BLAU SYNDROME RELATED **UVEITIS**

CASE REPORT

Pablo Mesa del Castillo B.

4th Insights in Autoinflammation

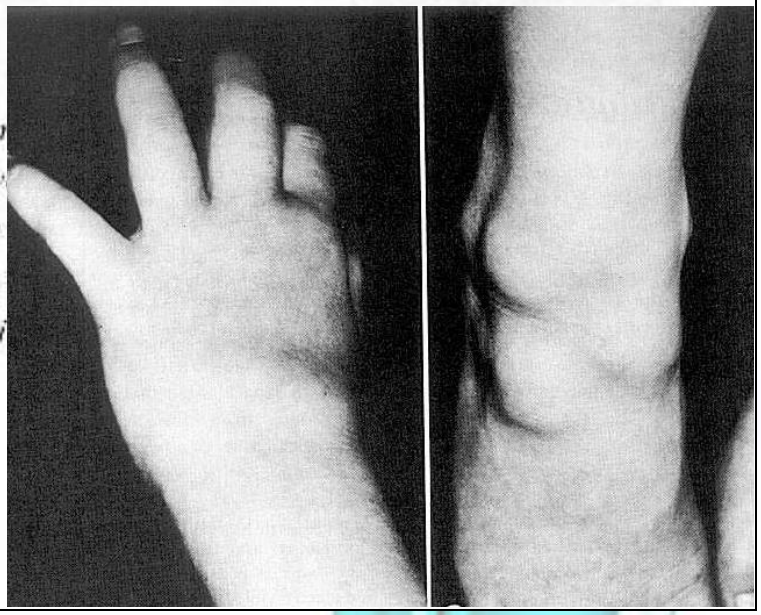
Baveno. June 2015.

Familial granulomatous arthritis, iritis, and rash

Eleven family members over four generations have had granulom joints. Ten have had arthritis; two had skin, eye, and joint involv disease, and one had iritis only. The disease is transmitted as an not associated with HLA-B27. The disease resembles sarcoidosis is probably a new syndrome. The major long-term problems are i

(J Pediatr 1985;107:689-693)

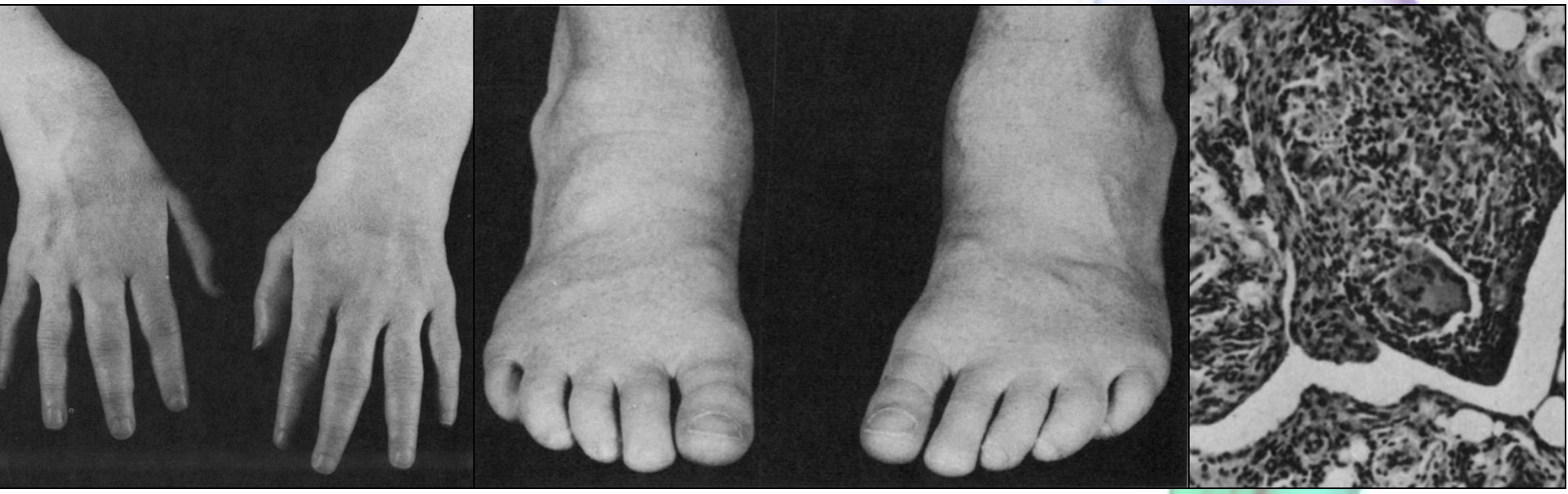
Edward B. Blau, M.D.
Marshfield, Wisconsin



•Douglas Jabs: Granulomatous **arthritis**, recurrent **uveitis** and cranial **neuropathies**. **AD** inheritance pattern. ANA, RF, HLA B27 negative. Synovium **biopsy**: granulomatous inflammation with giant cells. No dermatologic features described. Am J Med 1985; 78: 801-4.

JABS SYNDROME

EARLY ONSET SARCOIDOSIS



Miller. Early-onset "sarcoidosis" and "familial granulomatous arthritis": the same disease. *The Journal of pediatrics. 1986;109(2):387-8*.

Early Onset Sarcoidosis (EOS): sporadic.

Blau Syndrome: Familial.

JUVENILE GRANULOMATOUS ARTHRITIS

ARTHRITIS & RHEUMATISM
Vol. 60, No. 6, June 2009, pp 1797–1803
DOI 10.1002/art.24533

NOD2-Associated Pediatric Granulomatous Arthritis, an Expanding Phenotype

Study of an International Registry and a National Cohort in Spain

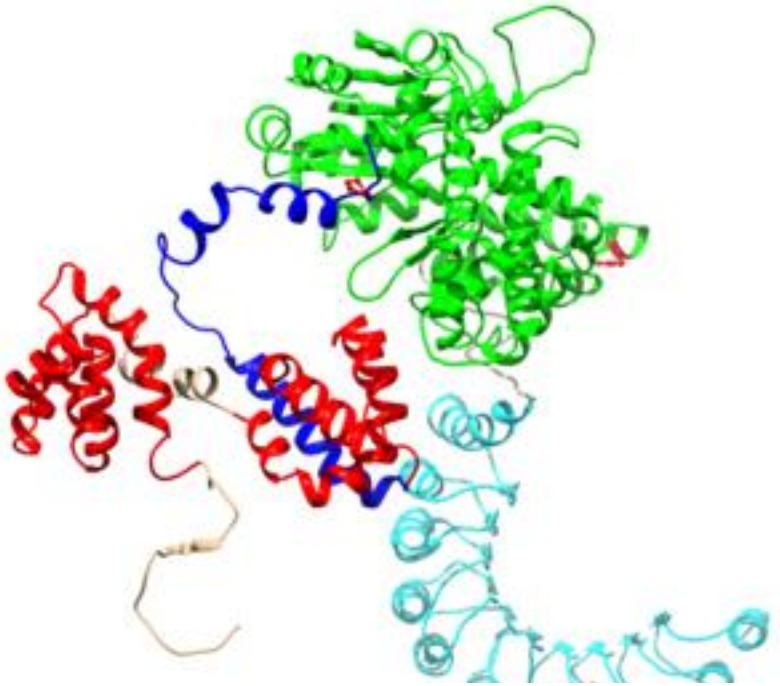
Carlos D. Rosé,[1] Juan I. Aróstegui,[2] Tammy M. Martin,[3] Graciela Espada,[4] Lisabeth Scalzi,[5] Jordi Yagüe,[2] James T. Rosenbaum,[6] Consuelo Modesto,[7] Maria Cristina Arnal,[7] Rosa Merino,[8] Julia García-Consuegra,[8] María Antonia Carballo Silva,[9] and Carine H. Wouters[10]

