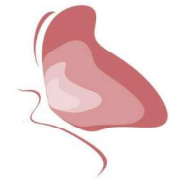




POLIANGEITIS GRANULOMATOSA (GPA) DE WEGENER

¿cómo se presenta? Afectación del SNC

Gonzalo De Luna
R5 Medicina Interna



Conflicto de interes:

Nada que declarar

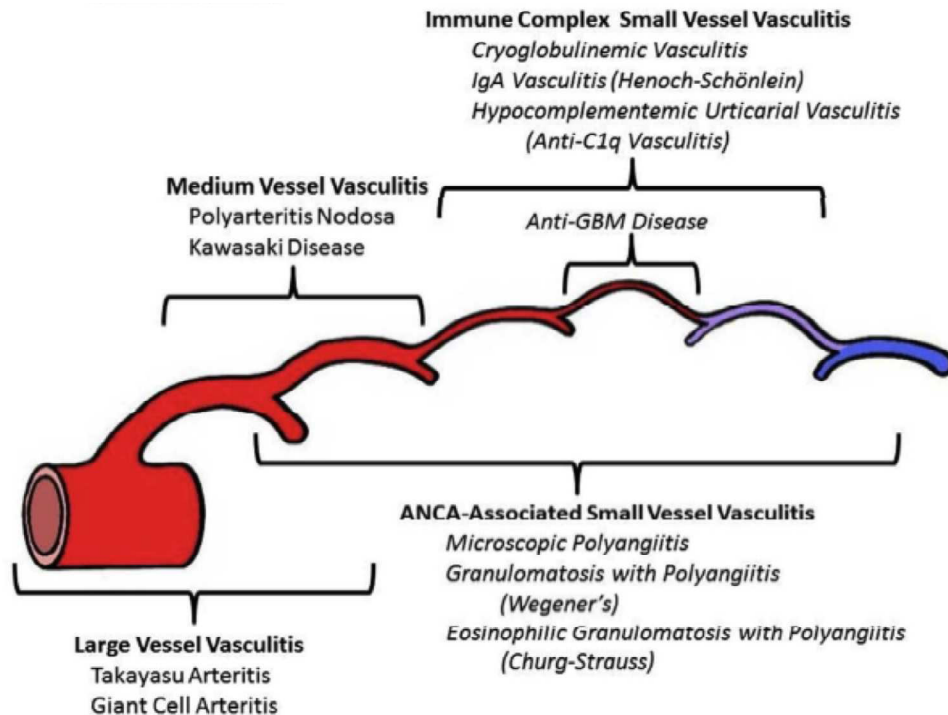
1. INTRODUCCION

2. MODELOS DE LESIÓN Y CORRELACIÓN RADIOLÓGICA

3. FENOTIPOS

4. ESTRATEGIAS TERAPEUTICAS. SEGUIMIENTO

GPA



Inflamación granulomatosa necrotizante con tropismo de vías respiratorias altas y bajas.

Vasculitis necrotizante de pequeño vaso a vaso mediano (capilar, vénula, arteriola, arterias y venas).

- 1. Glomerulonefritis necrotizante: *común***
- 2. Vasculitis ocular y capilaritis pulmonar con hemorragia: *frecuente***
- 3. Inflamación granulomatosa y no granulomatosa extravascular: *común*.**

2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides

Jennette JC et al. Arthritis & Rheumatism Arthritis & Rheumatism Accepted: Sep 18, 2012

Afectación neurológica en GPA

A Disease-Specific Activity Index for Wegener's Granulomatosis

VASCULITIS ACTIVITY SCORE		DEMOGRAPHY	
Tick box only if abnormality is newly present since last assessment or worse in the last few weeks (use the Vasculitis Damage Index, VDI to score items of damage) Tick box only if abnormality is due to active (but not new or worse) vasculitis Tick box if more information (specialist opinion/tests) is requested * oral/axillary temperatures; rectal temperatures are 0.5°C higher		Trial Number Visit Date / / Investigator	
PERSISTENT	NEW/WORSE	PERSISTENT	NEW/WORSE

1. GENERAL <input type="checkbox"/> (none)		
malaise	<input type="checkbox"/>	<input type="checkbox"/>
myalgia	<input type="checkbox"/>	<input type="checkbox"/>
arthralgia/arthritis	<input type="checkbox"/>	<input type="checkbox"/>
headache	<input type="checkbox"/>	<input type="checkbox"/>
fever (< 38.5°C) *	<input type="checkbox"/>	<input type="checkbox"/>
fever (> 38.5°C) *	<input type="checkbox"/>	<input type="checkbox"/>
wt loss (> 2kg)	<input type="checkbox"/>	<input type="checkbox"/>

2. CUTANEOUS <input type="checkbox"/> (none)		
infant	<input type="checkbox"/>	<input type="checkbox"/>
purpura	<input type="checkbox"/>	<input type="checkbox"/>
other skin vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
ulcer	<input type="checkbox"/>	<input type="checkbox"/>
gangrene	<input type="checkbox"/>	<input type="checkbox"/>
multiple digit gangrene	<input type="checkbox"/>	<input type="checkbox"/>

3. MUCOUS MEMBRANES/EYES <input type="checkbox"/> (none)		
mouth ulcers	<input type="checkbox"/>	<input type="checkbox"/>
genital ulcers	<input type="checkbox"/>	<input type="checkbox"/>
significant proptosis	<input type="checkbox"/>	<input type="checkbox"/>
red eye- conjunctivitis	<input type="checkbox"/>	<input type="checkbox"/>
red eye- episcleritis	<input type="checkbox"/>	<input type="checkbox"/>
blurred vision	<input type="checkbox"/>	<input type="checkbox"/>
sudden visual loss	<input type="checkbox"/>	<input type="checkbox"/>
ophthalmic opinion	<input type="checkbox"/>	<input type="checkbox"/>
no active vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
uveitis	<input type="checkbox"/>	<input type="checkbox"/>
retinal exudates	<input type="checkbox"/>	<input type="checkbox"/>
retinal haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>

4. ENT <input type="checkbox"/> (none)		
Nasal obstruction	<input type="checkbox"/>	<input type="checkbox"/>
Bloody nasal discharge	<input type="checkbox"/>	<input type="checkbox"/>
Nasal crusting	<input type="checkbox"/>	<input type="checkbox"/>
Sinus involvement	<input type="checkbox"/>	<input type="checkbox"/>
Hearing loss	<input type="checkbox"/>	<input type="checkbox"/>
Hoarseness/stridor	<input type="checkbox"/>	<input type="checkbox"/>
ENT opinion	<input type="checkbox"/>	<input type="checkbox"/>
no active vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
Granulomatous sinusitis	<input type="checkbox"/>	<input type="checkbox"/>
Conductive hearing loss	<input type="checkbox"/>	<input type="checkbox"/>
Sensorineural hearing loss	<input type="checkbox"/>	<input type="checkbox"/>
Significant Subglottic inflammation	<input type="checkbox"/>	<input type="checkbox"/>

5. CHEST <input type="checkbox"/> (none)		
persistent cough	<input type="checkbox"/>	<input type="checkbox"/>
dyspnoea or wheeze	<input type="checkbox"/>	<input type="checkbox"/>
Haemoptysis/haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>
chest radiology performed	<input type="checkbox"/>	<input type="checkbox"/>
no active vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
nodules or cavities	<input type="checkbox"/>	<input type="checkbox"/>
pleural effusion/pleurisy	<input type="checkbox"/>	<input type="checkbox"/>
infiltrate	<input type="checkbox"/>	<input type="checkbox"/>
massive haemoptysis or alveolar haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>
respiratory failure	<input type="checkbox"/>	<input type="checkbox"/>

6. CARDIOVASCULAR <input type="checkbox"/> (none)		
aortic incompetence	<input type="checkbox"/>	<input type="checkbox"/>
pericardial pain/rub	<input type="checkbox"/>	<input type="checkbox"/>
ischaemic cardiac pain	<input type="checkbox"/>	<input type="checkbox"/>
congestive cardiac failure	<input type="checkbox"/>	<input type="checkbox"/>
cardiology opinion/tests	<input type="checkbox"/>	<input type="checkbox"/>
no active vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
pericarditis	<input type="checkbox"/>	<input type="checkbox"/>
myocardial infarct/angina	<input type="checkbox"/>	<input type="checkbox"/>
cardiomyopathy	<input type="checkbox"/>	<input type="checkbox"/>

7. ABDOMINAL <input type="checkbox"/> (none)		
severe abdominal pain	<input type="checkbox"/>	<input type="checkbox"/>
bloody diarrhoea	<input type="checkbox"/>	<input type="checkbox"/>
surgical opinion/tests	<input type="checkbox"/>	<input type="checkbox"/>
no active vasculitis	<input type="checkbox"/>	<input type="checkbox"/>
gut perforation/infarct	<input type="checkbox"/>	<input type="checkbox"/>
acute pancreatitis	<input type="checkbox"/>	<input type="checkbox"/>

8. RENAL <input type="checkbox"/> (none)		
hypertension (diastol>95)	<input type="checkbox"/>	<input type="checkbox"/>
proteinuria >1+(>0.2g/24h)	<input type="checkbox"/>	<input type="checkbox"/>
haematuria>1+(>10 ⁶ /bclml)	<input type="checkbox"/>	<input type="checkbox"/>
creatinine 125-249 umol/l	<input type="checkbox"/>	<input type="checkbox"/>
creatinine 250-499 umol/l	<input type="checkbox"/>	<input type="checkbox"/>
creatinine >500 umol/l	<input type="checkbox"/>	<input type="checkbox"/>

9. NERVOUS SYSTEM <input type="checkbox"/> (none)		
organic confusion/dementia	<input type="checkbox"/>	<input type="checkbox"/>
seizures(not hypertensive)	<input type="checkbox"/>	<input type="checkbox"/>
stroke	<input type="checkbox"/>	<input type="checkbox"/>
cord lesion	<input type="checkbox"/>	<input type="checkbox"/>
sensory peripheral neuropathy	<input type="checkbox"/>	<input type="checkbox"/>
cranial nerve palsy	<input type="checkbox"/>	<input type="checkbox"/>
motor mononeuritis multiplex	<input type="checkbox"/>	<input type="checkbox"/>

