"ORBITAL PSEUDOTUMOR"

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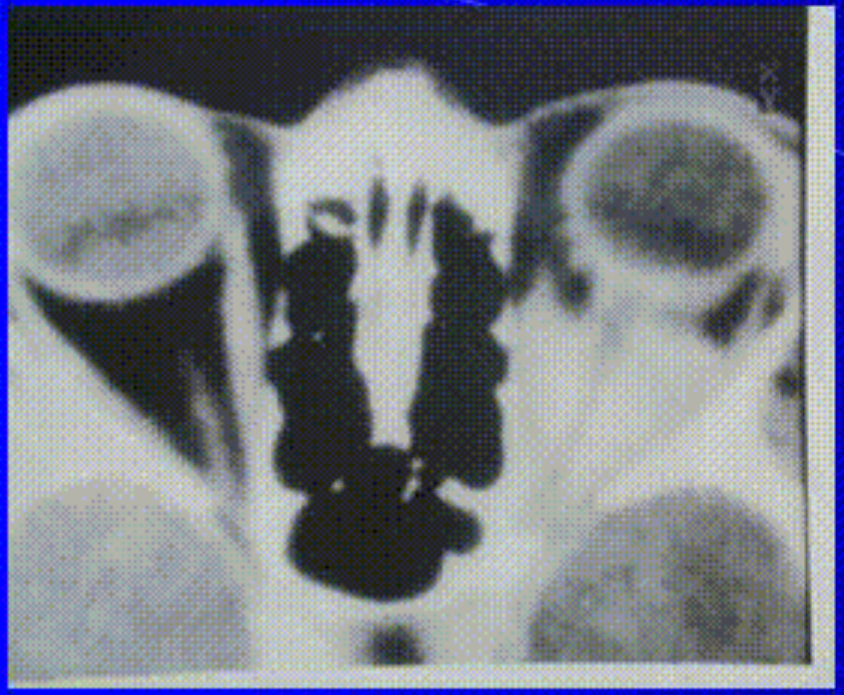
"Federico II"

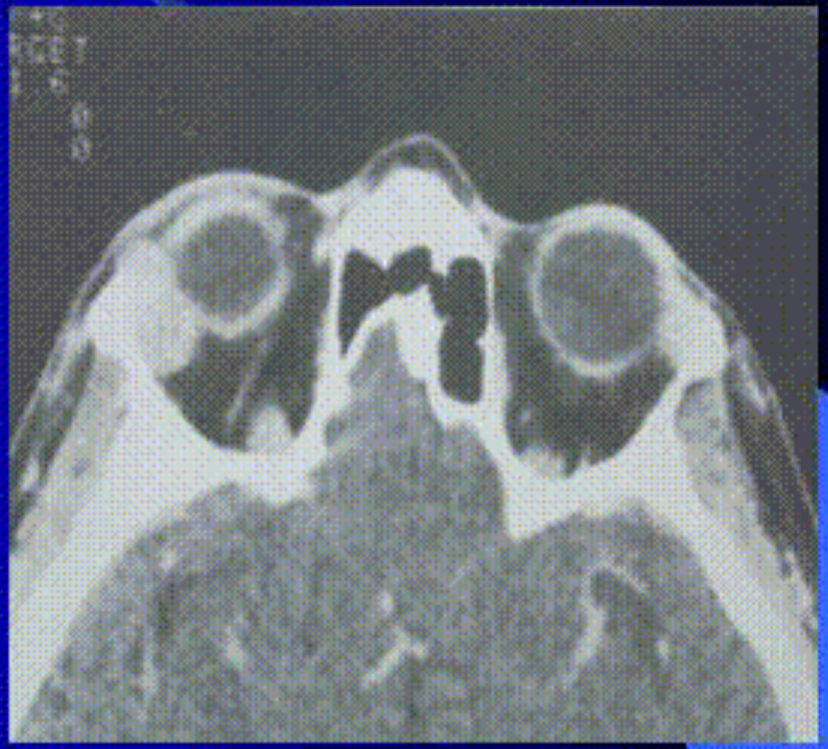
What's Orbital Pseudotumor?