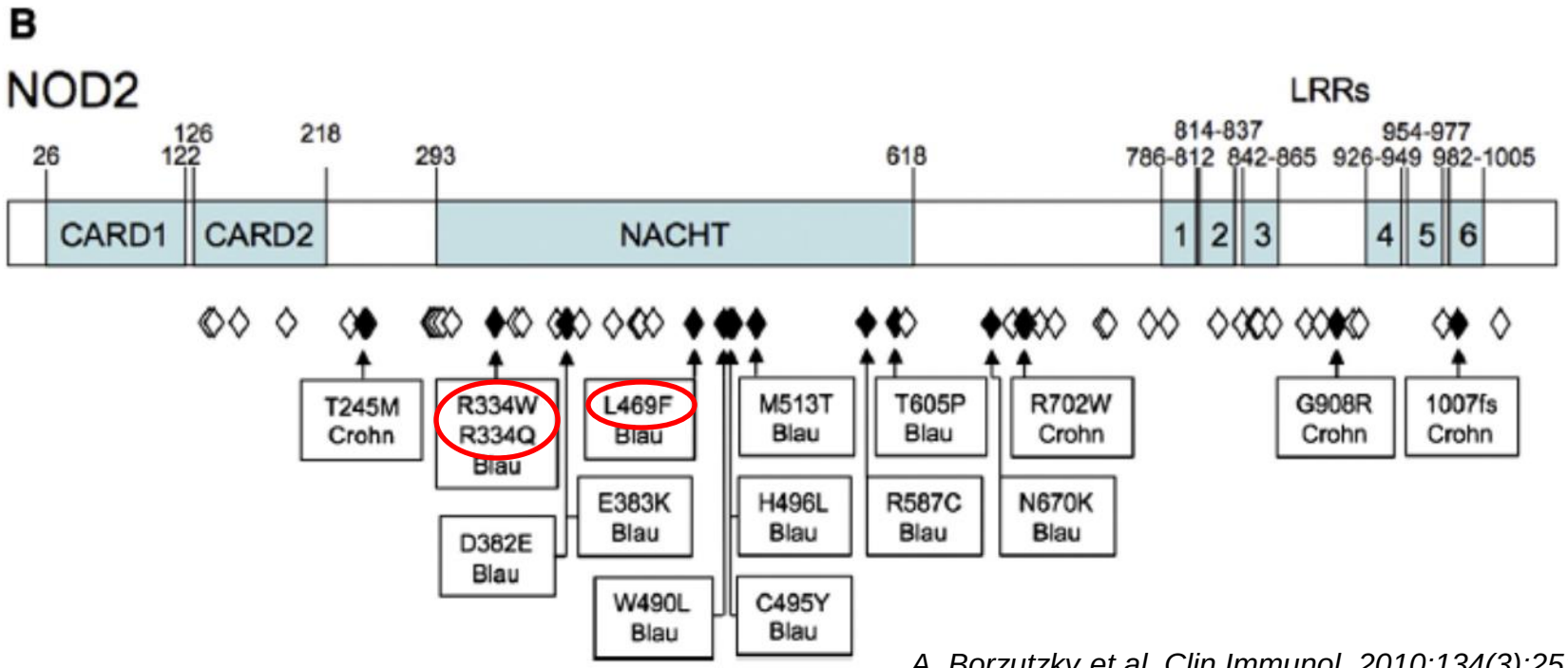
JUVENILE SYSTEMIC GRANULOMATOSIS

GENETICS

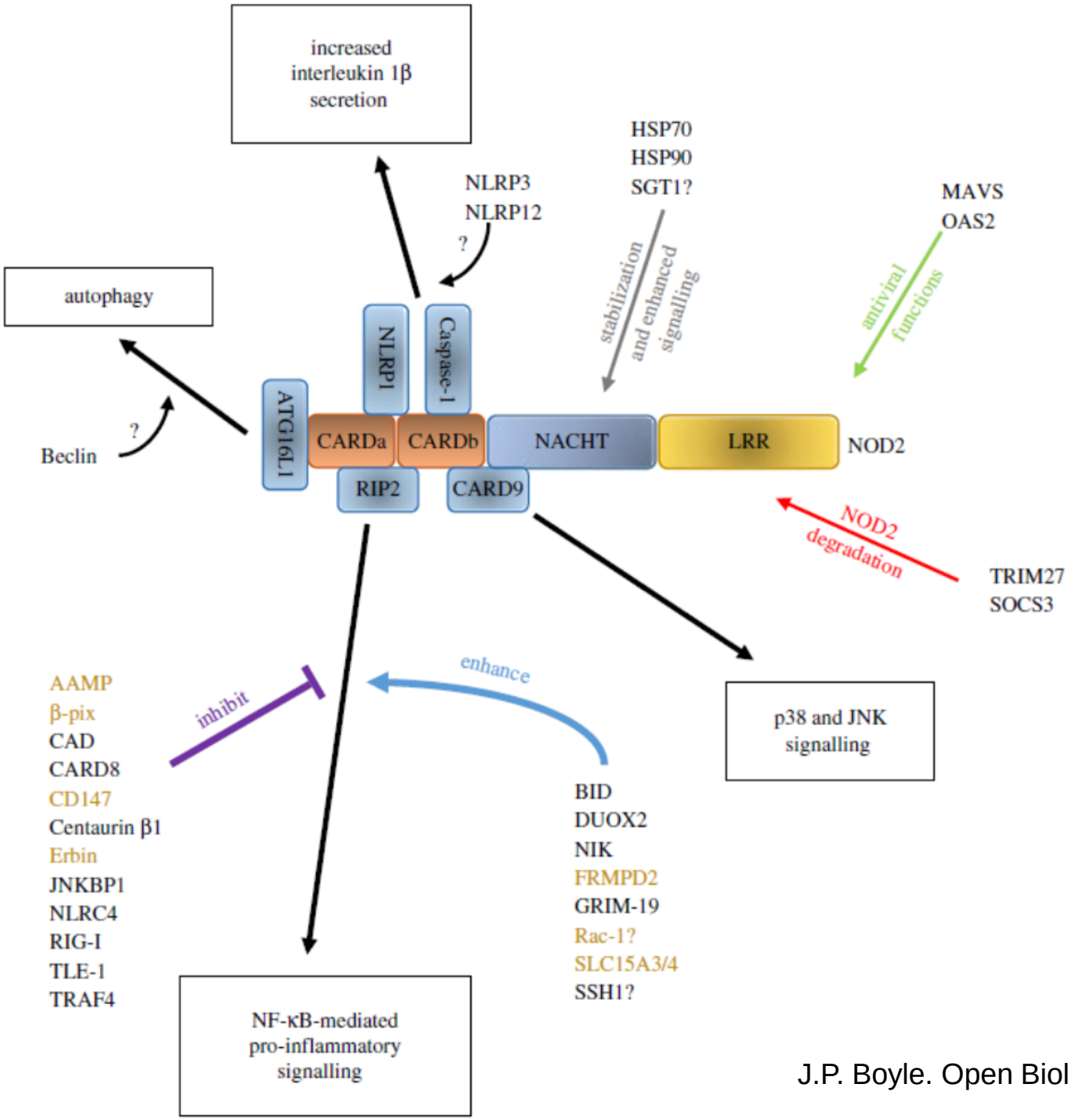
16Q12-21

NOD-2/CARD-15





A. Borzutzky et al. Clin Immunol. 2010;134(3):251-61.



J.P. Boyle. Open Biol. 4: 140178

Table 2 Comparison of typical genetic and clinical features of BS/EOS and CD.

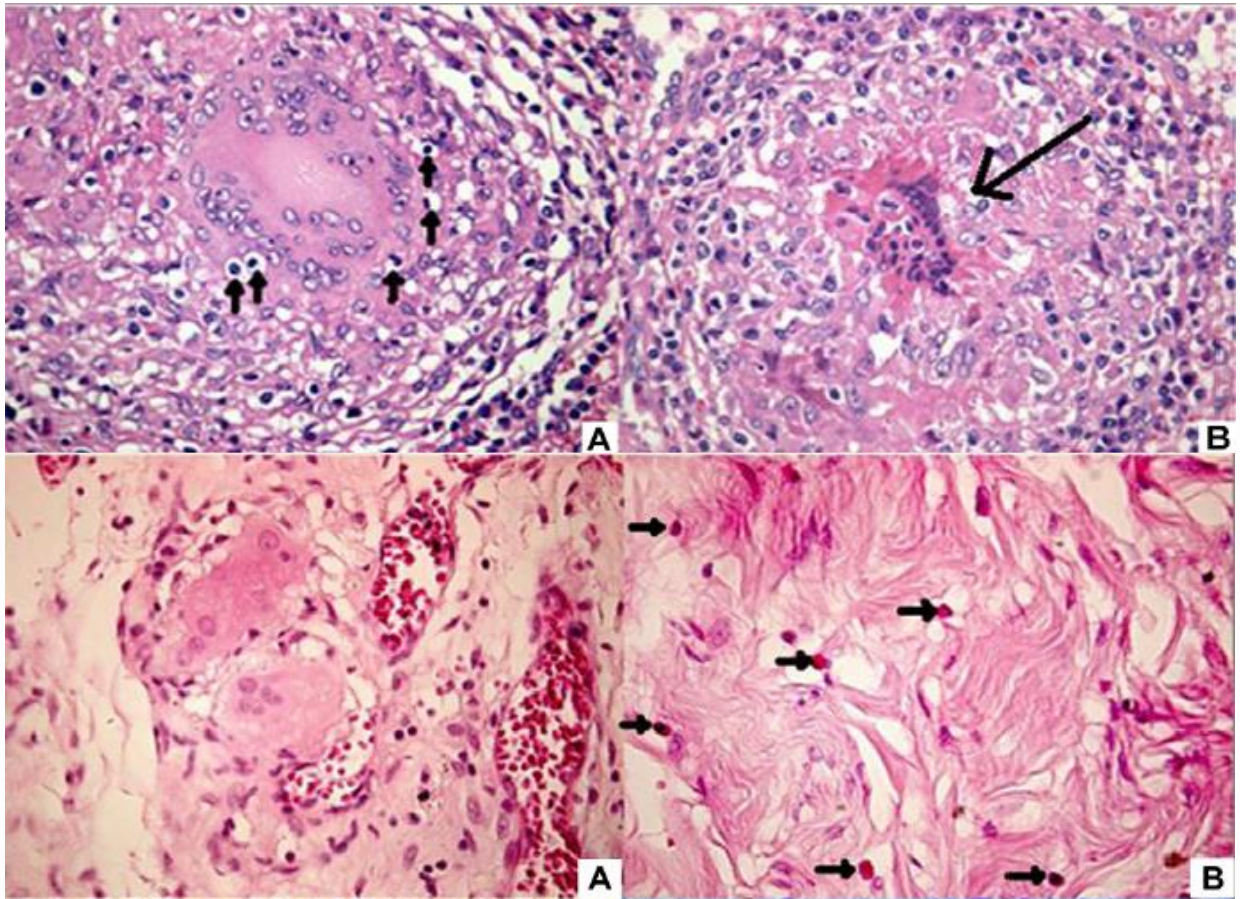
	Blau syndrome/early onset sarcoidosis	Crohn's disease
Genetic features		
Inheritance	Monogenic disorder (NOD2): dominant (BS) and recessive (EOS)	Complex polygenic disorder: NOD2 is a susceptibility gene
Location of NOD2 mutations	NACHT domain	LRR domain
Functional consequences	Increased NF-k B activity (gain-of-function)	Decreased NF-k B activity (loss-of-function)
Clinical features		
Age of onset	<4 years	Late childhood or young adulthood
Arthritis	>90%	10–35%
Skin manifestations	>90%	6–15%
Uveitis	>90%	4–6%
Gastrointestinal tract inflammation	Rare	100%
Location of granulomas	Multisystemic	Gastrointestinal
Treatment	Anti-inflammatory and immunosuppressive drugs	Anti-inflammatory and immunosuppressive drugs

A. Borzutzky et al. Clin Immunol. 2010;134(3):251-61.

Morphologic and immunohistochemical characterization of granulomas in the nucleotide oligomerization domain 2–related disorders Blau syndrome and Crohn disease

Carl E. I. Janssen, MBMS,[a,b] Carlos D. Rose, MD, CIP,[c] Gert De Hertogh, MD, PhD,[a] Tammy M. Martin, PhD,[d] Brigitte Bader Meunier, MD,[e,f,g] Rolando Cimaz, MD,[h] Miroslav Harjacek, MD,[i] Pierre Quartier, MD,[e,f,g] Rebecca Ten Cate, MD,[j] Caroline Thomee, MD,[k] Valeer J. Desmet, MD, PhD,[b] Alain Fischer, MD, PhD,[e,f,g] Tania Roskams, MD, PhD,[b] and Carine H. Wouters, MD, PhD[a] *Leuven, Belgium, Wilmington, Del, Portland, Ore, Paris, France, Florence, Italy, Zagreb, Croatia, Leiden, The Netherlands, and Luxembourg, Luxembourg*

J ALLERGY CLIN IMMUNOL
VOLUME 129, NUMBER 4



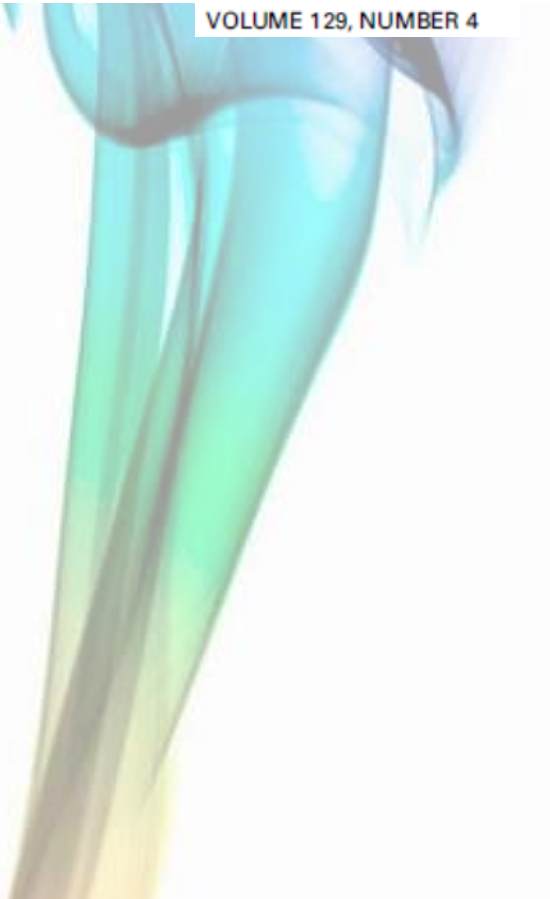


TABLE II. Morphologic and immunohistochemical features of granulomas from both patients with BS and patients with CD

NOD2-related granulomatous disease	BS	*NOD2*$^+$ pediatric CD
Genetics	Monogenic	Polygenic/multifactorial
	Gain-of-function (NOD/NACHT)	Loss-of-function (leucine-rich repeats
	Dominant inherited disease	Recessive familial predisposition
Morphology	n = 6	n = 7
Epithelioid macrophages	+++	+++
MGCs	+++	+++
Langhans-type MGCs	+++	+++
Polycyclic granulomas	+++	+
Lymphocytic coronas	+++	+
Refractive inclusions	+	+
Emperipolesis of lymphocytes	+++	+
MGC apoptosis	++	−
Fibrinoid necrosis	+	−
Caseating necrosis	−	−
Intragranulomatous fibrosis	+	−
Sclerosis of surrounding tissue	+	++
Neutrophils in surrounding tissue	++	+++
Eosinophils in surrounding tissue	+	++
Monocytes in surrounding tissue	+++	+++
Lymphocytes in surrounding tissue	+++	+++
Immunohistochemistry	n = 5	n = 7
CD68$^+$ MMLs	+++	+++
HLA-DR$^+$ MMLs and T lymphocytes	+++	+++
CD4>CD8 T lymphocytes	+++	+++
CD20$^+$ B lymphocytes	++ (n = 4)	++
IL-23R$^+$ MMLs and T lymphocytes	++ (n = 4)	++
TNF-α^+ MMLs and T lymphocytes	++ (n = 4)	+++
IL-6$^+$ MMLs and T lymphocytes	+++ (n = 4)	+
IL-10$^+$ MMLs and T lymphocytes	+ (n = 4)	+
IL-17$^+$ MMLs and T lymphocytes	+++	+
IFN-γ^+ MMLs and T lymphocytes	+++ (n = 4)	+++
TGF-β^+ T lymphocytes	++ (n = 4)	+

Features were scored by using a semiquantitative scoring system: −, absent; +, sporadic; ++, moderate; +++, prominent. Biopsy material of only 4 patients was available.