Modification of the Birmingham Vasculitis Activity Score

	Persistent	New/Worse	None													
6. GENERAL																
a. arthralgia/arthritis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
b. fever (>38.0 °C)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
7. CUTANEOUS																
a. purpura	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
b. skin ulcer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. * gangrene	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
8. MUCOUS MEMBRANES/EYES																
a. mouth ulcers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ												
b. conjunctivitis/episcleritis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. retro-orbital mass/proptosis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
d. uveitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
e. * scleritis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
f. * retinal exudates/hemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
9. EAR, NOSE & THROAT																
a. bloody nasal discharge/nasal crusting/ulcer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ												
b. sinus involvement	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. swollen salivary gland	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
d. subglottic inflammation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
e. conductive deafness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
f. * sensorineural deafness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
10. CARDIOVASCULAR																
a. pericarditis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
11. GASTROINTESTINAL																
a. * mesenteric ischemia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
12. PULMONARY																
a. pleurisy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
b. nodules or cavities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. other infiltrate secondary to WG	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
d. endobronchial involvement	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
e. * alveolar hemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
f. * respiratory failure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
13. RENAL																
a. hematuria (no RBC casts) (≥ 1+ or ≥ 10 RBC/hpf)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Δ ₁												
b. * RBC casts	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. * rise in creatinine >30% or full in creatinine clearance >25%	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
score only the RBC casts (the major item).																
14. NERVOUS SYSTEM																
a. * meningitis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
b. * cord lesion	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
c. * stroke	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
d. * cranial nerve palsy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
e. * sensory peripheral neuropathy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
f. * motor mononeuritis multiplex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
(describe all items and items deemed major)																
<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 25%; border-bottom: 1px solid black;"></td> <td style="width: 25%; border-bottom: 1px solid black;"></td> <td style="width: 25%; border-bottom: 1px solid black;"></td> <td style="width: 25%; border-bottom: 1px solid black;"></td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> <td style="text-align: center;"><input type="checkbox"/></td> </tr> </table>									<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>													
16. TOTAL NUMBER OF ITEMS:																
a.	b.	c.	d.													
Major New/Worse	Minor New/Worse	Major Persistent	Minor Persistent													
17. CURRENT DISEASE STATUS (check only one):																
Severe Disease/Flare ()																
Limited Disease/Flare ()																
Persistent Disease ()																
Remission ()																
18. PHYSICIAN'S GLOBAL ASSESSMENT (PGA)																
Mark line to indicate the amount of WG disease activity (not including longstanding damage) within the previous 28 days :																
<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center;">Remission</td> <td style="text-align: center;"> </td> <td style="text-align: center;">Maximum activity</td> </tr> <tr> <td style="text-align: center;">0</td> <td style="text-align: center;"> </td> <td style="text-align: center;">10</td> </tr> </table>					Remission		Maximum activity	0		10						
Remission		Maximum activity														
0		10														
19. Value in item #18: _____ (distance from 0 to tick mark in millimeters)																

A Disease-Specific Activity Index for Wegener's Granulomatosis

VASCULITIS ACTIVITY SCORE

Tick box **only** if abnormality is **newly present** since last assessment or **worse** in the

DEMOGRAPHY

Modification of the Birmingham Vasculitis Activity Score

Tick box **only** if abnormality is **newly present** since last assessment or **worse** in the

Persistent New/Worse None

8. NERVOUS SYSTEM (none)

organic confusion/dementia

seizures(not hypertensive)

stroke

cord lesion

sensory peripheral neuropathy

cranial nerve palsy

motor mononeuritis multiplex

	Persistent	New/Worse	None
retinal haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
renal impairment (creatinine >30% or fall in creatinine clearance >25%)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
alveolar haemorrhage (RBC casts the major item)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
respiratory failure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
neuropathy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
cranial nerve palsy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
motor mononeuritis multiplex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

retinal haemorrhage

4. ENT (none)

Nasal obstruction

Bloody nasal discharge

Nasal crusting

Sinus involvement

Hearing loss

Hoarseness/stridor

ENT opinion

no active vasculitis

Granulomatous sinusitis

Conductive hearing loss

Sensorineural hearing loss

Significant Subglottic inflammation

renal performance/mark acute pancreatitis

8. RENAL (none)

hypertension (diastol>95)

proteinuria >1+(>0.2g/24h)

haematuria>1+(>10/bc/ml)

creatinine 125-249 umol/l

creatinine 250-499 umol/l

creatinine >500 umol/l

rise in creatinine >30% or fall in creatinine clearance>25%

9. NERVOUS SYSTEM (none)

organic confusion/dementia

seizures(not hypertensive)

stroke

cord lesion

sensory peripheral neuropathy

cranial nerve palsy

motor mononeuritis multiplex

d. endobronchial involvement

e. * alveolar haemorrhage

f. * respiratory failure

DETERMINING DISEASE STATUS:

Severe Disease/Flare: ≥ 1 new/worse Major item.

Limited Disease/Flare: ≥ 1 new/worse Minor item.

Persistent Disease: Continued (but not new/worse) activity.

Remission: No active disease, including either new/worse or persistent items.

	Major New/Worse	Minor New/Worse	Major Persistent	Minor Persistent
retinal haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
renal impairment	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
alveolar haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
respiratory failure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
neuropathy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
cranial nerve palsy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
motor mononeuritis multiplex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

17. CURRENT DISEASE STATUS (check only one):

Severe Disease/Flare ()

Limited Disease/Flare ()

Persistent Disease ()

Remission ()

18. PHYSICIAN'S GLOBAL ASSESSMENT (PGA)

Mark line to indicate the amount of WG disease activity (not including longstanding damage) within the **previous 28 days**:



19. Value in item #18: _____ (distance from 0 to tick mark in millimeters)

Afectación neurológica en GPA

Afectación frecuente (22-54%) :

Sistema nervioso periférico y SNC

Condición más frecuentemente descrita: **neuropatía periférica como mononeuritis múltiple.**

La afectación del SNC es extremadamente rara si no incluimos PN (lesión de pares craneales):

Pares craneales se afectan predominantemente a lo largo del trayecto extracraneal.

Afectación **cerebral y meníngea**

Excepcional ocurriendo solamente del **2-8%** de los pacientes.

*Drachman et al (1963)

*Anderson et al (1975)

*Fauci et al (1983) *Seror

et al (2006)

French Vasculitis Study Group (FVSG)

FFS 1996

1. Proteinuria >1 g/dL
2. Renal insufficiency (stabilized peak creatinine 140 mmol/L)
3. Cardiomyopathy
4. Severe gastrointestinal manifestations
- 5. Central nervous system (CNS) involvement**

Changes in the 2009 FFS

- *To include GPA to evaluate prognosis at diagnosis
- *Absence of CNS involvement as a parameter of poor prognosis

The Five-Factor Score Revisited

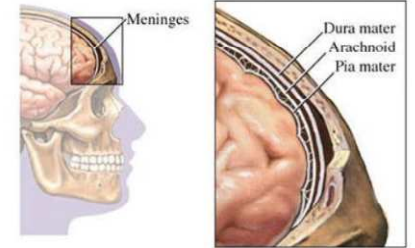
Assessment of Prognoses of Systemic Necrotizing Vasculitides
Based on the French Vasculitis Study Group (FVSG) Cohort .
Guillevin et al. Medicine & Volume 90, Number 1, January 2011

Tres modelos de lesión :

1) **Vasculitis** de pequeño calibre cerebrales o medulares.

2) **Masas granulomatosas** originarias del tracto superior respiratorio cartilaginoso y óseo contiguo, invadiendo estructuras del SNC como la órbita (afectación del nervio óptico), meninges o cerebro.

3) **Lesiones granulomatosas** cerebrales o meníngeas (paquimeningitis y lesiones aisladas).



Central Nervous System Involvement in Wegener Granulomatosis

Raphaelle Seror, MD, Loic Guillevin, MD. Medicine. Volume 85, Number 1, January 2006

MODELOS RADIOLÓGICOS DE AFECTACIÓN SNC EN GPA

Pachymeningitis (cerebral and/or medullary)

- ❑ Diffuse linear dural thickening and enhancement.
- ❑ Focal dural thickening and enhancement contiguous with orbital, nasal, or paranasal disease.
- ❑ Enlarged and enhancement of pituitary gland with infundibular thickening.

Granuloma

- ❑ Remote granulomatous lesions in brain or medullar parenchyma

Ischemic or hemorrhagic lesions due to vasculitis damage

- ❑ Infarcts (stroke) : ischemic or hemorrhagic
- ❑ Nonspecific white matter areas of high signal intensity
- ❑ Cerebral Vaculitides

Wegener Granulomatosis: MR Imaging Findings in Brain and Meninges.