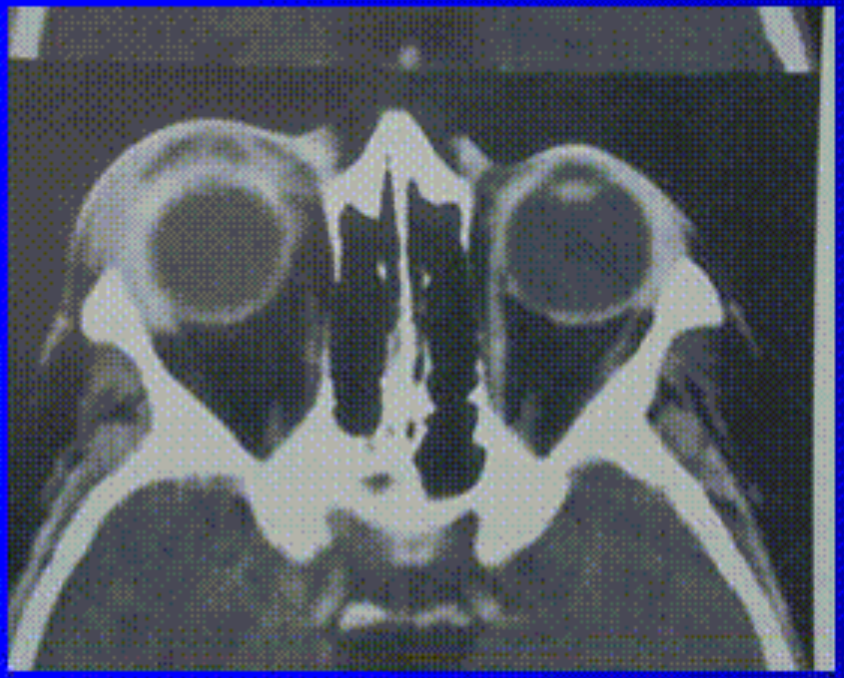
?

Terminology:

- Orbital Pseudotumor: Birc-Hirschfeld 1905
- Cellulitis Fibroplastica: Verebely 1926
- Orbital Granuloma: Reese
- Non specific Orbital Granuloma: Easton-Smith
- Orbital Lipogranuloma: Coop
- Inflammatory non neoplastic Orbital Pseudotumor: Hogan-Zimmerman
- Idiopathic inflammatory Orbital Pseudotumor: Jakobiec
- Lynphocytic inflammatory Orbital Pseudotumor >>>>> Non vasculitic inflammatory Orbital Tumor: Henderson
- Non Specific Orbital Inflammation: Rootman