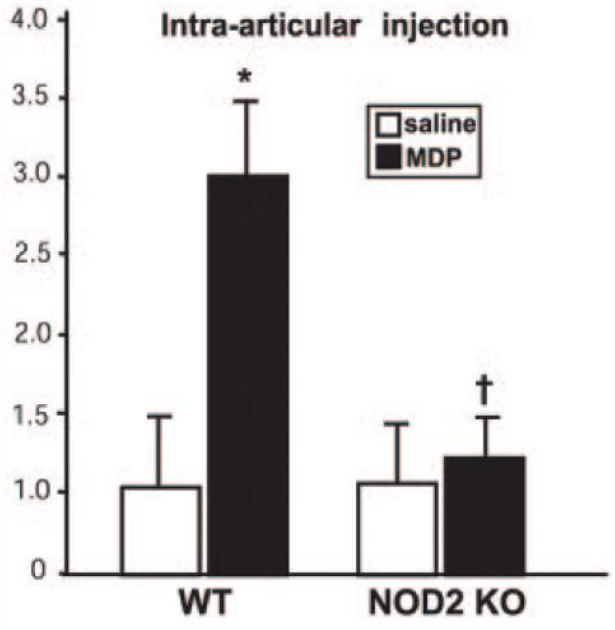
NOD 2 and disease

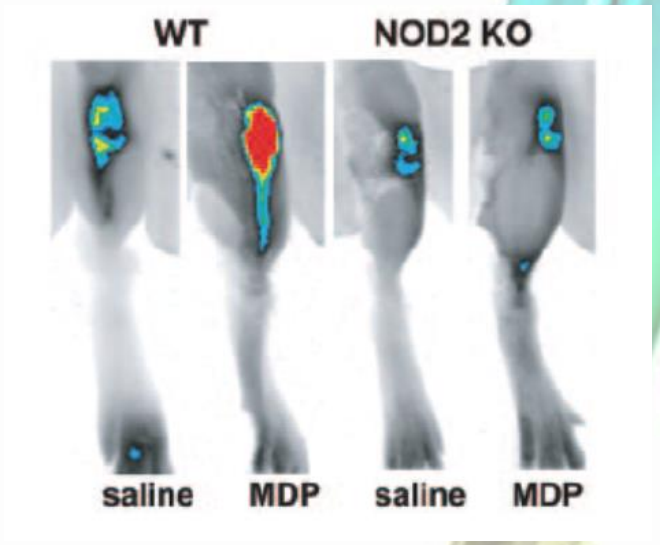
Journal of Leukocyte Biology Volume 85, April 2009

Activation of nucleotide oligomerization domain 2 exacerbates a murine model of proteoglycan-induced arthritis

H. L. Rosenzweig,*,[1] M. M. Jann,[†] T. T. Glant,[‡] T. M. Martin,* S. R. Planck,* W. van Eden,[§] P. J. S. van Kooten,[§] R. A. Flavell,[||] K. S. Kobayashi,[¶] J. T. Rosenbaum,* and M. P. Davey[†]

*Casey Eye Institute, Oregon Health and Science University, Portland, Oregon, USA; [†]Veterans Affairs Medical Center, Portland, Oregon, USA; [‡]Departments of Biochemistry and Orthopedics, Rush University Medical Center, Chicago, Illinois, USA; [§]Divisions of Immunology and Veterinary Medicine, University of Utrecht, Utrecht, The Netherlands; [||]Department of Immunology, Yale School of Medicine, New Haven, Connecticut, USA; and [¶]Department of Cancer Immunology and AIDS, Harvard Medical School, Boston, Massachusetts, USA

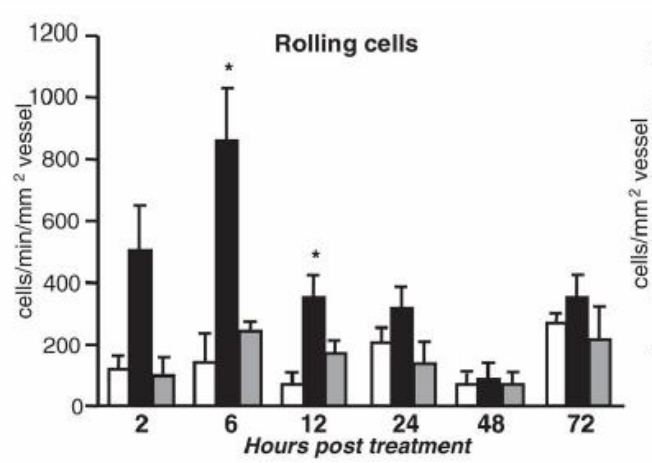


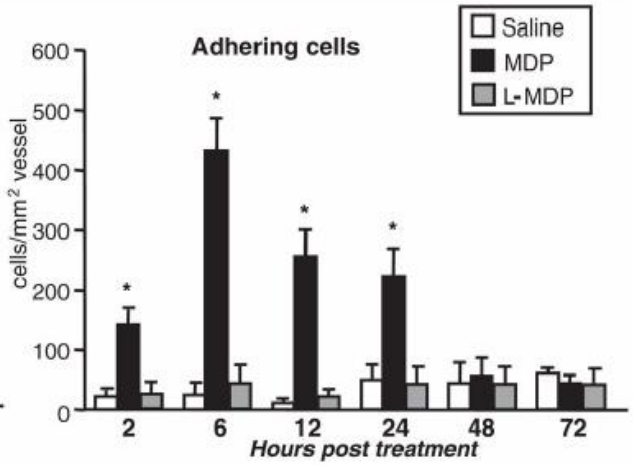


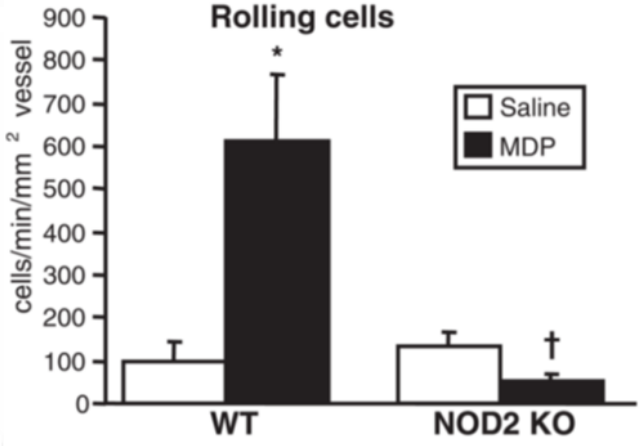
Invest Ophthalmol Vis Sci. 2008 April ; 49(4): 1518–1524.

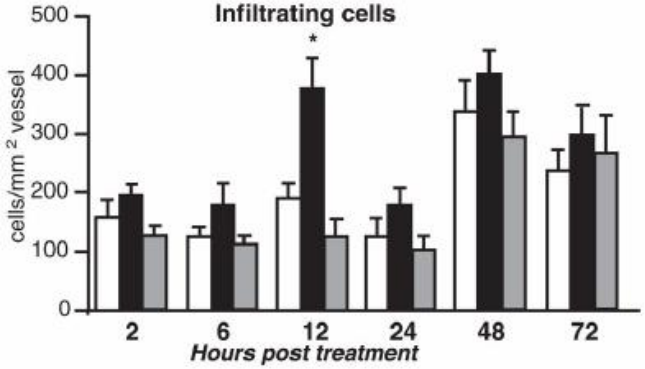
NOD2, the Gene Responsible for Familial Granulomatous Uveitis, in a Mouse Model of Uveitis

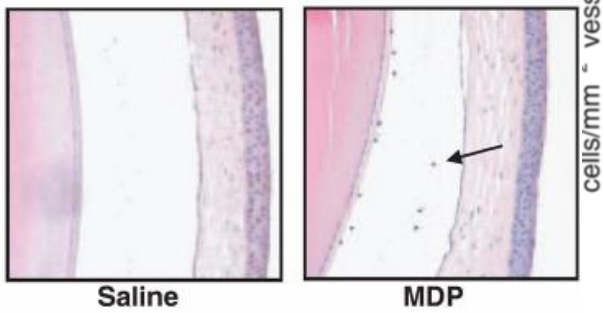
Holly L. Rosenzweig[1], Tammy M. Martin[1,2], Monica M. Jann[3], Stephen R. Planck[1,4,5], Michael P. Davey[2,3,4], Koichi Kobayashi[6], Richard A. Flavell[6], and James T. Rosenbaum[1,4,5]

