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INSUFFISANCE RENALE RAPIDEMENT PROGRESSIVE SURVENANT CHEZ UNE PATIENTE SCLERODERMIQUE : QUEL(S) DIAGNOSTIC(S) RETENIR ?

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INTRODUCTION

[i] Sclérodermie Systémique (ScS)

- **M**aladie systémique autoimmune :
  - Fibrose progressive atteignant la peau et les viscères,
  - Altérations vasculaires (microangioathie),
  - Autoanticorps : **AAN>95%** *(anti-topo1, ACA, anti-RNAP-III)*
- **A**tteintes viscérales :
  - Digestive, pulmonaire, cardiaque et/ou **rénale**

INTRODUCTION

[ii] Atteinte rénale au cours de la ScS

- **C**rise **R**énale **S**clérodermique (CRS) :
  - **2** à **5%** (premières années d'évolution de la ScS)
  - **IRA** oligoanurique & **HTA** maligne **(90%)**
  - **Microangiopathie thrombotique (43%)**
  - **Anti-ARN polymérase III (≈33%)**
- **A**utres étiologies :
  - Iatrogène, fonctionnelle ou **Glomérulonéphrite extracapillaire (vascularite à ANCA)**

INTRODUCTION

[iii] Vascularite associée aux ANCA & ScS

- **A**ssociation peu fréquente :
  - **ANCA** & **ScS** : **2** à **9%** **[2.9% : A. TAHIAT et al., 2013]**
  - **Vascularite à ANCA** & **ScS** : **<50** cas rapportés (2013)
- **S**ignes évocateurs :
  - Insuffisance rénale **normotensive (GNRP)** **(83%)**, hémorragie alvéolaire **(28%)**, ischémie digitale **(13%)**, vascularite cutanée **(10%)**,
  - pANCA/anti-MPO **(97%)**, anti-Scl-70 **(77%)**
- **B**iopsie rénale (GNRP) : Glomérulonéphrite extracapillaire

INTRODUCTION

[iii] Vascularite associée aux ANCA & ScS

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Letter to the Editor

Clinical relevance of antineutrophil cytoplasmic antibodies in Algerian scleroderma patients

ARTICLE INFO

Keywords:
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ANCA
Vasculitis

Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by vascular damage and progressive fibrosis involving

value obtained was more than 3.5 U/ml and 9 U/ml respectively. Other laboratory tests including inflammatory markers, urinalysis, rheumatoid factor (RF) and antinuclear antibodies (ANA) were also carried for each patient.

ANCA were positive in four cases (2.8%). Three patients were positive for p-ANCA with positivity for anti-MPO antibody. The fourth patient has shown negative result by IIFT but presented weak positivity for anti-PR3 antibody. Only one patient (Patient 1) had clinical features of AAV (Table 2). She presented with rapidly progressive renal failure with no evidence of scleroderma renal crisis (SRC) (lack of hypertension, microangiopathic hemolytic anemia and thrombocytopenia) and subsequently died from probable alveolar hemorrhage. The remaining three patients have shown no