Joseph M. Murphy. Radiology 1999; 213:794–799

Sinonasal and cerebral imaging findings in Wegener's granulomatosis

Silvera et al. Presse Md 2007 ; 36:913-21

**574 GPA Medicina Interna
Cochin/Avicenne**

Búsqueda de afectación SNC

**16 GPA (3%)
afectación
SNC**

**558 GPA no
afectación
SNC**

**Criterios de inclusión
GPA:
criterio ACR y/o
criterio Chapel Hill.**

Afectación del SNC

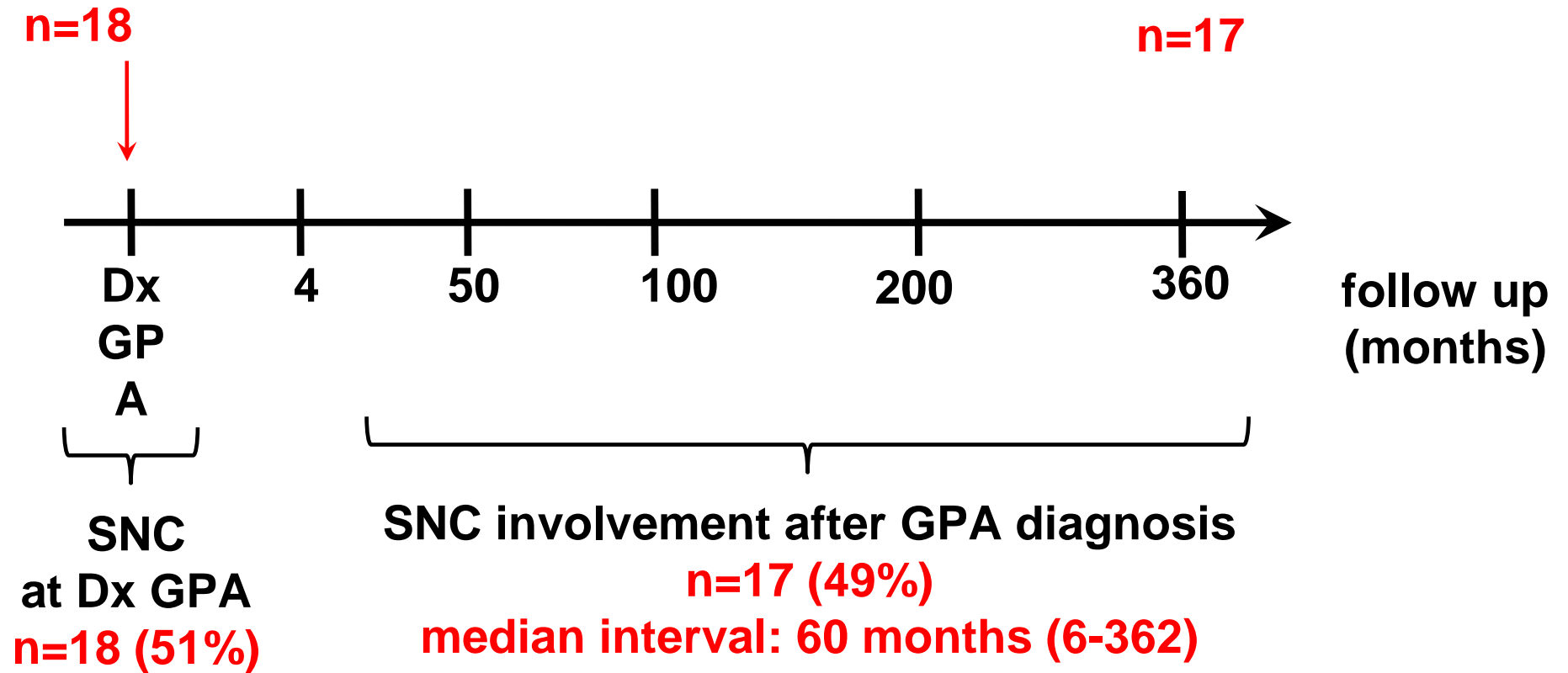
- Paquimeningitis medular y cerebral.**
- Meningitis aseptica**
- AVC Isquémico y/o hemorrágico.**
- Granuloma medulares/cerebrales**
- Afectación hipofisaria**

Granulomatose avec polyangéite : profil clinico-biologique et évolutif des atteintes du système nerveux central chez 16 patients.

De Luna G. , Guillevin L. Rev Med Int 2012. 33:2 (A1-A210)*

Treinta cinco observaciones (**n=35**) recogidas desde 7 departamentos de Medicina Interna incluyendo 6 en Francia y 1 en España.

Afectación de SNC y GPA



Características clínicas

Epidemiology

Age: 48 (2-78) years (GAP)
51 (2-79) years (SNC)

Male : 29/35 (83%)

ENT
n=28 (80%)

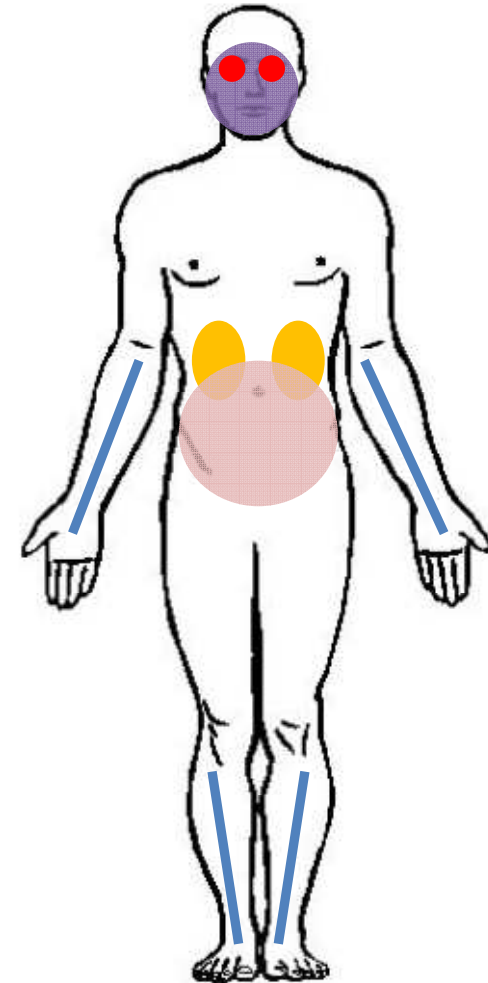
LUNG
n=20 (57%)

SNP
n=17 (48%)

RENAL
n=14 (40%)

OPHT
n=5 (33%)

DIGESTIVE
n=2 (11%)



Sintomas clínicos

CNS symptoms	n (%)
Headaches	23 (65 %)
Sensory impairment	15 (43 %)
Motor impairment	11 (31 %)
Vestibular syndrome	8 (23 %)
Hearing loss	8 (23 %)
Psychiatric/mood disorders	3 (8 %)
Diabetes insipidus	2 (6 %)

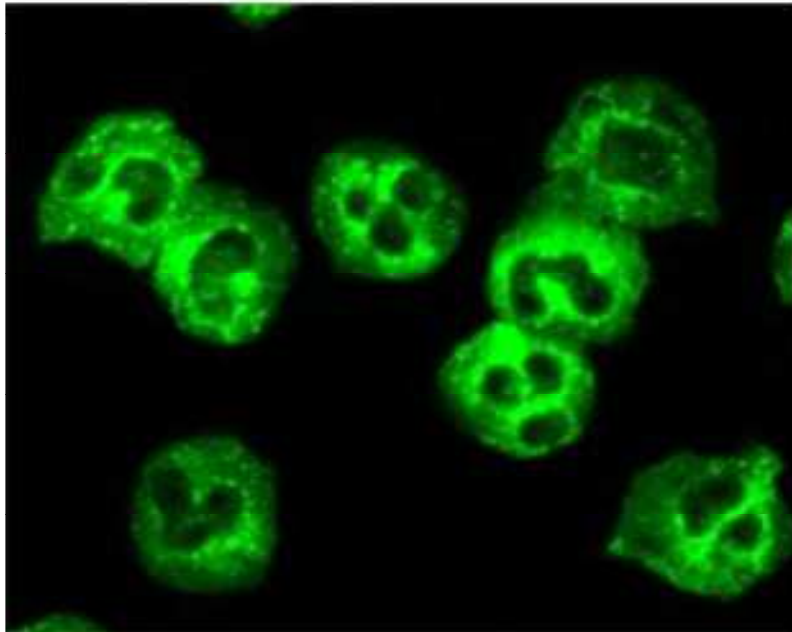
*

Características Inmunológicas

Immunology

ANCA positive in 31/35 (89%)

Anti-PR3: 26/35 (84%)



Anti-MPO: 5/35 (16%)



Líquido cefaloraquídeo

Lumbar ponction	n (%)
n=19	54
Normal	7 (37%)
Abnormal	12 (63%)
Protein level >0,40 g/L	8 (67%)
Lymphocyte (cell count)	6 (50%)
Low glucose level	3 (25%)

Características Radiológicas

Images TDM/IRM	n (%)
Cerebral pachymeningitis	16 (46 %)
Ischemic stroke and multi infarct areas	15 (43 %)
Cerebral vasculitides	7 (20 %)
Medullar pachymeningitis	4 (11 %)
Hypophyseal involvement	2 (6 %)
Hemorrhagic stroke	2 (6 %)
Isolated granuloma (cerebral)	1 (3 %)
Isolated granuloma (medullar)	1 (3 %)

*

Fenotipos clínico-radiológico

Granulomatous n=20	57%
Cerebral pachymeningitis	16 (80%)
Medullary pachymeningitis	3 (15%)
Hypophyseal involvement	2 (10%)
Isolated granuloma (cerebral and medullar)	0*
Vascular n=13	37%
Ischemic stroke (62%)	8
Cerebral vasculitides	6 (46%)
White matter areas of high signal intensity	5 (38%)
Hemorrhagic stroke	0*

*

Características clínicas: fenotipos

Vascular (V)
Granuloma (G)

ENT
77% (V) Vs 85% (G)

LUNG
54% (V) Vs 55% (G)

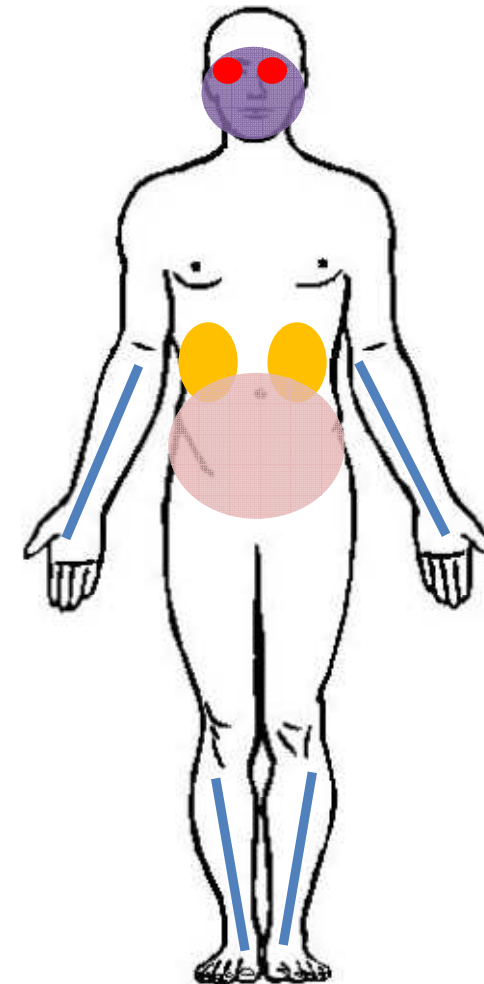
SNP
38% (V) Vs 55% (G)