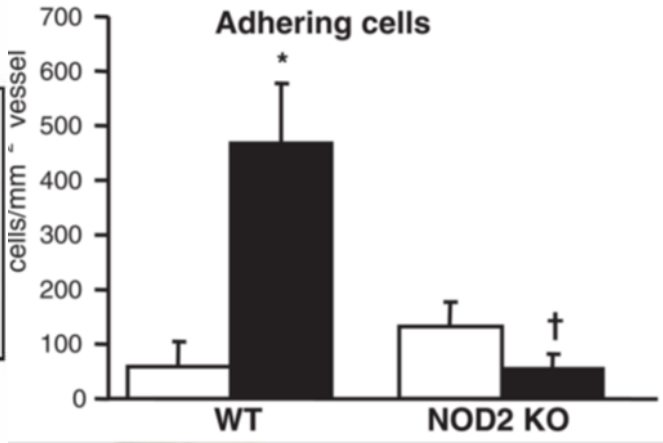






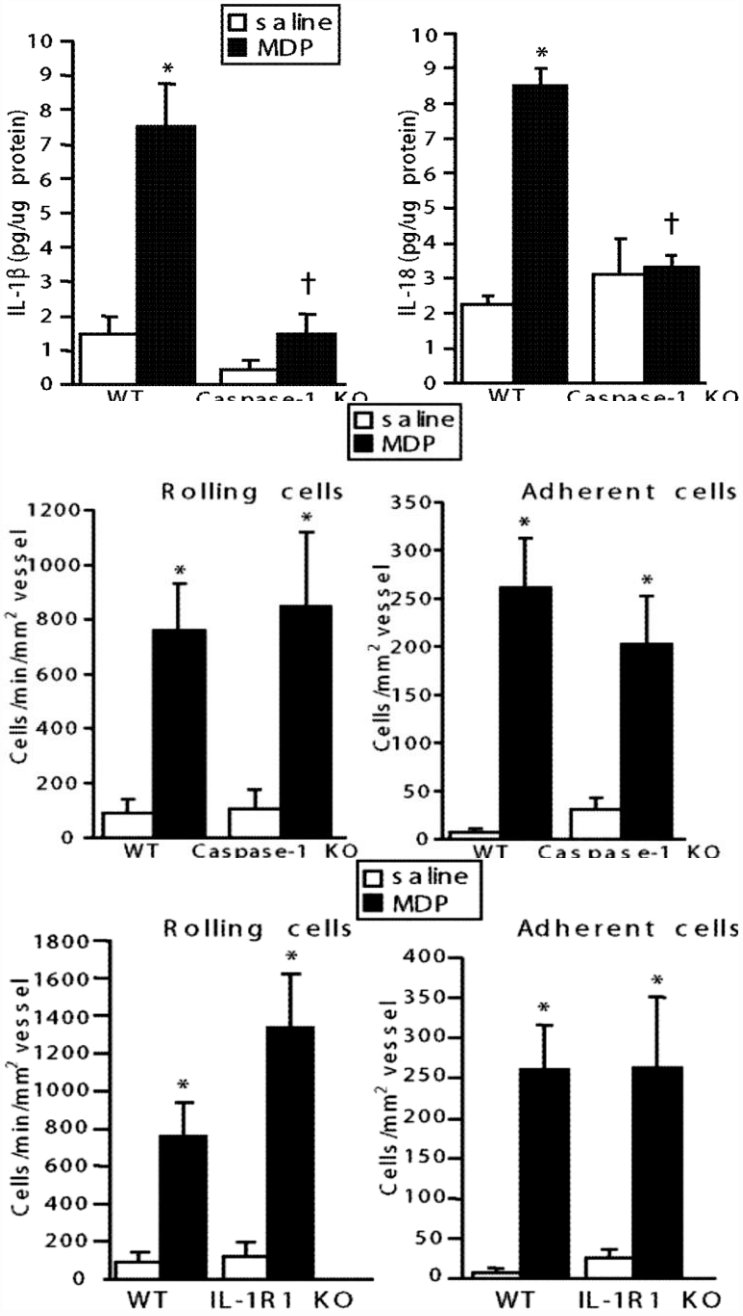


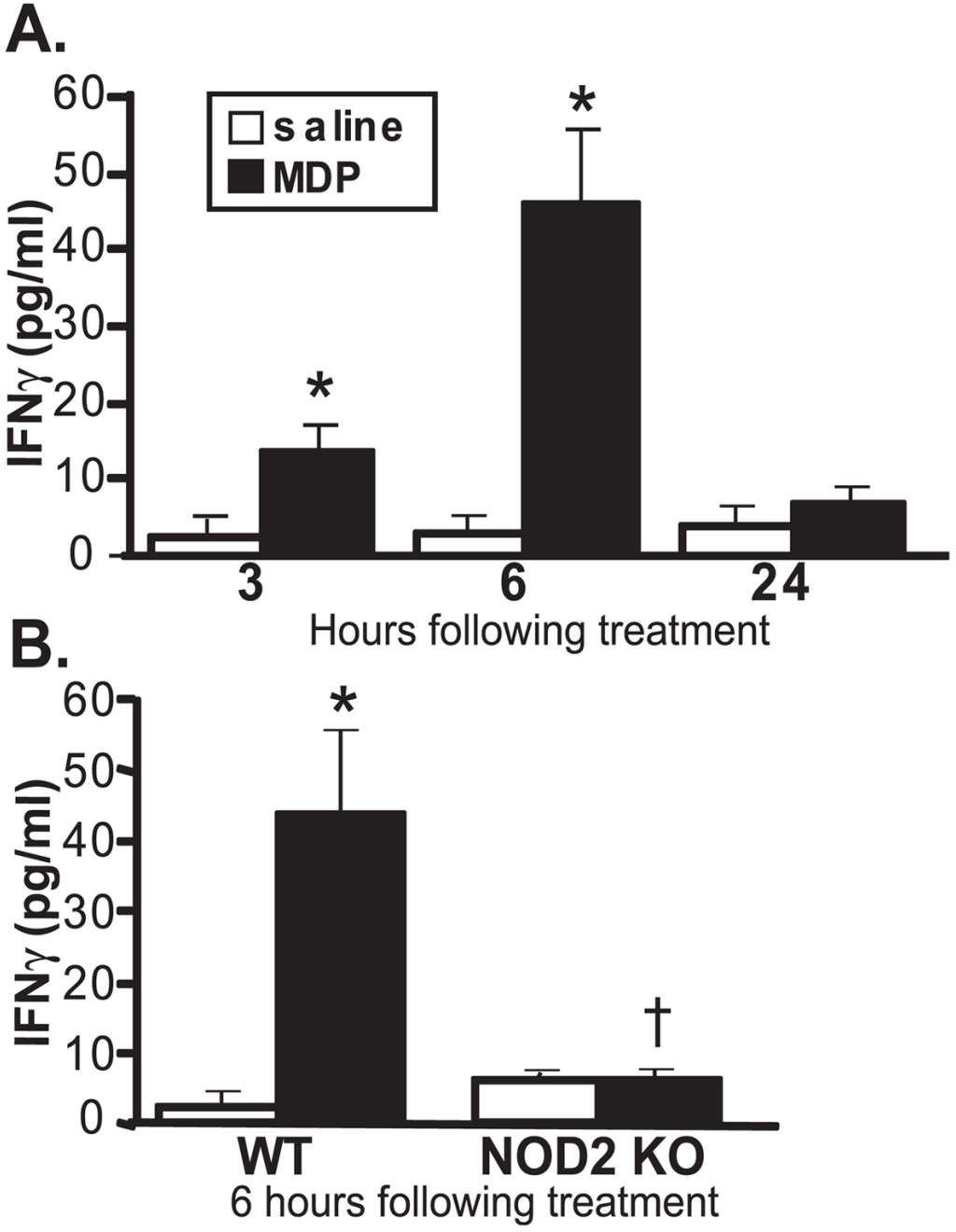




Journal of Leukocyte Biology Volume 84, August 2008

Invest Ophthalmol Vis Sci. 2009 April ; 50(4): 1739–1745.





FAMILIAL: 146

- 60 R334W
- 34 R334Q
- 9 E383K
- ….

SPORADIC: 62

- 24 R334W
- 15 R334Q
- 4 E383K
- ….

MONOGENIC AUTOINFLAMMATORY DISEASE

F. Caso et al. / Autoimmunity Reviews 13 (2014) 1220–1229

NATURAL HISTORY

ARTHRITIS & RHEUMATISM
Vol. 60, No. 6, June 2009, pp 1797–1803
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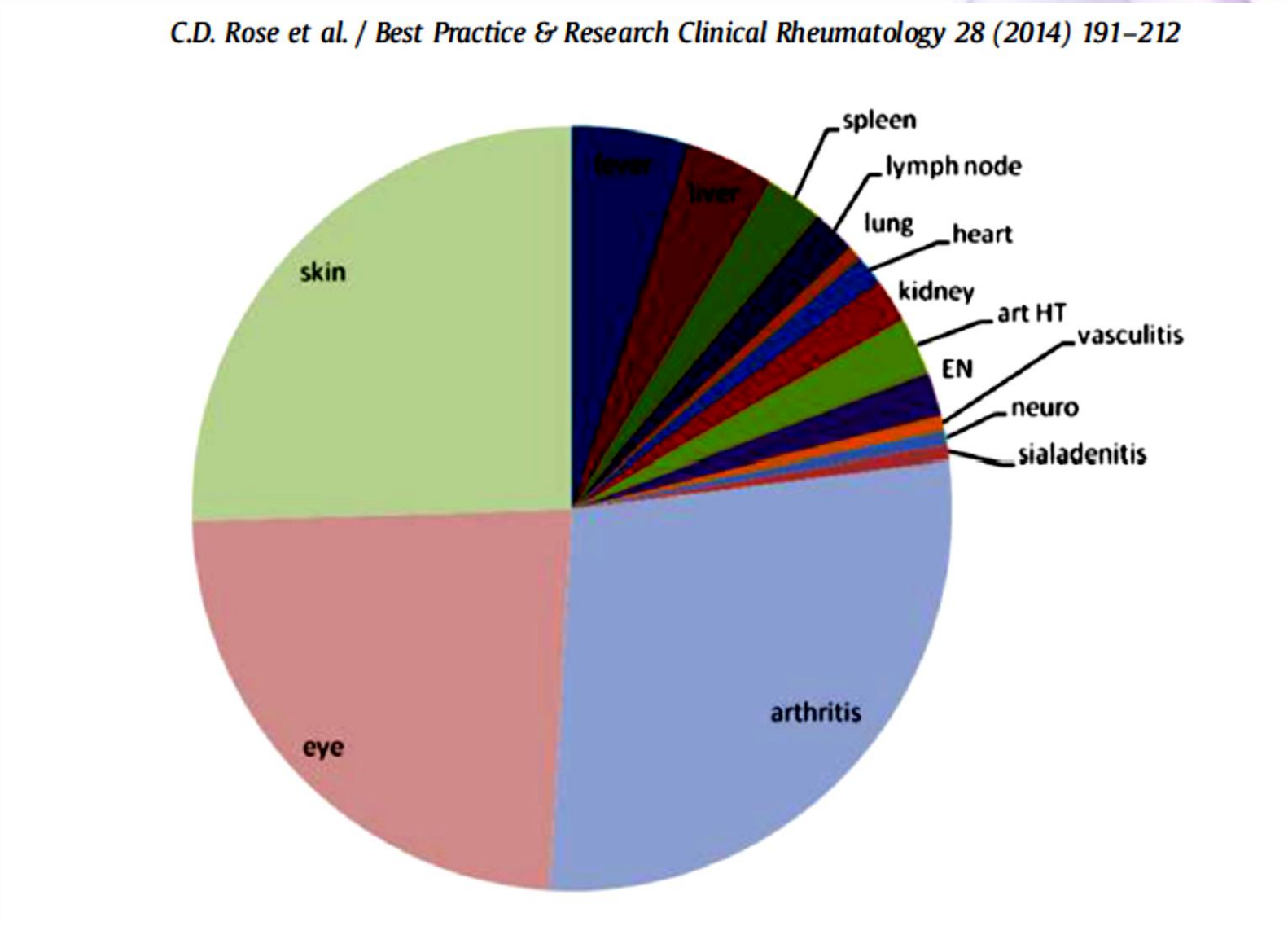
- Earliest: skin rash.
- Arthritis: poliarthritis with tenosynovitis.
- Uveítis: last but not least.