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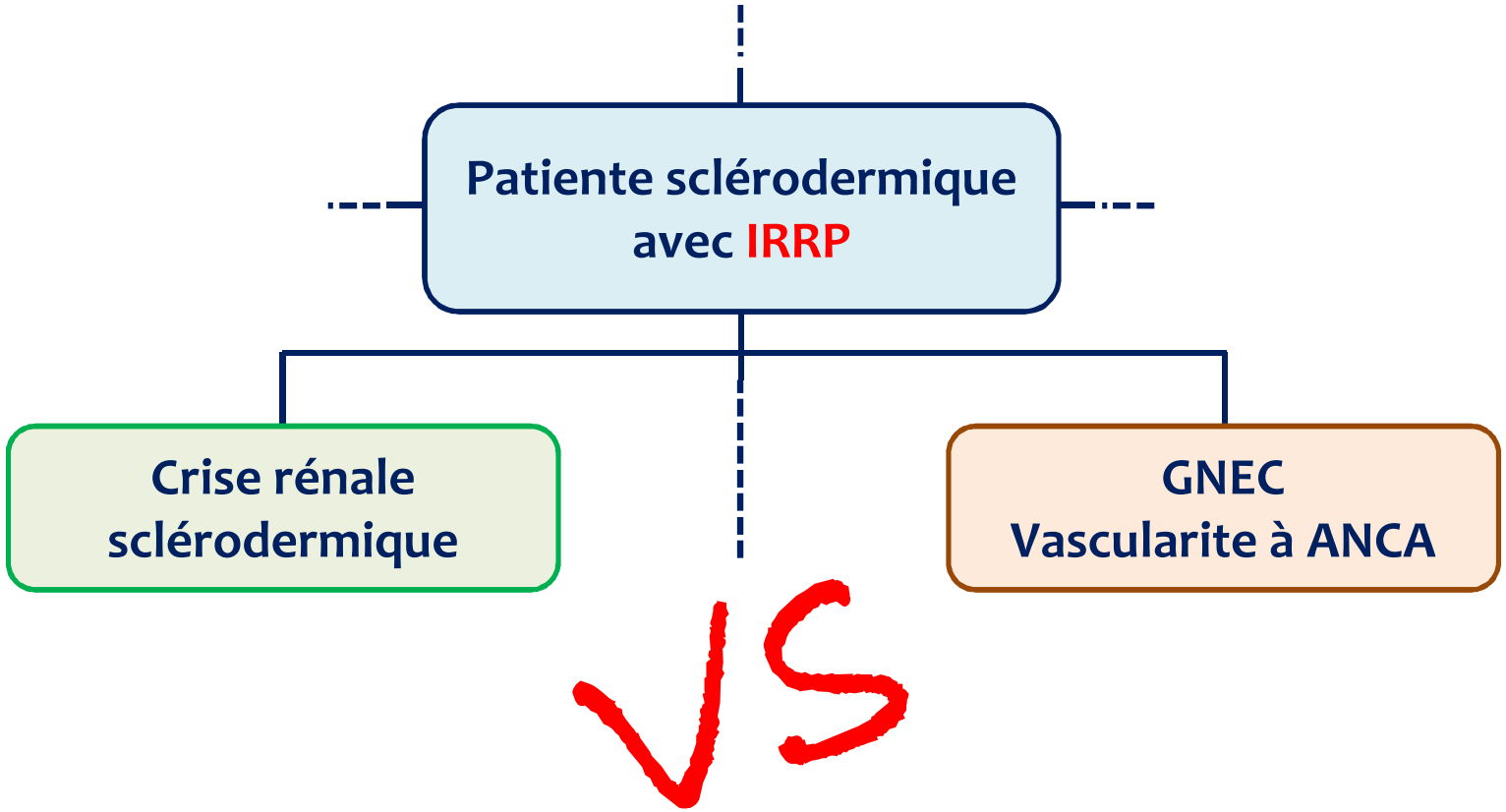

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F. C, 63 ans, ScS diffuse (3 ans) :

- Phénomène de Raynaud,
- Atteinte œsophagienne,
- Pneumopathie interstitielle diffuse, HTAP,
- Polyarthralgies,
- Syndrome de Sjögern secondaire.
- **AAN :**
  - **Positifs : Ac anti-SSA et anti-RNP ;**
  - **Négatifs :** Ac anti-CENP, anti-Scl-70, anti-RNA polymérase III, anti-Th/To, anti-Fibrillarin, anti-NOR90 et anti-PM-Scl (100 et 75)

Antécédents :

- Familiaux : RAS
- Personnels : **HTA** (depuis 6 ans)

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21/05/2012 : IRRP

- Insuffisance rénale aiguë,
- HTA sévère (220/120 mm Hg),
- Créatinine : 45mg/L, Urée : 1,05 g/L,
- Clearance : 17 ml/min
- NFS : HB : 10,4 g/dl, Plaquettes : 209,000,
- Frotti sanguin : **pas de schizocytes,**
- Vs : 90 mm (à la première heure),
- CRP : 48 mg/L,
- Chimie des urines : protéinurie +++ & hématurie.