RENAL
69% (V) Vs 20% (G)

OPHT
31% (V) Vs 35% (G)

DIGESTIVE
15% (V) Vs 10% (G)

*



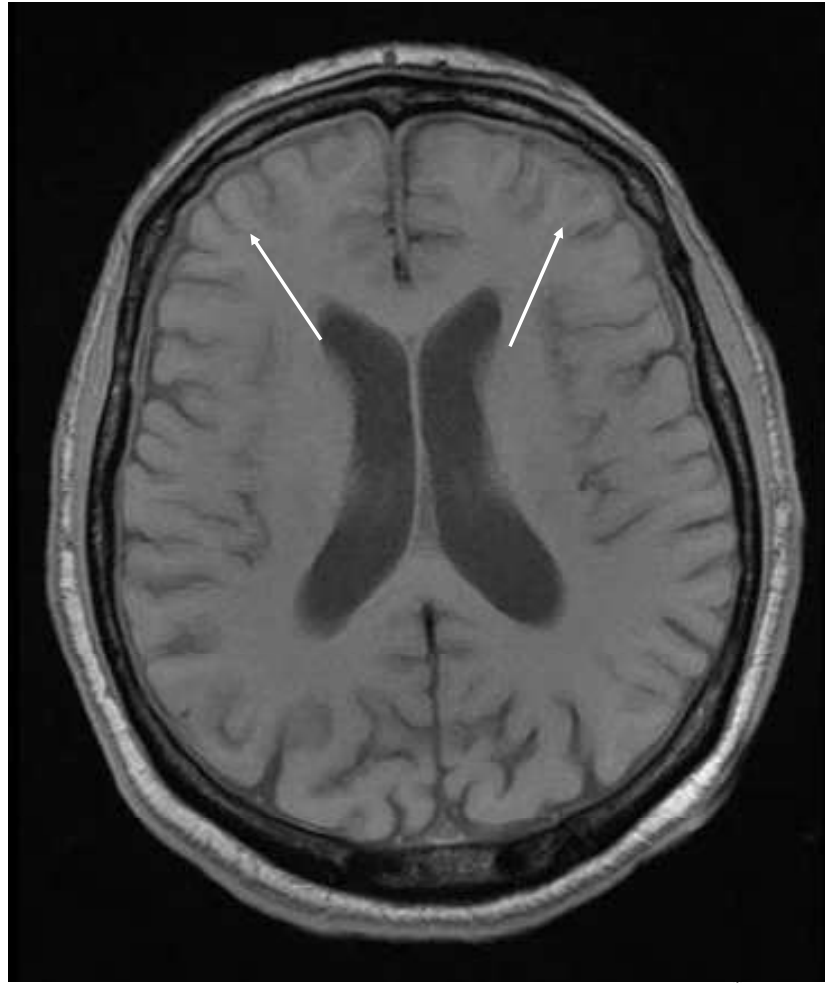
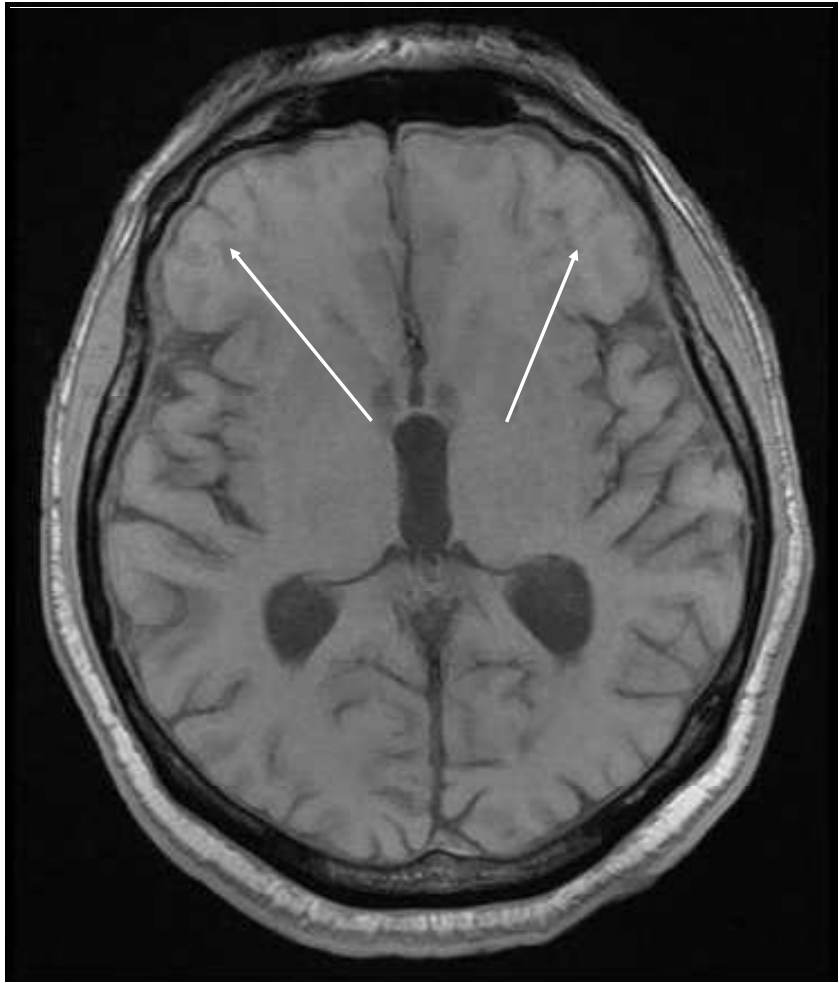
***p=0,01**

Sintomas clínicos

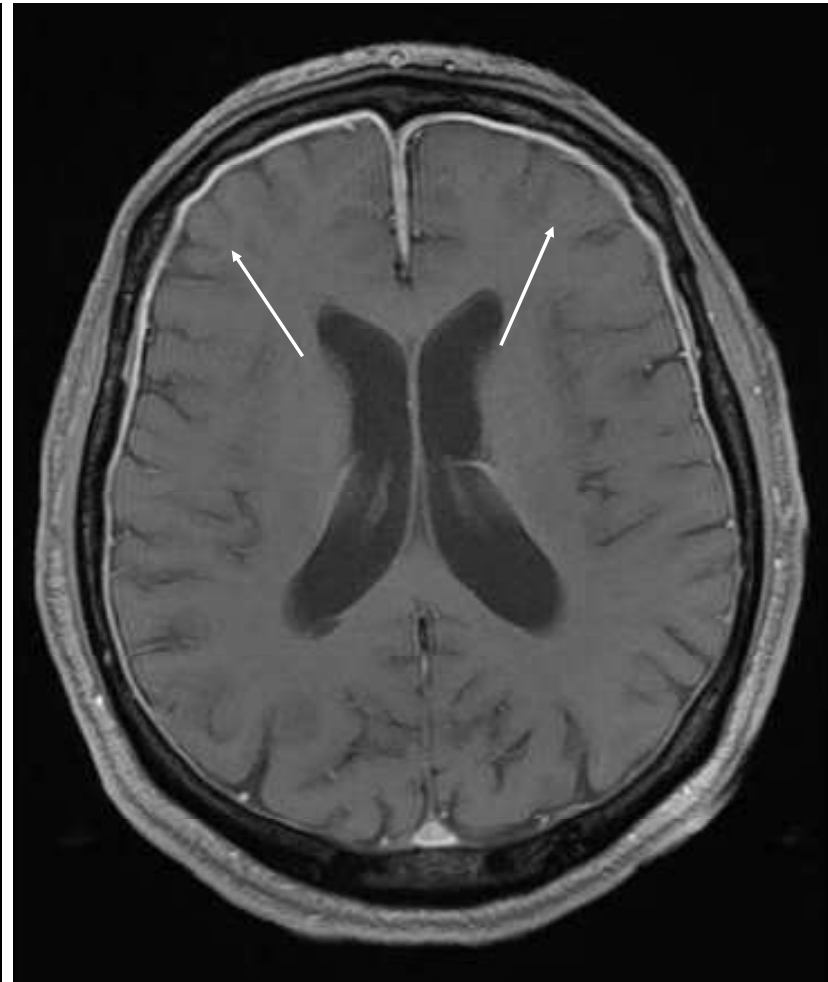
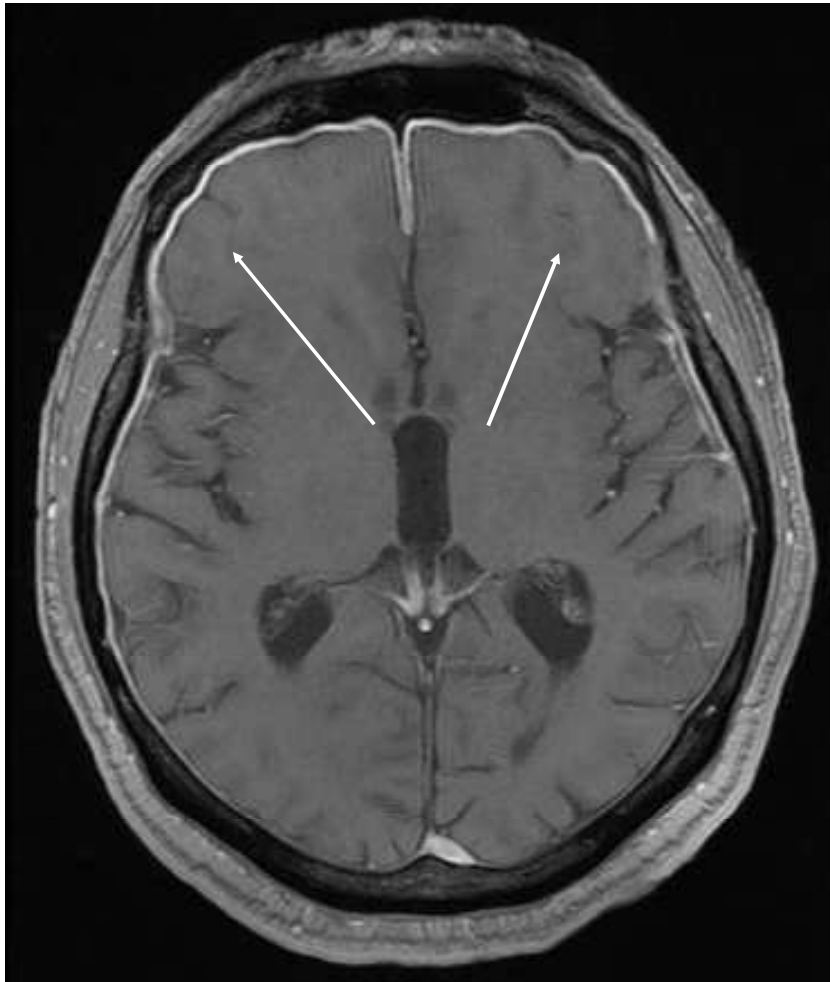
CNS symptoms	Granulome	Vascular	p
Headaches	19 (95 %)	4 (31%)	0,0002
Sensory impairment	10 (50 %)	5 (38%)	0,72
Motor impairment	1 (5 %)	9 (69%)	0,0002
Vestibular syndrome	4 (24 %)	3 (23%)	1
Hearing loss	7 (33 %)	1 (8%)	0,12
Psiquiatric/mood disorders	0 (0 %)	3 (23%)	0,005
Diabetes insipidus	2 (10 %)	0 (0%)	0,51

