Syndrome Inflammation Orbitaire

Bilan et prise en charge

Sébastien Abad

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UMR 1125

Orbitopathies inflammatoires

Bilan et prise en charge…..*à visée étiologique*

Sébastien Abad

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Survey of 1264 Patients with Orbital Tumors and Simulating Lesions

The 2002 Montgomery Lecture, Part 1

Jerry A. Shields, MD, Carol L. Shields, MD, Richard Scartozzi, MD

Table 2. Classification of 1264 Consecutive Patients with Orbital Lesions

Category	Number of Patients (%)*	Number Biopsy Proven (%)*	% Total Biopsy Proven*	Mean Age (yrs; median, range)
Cystic lesions	70 (6)	39 (56)	3	25 (19, 0–88)
Vasculogenic lesions	213 (17)	87 (41)	7	36 (39, 0–91)
Peripheral nerve lesions	23 (2)	18 (78)	1	38 (36, 0–84)
Optic nerve or meningeal lesions	105 (8)	27 (26)	2	33 (38, 0–90)
Fibrocytic lesions	13 (1)	13 (100)	1	25 (18, 0–65)
Osseous or fibro-osseous lesions	21 (2)	15 (71)	1	26 (20, 3–67)
Cartilaginous lesions	1 (<1)	1 (100)	<1	21 (21, 21–21)
Lipocytic or myxoid lesions	64 (5)	16 (25)	1	45 (54, 0–85)
Myogenic lesions	36 (3)	36 (100)	3	13 (7, 0–68)
Lacrimal gland lesions	114 (9)	77 (68)	6	49 (51, 0–90)
Primary melanocytic lesions	11 (1)	10 (91)	1	57 (65, 29–76)
Metastatic tumors to the orbit	91 (7)	50 (55)	4	60 (61, 5–91)
Lymphoid or leukemic lesions	130 (10)	111 (85)	9	63 (67, 2–92)
Secondary orbital tumors total	142 (11)	123 (87)	10	60 (65, 0–92)
Face origin	7 (1)	4 (57)	1	75 (71, 63–92)
Eyelid origin	25 (2)	23 (92)	2	69 (69, 44–88)
Conjunctival origin	22 (2)	22 (100)	2	68 (69, 44–89)
Intraocular origin	54 (4)	51 (94)	4	55 (65, 0–89)
Paranasal sinus origin	20 (2)	14 (70)	1	60 (62, 21–83)
Nasopharynx origin	6 (<1)	5 (83)	1	53 (51, 34–81)
Hard palate origin	1 (<1)	0 (0)	0	52 (52, 52–52)
Parotid gland origin	1 (<1)	0 (0)	0	71 (71, 71–71)
Lacrimal sac origin	2 (<1)	2 (100)	<1	53 (53, 44–62)
Brain origin	4 (<1)	2 (50)	<1	30 (29, 1–61)
Histiocytic lesions	17 (1)	15 (88)	1	27 (12, 0–81)
Thyroid-related orbitopathy	67 (5)	0 (0)	0	53 (54, 0–86)
Inflammatory lesions	133 (11)	61 (46)	5	43 (47, 0–92)
Miscellaneous	13 (1)	4 (31)	1	30 (18, 0–73)
Total orbital lesions	1264 (100.0)	703 (56)	56	45 (50, 0–92)

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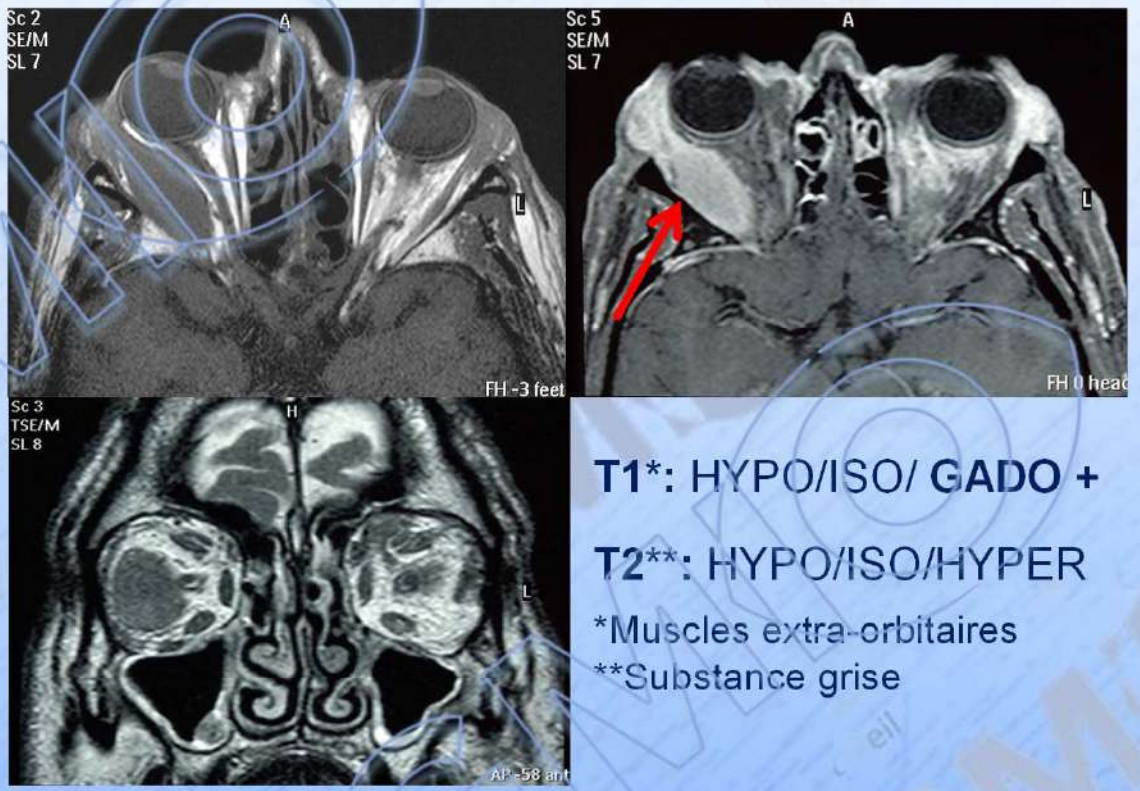
Diagnostic différentiel IO