Quel diagnostic évoquer ?

Une crise rénale sclérodermique ?

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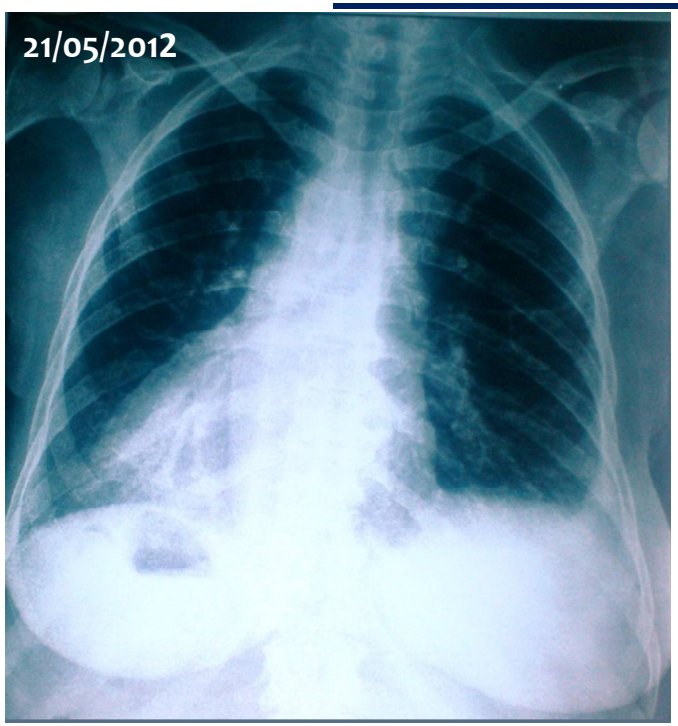
- **Traitement antihypertenseur :**
  - **Lopril** 75 mg/J **(IEC)**
  - **Loxen** parentérale puis per Os 100 mg/J **(Inhibiteur calcique)**

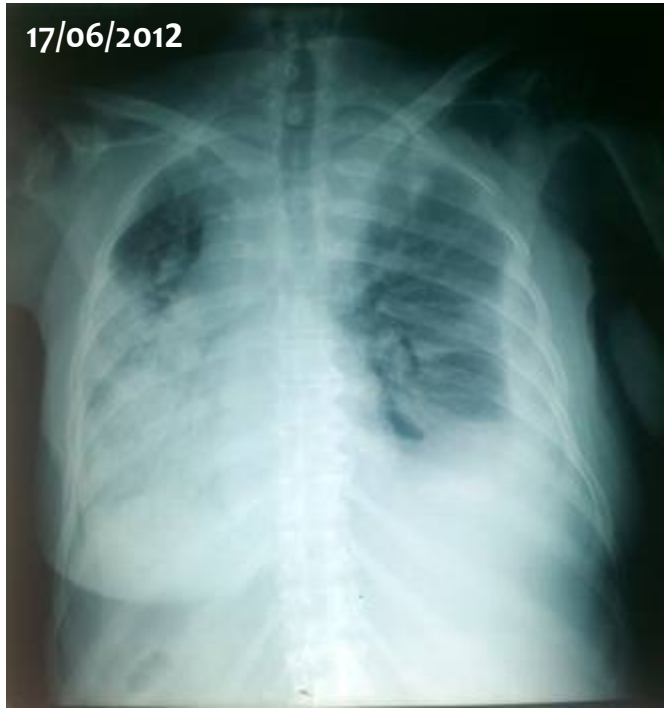
- **Après quelques jours d'observation :**
  - **Equilibre tensionnel :** 130/80 mm Hg
  - **Fonction rénale :** pas d'amélioration (créatinine à 54 mg/l)

INSUFFISANCE RENALE RAPIDEMENT PROGRESSIVE SURVENANT CHEZ UNE PATIENTE SCLERODERMIQUE. QUEL(S) DIAGNOSTIC(S) RETENIR ?