*

Engrosamiento linear difuso de duramadre (FLAIR)

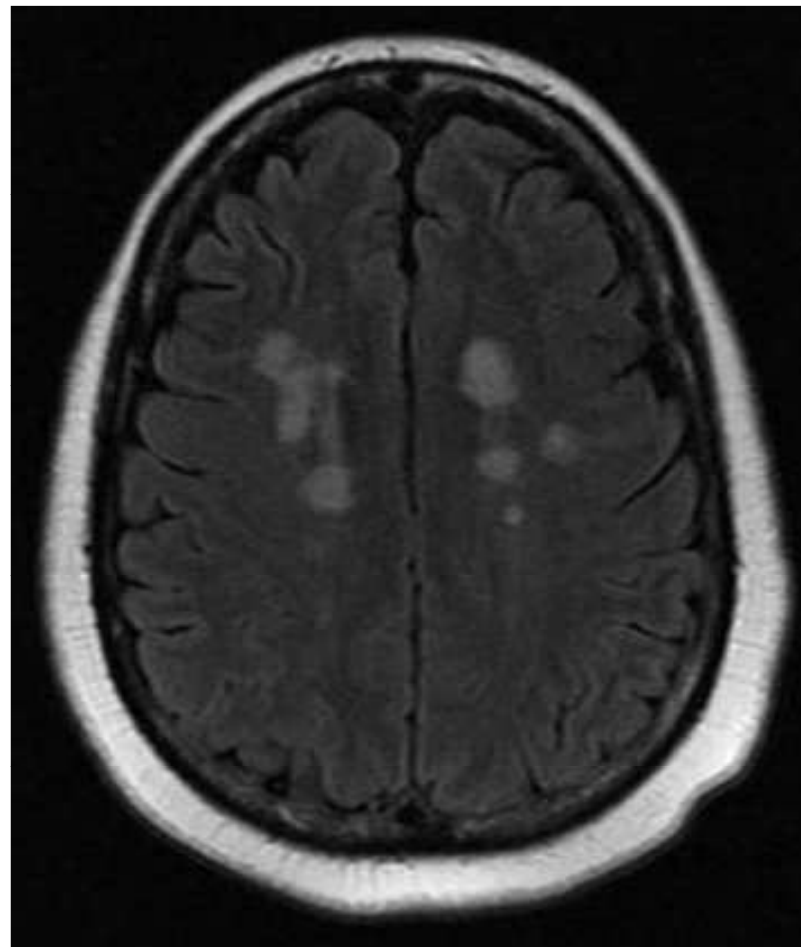
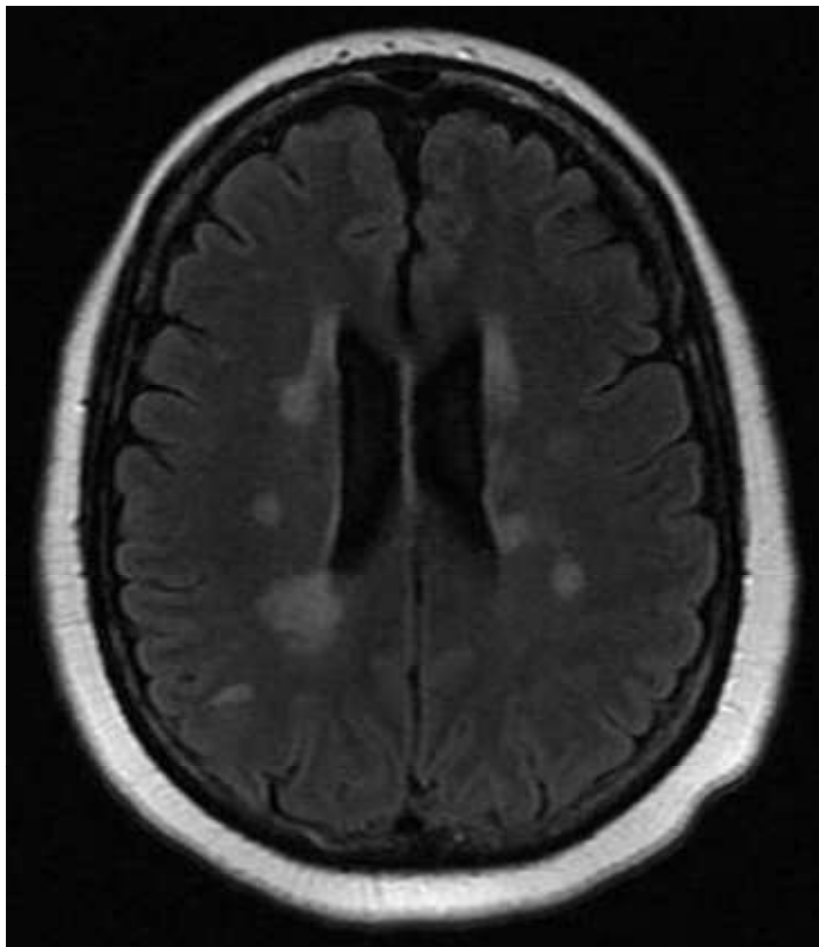


Realce linear difuso de duramadre (GADOLINIUM)



*

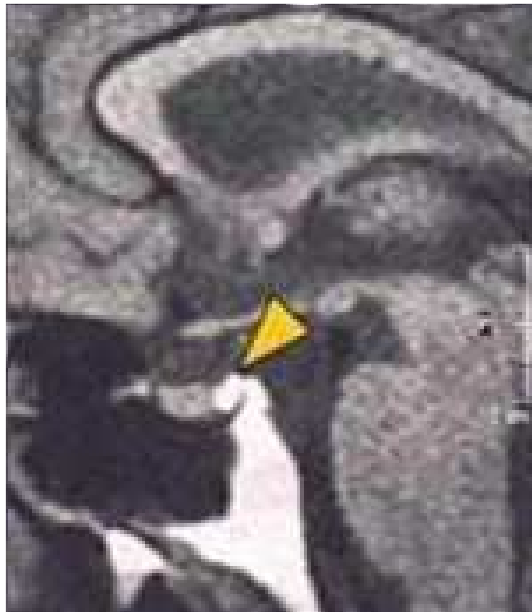
Múltiples áreas de hiperintensidad de señal sustancia blanca (T2)



Aumento y realce de glandula pituitaria con engrosamiento infundibular.