Lymphomes Non Hodgkiniens

- Type B 95%
- Bas grade 80% (MALT +++)
- Atteinte nodale 0➔24%
- Grade IV 15%



T1*: HYPO/ISO/ **GADO +**

T2**: HYPO/ISO/HYPER

*Muscles extra-orbitaires

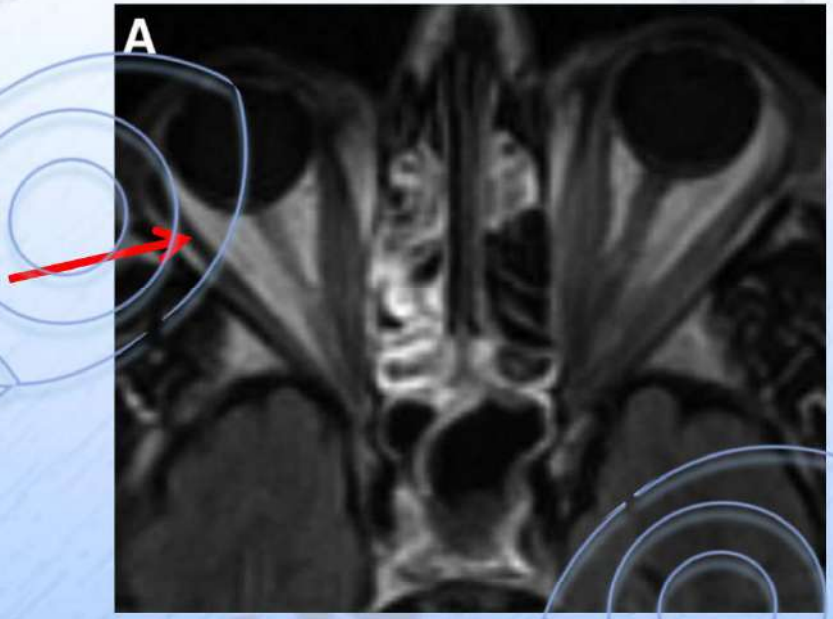
**Substance grise

Decaudin et al. Blood 2006;108:1451–1460 © 2004 by the American Society of Hematology.

