Vascularites systémiques et Inflammation oculaire

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CHU Pitié-Salpêtrière

Aucun conflit d'intérêts

INTRODUCTION

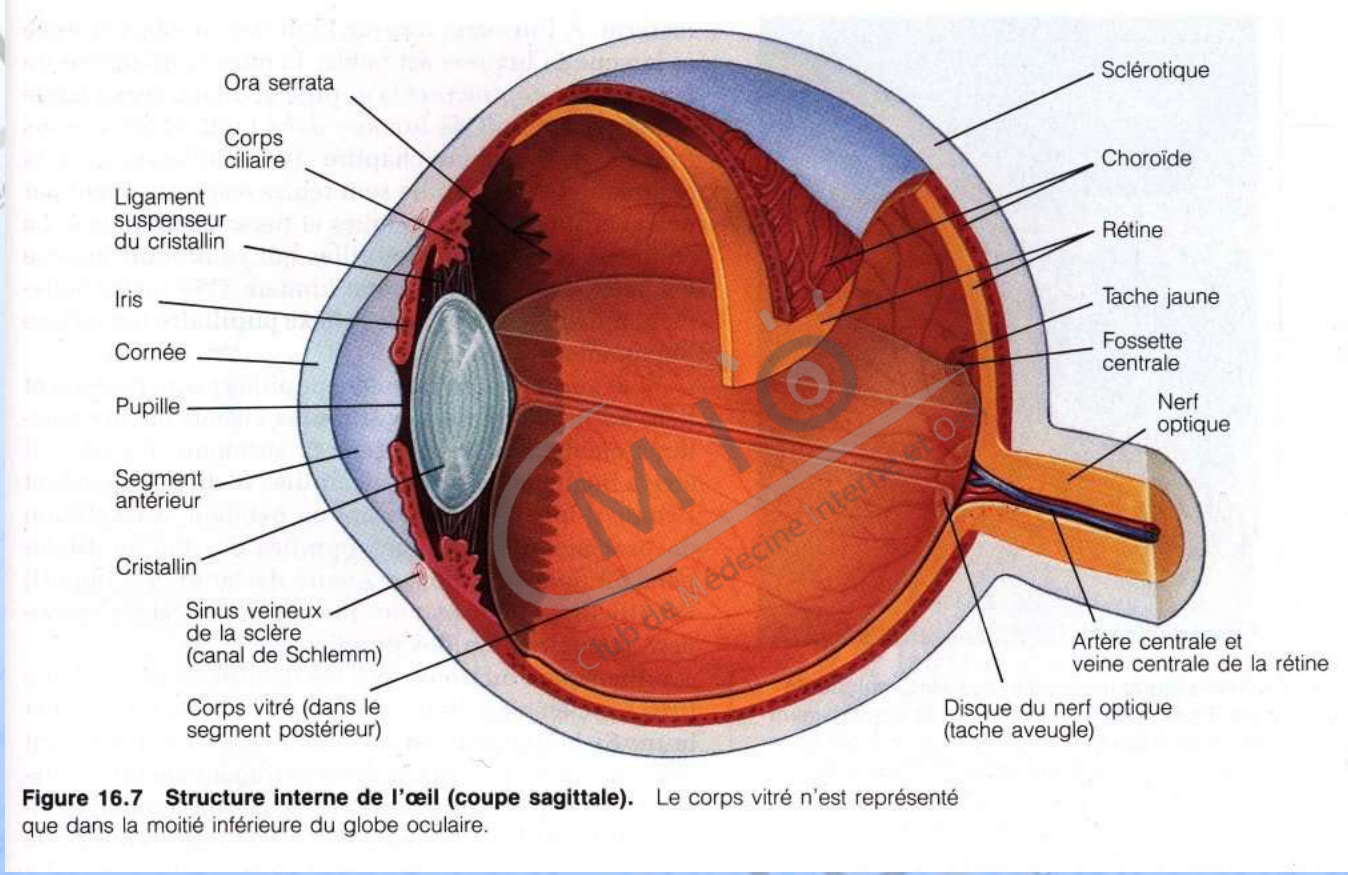


Figure 16.7 Structure interne de l'œil (coupe sagittale). Le corps vitré n'est représenté que dans la moitié inférieure du globe oculaire.

Œil: organe cible des vascularites systémiques

Toutes les structures peuvent être touchées

PLAN

1. Présentation générale des atteintes oculaires des Vascularites

   Conjonctivites
   Kératites
   Sclérites
   Vascularites rétiniennes

2. Exemple de la GPA

3. Exemple du TAKAYASU

Conjonctivite et Vascularites systémiques

Vascularites nécrosantes, Kawasaki

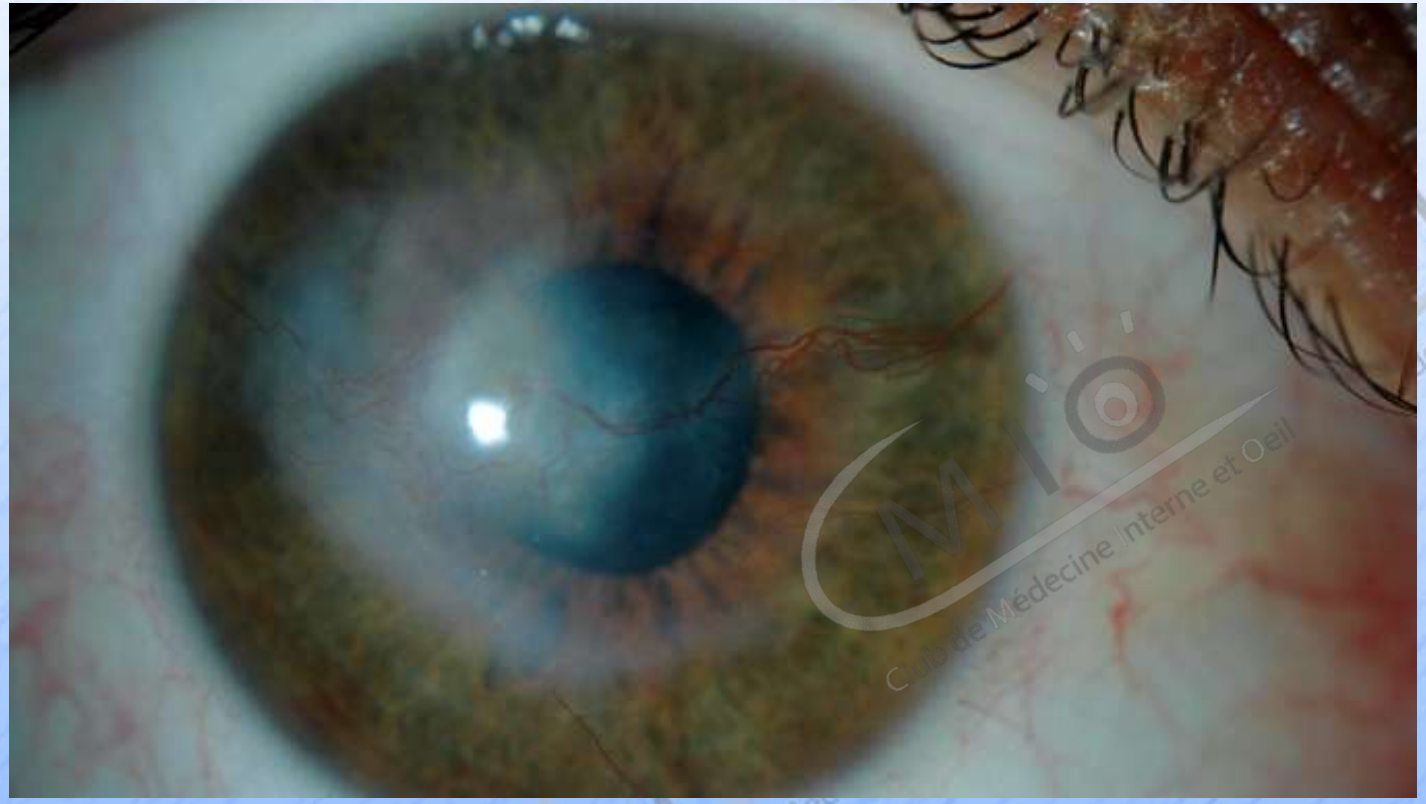
Kawasaki

- Uvéite antérieure ou Iridocyclite dans 80% des cas
- Inflammation oculaire corrélée au syndrome inflammatoire biologique
- Résolution sans séquelles en 2 à 8 semaines