Control

T1



GPA

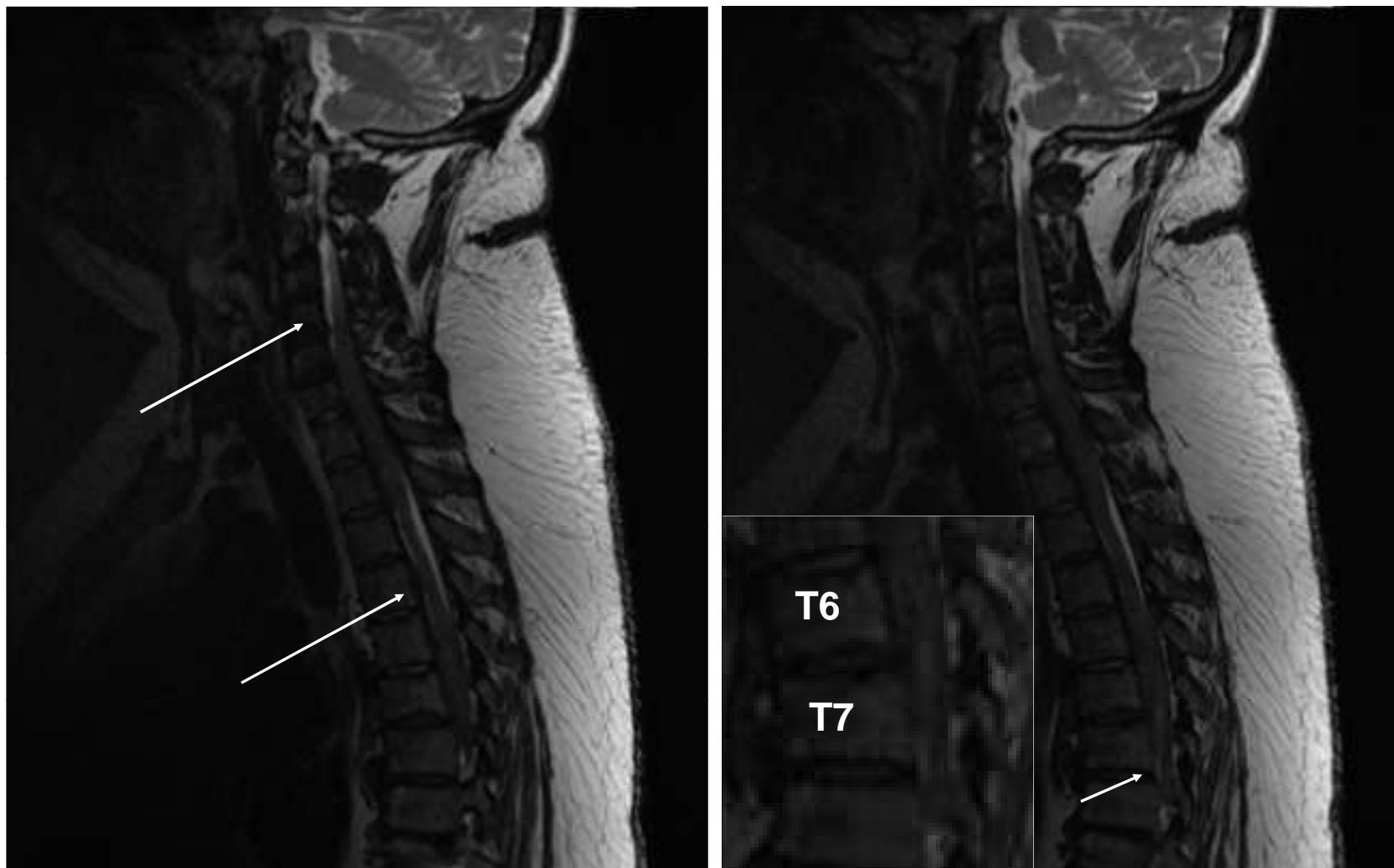
T1



T1 + gadolinium



Paquimeningitis medular e hiperseñal (T2)



Lesión granulomatosa intradural (GADOLINIUM)

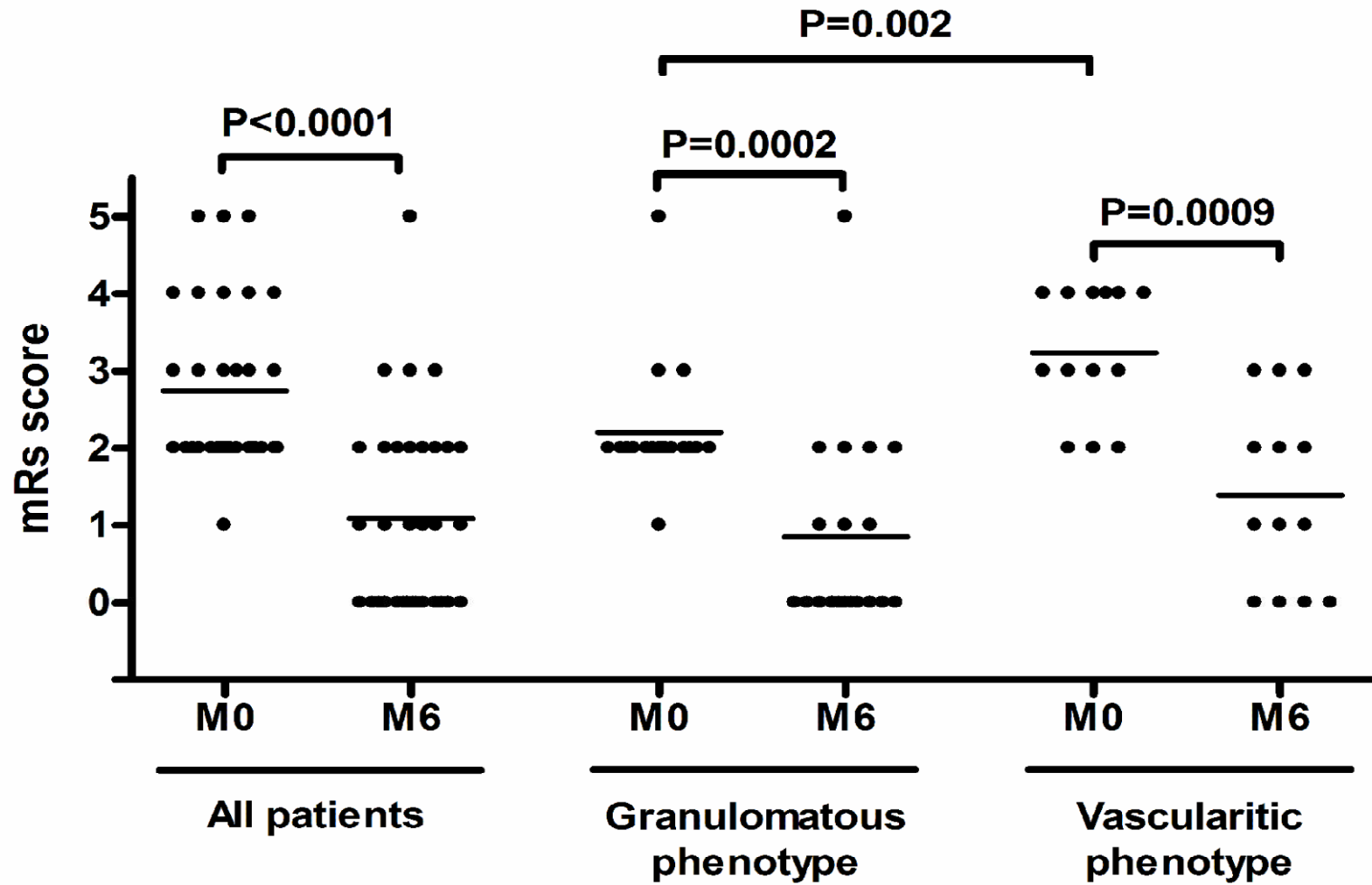


Terapia primera línea

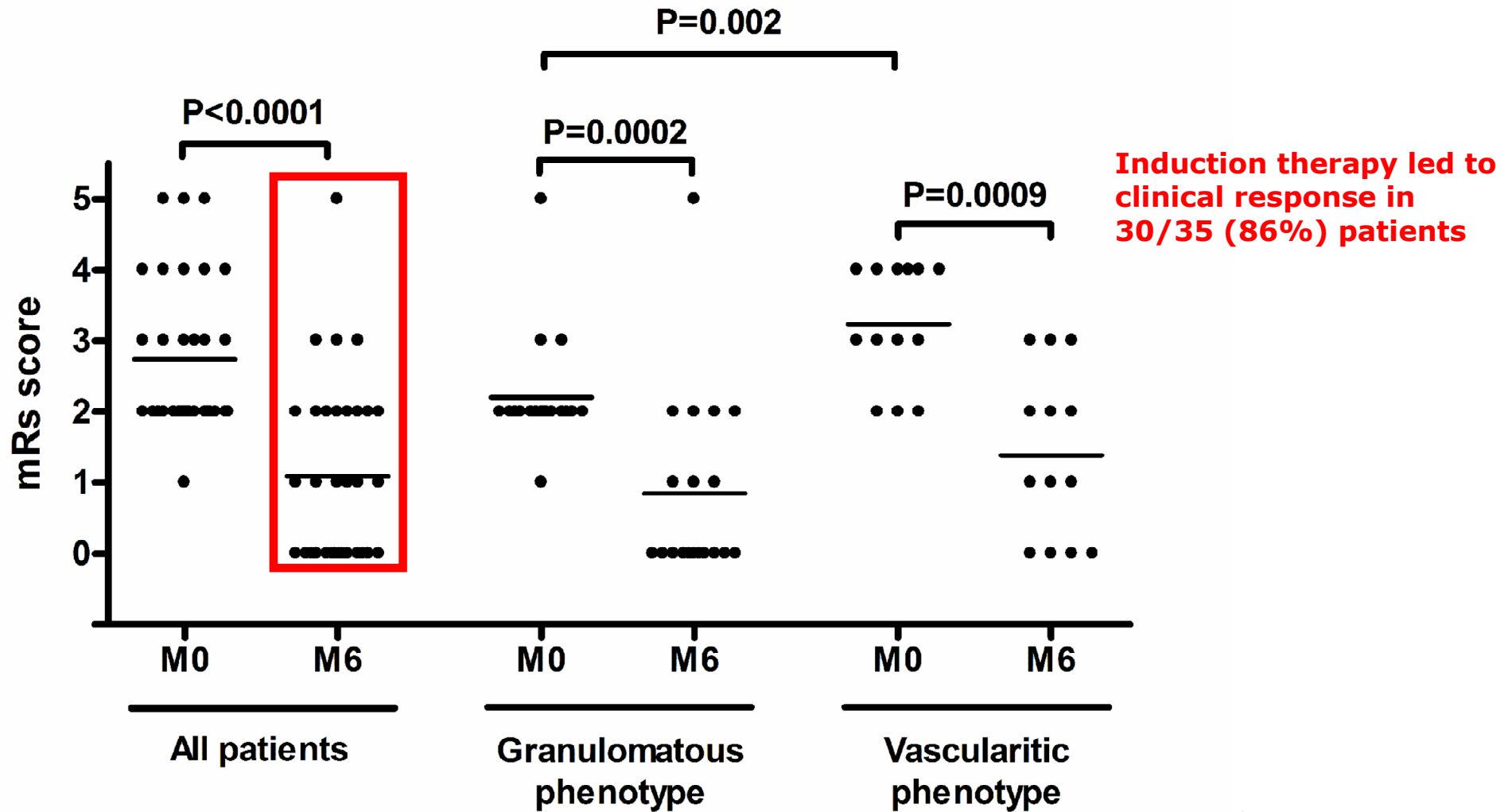
	Induction	Maintenance
Corticosteroids IV	35 (100%)	0 (0%)
Corticosteroids oral	35 (100%)	35 (100%)
Cyclophosphamid IV	25 (71%)	0 (0%)
Cyclophosphamid oral	11 (31%)	0 (0%)
Rituximab	1 (3%)	2 (7%)
Imurel	0 (0%)	18 (60%)
Methotrexate	0 (0%)	7 (23%)
IgIV	1 (3%)	1 (3%)