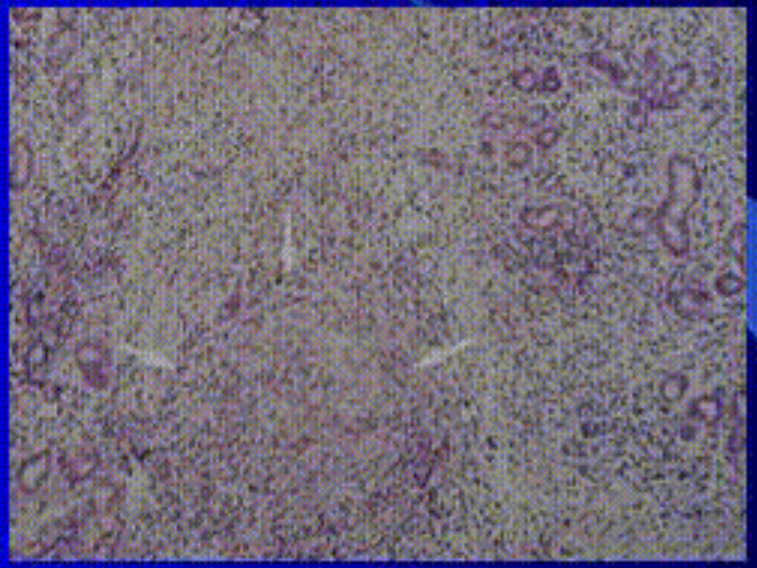


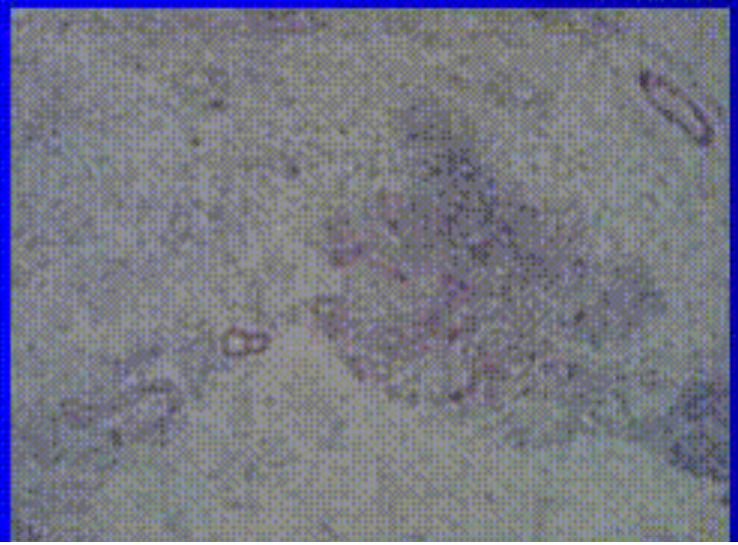
Hystologic Pattern

- ORGAN: eyelid, extraocular muscle, sclera, lacrimal gland….connective tessue
- TYPE OF CELLS: miscellaneous lynphocytic, plasma cells, fibroblasts.
- DISTRIBUTION: lymphoid follicle, perivascular, fibrous scarring,

Histologic Pictures:

lymphoid, granulomatous and sclerosing





"Orbital pseudotumor"

- **Inflammatory-Non Neoplastic:** with exclusions of reactive lymphoid hyperplasia, benign pseudolynphoma (true benign low grade lymphoma)
- **Idiopathic**
- **Non Specific:** with exclusions Syphilis, Tuberculosis, Graves ophthalmopathy, Wegener granulomatosis, Polyarteritis nodosa, Sarcoidosis, Amyloidosis, Forein body, ifection Cellulitis, Hemangioma, rupture Dermoid cyst.
- **Idiopathic Non-specific Orbital Inflammation (INOI)**

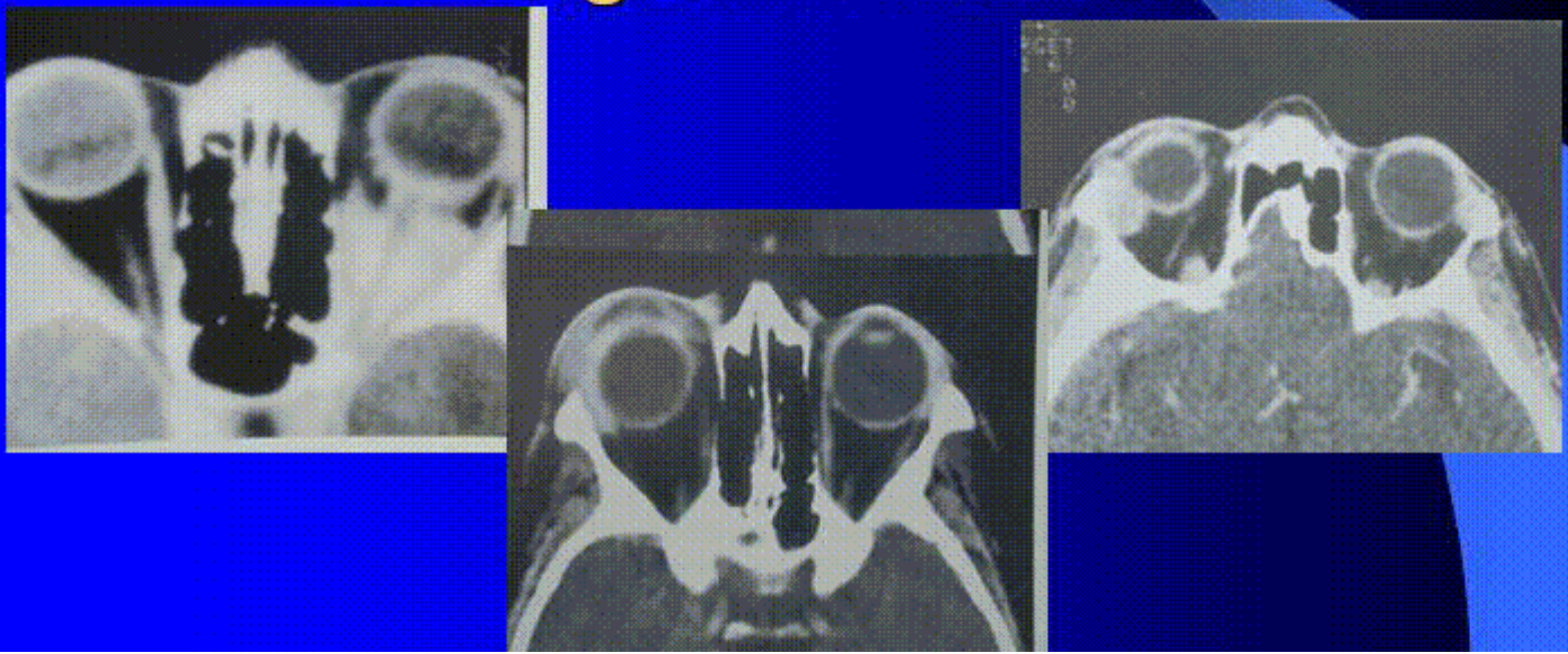
Questions ?