17/06/2012 : Syndrome de détresse respiratoire aiguë

Téléthorax : opacités alvéolaires diffuses bilatérales





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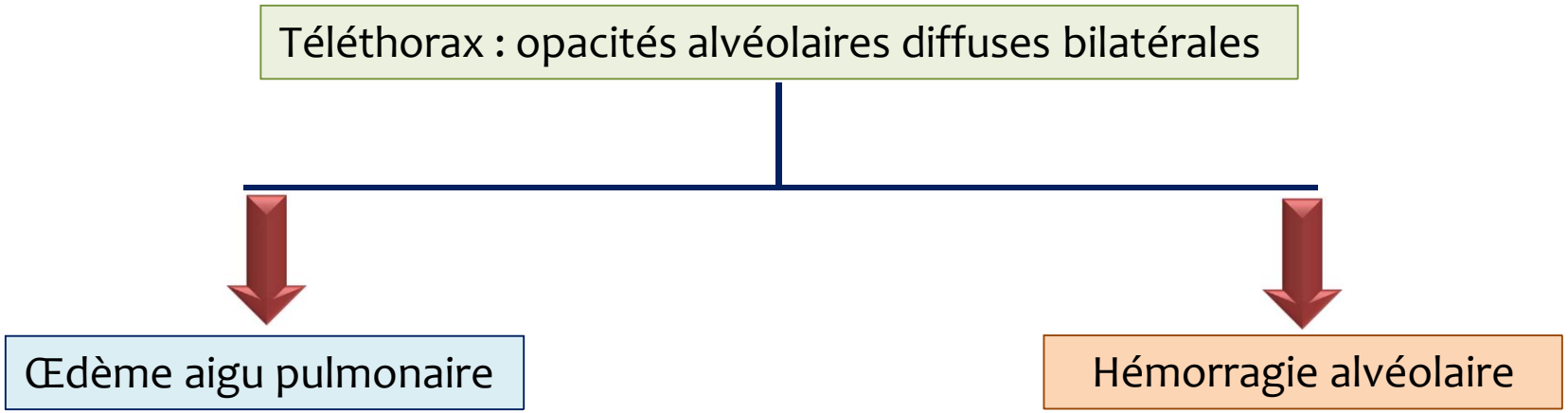

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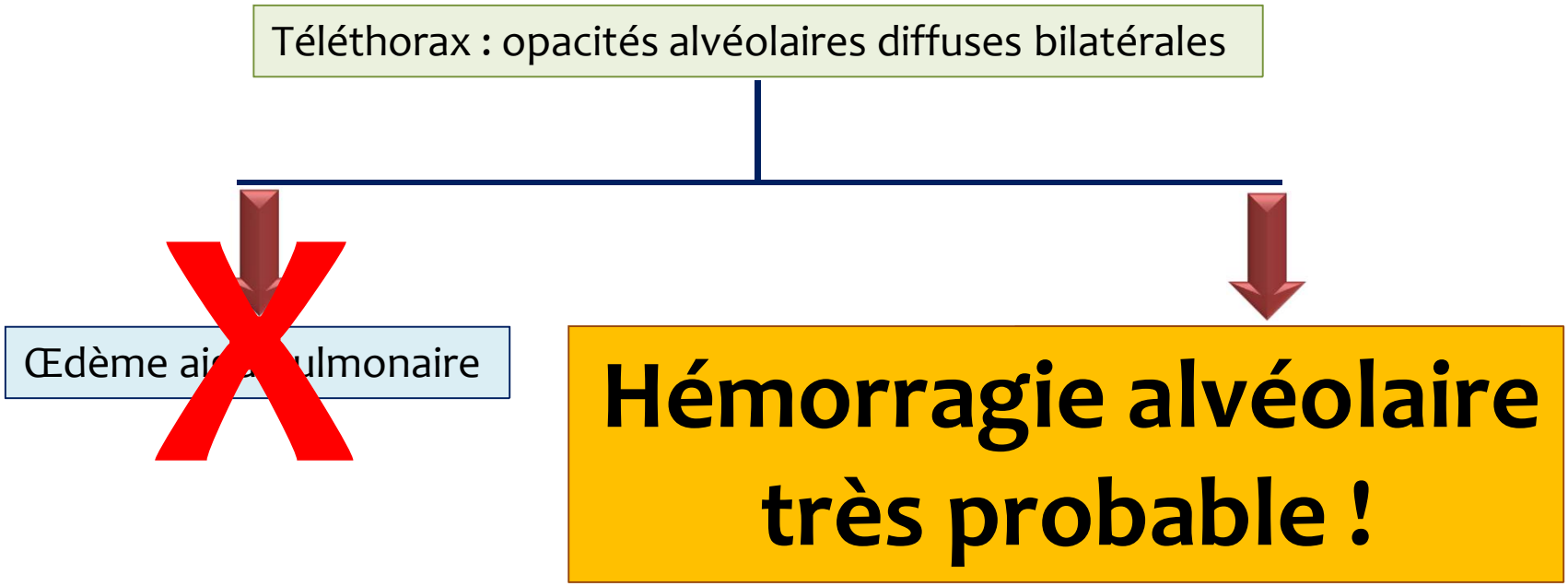