Kératite et Vascularites systémiques

Vascularites nécrosantes, Cogan et B7

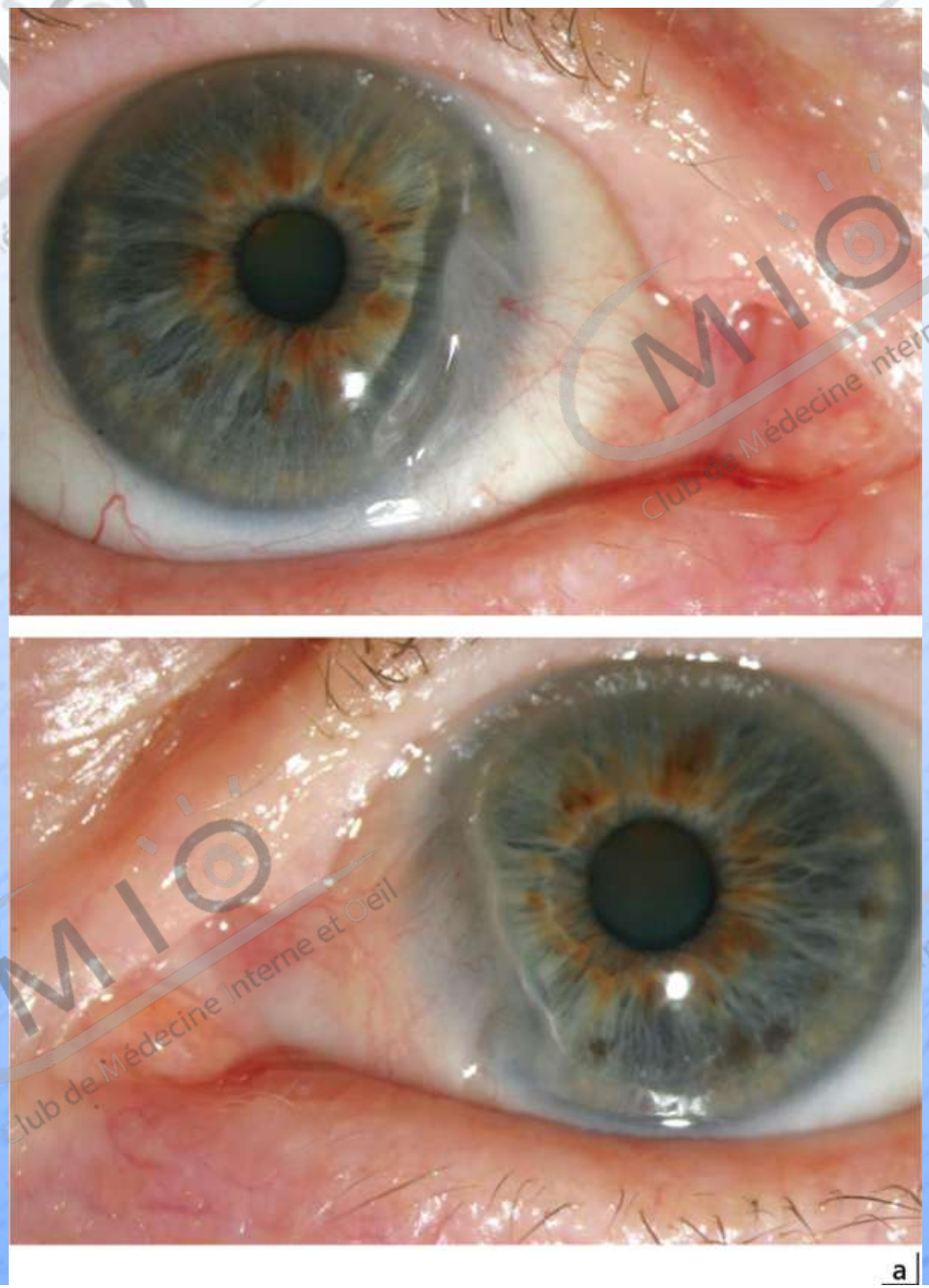
Kératite interstitielle du Cogan



- Associée à Sd vestibulaire, surdité souvent bilatérale d'emblée

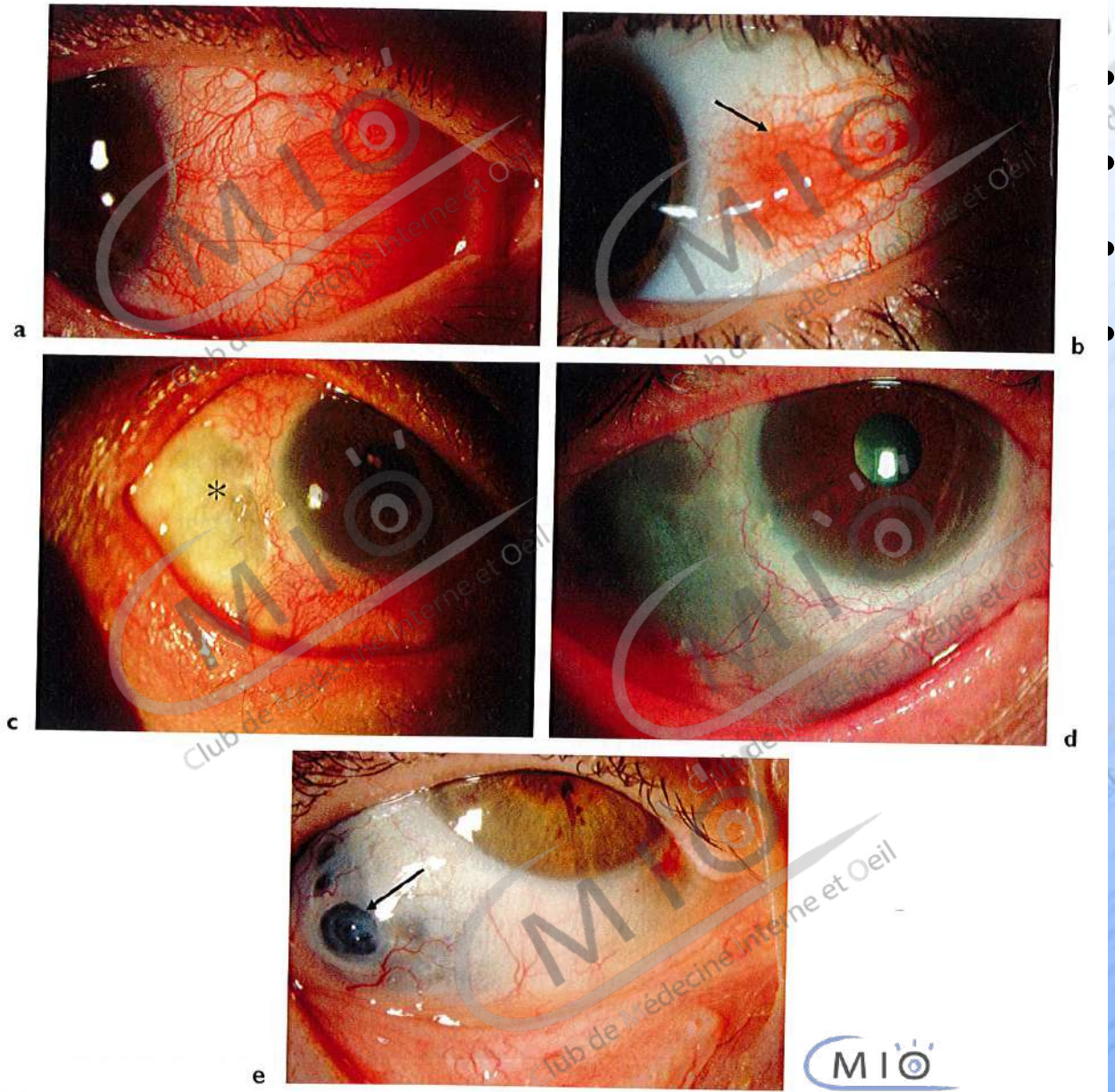
± fièvre, arthralgies/ites, aortite…

Kératite et Vascularite: GPA



Ulcère de cornée inflammatoire périphérique

Sclérites et Vascularites systémiques



- Vascularites nécrosantes
- B7
- Polychondrite
- *(PR, SPA, MICI, Lupus)*

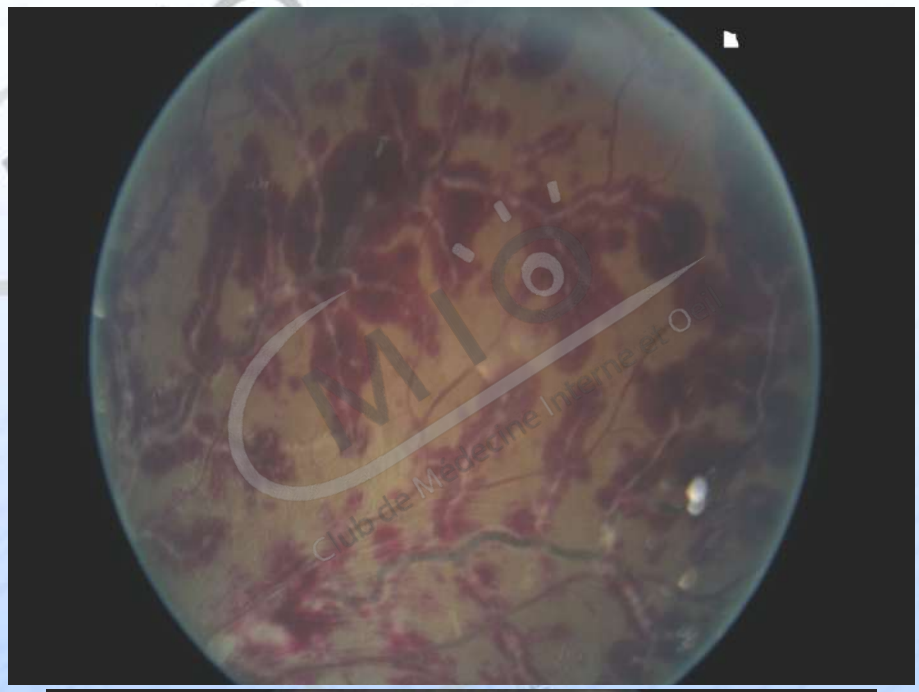
A antérieure diffuse
B antérieure nodulaire
C antérieure nécrosante
D séquelle nécrose
E scléromalacie perforante

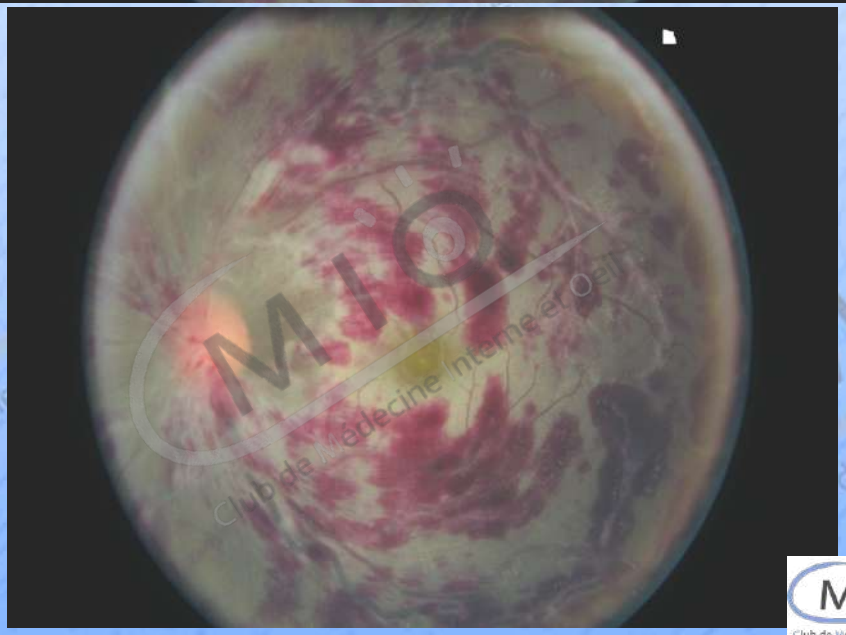
Vascularites rétiniennes et Vascularites systémiques

Atteinte	Diagnostic
Veines	Behcet, sarcoïdose, SEP,