- Are myositis, dacrioadenitis, tenonitis etc.. to be concidered as part of the whole group of INOI or they have its own clinical identity?
- Is INOI a systemic or a local inflammatory disease localized just to the Orbit? (like low grade limphoma or chronic infections)

PROJECTS

- Retrospective non-comparative case series on Management of Orbital Pseudotumor
- Prospective pilot study on possible Ethiologic role of Chlamydia and Mycoplasma infections in Orbital Pseudotumor

Management of INOI



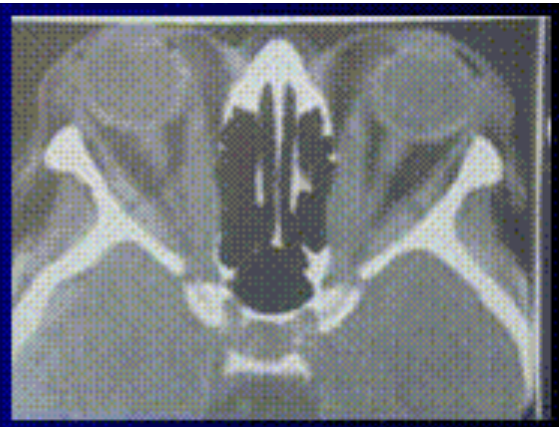
Methods

- We retrospectively analized 250 pz files with presumed diagnosis of INOI from 1976 to 2002
- We reviwed and recorded onto a data base: age, signs and symptoms, visual acuity, systemic diseases at presentation, diseases developed during follow up, imaging tests (MRI, CT, Ultrasound), diagnose, therapy (medical, surgical, both), recurrences, interval time therapy-recurrences, hystological diagose of recurrences.

Methods

- After re-evaluations of 250 pz. files only 120 with true INOI with adeguate follow up were included in the study. Pz who developed lymphoma or other sistemic or local diseases different from INOI were excluded. (lymphoma, Graves ophthalmopathy, meningioma, swhannoma)
- Based on radiological and hystological ground we classified diagnosis according to the orbital structure primarily affected: myositis (Myo), orbital mass (Ps), dacrioadenitis (dacrio), tenonitis, periostitis and Tolosa Hunt syndrome.

Methods



- Investigations:
- t3-t4, TRH, TSH, Thyroid-Abs were performed in pz with enlargment of extraocular muscles in order to exclude Graves Ophthalmopathy
- anti-nuclear Ab (ANA),antineutrophil-cytoplasmic Ab (ANCA), angiotensin-converting enzime (ACE), erithrocyte sedimentation rate (ESR), Reumatoid F. circulating immune ocomplexes.

