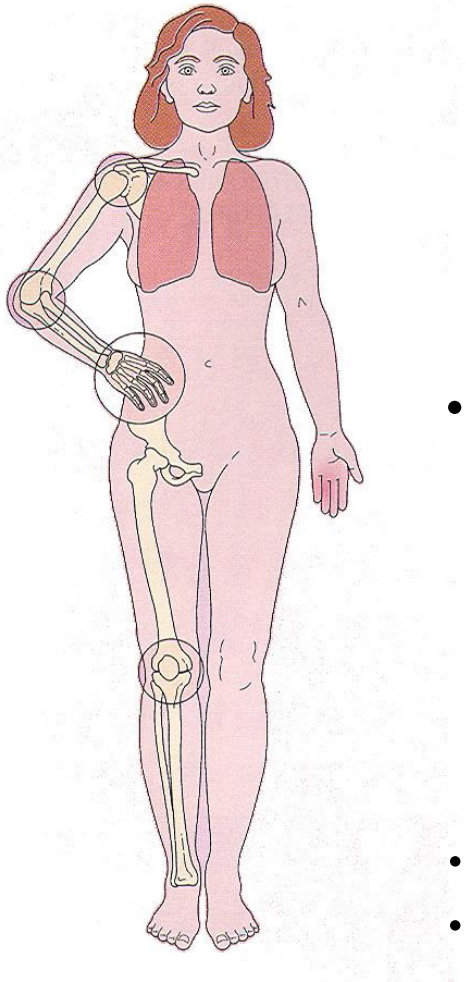
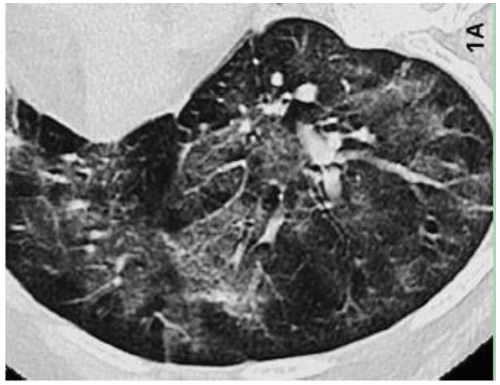
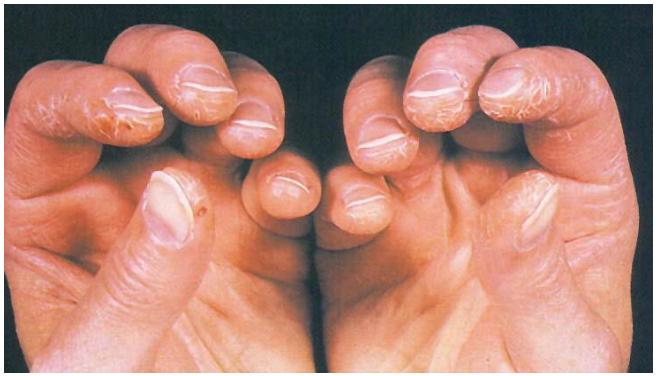
A propos du syndrome des anti-synthétases : les anti-TRIM21 : de la théorie à la pratique

GEAI : 22/01/15

Le syndrome des anti-synthétases







- **Clinique**
  - Pneumopathie interstitielle
  - Polyarthrite non érosive
  - Sd de Raynaud
  - Myosite souvent infraclinique (sauf si anti-Jo1)
  - Mains de mécanicien, hyperkératose fissuraire des mains
  - Fièvre, rash cutanés, Sd sec
- Association HLA : DR3 (Drw52)
- Sex ratio : 3 /1

Forte demande des cliniciens de recherche d'anticorps multiples

Hétérogénéité

- Au début PID et atteinte articulaire.
- Expression clinique, évolution et sévérité variable
- PID :
  - Présente chez 20 à 78% des myosites
  - conditionne le pronostic : augmentation de la morbidité et mortalité
  - Association +++ avec anti-synthétases (et aussi, anti-PM/Scl et anti–MAD-5)
- Importance de l'identification des anti-synthétases dans PID car réponse aux immunosuppresseurs vs PID idiopathiques

Facteurs « pronostiques »