- Séance d'hémodialyse avec perte de poids (>2Kg) : **aucun effet**,
- Echocardiographie doppler : **pas d'insuffisance VG.**

Reconsidérons le diagnostic !

Hémorragie alvéolaire très probable

+

Glomérulonéphrite rapidement progressive
Protéinurie > 1 g/24H + hématurie

↓

Tableau pneumo-rénal

Reconsidérons le diagnostic !

Tableau pneumo-rénal

+

Syndrome inflammatoire **CRP = 48, vs=90 mm**

+

Pas de signes biologiques de MAT

+

Ac anti-RNA polymérase III négatif | U1 RNP

=

Une vascularite associée aux ANCA ?

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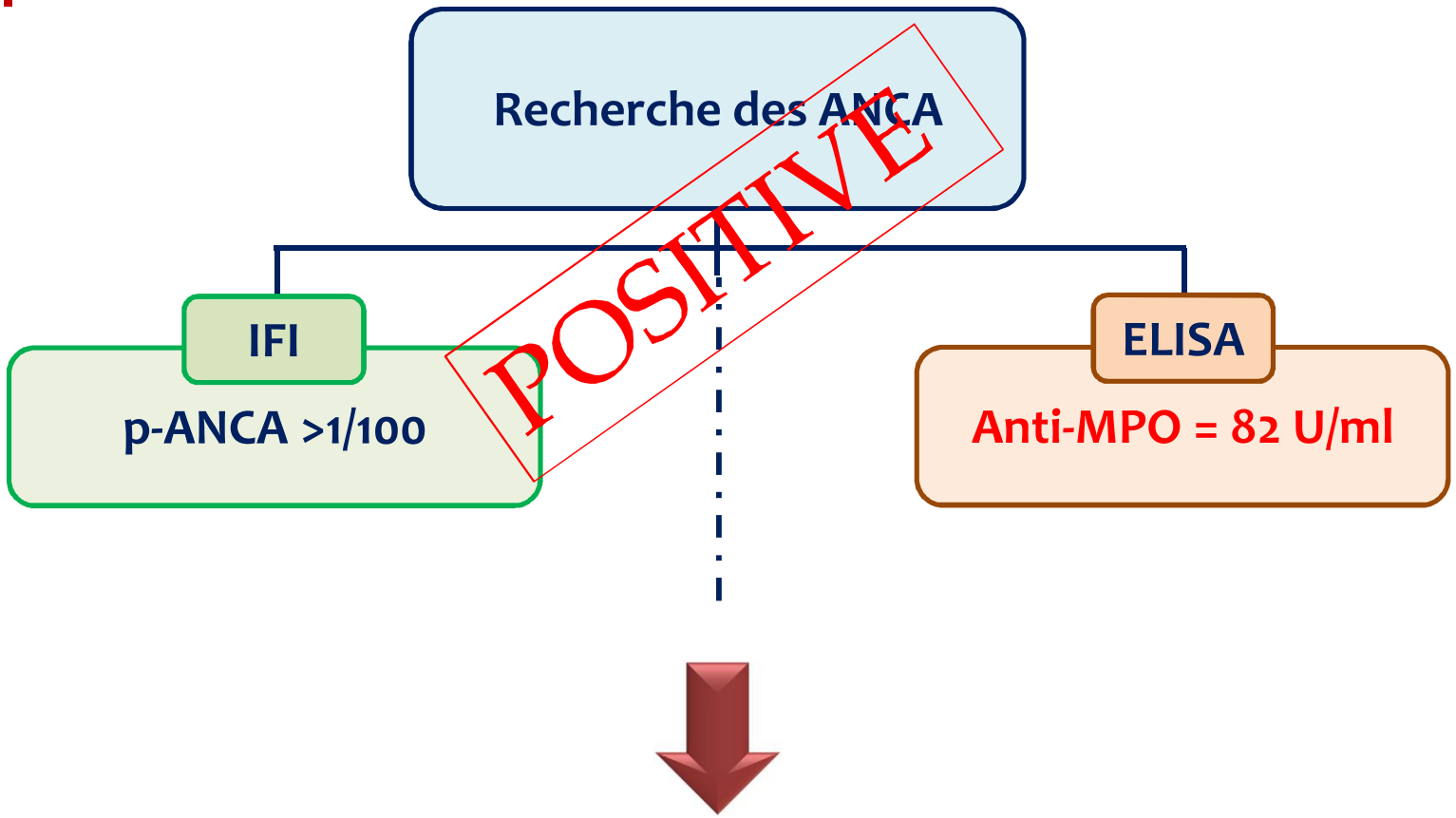