Artères	Vascularites (GPA, CSS, Takayasu...), Lupus, SAPL, SUSAC.
Infiltrats rétiniens	Behcet,
Ischémies rétiniennes	Behcet, SEP, sarcoïdose
Occlusions veineuses	Behcet, sarcoïdose
Occlusions artérielles	Lupus, vascularites systémiques, SUSAC,

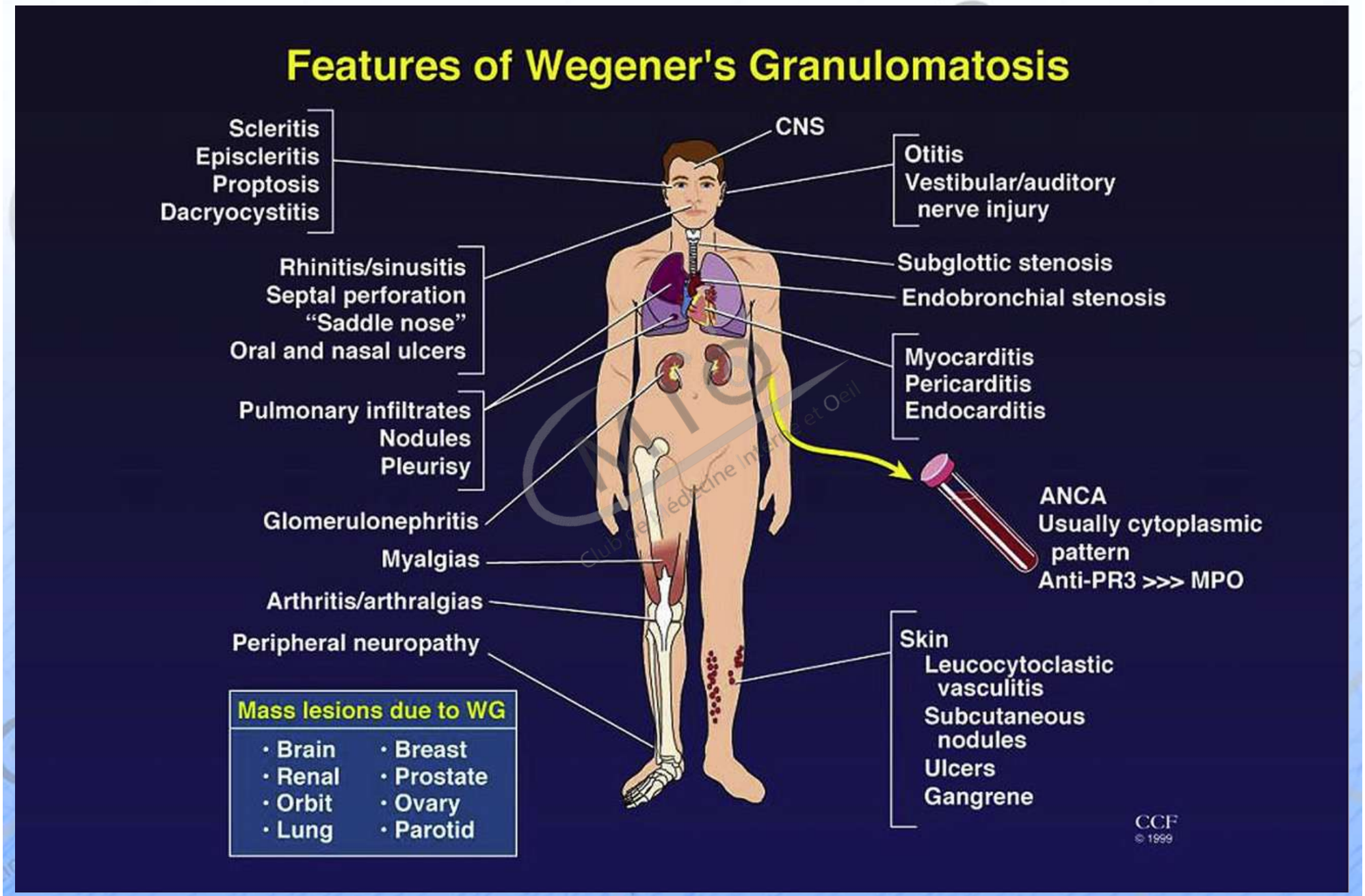
Vascularite veineuse et nodules cotonneux: B7

Vascularite artérielle et GPA





Œil et GPA



Hoffman G et al Survey of Ophtalmology 2010

GPA et atteinte oculaire

Pseudo tumeur orbitaire	**15%**
Sclérite/épisclérite	**10%**
Conjonctivite, kératite	**8%**
Dacryoadénite	**7%**
Nerf optique (névrite, Paralysie OM)	**5%**
Uvéite, rétinite, vascularite rétinienne	**<5%**

58% d'atteintes oculaires dans les GPA
8% de perte de vision

Mr L 25 ans, céphalées diffuses, otalgies, AEG -6kg en 1 mois
Rhinite crouteuse, **papillite et scotome œil G depuis 15 jours**

