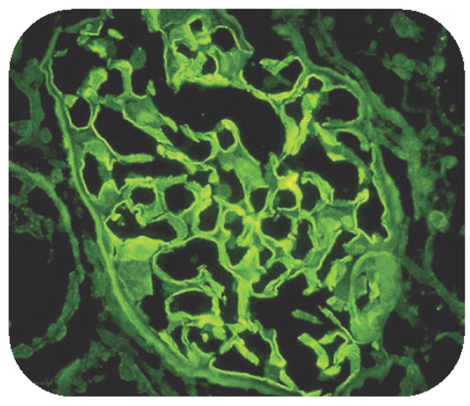




All patients presented with rapidly progressive glomerulonephritis, combining acute renal failure, proteinuria (from 0.9 to 26 g/L) and hematuria (macroscopic for 2 patients). The mean serum creatinine at diagnosis was 855±515 µmol/l. Eighteen patients started dialysis immediately after diagnosis.

Immunology and Pathology

Renal histology showed crescentic glomerulonephritis and constant linear immunofluorescence along the glomerular basement membrane. Sixteen patients (84%) had detectable serum anti-GBM antibody and all of them had detectable ANCA. Specificity of ANCA was anti-PR3 in 4 cases, anti-MPO in 15.



Linear deposits of anti-GBM antibody

Treatment and Prognosis

Except two patient who did not receive any immunosuppressive therapy, all the others were treated according to the local immunosuppression protocols. All of them received intraveinous corticosteroid and most of them (79%) received intravenous (74%) or oral (5%) cyclophosphamide
All treated patients had plasma exchanges (average number was 8±4 plasma exchanges).
Maintenance immunosuppressive therapy with low-dose corticosteroids (21%), azathioprine (26%) rituximab or MMF was given in 11 (58%) patients
None of the dialysis-depending patients had recovery of his renal function.
Only two patient had a relapse of the systemic vasculitis with extra-renal symptoms during subsequent follow-up.

Conclusion

The **double positive disease** shares several clinical characteristics, such as general and extra-renal symptoms (neurological, ENT…) with ANCA-associated vasculitis. Although recurrence of extra-renal vasculitis is rare, this risk may require maintenance immunosuppression, incontrast with typical anti-GBM disease.
On the other hand, its severe renal manifestations and prognosis is very similar to what has been described in anti-GBM disease (Goodpasture syndrome).

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