CLINICAL MANIFESTATIONS



Rheumatology Advance Access published February 15, 2015

RHEUMATOLOGY 53, 267

Original article

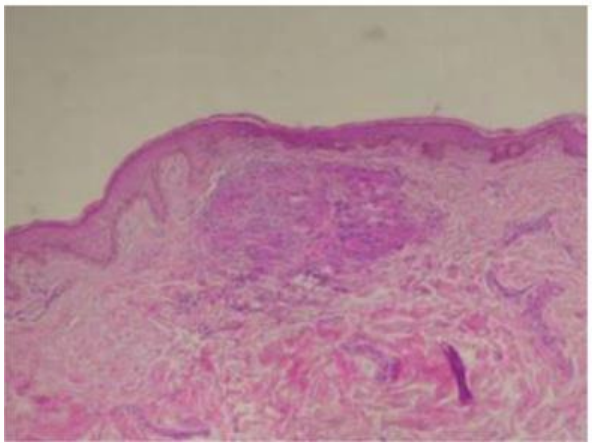
doi:10.1093/rheumatology/keu437

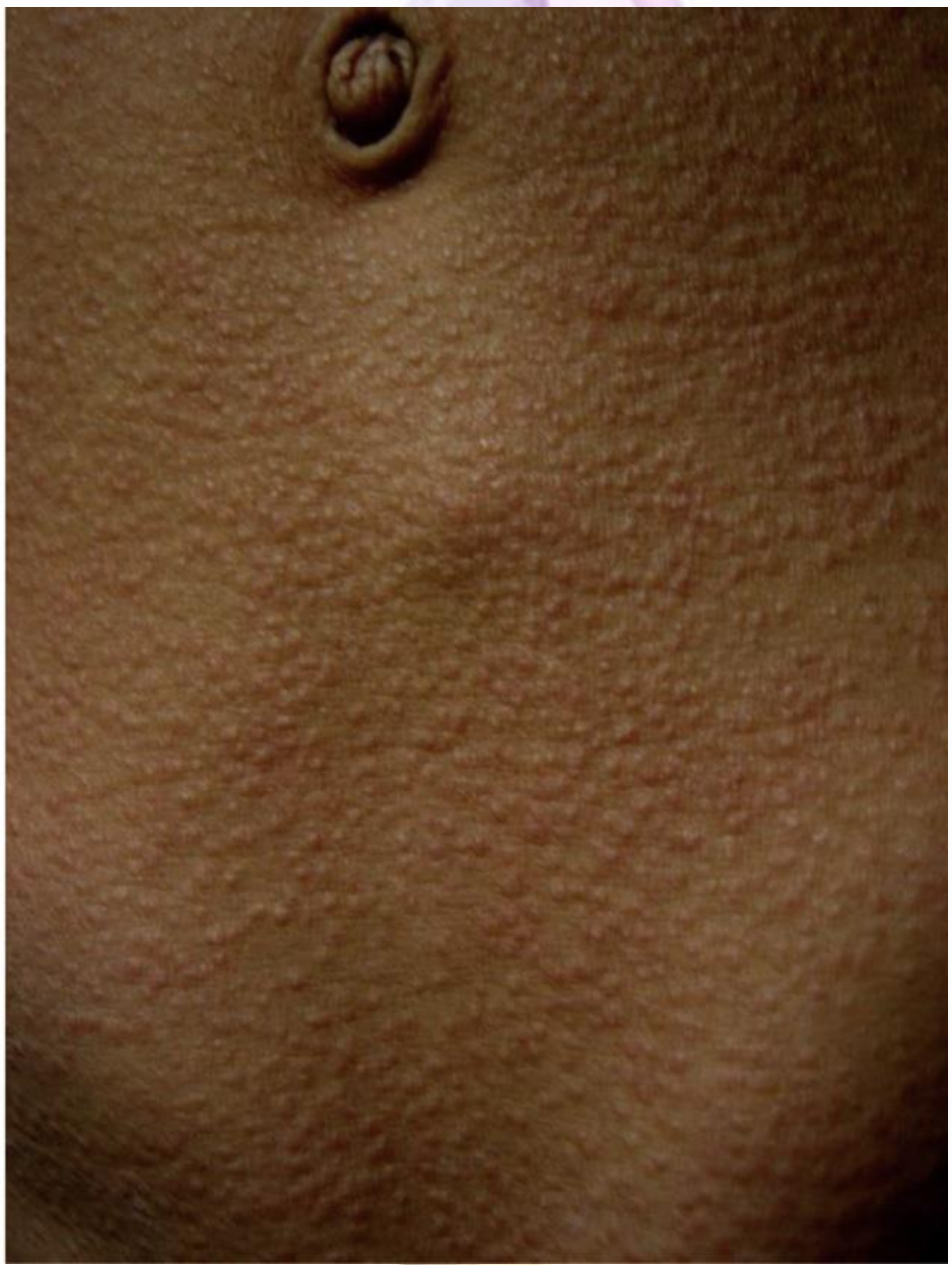
Blau syndrome: cross-sectional data from a multicentre study of clinical, radiological and functional outcomes

Carlos D. Rosé[1], Steven Pans[2], Ingele Casteels[3], Jordi Anton[4], Brigitte Bader-Meunier[5], Philippe Brissaud[6], Roland Cimaz[7], Graciella Espada[8], Jorge Fernandez-Martin[9], Eric Hachulla[10], Miroslav Harjacek[11], Raju Khubchandani[12], Friederike Mackensen[13], Rosa Merino[14], Antonio Naranjo[15], Sheila Oliveira-Knupp[16], Christine Pajot[17], Ricardo Russo[18], Caroline Thomée[19], Sebastiaan Vastert[20], Nico Wulffraat[21], Juan I. Arostegui[22], Kevin P. Foley[23], John Bertin[23] and Carine H. Wouters[24]

SKIN

- **Macular-papular-nodular**.
- **Lichenoid**-like.
- Others: **ptyriasis** lichenoid, leg **ulcers**, **ichtyosis** vulgaris, leuchocytoclastic **vasculitis**, eritema **nodosum**.





ARTHRITIS

Presentation:

OLIGOARTHRITIS (7/31). 22%.

POLYARTHRITIS (23/31). 78%.

- Wrists, ankles, knees, PIPs.
- MCP, elbow (1/3).
- Hip, spine, TMJ (rare).

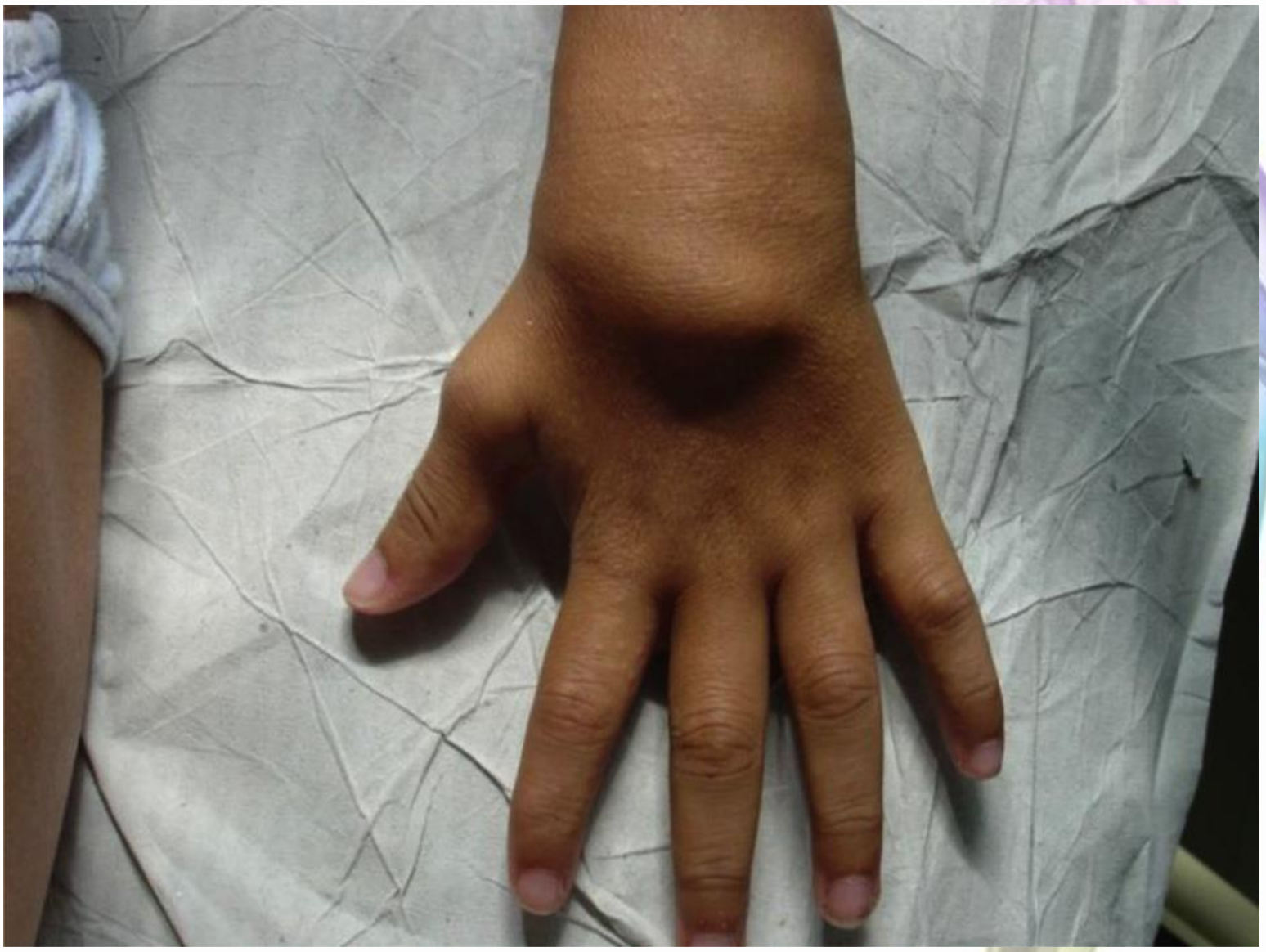
- Symetrical.

81% Limited ROM.

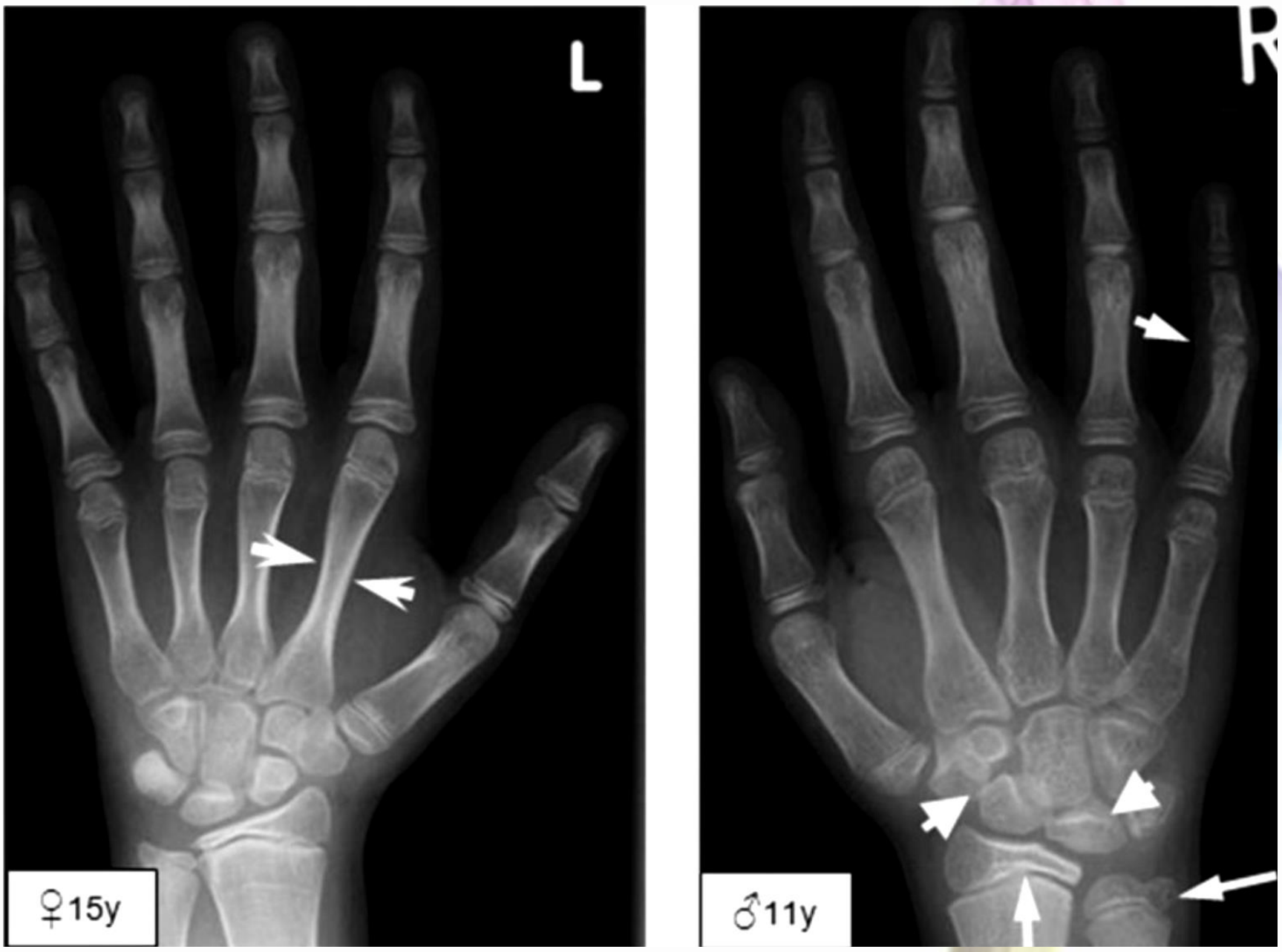
53% Joint deformities.