Ethmoïdite postérieure bilatérale et sphénoïdite
Neuropathie optique gauche

Pachyméningite de contiguité au niveau basi-frontal bilatéral

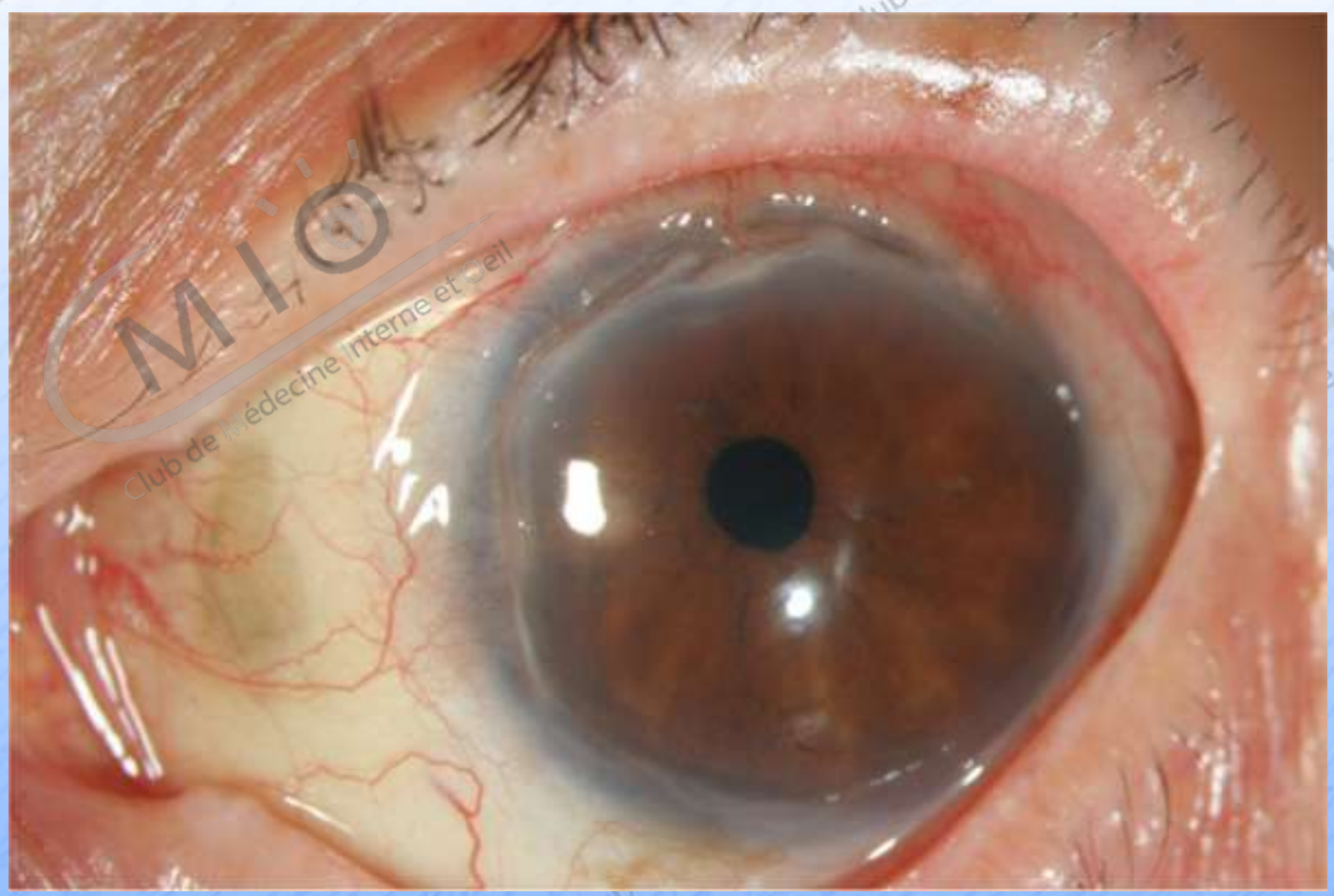
- cANCA anti PR3,
- CRP 17mg/l ,

- Biopsie ethmoidale: tissu nécrotique, réaction inflammatoire granulomateuse sans vascularite, microbiologie (BK, myco..) négative.

Rituximab, Bactrim, Corticoides

Rémission complète rapide
Rechute neuropathie optique en 2017 lors espacement rituximab

Patient 52 ans, ulcère cornéen G depuis 1 an
Echec Corticoides locaux, et par voie générale et ciclosporine 2%
Bilatéralisation ulcère cornéen 6 mois plus tard



Toux depuis 1 mois

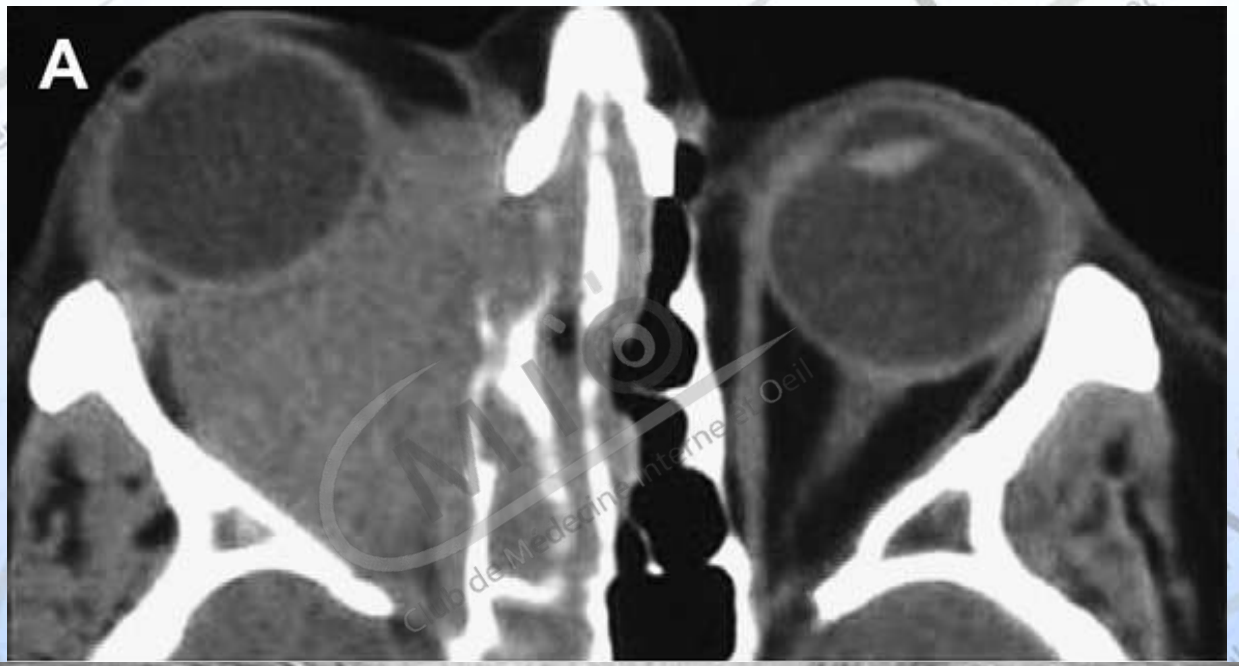
- cANCA anti PR3,
- biopsie bronchiques non contributives

- Corticoides, Endoxan,
- Greffe conjonctivaleOG

Mais cécité OG

- Rémission après 6 cures d' endoxan

GPA, exophtalmie, masse orbitaire Dte



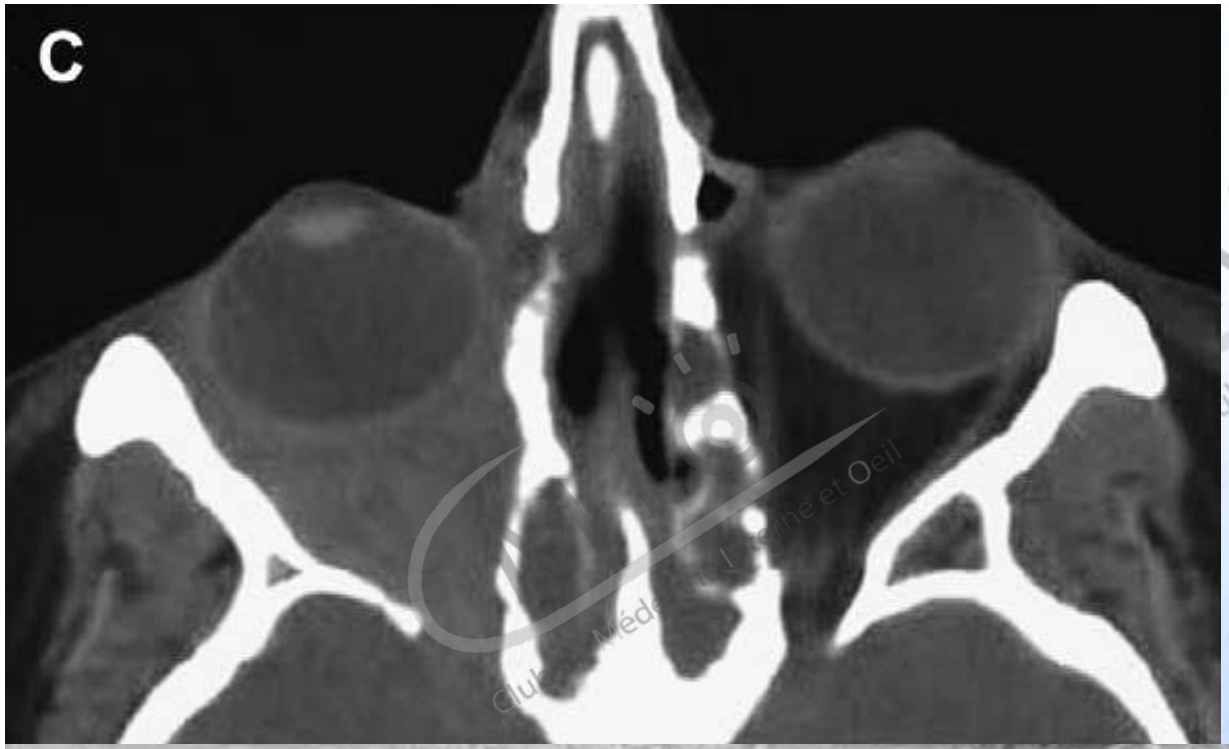
Rituximab et atteinte oculaire de GPA

- N=37 GPA avec atteinte oculaire (sclérite , n=20 et pathologie orbitaire, n=17) traitées par RTX