Histologie (PBR) ??

Patiente déjà décédée !!

Quel diagnostic retenir ?

Anti-Neutrophil Antibody Associated Vasculitis in Systemic Sclerosis

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Objectives: To report 3 cases ANCA-associated vasculitis (AAV) that developed in patients suffering from systemic sclerosis (SSc) and to review previously reported cases.

Methods: We describe 3 patients diagnosed with SSc who developed severe AAV that presented as crescentic glomerulonephritis (GN) and/or alveolar hemorrhage. A retrospective review of the literature was performed using the PubMed database.

Results: The first patient presented with rapidly progressive renal failure and then with 2 episodes of massive alveolar hemorrhage. She was partially refractory to treatment with corticosteroids and cyclophosphamide but responded promptly to treatment with rituximab. The second patient suffered from 2 episodes of fulminant alveolar hemorrhage; the first responded to intravenous corticosteroids, but the second was fatal despite aggressive immune suppression with corticosteroids and cyclophosphamide. The third patient presented with a clinical picture compatible with scleroderma renal crisis (SRC) but was later diagnosed with crescentic GN and subsequently died from probable alveolar hemorrhage. Thirty-seven cases of AAV in SSc patients have been described in the English literature. Clinical manifestations include rapidly progressive GN, alveolar hemorrhage, limb ischemia, and vasculitic skin rash. In contrast to SRC that usually develops early in the course of SSc, ANCA-associated GN in SSc patients occurred later, after several years of illness. Hypertension, microangiopathic hemolytic anemia, and thrombocytopenia that are the hallmark of SRC were observed only in a minority of AAV cases. Almost all cases of AAV in SSc were positive for MPO-ANCA.

Conclusions: AAV in the setting of SSc is a diagnostic challenge. Differential diagnosis from SRC is crucial as treatment approach for these conditions completely differs. High doses of corticosteroids and immune suppression are advocated in severe AAV. In resistant cases, treatment with rituximab may be considered.