Orbitopathies dysthyroïdiennes

- **Maladie de Basedow (95%)**
- **Rétraction palpébrale!**

- **TRAK +, TSH parfois normale**



- **IRM orbitaire:**

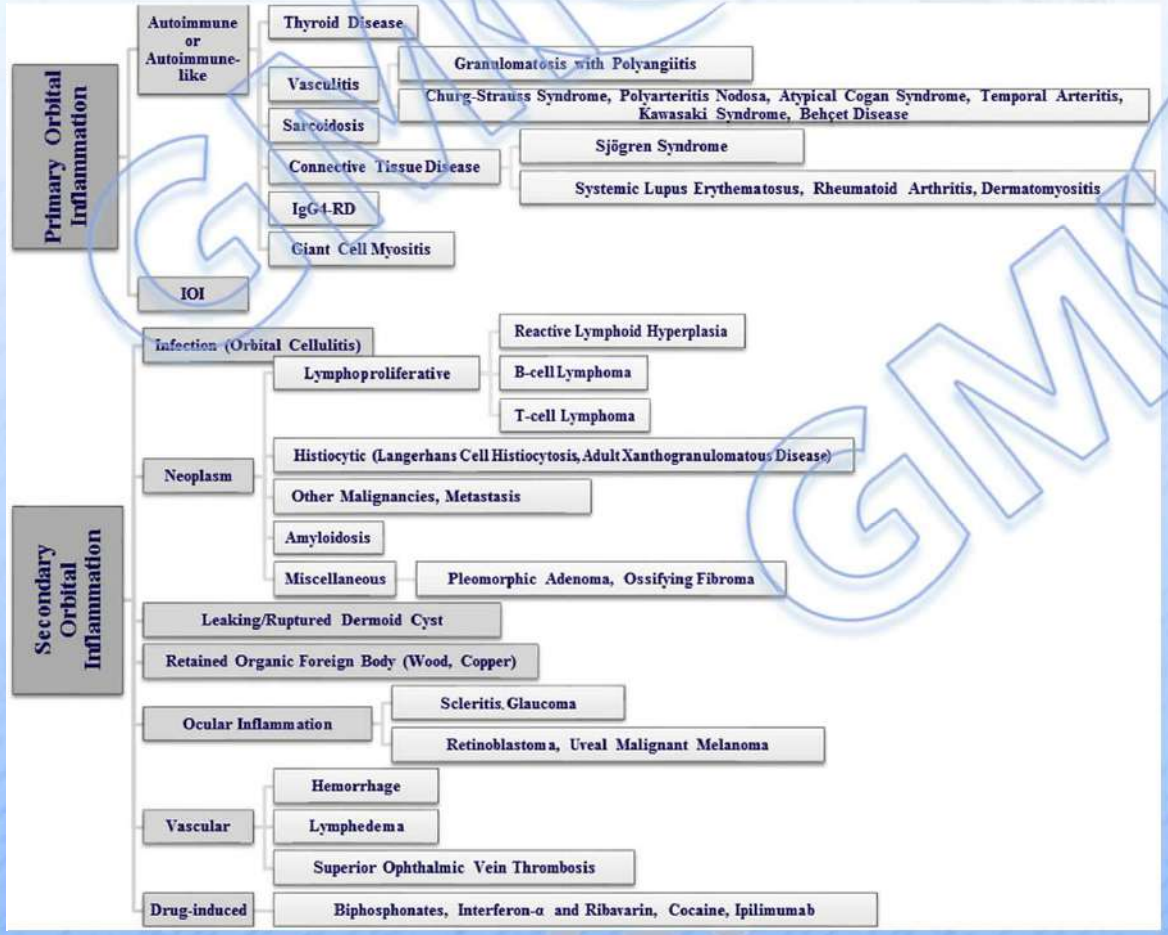
  T1*: HYPO/ISO/ **GADO +**

  T2:** HYPO/ISO/HYPER

*Muscles extra-orbitaires
**Substance grise

Lutt JR et al. Semin Arthritis Rhem 2008

Inflammation orbitaire: *Etiologies*



Mombaerts et al. Survey Ophthalmol 2016;61:664-669

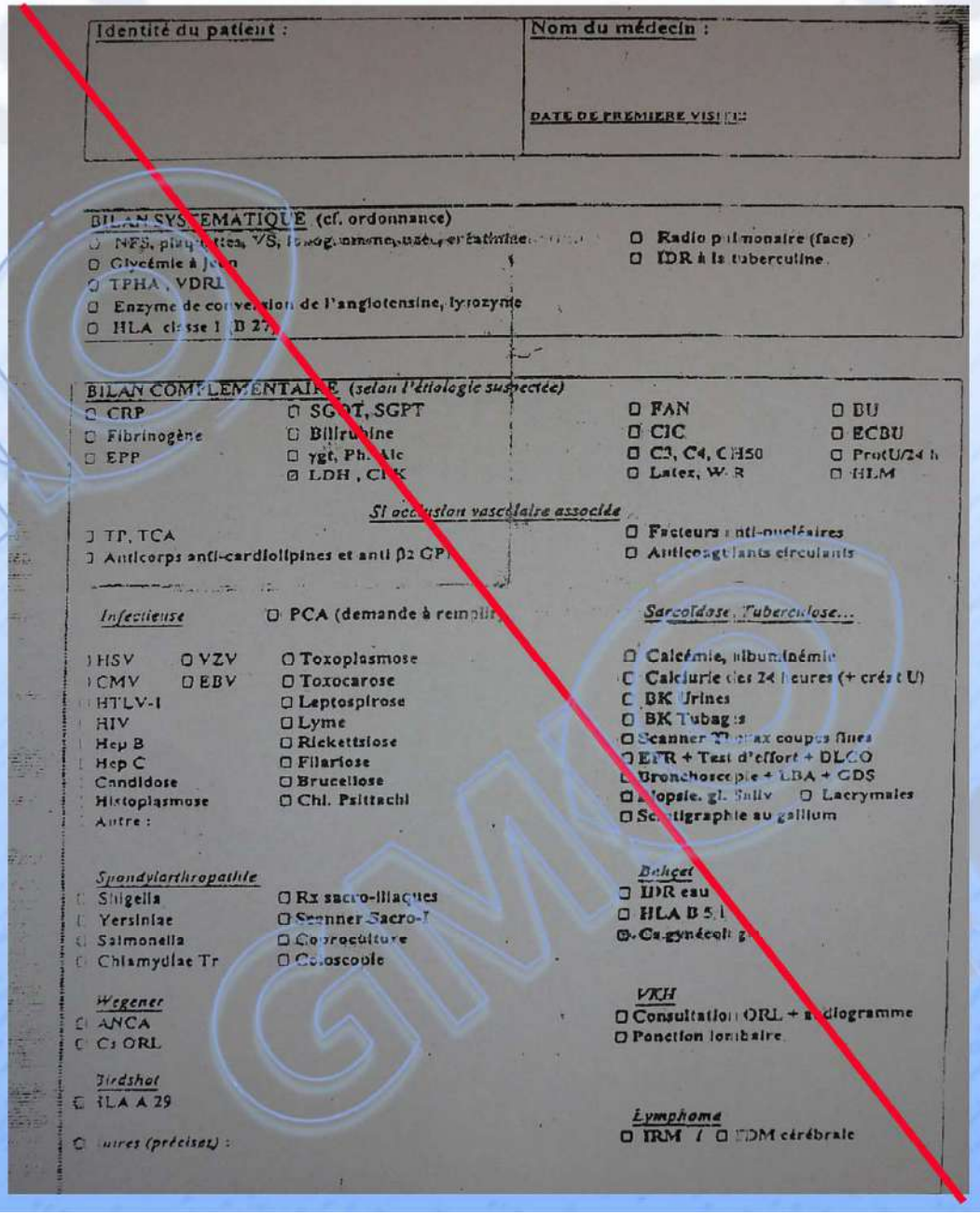


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Table 17. Subclassification of 133 Patients with Inflammatory Lesions among 1264 Consecutive Patients with Orbital Lesions

Subclassification	Number of Patients (%)*	% of Total Orbital Lesions*	Number Biopsy Proven (%)*	Mean Age in Years (median, range)
Idiopathic nongranulomatous (pseudotumor) « SIOI »	98 (74)	8	34 (35)	45 (48, 2–92)
Infectious	13 (10)	1	6 (46)	29 (11, 2–71)
Inflammation secondary to tumor necrosis				
Retinoblastoma related	4 (3)	<1	4 (100)	1 (1, 0–1)
Uveal melanoma related	2 (2)	<1	1 (50)	77 (77, 70–83)
Total intraocular lesions	6 (5)	<1	5 (83)	26 (1, 0–83)
Granulomatous inflammation				
Nonspecific	5 (4)	<1	5 (100)	57 (55, 40–83)
Wegener's granulomatosis « GPA »	4 (3)	<1	4 (100)	64 (65, 47–78)
Sarcoidosis	2 (2)	<1	2 (100)	24 (24, 14–34)
Vasculitis NOS	1 (1)	<1	1 (100)	82 (82, 82–82)
Total granulomatous	12 (9)	1	12 (100)	56 (55, 14–83)
Kimura's disease	4 (3)	<1	4 (100)	31 (34, 4–54)
Total inflammatory lesions	133 (100)	11	61 (46)	43 (47, 0–92)

NOS = not otherwise specified.
*Percents are rounded.

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Check for updates

Autoimmune markers in screening for orbital inflammatory disease

Terence Ang[1]✉, Valerie Juniat[2] and Dinesh Selva[2]