- Suivi médian de 36,5 mois après le 1er RTX

- GPA localisée (œil ± ORL, poumon) 57% vs GPA diffuse 43%

Lightman S et al Ophthalmology 2015



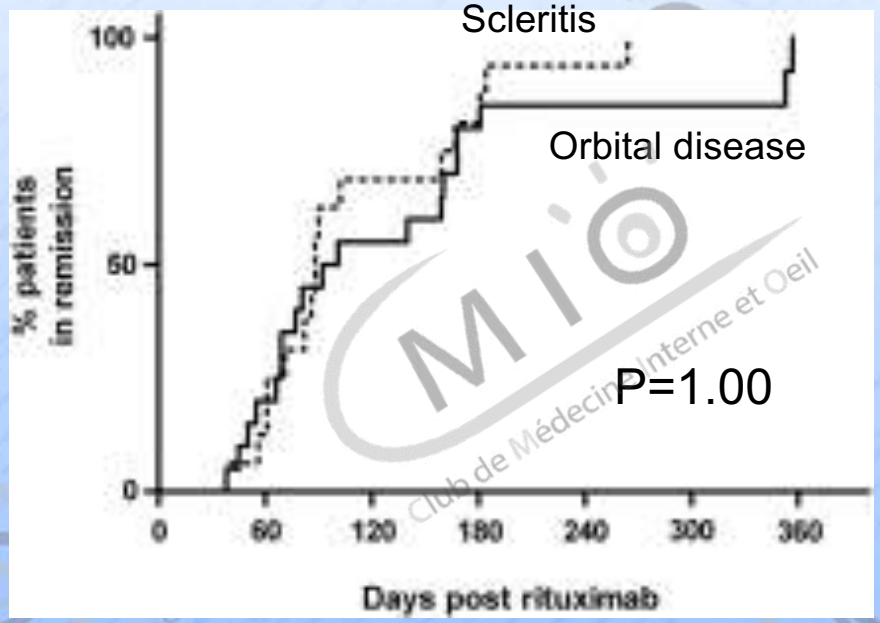
4 ans plus tard
Enophtalmie et
ophtalmoplégie

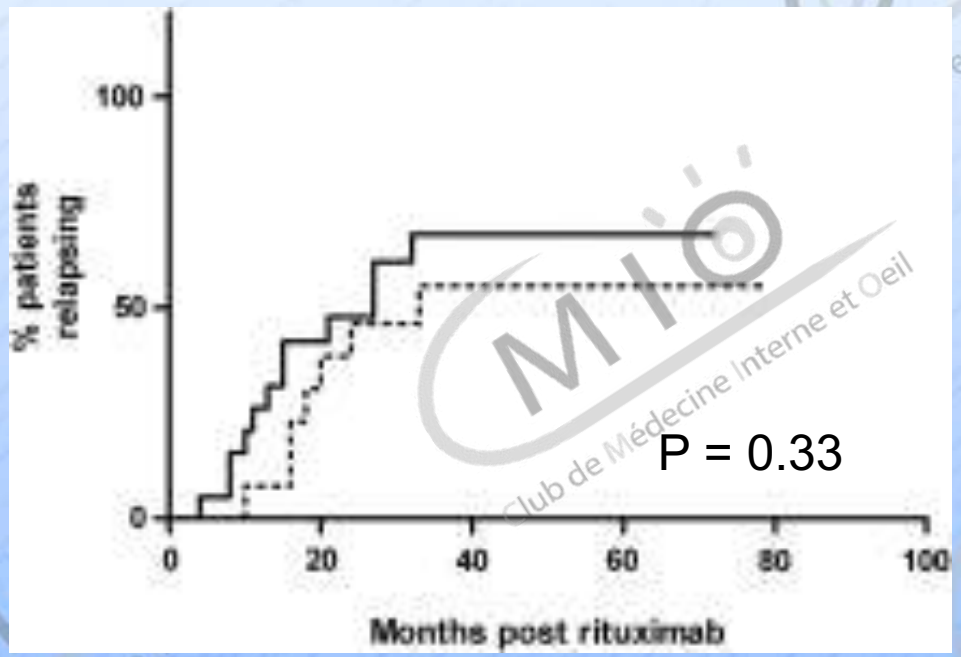
Hoffman G et al Survey of Ophtalmology 2010