- Anti-Jo1 versus autres anti-synthétases
- Marie I, 2012 :
  - 95 patients (75 anti-Jo1, 15 anti-PL7, 5 anti-PL12)
    - Patient avec anti-Jo1 : myosites plus sévères, arthrite +++ et plus de risque de cancer
    - Patients avec anti-PL7 PL12 : PID précoce et sévère, plus de complications gastro-intestinale
- Hervier B, 2012 : étude multicentrique rétrospective :
  - 203 patients (160 Jo1, 25 PL7, 48 PL12)
  - 2 groupes de patients
    - Jo1 : maladie plus diffuse
    - Autres : maladie plus limitée à PID, survie moins bonne, essentiellement liée à sévérité de atteinte pulmonaire
- Tomonaga M, 2014 : 7 anti-PL7, 15 anti-Jo1 : Différence sur nature de l'atteinte pulmonaire

Facteurs « pronostiques »

- Aggarwal et al, 2014 : comparaison survie à 5 et 10 ans de patients avec anti-Jo1 (122) et avec autre AS (80)
  - Survie à 5 et 10 ans : 90% et 70% pour anti-Jo1 versus 75% et 45% pour autres anti-synthétases
  - Facteurs d'influence : age au 1er diagnostic et délai de diagnostic (pas le sexe, ni l'ethnie, ni le type de connectivite)
  - Mais pas d'étude indépendante des différents facteurs et autres facteurs connu pour influer non testés
- Hamaguchi Y, 2013 : 166 japonais avec SAS
  - PID dans tous les groupes
  - Autres manifestations varient avec l'Ac présent
  - Inclusion des anti-synthétases dans critères diagnostic des myosites ?

Anti-Jo1 +/- anti-TRIM21 ?

Short-Term and Long-Term Outcome of Anti-Jo1-Positive Patients with Anti-Ro52 Antibody

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Luc Mouthon, MD, PhD,¶ Jean-François Menard, MD,#
Hervé Levesque, MD, PhD,* and Fabienne Jouen, MD**

- Dossiers de patients revus :
  - 89 patients avec SAS et anti-Jo1 revus, 36 avec anti-TRIM21
  - 13 patients avec anti-TRIM21 sans anti-Jo1

Table 1 Comparison of Clinical Characteristics Between Anti-Jo1-Positive Patients with and without Anti-Ro52 Antibody

	Presence of Anti-Ro52 Antibody (n = 36)	Absence of Anti-Ro52 Antibody (n = 53)	P
General characteristics			
Age (yr)	56 [range: 20-75]	53 [range: 18-79]	0.132
Sex: male/female	30.6%/69.4%	39.6%/60.4%	0.501
PM/DM subset[a]	66.7% PM/33.3% DM	62.3% PM/37.7% DM	1
Clinical characteristics			
Raynaud's phenomenon	50%	45.3%	0.672
Mechanic's hands	55.6%	32.1%	0.04
Esophageal involvement	25%	22.6%	0.997
Joint manifestations	69.4%	62.3%	0.368
ILD	77.8%	71.7%	0.624
Ventilatory insufficiency related to striated muscle weakness	13.9%	9.4%	0.517
Aspiration pneumonia	16.7%	9.4%	0.341
Cardiac impairment	13.9%	9.4%	0.517
Malignancy	19.4%	5.7%	0.02

ILD, interstitial lung disease; PM/DM, polymyositis/dermatomyositis.
[a]Except where indicated, values are median; P values were obtained with χ^2 or Fisher's exact tests.

Table 2 Comparison of ILD Characteristics Between Anti-Jo1-Positive Patients with and without Anti-Ro52 Antibody

	Presence of Anti-Ro52 Antibody (n = 28)	Absence of Anti-Ro52 Antibody (n = 38)	P
Presenting pulmonary symptoms			
Fever	16.7%	20%	0.438
Dyspnea	67.9%	42.2%	0.09
Cough	64.3%	36.9%	0.08
Asymptomatic	17.9%	57.8%	0.002
Time onset			
Before PM/DM	17.9%	18.4%	
Concomitant with PM/DM	64.2%	57.9%	0.762
After PM/DM	17.9%	23.7%	
PFT findings at ILD diagnosis			
FVC	71%	76%	0.277
VC	74%	75%	0.388
DLCO	57%	60%	0.550
HRCT-scan pattern			
HRCT score of fibrosis	16.1	11.9	0.275
COP	17.9%	15.8%	
NSIP	60.7%	65.8%	1
UIP	21.4%	18.4%	
Outcome of ILD			
Remission	25%	23.7%	
Improvement/ stabilization	53.6%	63.1%	0.470
Deterioration	21.4%	10.5%	