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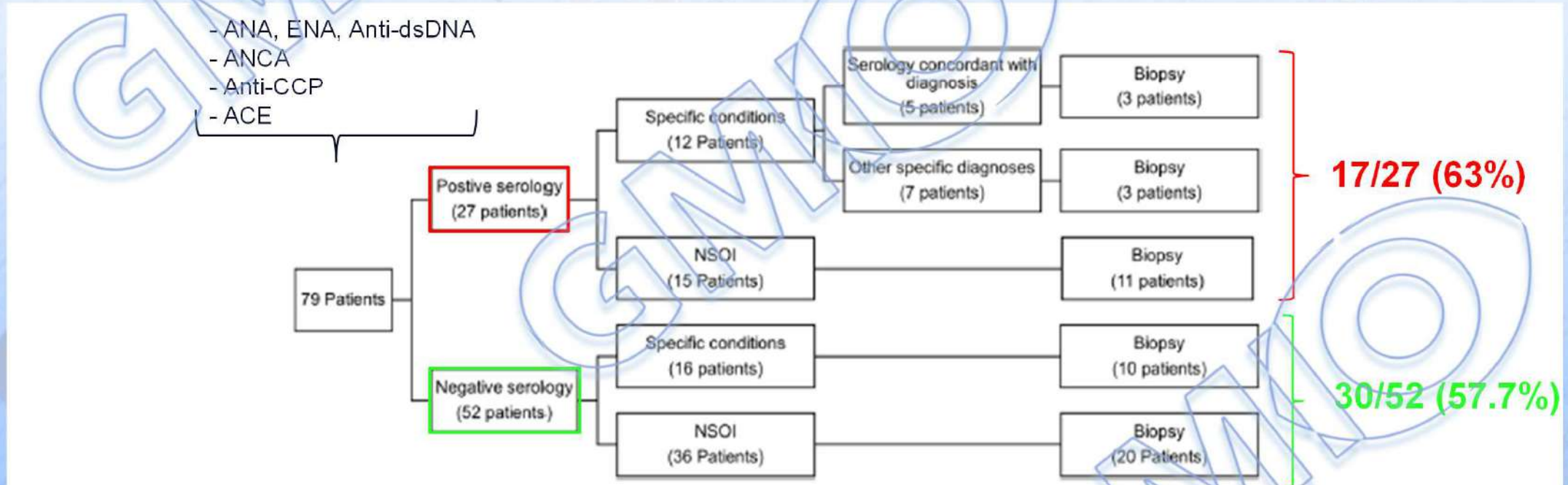

Fig. 1 Utility of autoimmune markers according to serological results. Flowchart demonstrating categorisation of patients according to serological results and subsequent diagnoses. NSOI non-specific orbital inflammation.

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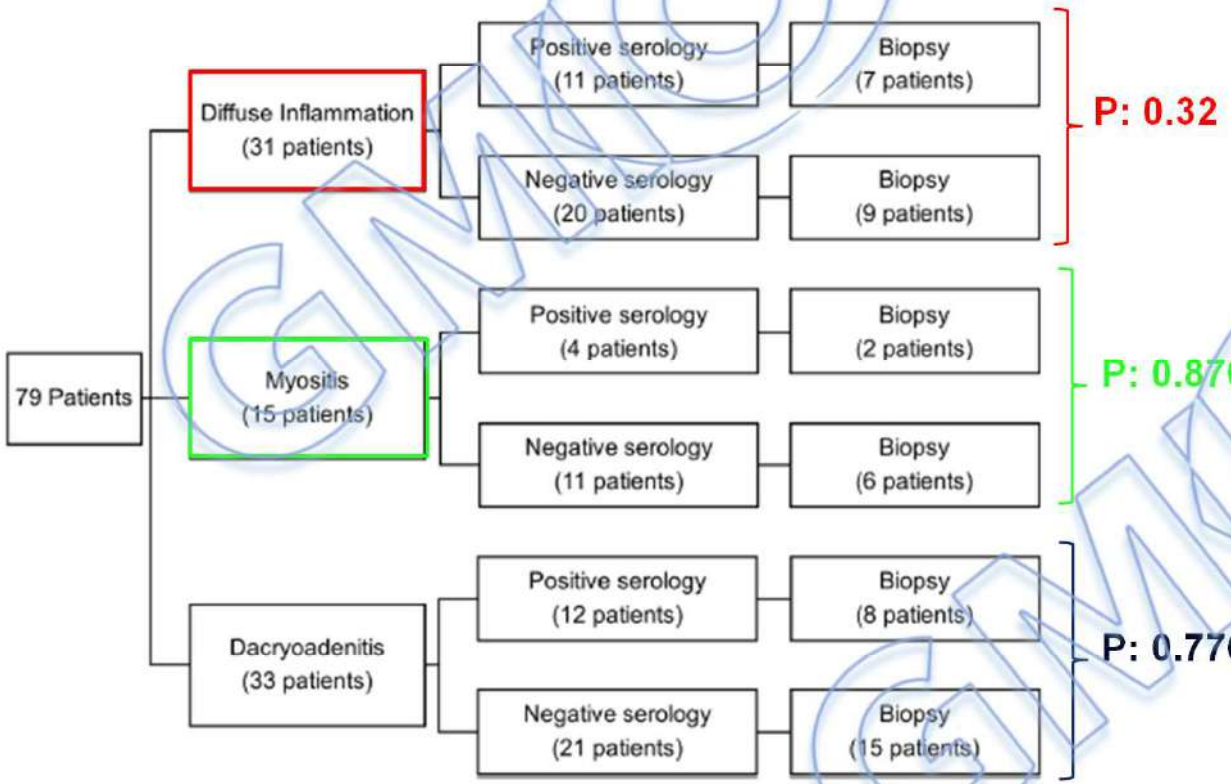

Fig. 2 Utility of autoimmune markers according to affected orbital structures. Flowchart demonstrating categorisation according to orbital structure and serological results.

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Autoimmune markers in screening for orbital inflammatory disease

Terence Ang[1], Valerie Juniat[2] and Dinesh Selva[2]

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- Sémiologie ophtalmologique
  - Uvéites: nomenclature SUN

Am J OPH 2005;140:509-516

- Topographie lésionnelle
  - Et Inflammations orbitaires……

In conclusion, autoimmune markers often have limited utility in screening for immunogenic OID. The choice of autoimmune markers in the initial diagnostic work-up of OID should be selective and rationalised by the clinico-radiological presentation, as a full panel approach may yield non-specific findings. In many

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Infectious	13 (10)	1	6 (46)	29 (11, 2–71)
Inflammation secondary to tumor necrosis				
Retinoblastoma related	4 (3)	<1	4 (100)	1 (1, 0–1)
Uveal melanoma related	2 (2)	<1	1 (50)	77 (77, 70–83)
Total intraocular lesions	6 (5)	<1	5 (83)	26 (1, 0–83)
Granulomatous inflammation				
Nonspecific	5 (4)	<1	5 (100)	57 (55, 40–83)
Wegener's granulomatosis « GPA »	4 (3)	<1	4 (100)	64 (65, 47–78)
Sarcoidosis	2 (2)	<1	2 (100)	24 (24, 14–34)
Vasculitis NOS	1 (1)	<1	1 (100)	82 (82, 82–82)
Total granulomatous	12 (9)	1	12 (100)	56 (55, 14–83)
Kimura's disease	4 (3)	<1	4 (100)	31 (34, 4–54)
Total inflammatory lesions	133 (100)	11	61 (46)	43 (47, 0–92)

NOS = not otherwise specified.
*Percents are rounded.