Camptodactily PIPs.

Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16



C.D. Rose et al. / Best Practice & Research Clinical Rheumatology 28 (2014) 191–212



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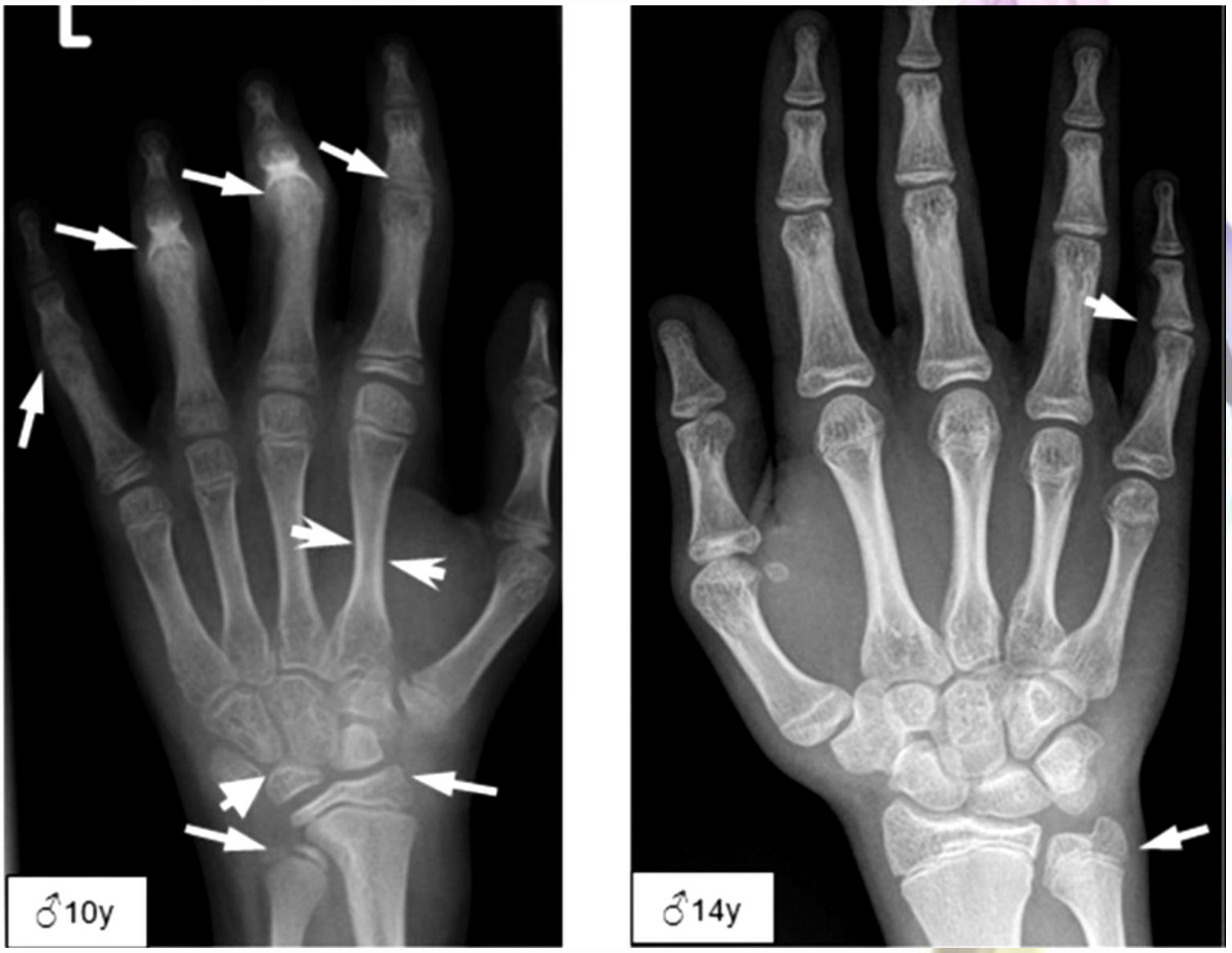

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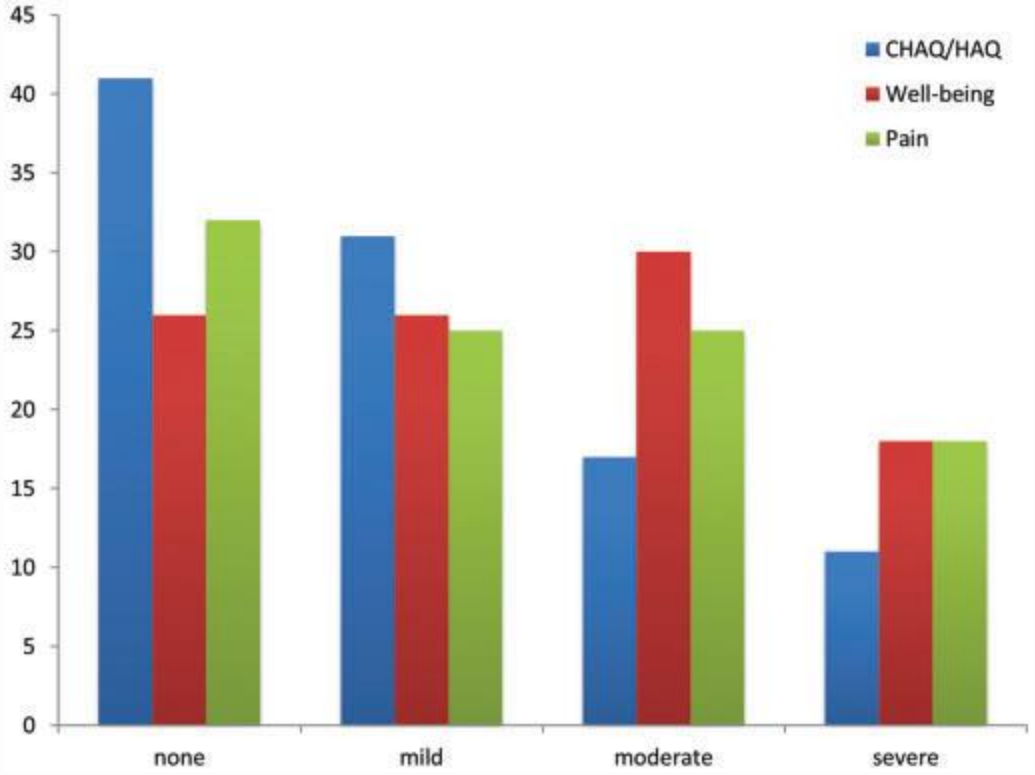


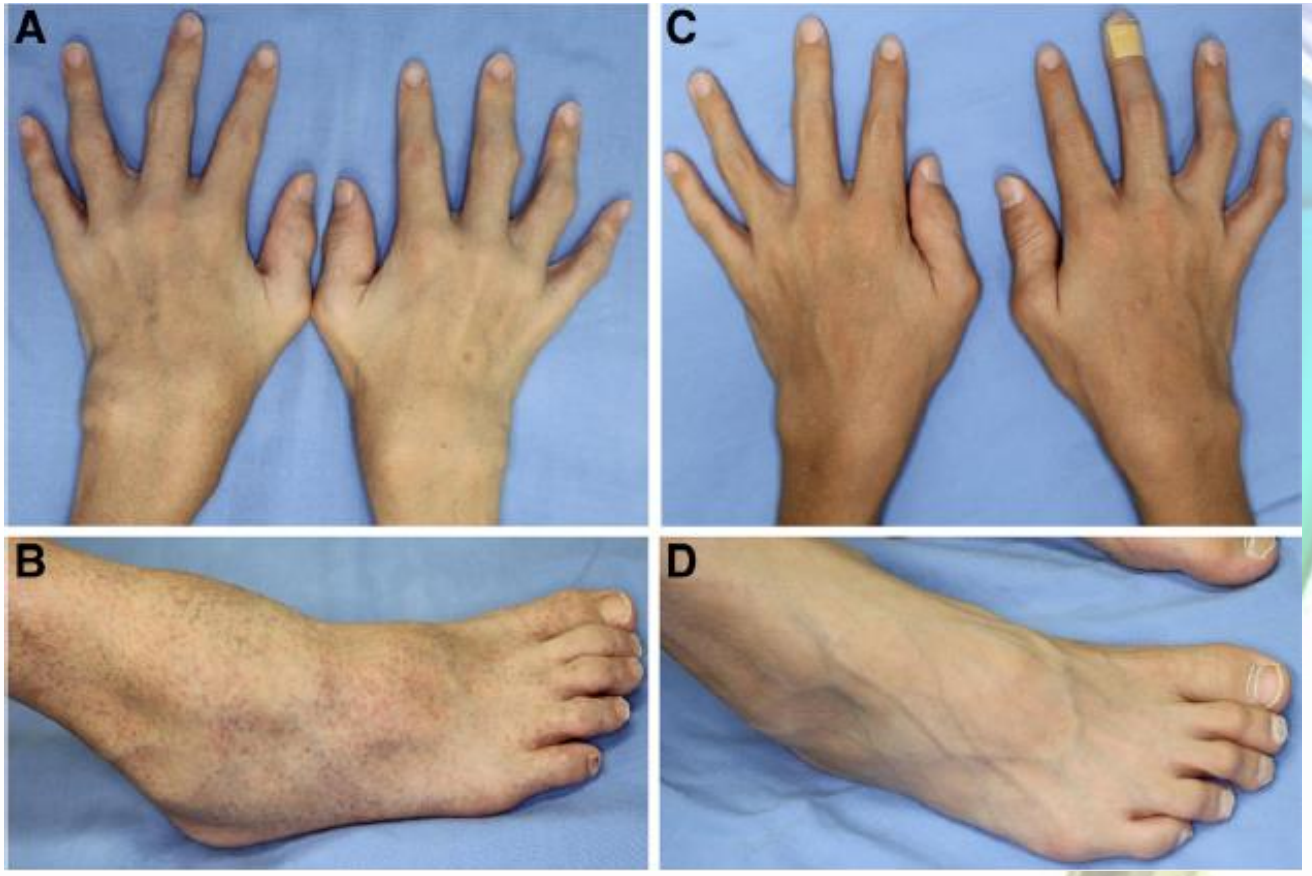
48% moderate to severe impact on well being.

31% no pain at all.