Methods

- Open orbital biopsy were performed on 51(42%) of pz while pz with pain ophthalmoplegia and radiologic absence of infiltration (Tolosa Hunt syndrome) and those who did not receive histologic examination the diagnosis of INOI was supported by combined clinical findings, radiological incontrovertible appearance of infiltration and long term follow up (mean 13 years)

Methods

- None of pz had received treatment before
- Treatment criteria was based empirically on the ammount of inflammation and on clinical and radiological appearance, regardless of discriminating on the base of single structure envolved in the orbit
- Medical (MT): 1-1,5 mg/kg prednisolon in 65(54%) of pz
- Surgical (ST): debulking in 29(24%) of pz
- Steroids+Surgical (MST): in 22(18%) of pz
- 12/26 pz who recurred (47%) underwent open orbital biopsy in order to exclude diagnosis different from INOI even though already had ST as first terapeutic approach

Results

- Mean age: 42 years (ranged between 5-84)
- Bilateral cases were not observed
- 63/120 pz (52%) mass located in a variable infiltraded manner
- 25 pz (20%) lacrimal gland envolvement
- 23 pz (19%) myositis
- 2 pz (1%) tenonitis
- 5 pz (4%) periostitis
- 2 pz (1%) Tolosa Hunt syndrome

Symptoms

	Freq.	%	% valid.	% add.
None	44	36,7	36,7	36,7
Pain	35	29,2	29,2	65,8
Diplopia	22	18,3	18,3	84,2
Dip + pain	19	15,8	15,8	100,0
Total	120	100,0	100,0	

Signs

	Freq.	%	% valid.	% add.
None	10	8,3	8,3	8,3
Exophthalm	41	34,2	34,2	42,5
Ptosis	10	8,3	8,3	50,8
Exophthalm + ptosis	25	20,8	20,8	71,7
Edema	24	20,0	20,0	91,7
Retraction	1	8	8	92,5
s-shaped	1	8	8	93,3
Exophthalm + edema	2	1,7	1,7	95,0
edema+ptosis	6	5,0	5,0	100,0
Total	120	100,0	100,0	

Therapies

	Freq.	%	% valid.	% add.
No therapy	4	3,3	3,3	3,3
ST	29	24,2	24,2	27,5
MST	22	18,3	18,3	45,8
MT	65	54,2	54,2	100,0
Total	120	100,0	100,0	

Recurrences

		TREAT.				Total
		No therapy	ST	MST	MT	
RECUR:	Negative	4	23	17	50	94
	Positive		6	5	15	26
Total		4	29	22	65	120

Recurrences-Treatments (M&S)

	Valore	df	Sig. asint. (2 vie)	Sig. esatta (2 vie)	Sig. esatta (1 via)
K-Pearson	,066	1	,797		
Correction	,000	1	1,000		
Fisher T.				1,000	,512
Asso.	,065	1	,799		
N.	94				

Histopathology of pz recurred:

	Freq.	%	% valid.	% add.
None	14	53,8	53,8	53,8
Ps	2	7,7	7,7	61,5
dacrio	2	7,7	7,7	69,2
Ps sclerosis	7	26,9	26,9	96,2
Ps eosinophil	1	3,8	3,8	100,0
Total	26	100,0	100,0	

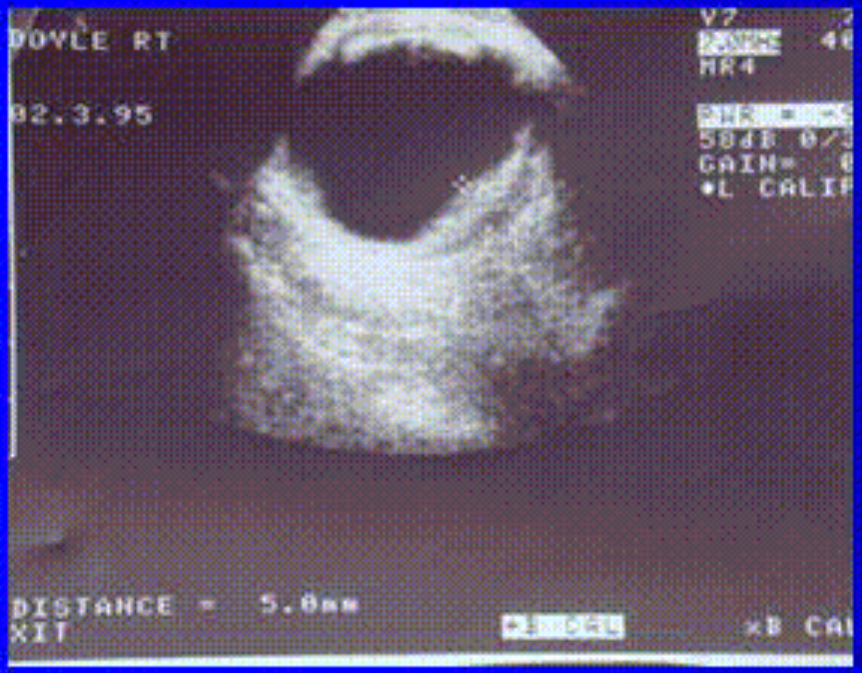
Times disease-recurrence (years)