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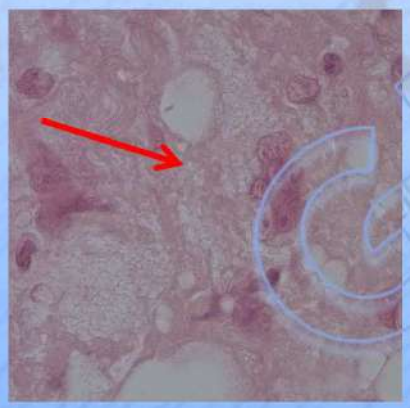
Survey of 1264 Patients with Orbital Tumors and Simulating Lesions

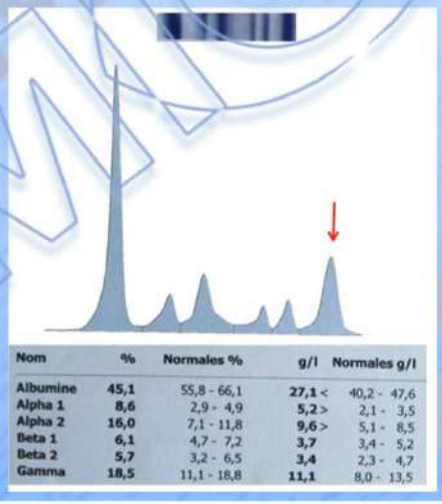
The 2002 Montgomery Lecture, Part 1

Jerry A. Shields, MD, Carol L. Shields, MD, Richard Scartozzi, MD

Table 16. Subclassification of 16 Patients with Histiocytic Lesions among 1264 Consecutive Patients with Orbital Lesions

Subclassification	Number of Patients (%)*	% of Total Orbital Lesions*	Number Biopsy Proven (%)*	Mean Age in Years (median, range)
Eosinophilic granuloma	9 (53)	1	7 (78)	14 (6, 1–81)
Xanthogranuloma	7 (41)	<1	7 (100)	
Erdheim Chester syndrome	4 (25)	<1	4 (100)	54 (56, 28–77)
Adult onset asthma	1 (6)	<1	1 (100)	46 (46, 46–46)
Juvenile xanthogranuloma	1 (6)	<1	1 (100)	0 (0–0)
Angiohistiocytoma	1 (6)	<1	1 (100)	30 (30–30)
Total histiocytic lesions	16 (100)	1	14 (88)	26 (12, 0–81)





Nom	%	Normales %	g/l	Normales g/l
Albumine	45,1	55,8 - 66,1	27,1 <	40,2 - 47,6
Alpha 1	8,6	2,9 - 4,9	5,2 >	2,1 - 3,5
Alpha 2	16,0	7,1 - 11,8	9,6 >	5,1 - 8,5
Beta 1	6,1	4,7 - 7,2	3,7	3,4 - 5,2
Beta 2	5,7	3,2 - 6,5	3,4	2,3 - 4,7
Gamma	18,5	11,1 - 18,8	11,1	8,0 - 13,5

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Clinical characteristics of inflammatory ocular disease in anti-neutrophil cytoplasmic antibody associated vasculitis: a retrospective cohort study

1171 patients entre 2003-13

Treatment	Negative ANCA (n = 27)	p-ANCA/ MPO-ANCA (n = 39)	c-ANCA/ PR3-ANCA (n = 117)	Total (n = 183)	P-value
Demographics					
Age at diagnosis of IOD, mean (S.D.), years	51.0 (20.6)	53.9 (17.9)	46.9 (16.3)	49.0 (17.5)	0.053
Female, n (%)	16 (59)	20 (51)	57 (49)	93 (51)	0.613
Ethnicity, n (%)					0.131
Caucasian	26 (96)	36 (92)	112 (96)	174 (95)	
African-American	0 (0)	1 (3)	0 (0)	1 (1)	
Native Hawaiian/other Pacific islander	1 (4)	0 (0)	0 (0)	1 (1)	
Asian	0 (0)	1 (3)	3 (3)	4 (2)	
Native American	0 (0)	1 (3)	0 (0)	1 (1)	
Other	0 (0)	0 (0)	2 (2)	2 (1)	
Duration of follow-up[a], median (IQR), years	6.0 (3.3–9.7)	5.5 (2.1–9.9)	7.0 (3.9–10.9)	6.6 (3.4–10.7)	0.318
Clinical characteristics					
IOD onset prior or at diagnosis of AAV, n (%)	18 (67)	27 (69)	52 (44)	97 (53)	0.008
IOD onset after diagnosis of AAV, n (%)	9 (33)	12 (31)	65 (56)	86 (47)	
Time from IOD to AAV diagnosis for those with IOD onset prior to/at diagnosis of AAV, mean (S.D.), months	11.1 (11.3)	6.0 (13.8)	5.9 (11.7)	6.9 (12.3)	0.035
Time from AAV diagnosis to IOD for those who had IOD onset after AAV, mean (S.D.), months	92.2 (89.5)	25.9 (22.4)	64.4 (64.9)	61.9 (65.4)	0.084
BVAS/GPA at IOD onset, mean (S.D.)	2.7 (2.6)	5.7 (4.2)	5.3 (3.9)	5.0 (3.9)	0.002

Rheumatology 2017;56:1663–1770

Clinical characteristics of inflammatory ocular disease in anti-neutrophil cytoplasmic antibody associated vasculitis: a retrospective cohort study

Patompong Ungprasert[1], Cynthia S. Crowson[1,2], Rodrigo Cartin-Ceba[3], James A. Garrity[4], Wendy M. Smith[4], Ulrich Specks[5], Eric L. Matteson[1,6] and Ashima Makol[1]