Rituximab et atteinte oculaire de GPA

RC 85 vs 82%

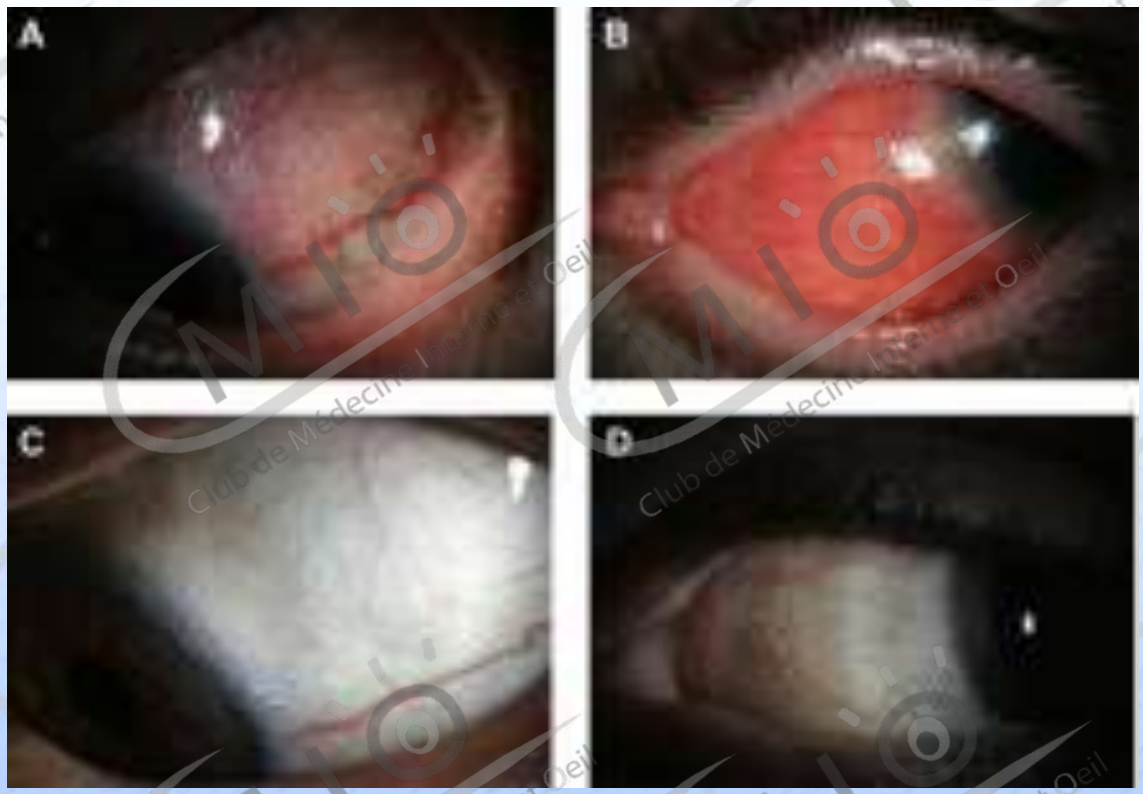
Rechute ≈ 50%

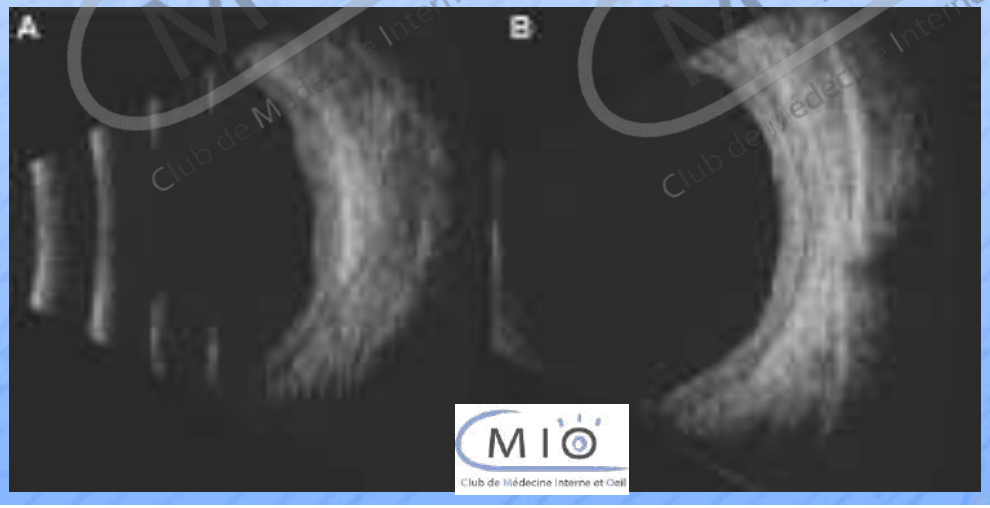




Lightman S et al Ophthalmology 2015

Rituximab et sclérite de GPA





Rituximab in the Treatment of Refractory Noninfectious Scleritis

TABLE 3. Treatment and Outcomes of Refractory Scleritis Using Rituximab

				Response		Adverse Events		Relapse		Last Follow-up	
Patient	Diagnosis	Previously Failed Medications	Rituximab Dose[a]	Response (Y/N)	Remission (Y/N)	Event (Y/N)	Lead to Cessation (Y/N)	Relapse (Y/N)	Time to Relapse (mo)	Current Regimen	Remission (Y/N)
1	GPA	MTX, MM, AZA, CYC	Rheumatologic	Y	Y	N	-	Y	20	RTX + IVIG	N
2	RA	LEF, MTX, IFX, ADA, ETN, NSAIDs, Doxycycline,	Rheumatologic	Y	Y	N	-	N	-	RTX	Y
3	RA	NSAIDs, MM, AZA, IFX, ADA, Chlorambucil	Rheumatologic	Y	Y	Y	Y	-	-	ABT + IVIG	N
4	Idiopathic	NSAIDs, CYC	Rheumatologic	Y	Y	N	-	N	-	RTX	Y
5	Idiopathic	NSAIDs, HCQ, LEF, MTX, AZA, IFX, TCZ, CYC, Ara-C	Ocular inflammation	N	N	N	-	N	-	IVIG	Y
6	GPA	MTX, ADA	Oncologic	Y	Y	N	-	Y	5	IVIG	Y
7	RA	MTX, IFX, ETN, CYC	Rheumatologic	Y	Y	N	-	N	-	Drug-free	Y
8	Idiopathic	NSAIDs	Rheumatologic	Y	Y	N	-	N	-	Drug-free	Y
9	GPA	MTX, MM	Rheumatologic + CYC	Y	Y	N	-	N	-	RTX	Y
10	Idiopathic	NSAIDs, MM	Ocular inflammation	Y	N	N	-	Y	5	CYC	Y
11	GPA	AZA	Rheumatologic	Y	Y	N	-	N	-	RTX + IVIG	Y
12	MCTD, Scl	MTX	Ocular inflammation	Y	Y	N	-	N	-	MTX	Y
13	RA	CYC	Ocular inflammation	Y	Y	N	-	N	-	RTX + CYC	LTF
14	GPA	CYC	Rheumatologic	Y	Y	N	-	N	-	RTX + CYC	LTF
15	GPA	NSAIDs, CYC	Rheumatologic	Y	Y	N	-	N	-	RTX	Y

ABT = abatacept; ADA = adalimumab; Ara-C = cytarabine; AZA = azathioprine; CYC = cyclophosphamide; ETN = etanercept; GPA = granulomatosis with polyangiitis; HCQ = hydroxychloroquine; IFX = infliximab; IVIG = intravenous immunoglobulin; LEF = leflunomide; LTF = lost to follow-up; MCTD = mixed connective tissue disease; MM = mycophenolate mofetil; MTX = methotrexate; NSAIDs = nonsteroidal anti-inflammatory drugs; RA = rheumatoid arthritis; RTX = rituximab; Scl = scleroderma; TCZ = tocilizumab; Y/N = Yes/No.

[a]Rheumatologic dose was 1 g x2 separated by 14 days, cycled every 4 months; oncologic dose was 375 mg/m^2 weekly x4; ocular inflammation dose was 375 mg/m^2 weekly x8 followed by monthly with extension as tolerated.

Am J Ophthalmol 2016

Œil et Takayasu

Madame P 40 ans
Asthénie et BAV bilatérale depuis 6 mois.

Pas d'ATCD CV

Examen ophtalmologique:

AV 5/10 OD et 8/10 OG

FO: paleur NO et VR bilatérale

Angiographie: ischémie rétinienne périphérique ODG

Examen clinique

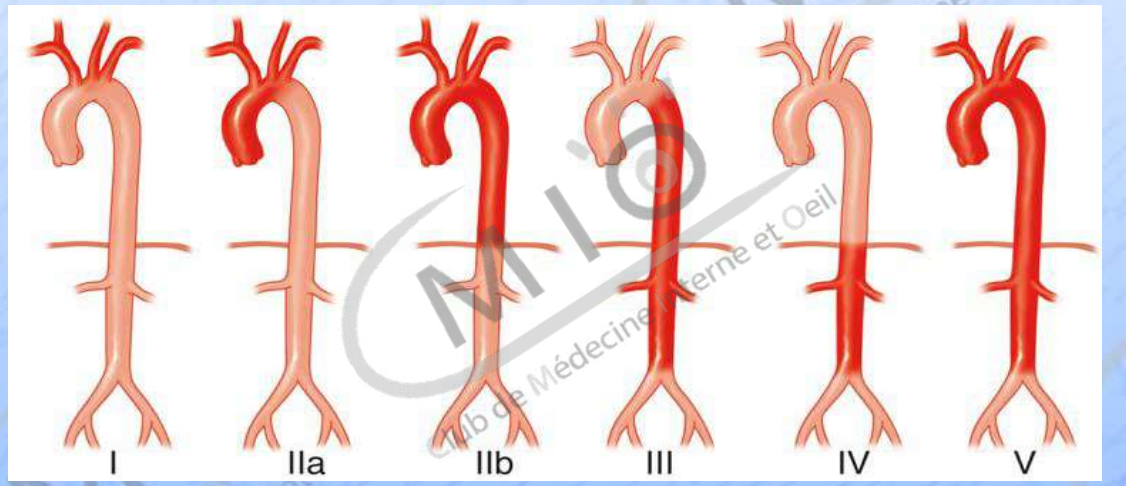
Claudication MSG

Souffle sous clavier et carotidien

Madame P 40 ans
Asthénie et BAV bilatérale depuis 6 mois.