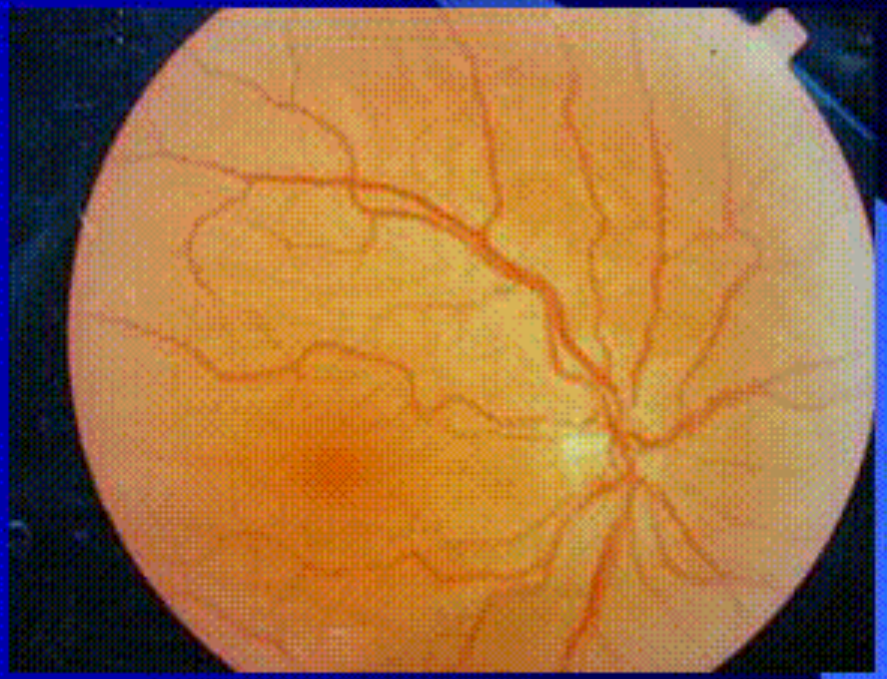
	N.	Media	D.S.	Error std.	Interv. Conf. 95% Lim.	Lim.	Min	Max
No therap	4	,00	,00	,00	,00	,00	0	0
ST	29	,55	1,72	,32	-,10	1,21	0	9
MST	22	1,05	3,26	,69	-,40	2,49	0	15
MT	65	,74	2,06	,26	,23	1,25	0	10
Total	120	,73	2,21	,20	,33	1,12	0	15

Multiple analysis (Bonferroni): Therapies/recurrences

(I) TREATT	(J) TREATT	Diff. medie (I-J)	Error std.	Sig.	Interval conf. 95% Limit	Limit
no therapy	ST	-,55	1,19	1,000	-3,74	2,64
	MST	-1,05	1,21	1,000	-4,30	2,21
	MT	-,74	1,15	1,000	-3,82	2,34
ST	no therapy	,55	1,19	1,000	-2,64	3,74
	MST	-,49	,63	1,000	-2,19	1,20
	MT	-,19	,50	1,000	-1,52	1,15
MST	no therapy	1,05	1,21	1,000	-2,21	4,30
	ST	,49	,63	1,000	-1,20	2,19
	MT	,31	,55	1,000	-1,17	1,78
MT	no therapy	,74	1,15	1,000	-2,34	3,82
	ST	,19	,50	1,000	-1,15	1,52
	MST	-,31	,55	1,000	-1,78	1,17

Scleritis and Choroidal folds





Conclusion

Is INOI a local or a systemic disease?

- Since systemic diseases are by definition characterized by a multisystemic involvement it appears controversial consider the INOI a sistemic disease limited just to the orbit; in our study the absence of any other systemic sign or other localization on long term follow-up (mean 13 years) corroborate the hypothesis that **INOI** is a local disease

Conclusion

Are myositis, dacrioadenitis, tenonitis etc.. to be concidered as part of the whole group of INOI or they have its own clinical identity?