ILD, interstitial lung disease; PM/DM, polymyositis/dermatomyositis; ILD, interstitial lung disease; PFT, pulmonary function tests; FVC, forced vital capacity; VC, vital capacity; DLCO, diffusing capacity of carbon monoxide; HRCT, high-resolution computed tomography; COP, cryptogenic organizing pneumonia; NSIP, nonspecific interstitial pneumonia; UIP, usual interstitial pneumonia.

Table 3 Comparison of Musculoskeletal Outcome Between Anti-Jo1-Positive Patients with and without Anti-Ro52 Antibody

	Presence of Anti-Ro52 Antibody (n = 36)	Absence of Anti-Ro52 Antibody (n = 53)	P
Outcome of myositis			
Median score of muscle power at last follow-up	77	84	0.04
Remission	25%	32%	
Improvement	52.8%	62.3%	0.07
Deterioration	22.2%	5.7%	
Recurrence	63.9%	58.4%	0.08
Outcome of joint involvement			
Onset of periarticular calcifications and erosions of hand and wrist joints	8.3%	0%	0.06
Remission	40%	45.4%	
Improvement	36%	51.5%	0.04
Deterioration	24%	3.1%	
Mortality	16.7%	7.5%	0.304

Except where indicated, values are median; P values were obtained with χ^2 or Fisher's exact tests.

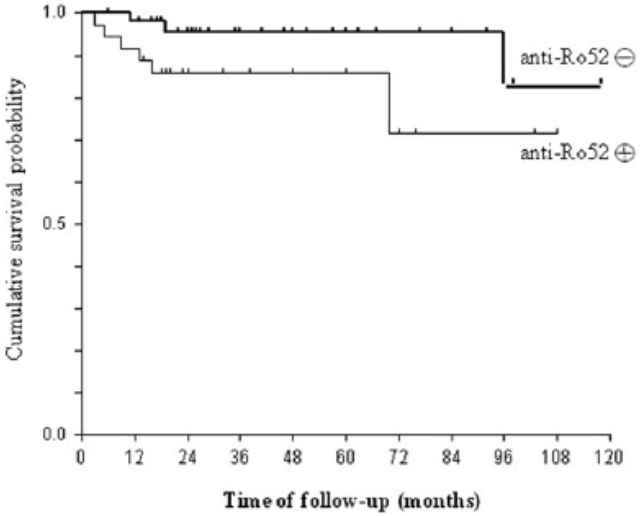

Figure 1 Survival curves in anti-Jo1-positive patients with and without anti-Ro52 antibody.

Table 4 Comparison of Clinical Characteristics Between Anti-Ro52-Positive Patients with and without Anti-Jo1 Antibody

	Presence of Anti-Jo1 Antibody (n = 36)	Absence of Anti-Jo1 Antibody (n = 13)	P
General characteristics			
Age (yr)	56 [range: 20-75]	46 [range: 26-69]	0.007
Sex: male/female	30.6%/69.4%	7.7%/92.3%	0.142
PM/DM subset*	66.7% PM/33.3% DM	38.5% PM/61.5% DM	0.104
Clinical characteristics			
Raynaud's phenomenon	50%	25%	0.114
Mechanic's hands	55.6%	0%	0.0002
Esophageal involvement	25%	30.8%	0.723
Joint manifestations	69.4%	46.1%	0.338
ILD	77.8%	38.5%	0.009
Ventilatory insufficiency related to striated muscle weakness	13.9%	7.7%	0.523
Aspiration pneumonia	16.7%	7.7%	0.341
Outcome			
Deterioration of myositis	22.2%	7.7%	0.411
Deterioration of ILD	21.4%	0%	0.001

Except where indicated, values are median; P values were obtained with χ^2 or Fisher's exact tests.
ILD, interstitial lung disease; PM/DM, polymyositis/dermatomyositis.

Conclusion : des questions

- Que faire des anti-TRIM21 : les rendre ou pas ?

- Que peut-on mettre en commentaire à propos de la valeurs des résultats d’autoanticorps?

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