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Keywords: *systemic sclerosis, vasculitis, ANCA, alveolar hemorrhage*

Systemic sclerosis (SSc) is an idiopathic disease characterized by progressive thickening of the skin and characteristic fibrotic involvement of multiple internal organs, most notably the kidneys, lungs, gastrointestinal tract, and heart. The pathogenesis is incompletely understood, but entails a cellular and humoral autoimmune reaction that leads to vasculopathy and progressive visceral and vascular fibrosis. The most important renal complication in SSc is scleroderma renal crisis (SRC), estimated to affect 5 to 10% of all SSc patients (reviewed in (1,2)). SRC typically presents as a rapid onset of accelerated and often malignant hypertension, acute renal failure, and microangiopathic hemolytic anemia. Therapy with angiotensin-converting enzyme inhibitors dramatically improves the survival of patients with SRC. Overall, approximately two thirds of patients with SRC require renal replacement therapy and approximately one half of these patients will eventually recover sufficiently to discontinue dialysis (1). Renal recovery can occur up to 24 months after SRC.

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with high titers of RF. D-penicillamine was discontinued, and treatment with weekly oral methotrexate (15 mg), low-dose prednisone (10 mg/daily), and hydroxychloroquine was instituted. Over the next several years, her disease gradually progressed with worsening sclerodactyly and gradual deterioration of the interstitial lung disease.

hips necessitated treatment with tumor necrosis factor-α blockers.

In 2006, while treated with etanercept, the patient sud-

Two days later, her hemoglobin level dropped from 12.3 g/dL to 10 g/dL and schistocytes were seen on blood smear. Hypertension persisted and the diagnosis of SRC was made. At this point, angiotensin-converting enzyme inhibitors were initiated. Serologic tests were positive for ANA with homogenous pattern, Scl-70, p-ANCA by immunofluorescence, and MPO by ELISA, whereas antibodies against dsDNA, GBM, Hepatitis B and C viruses, and cryoglobulins were all negative.

Renal biopsy, obtained on the fourth day of hospitalization, yielded 14 glomeruli, of which 1 was sclerotic and 10 contained epithelial crescents with fibrin deposits, and mixed lymphocytic and neutrophilic interstitial infiltrates. Blood vessels appeared normal.

The diagnosis of crescentic AAGN was made and treatment with IV methylprednisolone for 3 consecutive days, followed by high-dose oral prednisone and IV CYC (500 mg/m^2), was initiated. During the following days, she developed progressive respiratory failure. Chest CT showed diffuse alveolar infiltrates. Despite an adequate

administration of high-dose IV immunoglobulins. Despite this treatment, the patient's condition continued to deteriorate and she died on the 32nd day of hospitalization.

Case 3

In February 2009, a 69-year-old woman was admitted to the internal medicine ward for investigation of weakness of 2 weeks' duration accompanied by mild abdominal pain, microscopic hematuria, and new onset renal failure.

On admission, she appeared comfortable. Her blood pressure was 180/95 mm Hg; heart rate was 90 beats per minute, and her temperature was 37.5°C. The physical

Diffuse	57% (12/21)
Limited	38% (8/21)
Sine	5% (1/21)
Serology %, No.	
Scl-70	77% (27/35)
ACA	20% (7/35)
Scl-70 + ACA negative	5.7% (2/35)
p-ANCA	97% (32/33)
c-ANCA	3% (1/33)
MPO	97% (34/35)
PR3	3% (1/35)
MPO+PR3 negative	3% (1/35)
Clinical manifestation %, no.	
RPGN	83% (33/40)
Alveolar hemorrhage	28% (11/40)
Limb ischemia	13% (5/40)
Skin vasculitis	10% (4/40)
Outcome %, no.	
Improved	51% (18/35)
ESRD	14% (5/35)
Death	34% (12/35)

until the appearance of overt AAV is about 9 years. The majority of patients suffered from the diffuse variant of SSc (57%), while about 38% had limited SSc.

In the AAV cohort, positive serology for Scl-70 was common (77%), while the frequency of this antibody

CONCLUSION

- Le diagnostic d'une GNEC, rentrant dans le cadre d'une vascularite à ANCA, chez un patient atteint d'une ScS constitue un véritable **challenge !!**

- **La mise en évidence d'ANCA par IFI et/ou par ELISA** est d'une aide incontestable au diagnostic différentiel que l'on peut préciser par biopsie rénale.

Merci pour votre attention

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