Treatment	Negative ANCA (n = 27)	p-ANCA/ MPO-ANCA (n = 39)	c-ANCA/ PR3-ANCA (n = 117)	Total (n = 183)	P-value
Type of eye disease, n (%)					
Scleritis	1 (4)	5 (13)	34 (29)	40 (22)	0.005
Episcleritis	1 (4)	10 (26)	28 (24)	39 (21)	0.052
Orbital inflammation	12 (44)	6 (15)	15 (13)	33 (18)	0.001
Lacrimal duct stenosis	3 (11)	0 (0)	16 (14)	19 (10)	0.053
Uveitis	1 (4)	1 (3)	14 (12)	16 (9)	0.120
Conjunctivitis	1 (4)	5 (13)	6 (5)	12 (7)	0.197
Cranial nerve II, IV or VI palsy	3 (11)	6 (15)	2 (2)	11 (6)	0.004
Peripheral ulcerative keratitis	0 (0)	4 (10)	3 (3)	7 (4)	0.051
Dacryoadenitis	3 (11)	2 (5)	3 (3)	8 (4)	0.142
Optic neuritis	1 (4)	3 (8)	3 (3)	7 (4)	0.351
Amaurosis fugax	2 (8)	2 (5)	3 (3)	7 (4)	0.443
Retinal vasculitis	1 (4)	1 (3)	1 (1)	3 (2)	0.505
Laterality of IOD, n (%)					0.927
Unilateral	17 (63)	23 (59)	69 (59)	109 (60)	
Bilateral	10 (37)	16 (41)	48 (41)	74 (40)	

Rheumatology 2017;56:1663–1770.

Clinical characteristics of inflammatory ocular disease in anti-neutrophil cytoplasmic antibody associated vasculitis: a retrospective cohort study

1171 patients entre 2003-13

Treatment	EGPA (n = 8)	GPA (n = 152)	MPA (n = 23)	Total (n = 183)	P-value
Type of eye disease, n (%)					
Scleritis	0 (0)	36 (24)	4 (17)	40 (22)	0.246
Episcleritis	2 (25)	32 (21)	5 (22)	39 (21)	0.964
Orbital inflammation	0 (0)	32 (21)	1 (4)	33 (18)	0.060
Lacrimal duct stenosis	0 (0)	19 (13)	0 (0)	19 (10)	0.115
Uveitis	0 (0)	15 (10)	1 (4)	16 (9)	0.457
Conjunctivitis	0 (0)	9 (6)	3 (13)	12 (7)	6
Cranial nerve II, IV or VI palsy	3 (38)	4 (3)	4 (17)	11 (6)	1
Peripheral ulcerative keratitis	0 (0)	5 (3)	2 (9)	7 (4)	0.383
Dacryoadenitis	0 (0)	8 (5)	0 (0)	8 (4)	0.426
Optic neuritis	1 (13)	5 (3)	1 (4)	7 (4)	0.412
Amaurosis fugax	2 (25)	5 (3)	0 (0)	7 (4)	0.005
Retinal vasculitis	0 (0)	2 (1)	1 (4)	3 (2)	0.528
Laterality of IOD, n (%)					0.243
Unilateral	5 (63)	94 (62)	10 (43)	109 (59)	
Bilateral	3 (38)	58 (38)	13 (57)	74 (41)	

2,8%

0.7%

Rheumatology 2017;56:1663–1770

Orbital and Adnexal Involvement in Sarcoidosis: Analysis of Clinical Features and Systemic Disease In 30 Cases

379 patients entre 2000-08

HAKAN DEMIRCI AND MURRAY D. CHRISTIANSON

TABLE 1. Anatomic Localization of Involvement in 30 Consecutive Patients with Histopathologically Confirmed Orbital and Adnexal Sarcoidosis

	No. of Eyes (%)
Anteroposterior location of orbital and adnexal sarcoidosis	
Anterior orbit	29 (97%)
Midorbit	1 (3%)
Posterior orbit	0 (0%)
Radial location of orbital and adnexal sarcoidosis	
Superior	20 (67%)
Inferior	4 (13%)
Nasal	2 (7%)
Diffuse	4 (13%)
Conal location of orbital and adnexal sarcoidosis	
Extraconal	29 (97%)
Intraconal	1 (3%)
Muscle involvement	
Superior rectus	1 (3%)
Involved orbital and adnexal organs	
Lacrimal gland	19 (63%)
Eyelid	5 (17%)
Orbit	4 (13%)
Lacrimal sac	2 (7%)

5%

1%

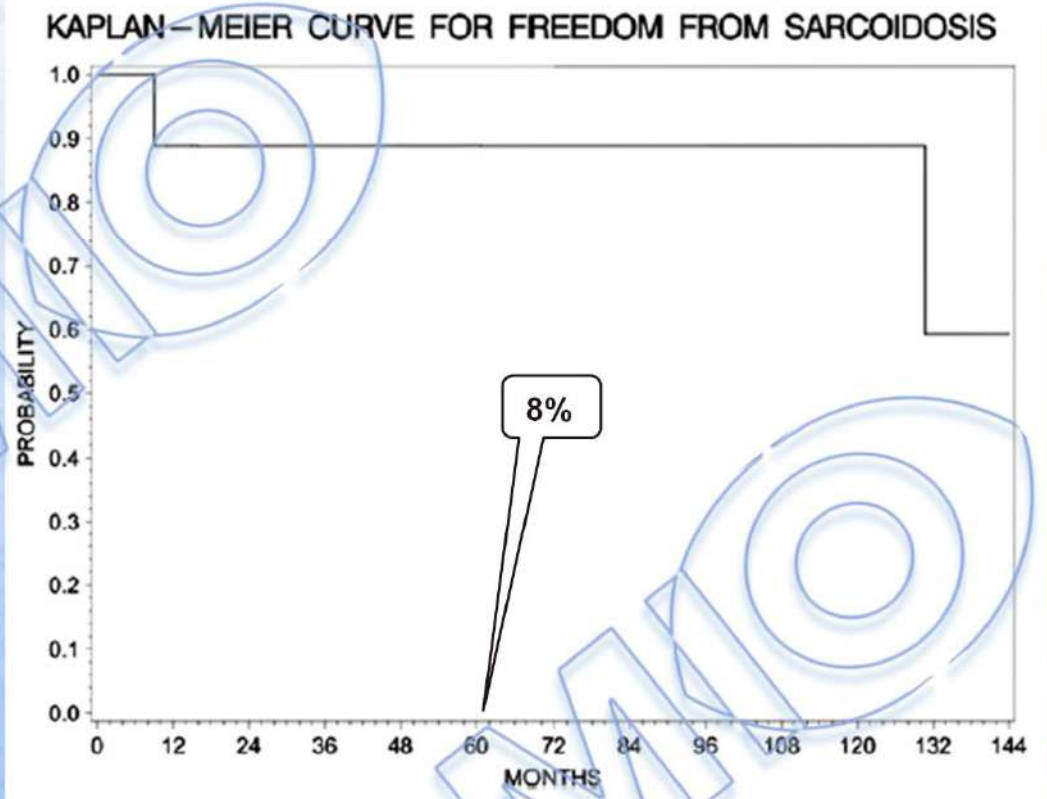

FIGURE 3. Kaplan-Meier survival analysis of 19 patients with orbital and adnexal sarcoidosis and no evident systemic sarcoidosis at presentation.