*

Evolution of the **modified Rankin** scale after induction regimen M0/M6



Evolution of the **modified Rankin** scale after induction regimen M0/M6



Terapia segunda línea: lesión SNC

Refract:

al tratamiento de inducción: 14%

Recaída:

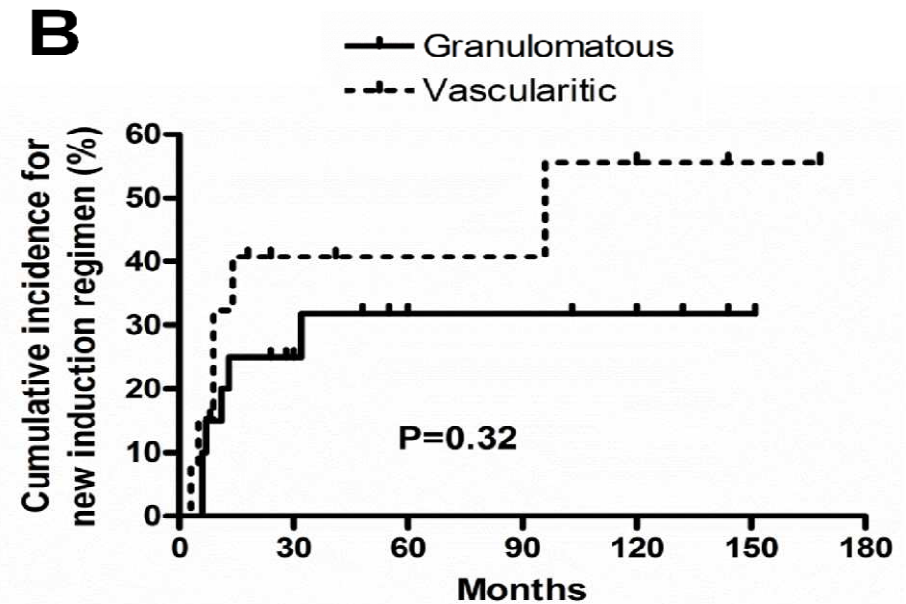
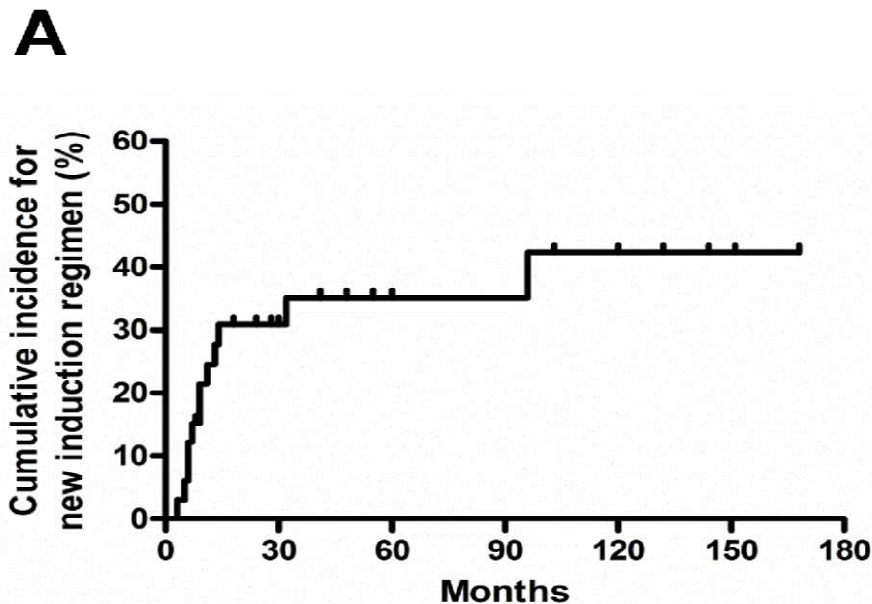
seguimiento medio 14 m (rango 9-96): 27%

CNS involvement		n (%)
Ischemic stroke and multi infarcts areas	(V)	7 (54%)
Medullar pachymeningitis	(G)	4 (31%)
Cerebral Pachymeningitis	(G)	3 (23%)
Hemorrhagic stroke	(V)	1 (8%)
Hypophyseal involvement	(G)	1 (8%)

*

Time from first to new induction regimen for relapsing and/or refractory CNS disease

Refractarios / Recaida



Cumulative incidence for a new induction regimen because of relapsing and/or refractory CNS involvement for the whole population (**A**) and according to the granulomatous or the vascularitic phenotype of CNS involvement (**B**).

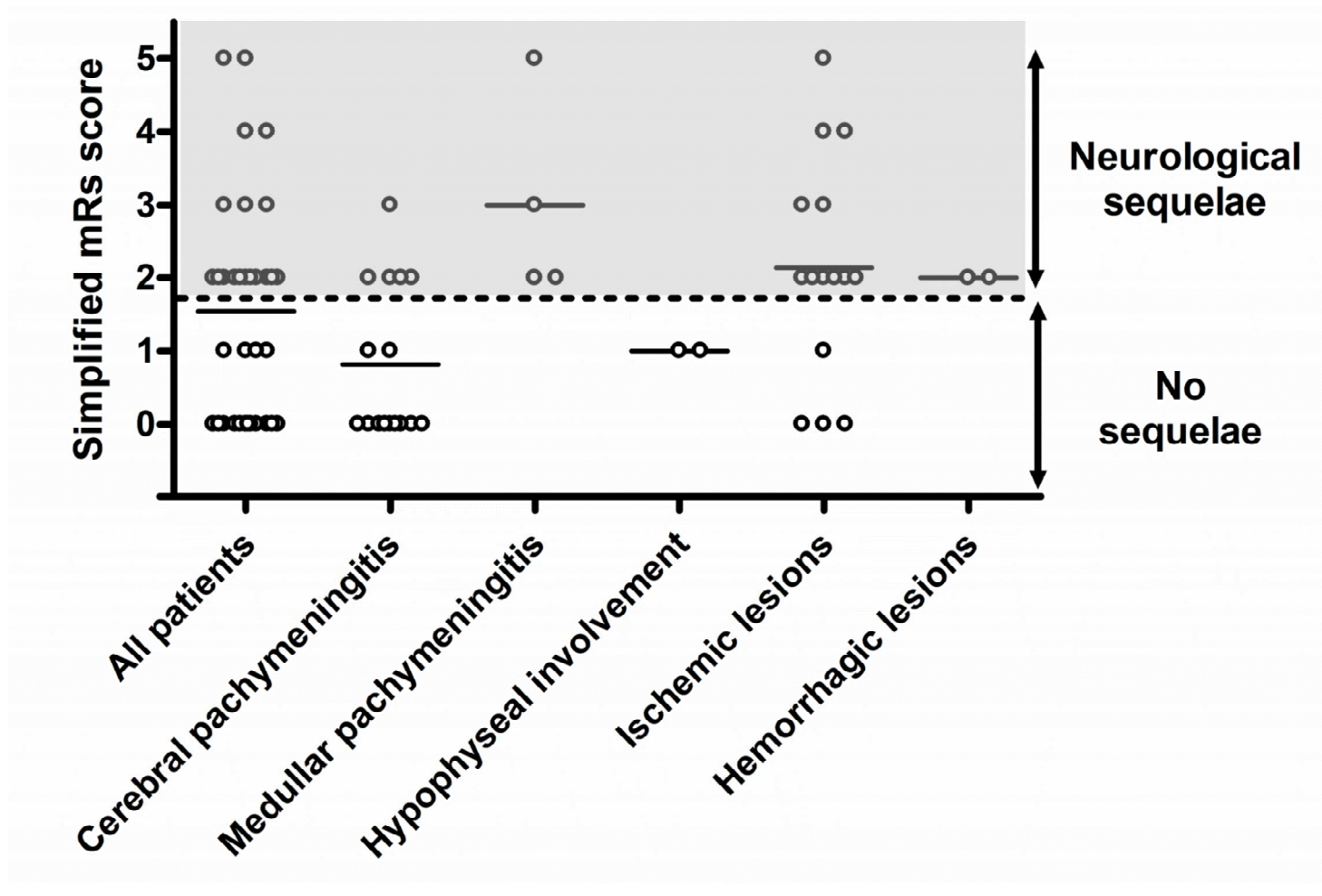
Terapia segunda línea

Refractarios / Recaida

	Induction	Maintenance
Corticosteroids IV	13 (100%)	0 (0%)
Corticosteroid oral	13 (100%)	13 (100%)
Cyclophosphamid oral	3 (23%)	0 (0%)
Cyclophosphamid IV	2 (15%)	0 (0%)
* Rituximab	8 (61%)	8 (61%)
Methotrexate	0 (0%)	4 (31%)
Imurel	0 (0%)	1 (8%)

* None of the patients treated with RTX as induction were found to be relapsing and/or refractory after a median follow-up of 17 months

Neurological sequelae at the end of follow-up: 51% (smRs ≥ 2)
Median follow-up 60 months (range 19-201)