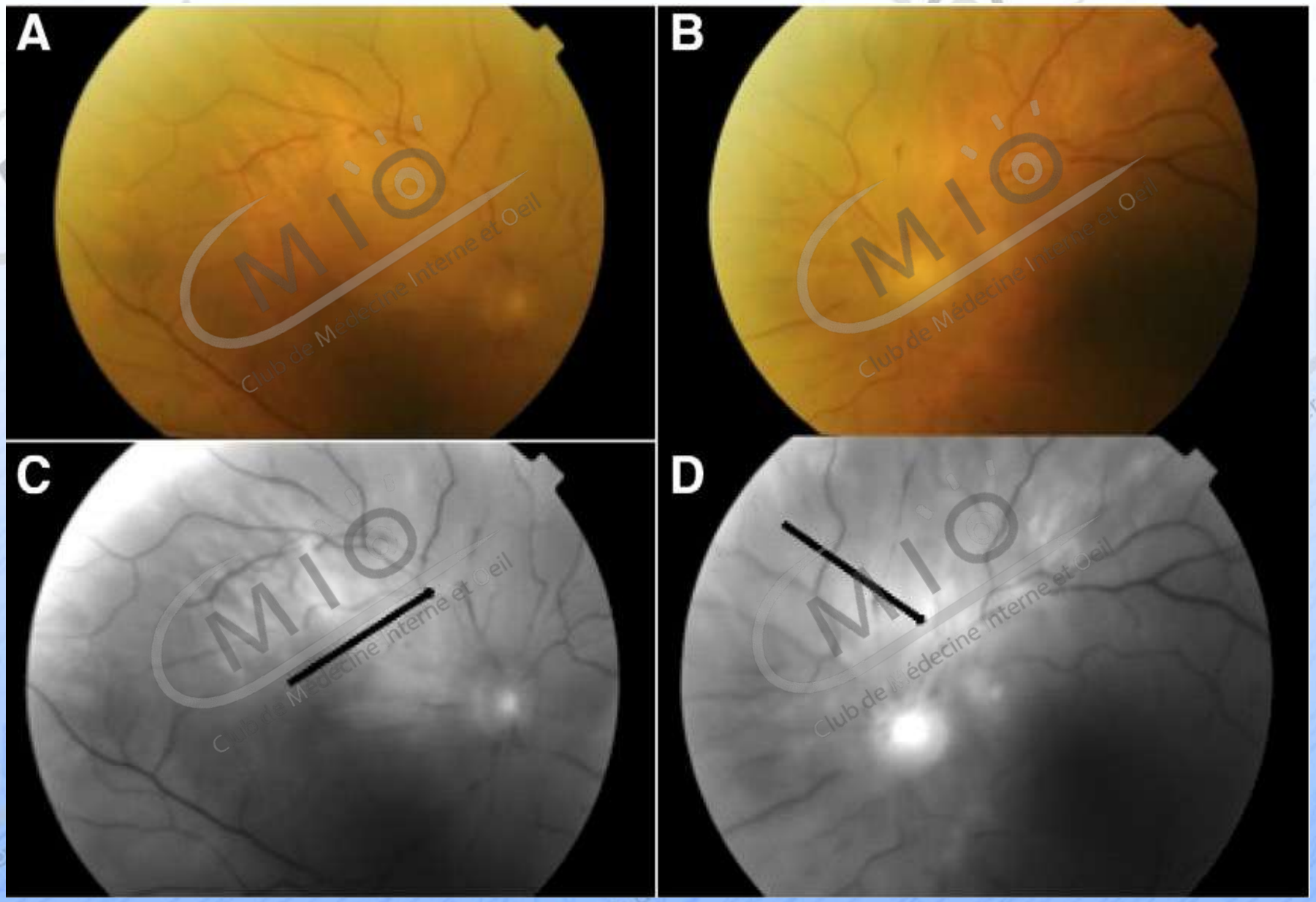
Imagerie :
Takayasu type V
Sténose TABC, sous clav G, aorte abdo, art iliaques

VS 22, CRP 7mg/l



Traitement:
Corticoides (1mg/kg/j)
MTX 20mg/sem
Aspegic
Photocoagulation Laser

Madame P 40 ans
Cécité bilatérale 2 mois plus tard.



OACR bilatérale

Demographic and global characteristics of the 9 TA patients with small retinal vessel involvement.

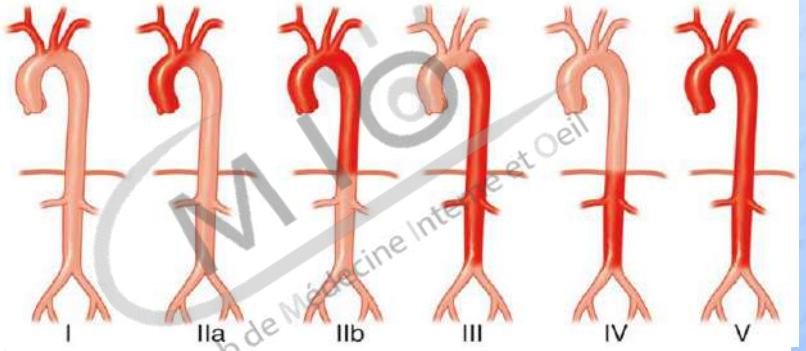
Case	Sex age (y)	Origin	TA type	Other manifestation	Duration of TA at ocular manifestation
#1, 1st episode	F 58	Caucasian	V	Asthenia, left leg claudication, carotid and subclavian bruit	Inaugural
#1, 2nd episode	F 58	Caucasian	V	–	3 months
#2	M 47	Caucasian	V	None	5.5 years
#3	F 63	Caucasian	I	Asthenia	6 years
Ramteke V et al. [53]	F 48	India	V	Headache, hypertension, right carotid and right iliac artery stenosis	6 years
Balaskas K et al. [30]	F 35	Mediterranean	II a	Arm weakness, left carotid and subclavian artery occlusion	5 years
Das D et al. [33]	F 16	India	II a	Headache + aortic arch syndrome	Inaugural
Kaushik et al. [40]	F 40	India	II a	Headache + aortic arch syndrome	Inaugural
Karam E et al., case #8 [39]	F 30	NA	V	Leg claudication, leg ulcer, ombilical bruit	5 months
Conrath J et al. [32]	F 28	Mediterranean	III	Coeliac artery stenosis	Inaugural

Noel N et al, Autoimmunity reviews 2012

Patient/study	Eye involvement	Ophtalmoscopy	Systemic therapies	Outcome
#1, 1st episode	BRAO (BE)	Peripheral retinal ischemia, choroidal neovessels	MP (1 g/d×3d), CST (1 mg/kg/d), MTX (20 mg/w)	Aggravation
#1, 2nd episode	CRAO (BE)	Retinal palor	MP (1 g/d×3d), CST (1 mg/kg/d), MTX (20 mg/w), IFX (5 mg/kg S0-S2–S6)	Stabilization after 1 year follow up
#2	BRAO (LE)	Stade II HR	CST (10 mg/d)	Spontaneous improvement
#3	BRVO (LE)	Superior temporal BRVO	CST (20 mg/d) + MTX (30 mg/2w)	Remission
Ramteke V et al. [53]	BRAO (RE)	Superior temporal BRAO, macular edema	CST (1 mg/kg/d), aspirin, heparin, MTX (15 mg/sem)	Improvement of the vision (2 weeks)
Balaskas K et al. [30]	BRAO (LE)	Upper temporal BRAO + 2 microaneurysm	CST (5 mg/d), acetazolamid	Improvement of the vision (3 months)
Das D et al. [33]	BRAO (LE)	Lower temporal BRAO + microaneurysms	CST (40 mg/d)	Improvement in visual acuity, but LE's synechial closure of the angle. Lost in follow up.
Kaushik et al. [40]	BRAO (LE)	Sheathed nasal BRA + absence of tertiary lower temporal arterioles	CST (40 mg/d)	Degradation (optic disk palor) in 3 months
Karam E et al., case #8 [39]	BRAO (RE) + TR	"Embolus" in the inferotemporal BRA	CST	Spontaneous improvement
Conrath J et al. [32]	BRVO (LE)	Foveal and peripheral haemorrages,retinal palor	CST, heparin	Unsuccessful, retinal ischemia, panphotocoagulation

Atteintes oculaires et Takayasu

	Estimated prevalence in TA	TA type
Retinal involvement		
TR [8,9,17–21,27]	13–33%	Mainly I, II or V (aortic arch and/or subclavian arteries)
HR [8,19,20]	16–37%	Mainly III, IV or V (renal artery involvement)
BRAO [30,33,39,40,53]	Rare	V (4/7) or II a (3/7)
BRVO [32]	Exceptional	–
Other ocular manifestations		
Uveitis [12,31,37,41,44]	1.6%	–
Scleritis [29,36,51,54]	ND (4 reported cases)	–
Glaucoma [19,38,55]	3.3%	–
Cataract [11,19,35]	1.6–23%	–
AION [13,14,43,49]	3.3%	–



TR: Takayasu's retinopathy; HR: hypertensive retinopathy; BRAO: branched retinal artery occlusion; BRVO: branched retinal vein occlusion; AION: anterior ischemic optic neuropathy. ND: not determined.

Atteintes oculaires et Takayasu

	Occurrence in TA setting	Improvement
Retinal involvement		
TR [8,9,17–21,27]	Usually late (retinal hypoperfusion)	Yes if <stage 3
HR [8,19,20]	Secondary to reno-vascular hypertension	Difficult
BRAO [30,33,39,40,53]	May be inaugural	Yes (IS)
BRVO [32]	May be inaugural	–
Other ocular manifestat		
Uveitis [12,31,37,41,44]	May be inaugural or secondary to chronic ischemia	Yes (IS)
Scleritis [29,36,51,54]	May be inaugural	Yes
Glaucoma [19,38,55]	Secondary to chronic ischemia and neoproliferation	Yes (local therapy)
Cataract [11,19,35]	Secondary to chronic hypoperfusion	Yes
AION [13,14,43,49]	May be inaugural	Yes if begun promptly

TR: Takayasu's retinopathy; HR: hypertensive retinopathy; BRAO: branched retinal artery occlusion; BRVO: branched retinal vein occlusion; AION: anterior ischemic optic neuropathy. ND: not determined.