Ophthalmology 2011;151:1074–1080 © 2011 by the American Academy of Ophthalmology.

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Infectious	13 (10)	1	6 (46)	29 (11, 2–71)
Inflammation secondary to tumor necrosis				
Retinoblastoma related	4 (3)	<1	4 (100)	1 (1, 0–1)
Uveal melanoma related	2 (2)	<1	1 (50)	77 (77, 70–83)
Total intraocular lesions	6 (5)	<1	5 (83)	26 (1, 0–83)
Granulomatous inflammation				
Nonspecific	5 (4)	<1	5 (100)	57 (55, 40–83)
Wegener's granulomatosis « GPA »	4 (3)	<1	4 (100)	64 (65, 47–78)
Sarcoidosis	2 (2)	<1	2 (100)	24 (24, 14–34)
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NOS = not otherwise specified.
*Percents are rounded.

Maladie associée aux IgG4 ?

Ophthalmology 2004;111:997–1008 © 2004 by the American Academy of Ophthalmology.

Orbitopathies associées aux IgG4

Ophthalmologic characteristics according to IgG4 immunostaning in patients with biopsy proven IOIS from the literature review and cohort SIOI

37%

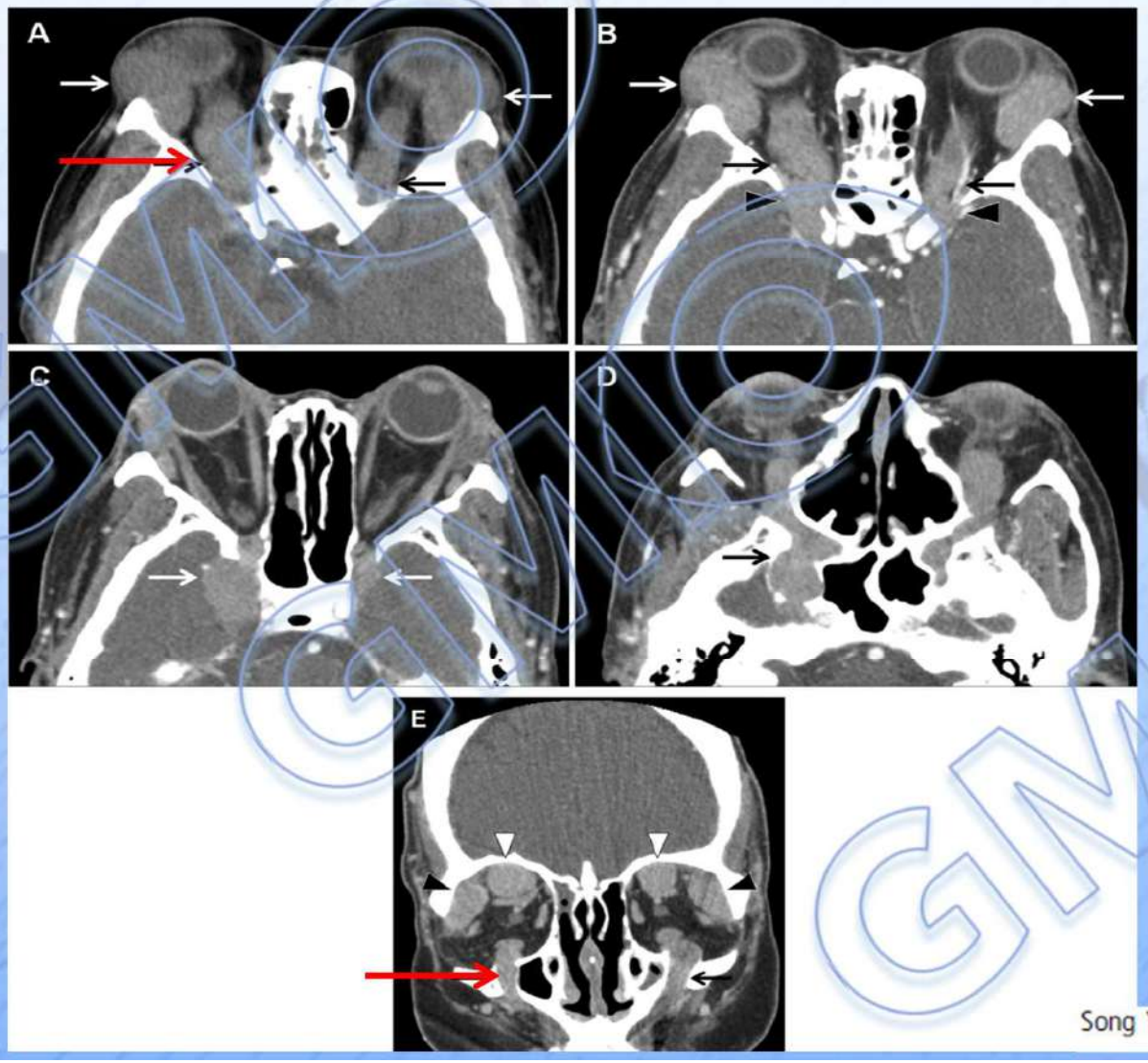
	Plaza et al. 2011		Deschamps et al. 2013		Andrew et al. 2015		Sa et al. 2015		Abad et al. 2019			Pooled data[+]		
	IgG4+ n: 11	IgG4- n: 10	IgG4+ n: 10	IgG4- n:15	IgG4+ n: 18	IgG4- n: 47	IgG4+ n: 11	IgG4- n: 13	IgG4+ n: 13	IgG4- n: 21	*P*	IgG4+ n: 63	IgG4- n: 106	Total n: 169
Ophthalmologic locations, n°(/n%)														
- Lacrimal gland	10(91)	8(80)	8(80)	10(66)	14(77)	34(73)	10(91)	4(30)	8(61.5)	10(47)	0.43	50(79)	66(62)	116(68)
- Extra ocular muscles	5(45)	4(36)	4(40)	5(33)	6(33)	21(46)	0	4(30)	4(31)	5(31)	0.7	19(30)	39(36.8)	58(34)
- Globe/ sclera	0	0	0	0	1(6)	2(5.4)	0	0	2(15.5)	4(19)	1	3(4.75)	6(5.5)	9(5.5)
- Orbital fat	2(18)	1(10)	6(60)	8(53)	8(44)	15(32)	1(9)	9(70)	10(77)	13(62)	0.46	27(43)	46(43)	73(43)
- Apex	0	0	1(10)	1(6)	0	0	0	0	4(31)	4(19)	0.68	5(8)	5(4.5)	10(6)
- Optic nerve	1(9)	0	3(30)	6(40)	NA	NA	NA	NA	4(31)	9(43)	0.7	8(12.5)	15(14)	23(13.5)
-Trigeminal nerve	/	/	/	/	/	/	/	/	4/10°(40)	1/16°(6.2)	0.055			
- Bilateral presentation	6(55)	0	2(20)	2(13)	6(35)	6(13)	10(91)	5(39)	6(46)	5(24)	0.26	30(47.5)	18(14)	48(28.5)