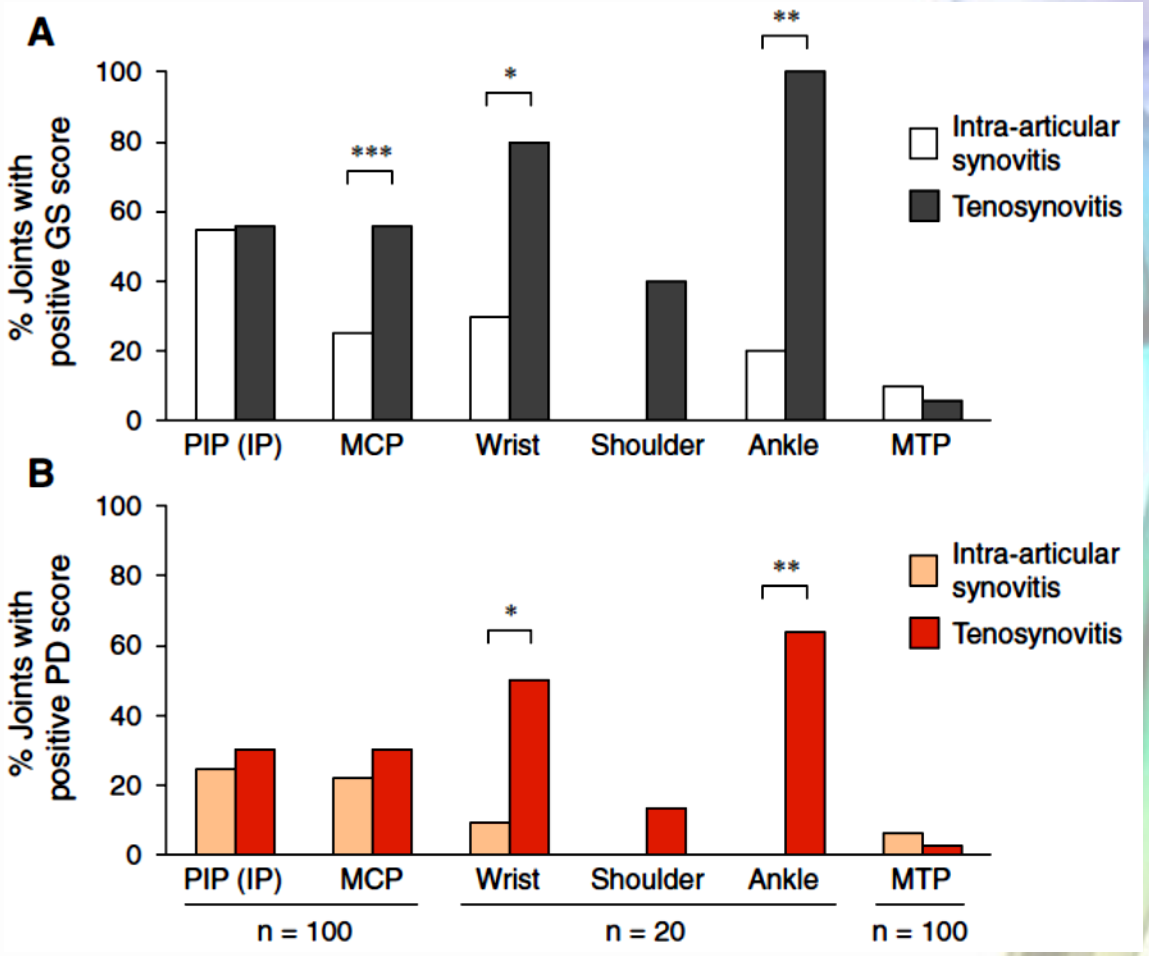
41% normal function.

Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16

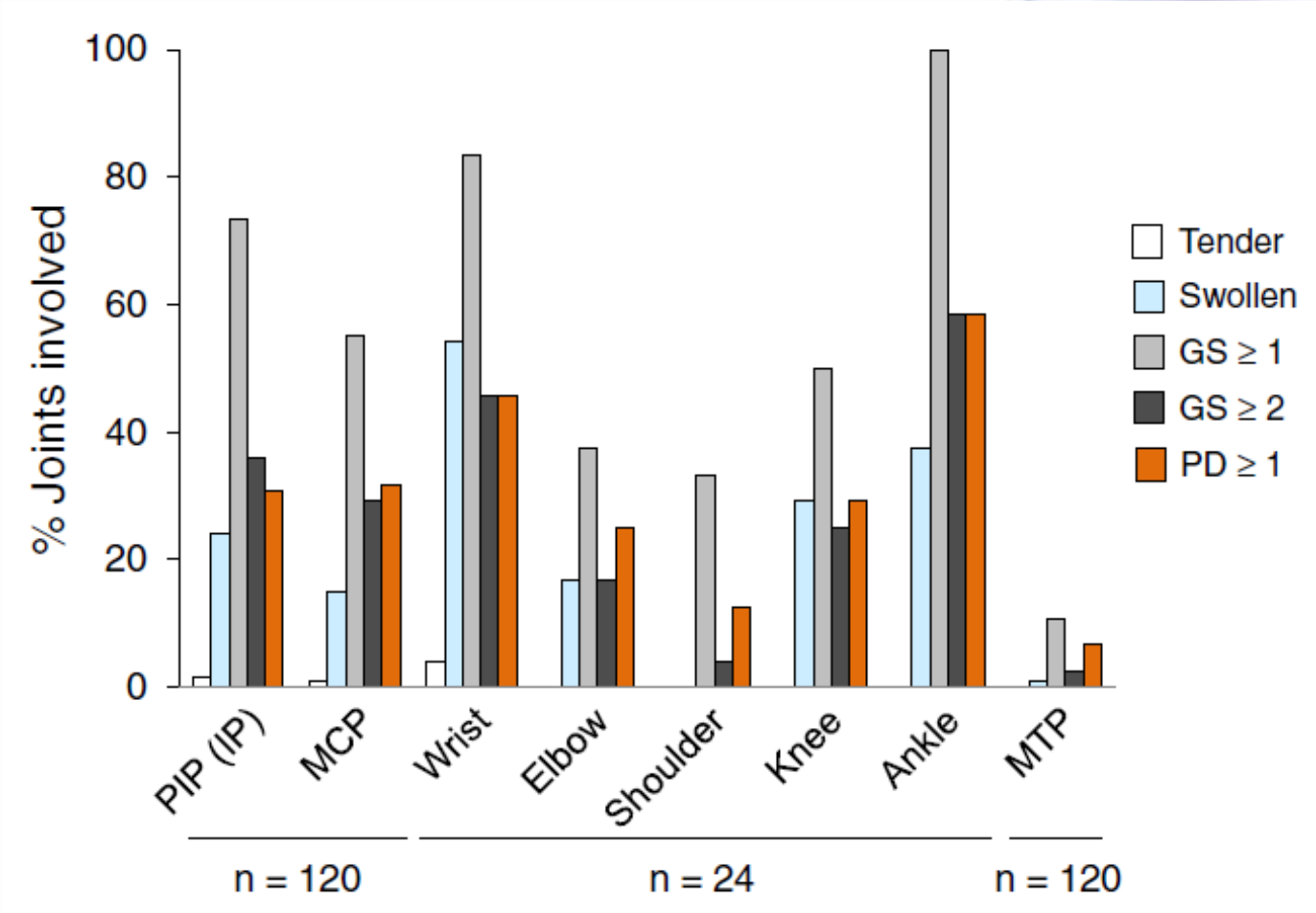
Ultrasonographic assessment reveals detailed distribution of synovial inflammation in Blau syndrome



Ikeda *et al. Arthritis Research & Therapy* 2014, **16**:R89



Ikeda *et al. Arthritis Research & Therapy* 2014, **16**:R89

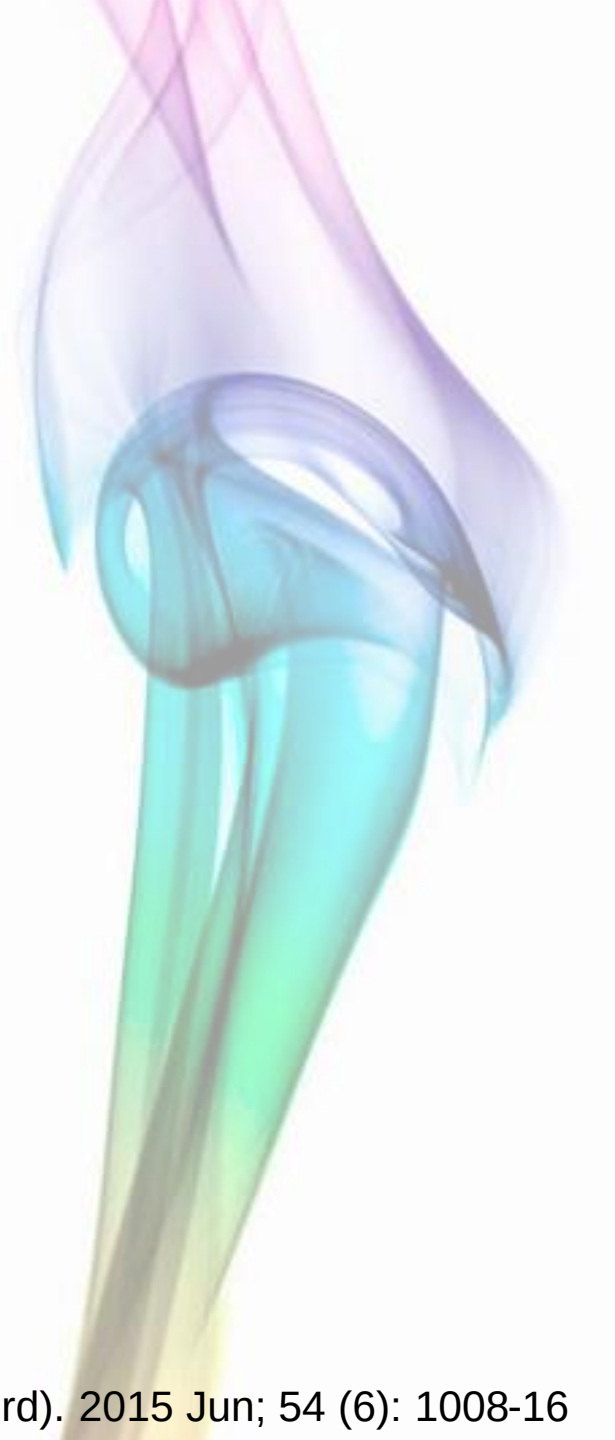


Ikeda *et al. Arthritis Research & Therapy* 2014, **16**:R89

UVEITIS (81%)

Bilateral (96%).

- ANTERIOR (100%)
- INTERMEDIATE (52%)
- POSTERIOR (72%)
- HTO (36%).



Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16

SEQUELAE

ANTERIOR POLE

- Sinechiae 64%
- Cataracts 55%
- Band Cheratopathy 23%

POSTERIOR POLE

- Optic atrophy 14%
- Macular edema 14%
- Retinal detachment 9%

logMAR scale:
- 68% AVC normal
- 18% AVC moderate
- 14% AVC severe

Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16

Optic nerve and retinal features in uveitis associated with juvenile systemic granulomatous disease (Blau syndrome)

Ester Carreño,[1] Catherine M. Guly,[1] Michael Chilov,[2] Annie Hinchcliffe,[1] Juan I. Arostegui,[3] Richard W. J. Lee,[1,4] Andrew D. Dick[1,4] and Athimalaipet V. Ramanan[5]

[1]Bristol Eye Hospital, University Hospitals Bristol NHS Foundation Trust, Bristol, UK
[2]Save Sight Institute, University of Sydney, Sydney, New South Wales, Australia
[3]Department of Immunology-CDB, Hospital Clinic-IDIBAPS, Barcelona, Spain
[4]School of Clinical Sciences, Faculty of Medicine, University of Bristol, Bristol, UK
[5]Department of Pediatric Rheumatology, Bristol Royal Hospital for Children, Bristol, UK

89% BILATERAL

100% CHRONIC

Duration 15 yrs.