Rétinopathie ischémique du Takayasu

4 stades de Uyama and Asayama basés sur l'examen par angiographie à la fluorescéine

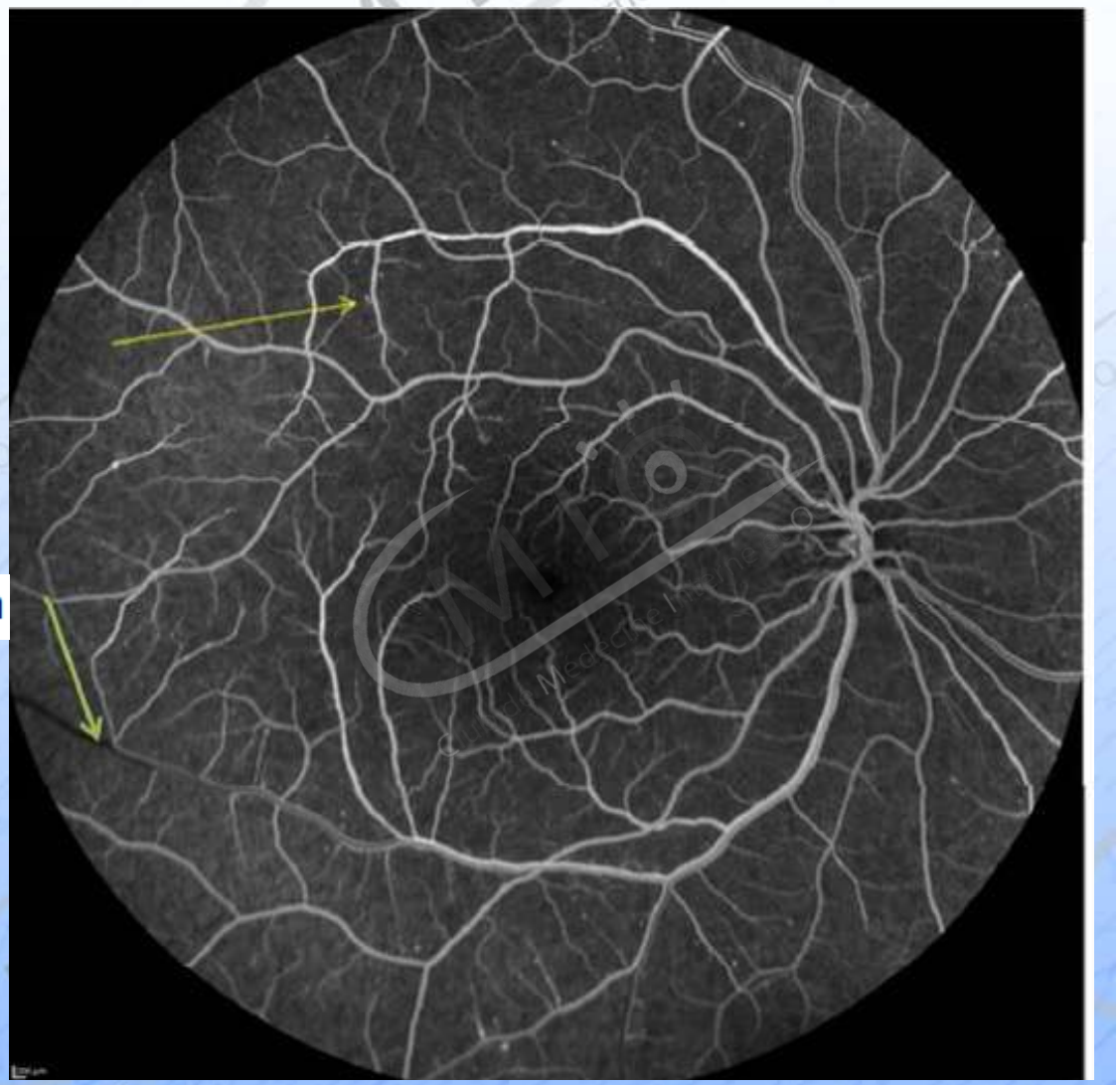
- Stage 1: dilatation of retinal veins
- Stage 2: **microaneurysms**, most likely located in the posterior pole
- Stage 3: **arteriovenous shunt**, most likely peripapillar than peripheric.
- Stage 4: **ischemic complications**: retinal neovascularisation, iris rubeosis, vitreous hemorrhage and neovascular glaucoma.

Uyama M, et al. Retinal vascular changes in Takayasu's disease (pulseless disease). Doc Ophthalmol Proc Ser 1976;9:549–54.

Takayasu: Rétinopathie ischémique stade II

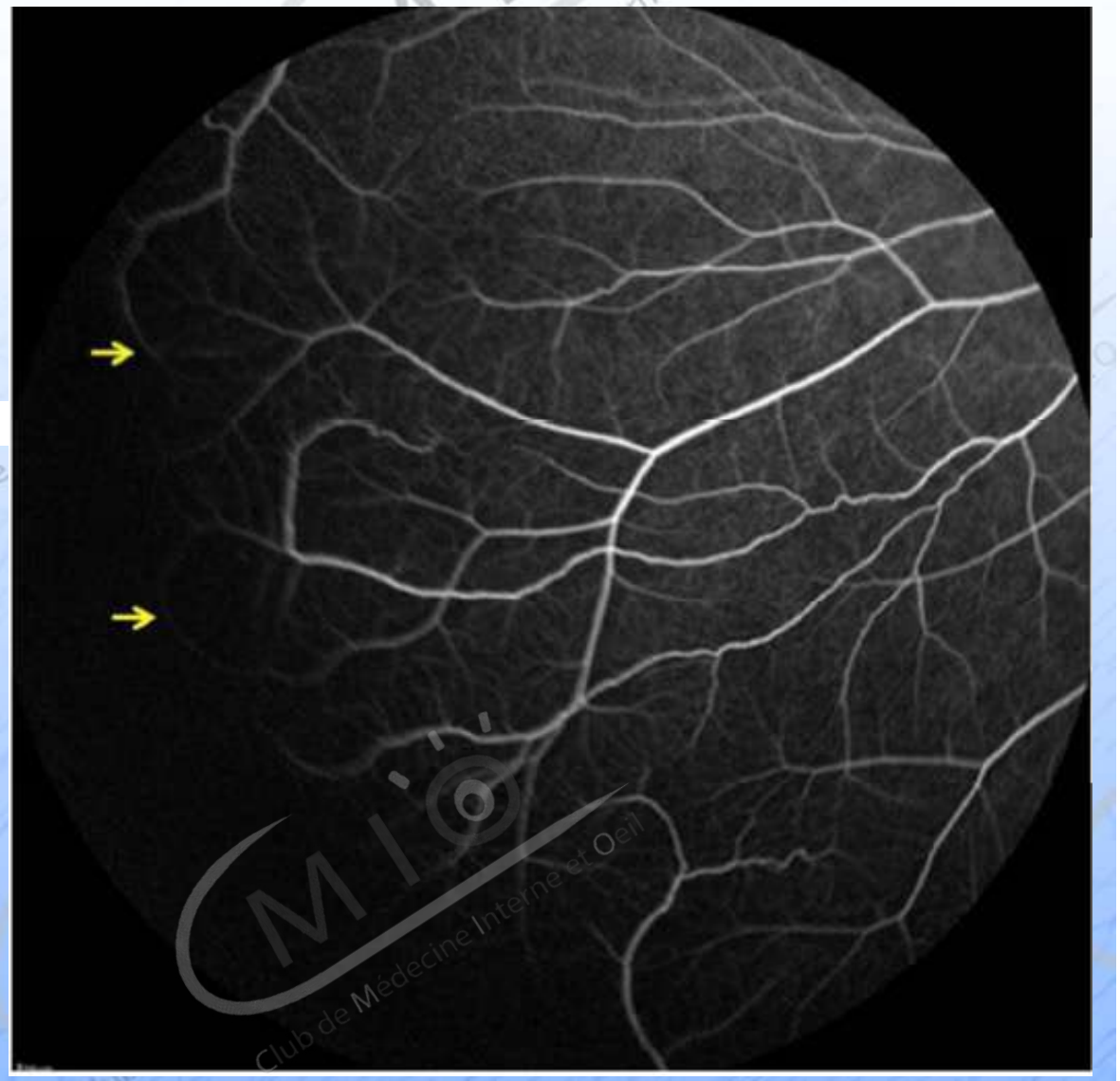
Microaneurysms (yellow arrow)

vein branch occlusion



Takayasu: Rétinopathie ischémique stade III

Multiple peripheric arteriovenous shunts



Points clés

- Œil = Organe cible des maladies systémiques
- Avancées thérapeutiques considérables
- Thérapies ciblées+++
- Interaction entre l'Ophtalmologiste et l'Interniste

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