- we demostrate they should be concidered all together as single disease because of shearing the unknown aethiology and the same clinical, therapeutic and prognostic course irrispective of their original tessue location

Ethiologic role of Chlamydia and Mycoplasma infections in INOI

Questions ?

- Are myositis, dacrioadenitis, tenonitis etc.. to be concidered as part of the whole group of INOI or they have its own clinical identity?
- Is INOI a systemic or a local inflammatory disease localized just to the Orbit? (like low grade limphoma or chronic infections)

Scientific evidence:

- inflammatory pseudotumor of the lung manifested as a mediastinal mass can be associated with Mycoplasma pn. infection: Kim at all. Pediatr Radiol 1992
- fluorescence with monoclonal Abs against the major outer membrane proteins of Chlamydia species have been found in patients with spindle-cell nodule of the urinary bladder (inflammatory pseudotumor): Lo JW at all. Diagn Cytopatol 1992

Scientific evidence:

- Rectal pseudotumor due to Chlamidia tracomatis in a male homosexual. Ruther U. at all.: Endoscopy 1990
- Pseudotumor of the orbit and retroperitoneal fibrosis. A form of multifocal fibrosclerosis. Richards AB at all. Arch.Ophthalmol 1980

Methods

- We analized 8 pz (3M and 5F) with clinical presentations (sings and symptoms), imaging study (MRI, CT scan and echography) and histological result compatible with INOI.
- All patients underwent a complete laboratory investigations and imaging analysis in order to exclude local and systemic disease of known aetiology

Methods

- Specifically serum t3 –t4, thyrotropin releasing hormone, thyroid antibodies and thyroid stimulating hormone levels was performed in patients with primarily muscles involvement in order to exclude Graves Ophthalmopathy.
- anti-nuclear antibodies, antineutrophil-cytoplasmic auto-antibodies, angiotensin-converting enzyme, erythrocyte sedimentation rate, rheumatoid factor and circulating immune complexes were also tested to exclude sarcoidosis, Wegner's granulomatosis, autoimmune and infectious diseases

Methods

- All patients underwent a surgical approach (debulking) with open orbital biopsy
- All tissue biopsy specimens were fixed in 4% formalin and embedded in paraffin for conventional histological staining (hematoxilin&eosin, Giemsa and periodic a acid-Schiff).
- Immunologic studies were performed on each fresh tissue specimen, which was storage at –80 C° and frozen sections were prepared for the immunofluorescence tests.

Methods

- On histological samples: to detect Chlamydia at all stages of its development cycle (elementary bodies, reticulate bodies and inclusion bodies) direct fluorescent Ab technique (Chlamydia direct IF: bio-Mèrieux) was used
- On the blood samples immunoenzimatic ELISA test (Eurospital Ct, Cp) was used to detect respectively Ig A and Ig G Ab against Ch. trachomatis and Ig.M and Ig.G Ab against Ch. Pneumonia; immunoenzimatic ELISA test (Eurospital Myp) was used to detect Ig M and Ig G Ab against Mycoplasma.

Results

- On histological examination:lesions were all classified as chronic non specific inflammations
- On immunofluorescence: the histological sections fail to show monoclonal antibody staining pattern against Chlamydia species in all cases
- On blood samples: none of autoantibodies against Chlamydia and Mycoplasma species were detected in the serum of patients involved in the study.

Conclusions

- if we consider that 40% and 50% of normal population are blood positive for anti-Mycoplasma antibody and anti-Chlamydia pneumonia respectively, the total negativity of our patients do not support our hypothesis that orbital pseudotumor could be do to infection.
- Similarly at immunofluorescence test we were not able to show Chlamydia trachomatis or pneumonia inclusions on frozen sections which also do not corroborate our assumption

Guidelines

- Mainstay of therapy in INOI: never-ever use steroids as first line of treatment if you suspect INOI (NSAD) a part from Myositis and Tolosa-Hunt S. characterized by 24h dramatic pain and motility deficienzy in abcense of infiltration (use of steroids is unjustified-confiusing-dangerous and nowdays negligent on medical legal base)
- If you suspect orbital cellulitis in a little child starting intravenous anibiotics is imperative