[+] P values are based on the chi-square test or Fisher's exact test, as appropriate. P values below 0.05 were considered to denote significant differences.
° Imaging analysis was inconclusive for three IgG4-positive patients and five IgG4-negative patients.

Abad et al. Acta Ophthalmologica 2019

Ocular adnexal IgG4-related disease: CT and MRI findings

Yong Sub Song,[1] Ho-Kyung Choung,[2,3] Sun-Won Park,[1,4] Ji-Hoon Kim,[1] Sang In Khwarg,[3] Yoon Kyung Jeon[5]



Song YS, *et al. Br J Ophthalmol* 2013;**97**:412–418.

Acta Ophthalmologica

– Acta Ophthalmologica 2019

0,1-0,4% *Minh LJ et al. Prog Retin Eye Res. 2020*

Aminobisphosphonate-associated orbital and ocular inflammatory disease

Shay Keren,[1,†] Igal Leibovitch,[1,†] Ran Ben Cnaan,[1] Meira Neudorfer,[1] Ortal Fogel,[1] Yona Greenman,[2] Shiri Shulman,[1] Dinah Zur[1] and Zohar Habot-Wilner[1]

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ABSTRACT.

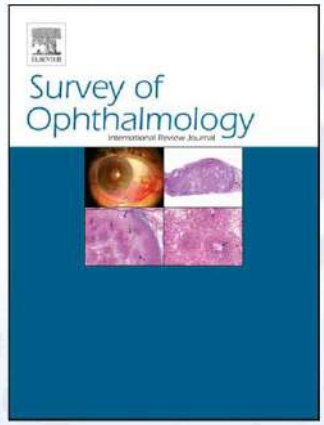
Purpose: Aminobisphosphonates may cause orbital/ocular inflammation. Awareness of the clinical presentation and disease course is crucial. The purpose of this study was to analyse demographics, clinical presentation, disease course and treatment of aminobisphosphonate-associated orbital/ocular inflammation in a large series of patients.

Methods: A retrospective study of patients with aminobisphosphonate-associated orbital/ocular inflammation and a literature review to differentiate disease presentation and course between various aminobisphosphonates.

Results: Eight patients from our institution (6 women and 2 men, median age 62 years) were included. The used drugs were zoledronate, alendronate and risedronate. The most common clinical presentation was conjunctival hyperaemia/chemosis. Scleritis was the most common manifestation, followed by diffuse orbital inflammation and anterior uveitis. Ultrasound aided in diagnosis in all our patients. The aminobisphosphonate was halted in all patients, and some patients had anti-inflammatory treatment. Literature review included 68 patients (83 eyes), of them the most abundant drugs causing orbital/ocular inflammation were pamidronate (38 eyes) and zoledronate (35 eyes). Overall, among 76 patients, all drugs induced orbital disease, while uveitis was induced mostly by zoledronate and pamidronate, less by alendronate and not found among risedronate users. Time interval from drug administration to symptoms was hours to 28 days. Resolution was achieved in all patients, after 1–60 days from disease presentation, and the longer resolution period was found among alendronate users.

Conclusion: Orbital/ocular inflammation was mostly caused by intravenous aminobisphosphonates. Uveitis was not induced by risedronate. The putative aminobisphosphonate should be halted at the onset of orbital/ocular involvement and prognosis is favourable.

Inflammations orbitaires et inhibiteurs de chek point immunitaires



Inflammatory orbital disease			
Graves–Basedow-like	Ipilimumab	McElna,[58] Borodic,[12]	Oral corticosteroids
	Pembrolizumab	Conrady,[20] Sun[59]	Oral corticosteroids
Idiopatic orbital inflammation	Ipilimumab	Lacouflat,[52]	Oral corticosteroids
	Durvalumab + Tremelimumab (Ac CTLA4)	Carrera,[16] — Myosites	
Tolosa–Hunt syndrome	Ipilimumab	Voskens[93]	Checkpoint inhibitor withdrawal Oral corticosteroids Intravenous corticosteroids
Myasthenia-gravis-like	Nivolumab Ipilimumab Pembrolizumab	Polat,[74] Montes,[61]	Checkpoint inhibitor withdrawal Oral corticosteroids Plasmapheresis Immunoglobulins

Alba-Linero C et al. Surv Ophthalmol 2021

Examen Ophtalmologique
- Formes anatomocliniques
- Signes orbitopalpébraux

Manifestations orbitaires caractéristiques
Maladie de Basedow +++

Médicaments!

Manifestations systémiques

Signes cliniques
Asthme, sinusite, sarcoïdes…….

GRADES C !

Topographie lésionnelle

Myosite

TSHus/
TRAK/ Ac anti-TPO

NFS-Plaquettes
CRP-Fibrinogène
Créatininémie - BU- Prot/creat U
gGT/PAL/ASAT/ALAT
EPP

Xanthogranulomatoses périorbitaires

+ Immunofixation

Scanner thoracique (TEP scan ?)
ECA/ BGSA
ANCA

Dacryoadénites

Nerf Trijumeau

IgG4 sériques

+/-

BIOPSIE → **SIOI (si IgG4-)**


Merci
pour votre
attention