*

Para casa

1. Afectación de SNC en GPA es infrecuente 3-8%

1. Lesión cerebral o medular (RM) determinan 2 fenotipos : vascular y granulomatoso

1. Cefaleas

1. Secuelas a pesar del control de la enfermedad

1. Formas refractarias: Rituximab?

Gracias Madrid-Paris-Barcelona

V
DEUX CAS D'ATROPHIE MUSCULAIRE PROGRESSIVE

AVEC LÉSIONS DE LA SUBSTANCE GRISE

ET DES FAISCEAUX ANTÉRO-LATÉRAUX DE LA MOELLE ÉPINIÈRE

Par J.-M. CHARCOT et A. JOFFROY

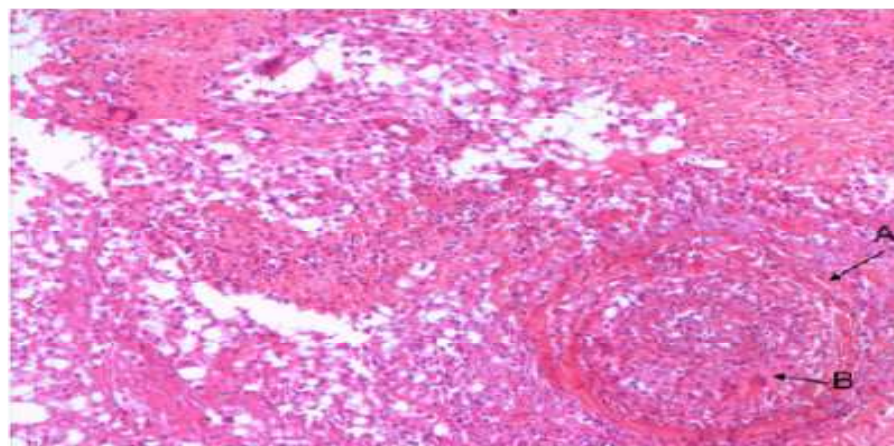
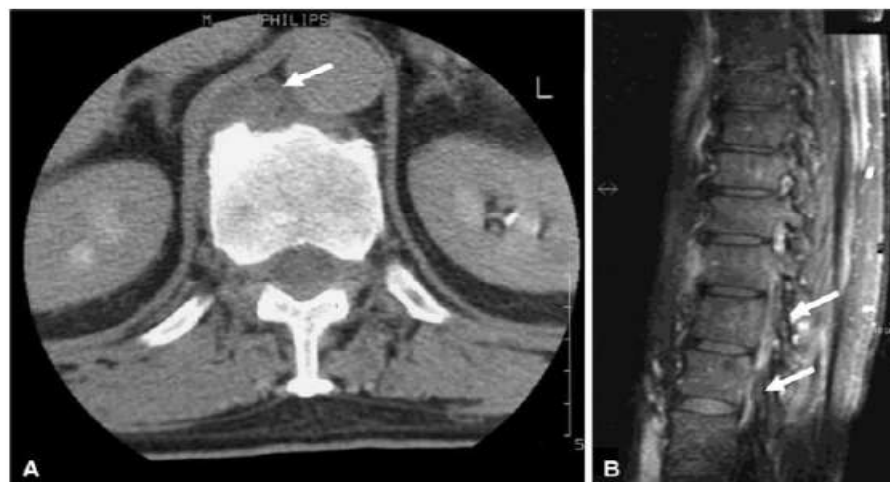
(Suite et fin.)

La sclérose symétrique des cordons latéraux de la moelle épinière et l'altération particulière des cellules nerveuses que nous avons rencontrées dans l'observation de Catherine A. (obs. I), se sont retrouvées, avec leurs caractères principaux, chez la malade dont nous venons de rapporter l'histoire. Mais elles se sont montrées, dans ce second cas, associées à d'autres altérations, et nous devons entrer à ce propos dans quelques développements.

Pour ce qui concerne d'abord les altérations des faisceaux blancs de la moelle observées chez Adèle C... (obs. II), il y a lieu de remarquer que, à la région cervicale, siège principal des lésions scléreuses, celles-ci occupaient à peu près indistinctement toute l'étendue des divers faisceaux : mais elles prédominaient toutefois d'une manière remarquable à la partie la plus postérieure des cordons latéraux. Ainsi c'est en ce lieu seulement que l'hyperplasie conjonctive s'était développée et généralisée au point d'amener les lésions de la sclérose proprement dite, avec production de tissu fibrillaire et destruction de la majeure partie des tubes nerveux. Partout ailleurs et, en parti-

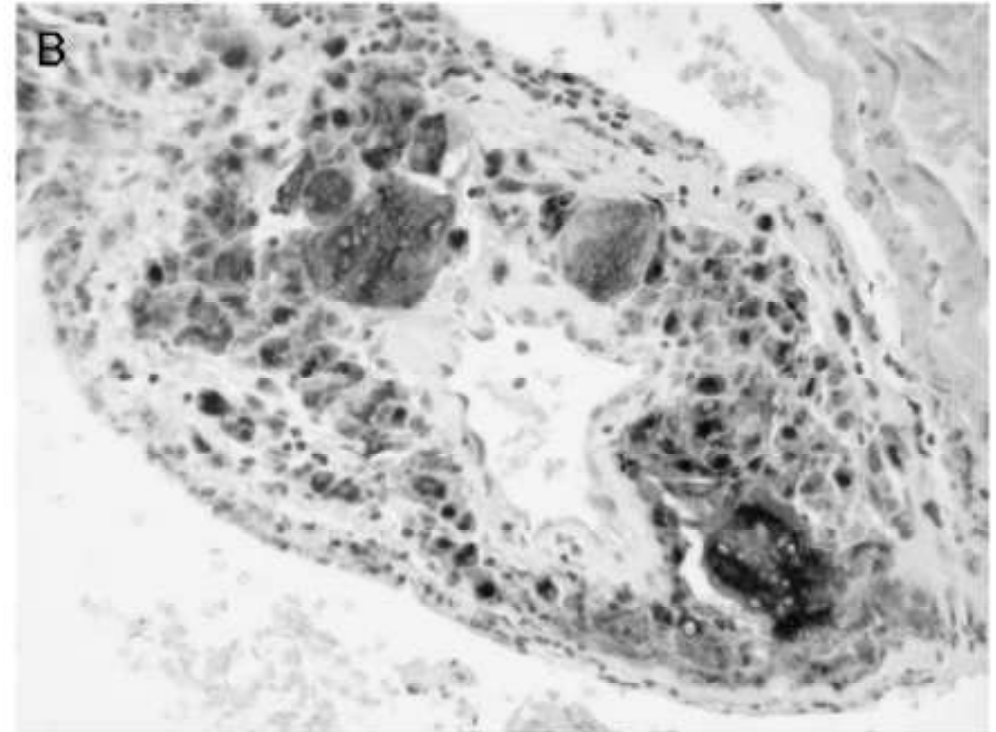
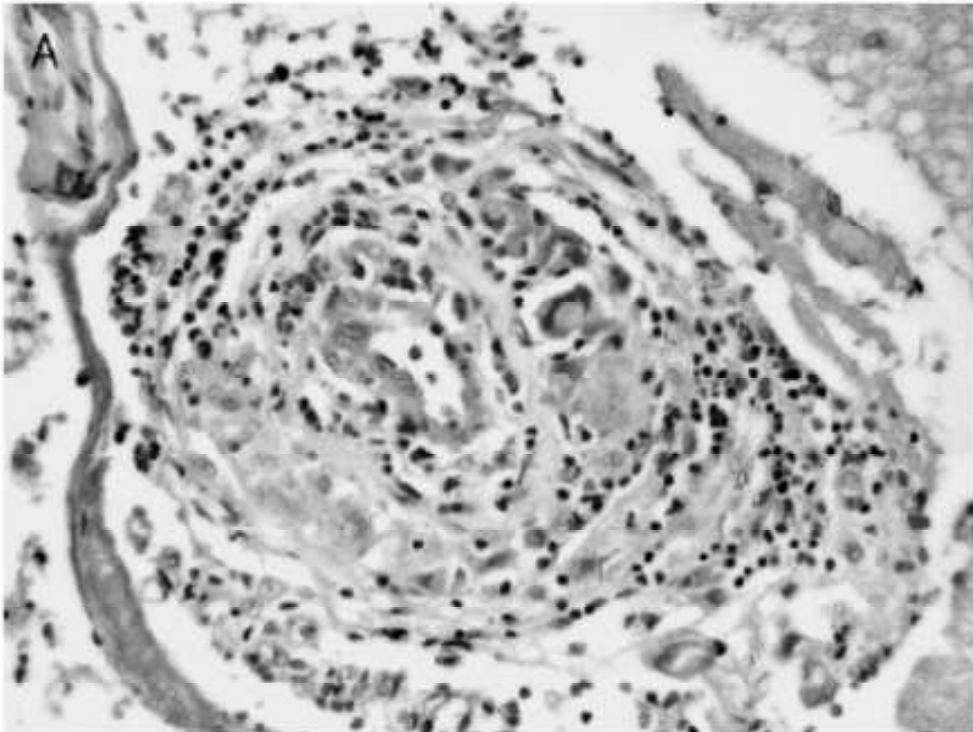
¹ Voy. le numéro de septembre 1899.

Exceptional osseous and meningeal spinal localization of ANCA-associated granulomatous vasculitis with hypertrophic spinal pachymeningitis



Central Nervous System Involvement in Wegener Granulomatosis

*Raphaèle Seror, MD, Alfred Mahr, MD, Jacky Ramanoelina, MD,
Christian Pagnoux, MD, Pascal Cohen, MD, and Loïc Guillevin, MD*



IgG4-Related Disease and Hypertrophic Pachymeningitis

Zachary S. Wallace, MD, Mollie N. Carruthers, MD, Arezou Khosroshahi, MD, Robert Carruthers, MD, Shweta Shinagare, MD, Anat Stemmer-Rachamimov, MD, Vikram Deshpande, MD, and John H. Stone, MD, MPH

TABLE 2. Histopathologic Features of Pachymeningitis Patients

Case	Diagnosis	Lymphoplasmacytic Infiltrate	Storiform Fibrosis	Plebitis	EOS	Granulomas	Giant Cells
1	IgG4-RD	Y	Y	N	N	N	Y
2	IgG4-RD	Y	Y	Y	Y	Y (few)	N
3	IgG4-RD	Y	Y	N	N	N	N
4	IgG4-RD	Y	Y	Y	Y	N	N
5	GPA	Y	N	N	Y	Y	Y
6	GPA	N	Y	N	N	N	Y
7	GPA	Y	Y	N	N	Y	Y
8	Rheumatoid arthritis	Y	N	N	N	Y	Y
9	Giant cell arteritis	N	N	N	N	N	N
10	Sarcoidosis	Y	N	N	N	Y	N
11	Lymphoma	Y	N	N	N	N	N
12	Lymphoma	Y	N	N	N	N	N
13	Undifferentiated	Y	N	N	N	N	Y
14	Undifferentiated	N	N	N	N	N	N

Abbreviations: EOS = eosinophilia.