29% ANTERIOR

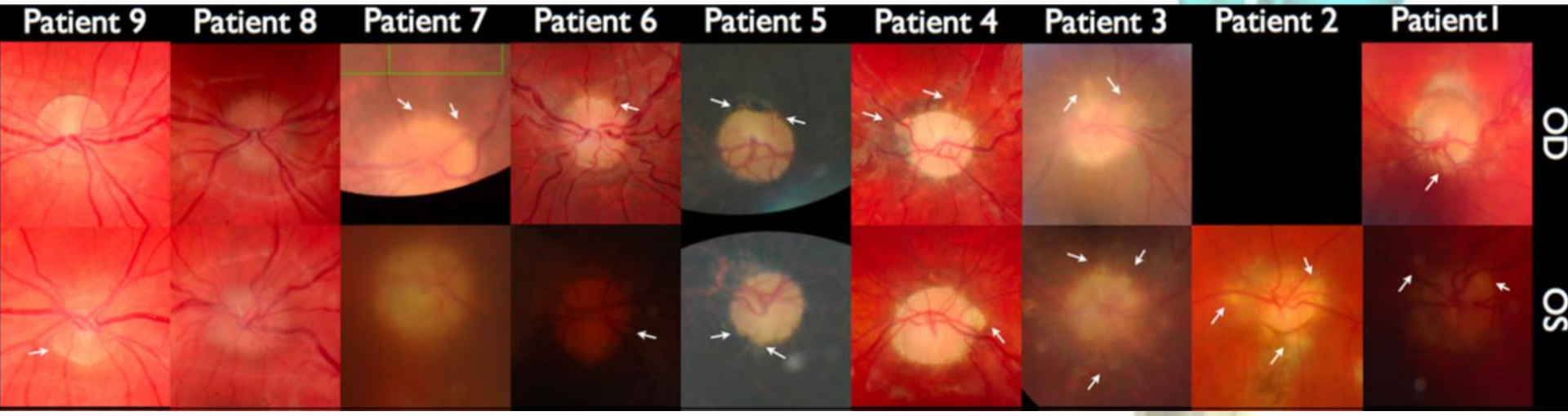
12% INTERMEDIATE

59% PANUVEITIS

Acta Ophthalmol. 2015 May;93(3):253-7

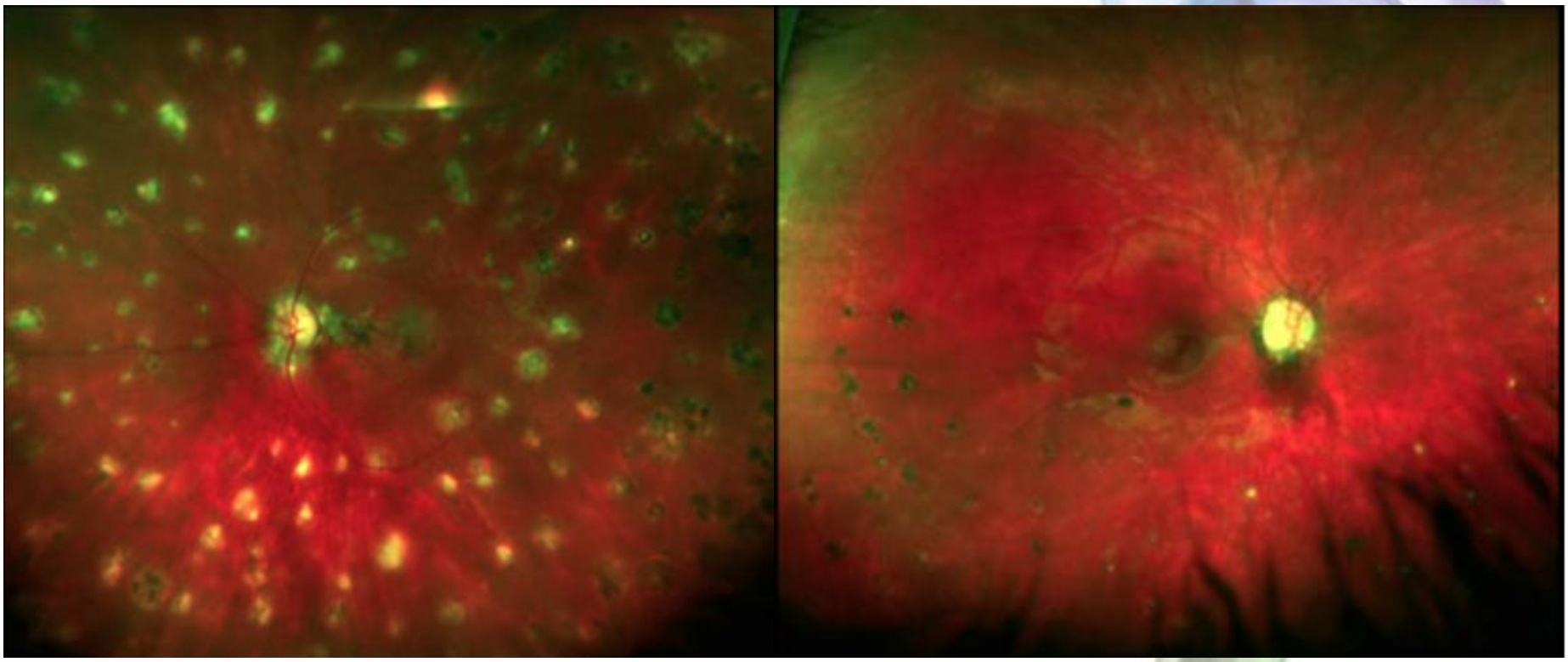
G	Age at onset (months)	Laterality		VA	Anatomical classification	Course	Ocular phenotype	Localization lesions	On margin	On colour	On vessels	Peripapillary area colour	Peripapillary excrescence	NOD2 genotype
F	60	BE	OD	1.3	Panuveitis	Chronic	MFC	Outside	Normal	Pale	Normal	Hypopigmented	Nodular	p.R334W/wt
			OS	0.8	Panuveitis	Chronic	MFC	Outside	Normal	Normal	Normal	Mixed	Nodular	
M	36	BE	OD	3	Panuveitis	Chronic	MFC	Inside + outside	U	U	U	U	U	p.Q809K/wt
			OS	0.3	Panuveitis	Chronic	MFC	Inside + outside	Normal	Normal	Normal	Mixed	Nodular	
M	3	BE	OD	0.8	Panuveitis	Chronic	MFC	Outside	Blurred	Pale	Sheathed	Mixed	Nodular	p.E383D/
			OS	0.2	Panuveitis	Chronic	MFC	Outside	Blurred	Pale	Sheathed	Hypopigmented	Nodular	p.D390V
M	15	BE	OD	0	Panuveitis	Chronic	MFC	Outside	Normal	Pale	Normal	Mixed	Nodular	P.h520y/wt
			OS	0	Panuveitis	Chronic	MFC	Outside	Normal	Pale	Normal	Mixed	Nodular	
F	1	BE	OD	0.4	Panuveitis	Chronic	MFC	Outside	Normal	Normal	Normal	Mixed	Nodular	p.R334Q/wt
			OS	0.1	Panuveitis	Chronic	MFC	Outside	Normal	Normal	Normal	Mixed	Nodular	
M	60	BE	OD	0	Anterior	Chronic	No MFC	N/A	Normal	Normal	Normal	Hypopigmented	Nodular	p.R334Q/wt
			OS	0	Anterior	Chronic	No MFC	N/A	Normal	U	Normal	U	Nodular	
F	–	BE	OD	0.3	Anterior	Chronic	No MFC	N/A	Blurred	Normal	Normal	Hypopigmented	Nodular	p.R334W/wt
			OS	0.5	Anterior	Chronic	No MFC	N/A	Blurred	Pale	Normal	Hypopigmented	None	
F	18	BE	OD	0.1	Intermediate	Chronic	No MFC	N/A	Blurred	Normal	Sheathed	Hypopigmented	None	p.R334W/wt
			OS	0.4	Intermediate	Chronic	No MFC	N/A	Blurred	Normal	Sheathed	Normal	None	
M	18	OS	OS	0	Anterior	Chronic	No MFC	N/A	Normal	Normal	Normal	Normal	Nodular	p.R334W/wt

LogMAR scale
Median 0,48



Acta Ophthalmol. 2015 May;93(3):253-7

MULTIFOCAL CORIORETINITIS



10%

90%

Acta Ophthalmol. 2015 May;93(3):253-7

EXPANDED MANIFESTATIONS (52%)

Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16

TABLE 2 Clinical description and *NOD2* mutations observed in 16 patients with expanded manifestations

Patient	*NOD2* mutation	Expanded manifestations
4	R334Q	GL
5	R334Q	Transient facial palsy
6	R334Q	ILD, pulmonary embolism (single episode)
7	R334Q	Hepatomegaly (hepatic granuloma), GL (granulomatous), ILD, sialadenitis, EN
9	R334Q	HT
10	R334W	HT, GL
13	R334W	Recurrent fever, GL
14	R334W	Recurrent fever, GL, interstitial nephritis (granulomatous)
16	A755V	Recurrent fever, EN, HT, ILD, interstitial nephritis
17	G481D	GL, splenomegaly (required splenectomy), ILD, transient facial palsy, HT, ischaemic stroke, nephrocalcinosis
19	R334W	EN
21	E383K	GL, hepatomegaly, splenomegaly
24	G464W	HT, large vessel vasculitis (Takayasu's-like), hepatomegaly
25	C495Y	Hepatitis (granulomatous), splenomegaly
27	R334W	ILD, nephrocalcinosis
28	R334Q	Recurrent fever, EN, leucocytoclastic vasculitis, interstitial and glomerulonephritis (granulomatous)

HT: hypertension; EN: erythema nodosum; GL: generalized lymphadenopathy; ILD: interstitial lung disease.

Rheumatology (Oxford). 2015 Jun; 54 (6): 1008-16

Patient	Systemic drugs	Topical steroids	Articular control	Ocular control	Expanded disease resolved
1	—	Yes	Yes	No	NA
2	MTX, CS	No	No	NA	NA
3	MTX	No	No	NA	NA
4	MTX, CS	Yes	No	No	No
5	A, MTX, CS	Yes	No	No	Yes
6	CS	No	No	Yes	Yes
7	CS, I	No	No	No	Yes
8	I	Yes	No	No	NA
9	CS, A	Yes	No	No	Yes
10	CS, A	Yes	No	No	Yes
11	MTX	NA	No	NA	NA
12	CS, MTX, C	Yes	Yes	No	NA
13	A, MTX	Yes	No	No	Yes
14	MTX, CS, A	Yes	No	No	Yes
15	MTX, A	Yes	Yes	No	NA
16	MTX, A	NA	NA	NA	Yes
17	Th, CS	Yes	No	No	No
18	MTX, A	Yes	Yes	No	NA
19	CS, A	Yes	No	No	No
20	MTX, A	Yes	No	No	NA
21	I	Yes	Yes	Yes	Yes
22	MTX, I	No	Yes	No	NA
23	CS	Yes	No	No	NA
24	CS, MTX	NA	Yes	NA	No
25	CS	No	No	No[a]	No[b]
26	MTX, A	No	Yes	Yes	NA
27	CS, MTX, A	Yes	No	No	Yes
28	CS, MMF	No	No	No	No[c]
29	CS, A	No	No	No	NA
30	CS	NA	No	NA	NA
31	MTX	No	No	No	NA

CS: systemic corticosteroids; I: Infliximab; A: adalimumab; C: canakinumab; TH: thalidomide; NA: manifestation not present. [a]Had end-stage eye disease. [b]Hepatomegaly resolved, splenomegaly persisted. [c]Fever persisted.

TREATMENT

- 5/9: Combination therapy: CS + IS (2 MMF, 2 MTX, 1 MMF + MTX) + anti TNF (3 A, 2 I).
- 1/9: CS + IV MP + I
- 2/9: CS + I (1 intraocular dexametasone implant).
- 1/9: Topical CS.

Acta Ophthalmol. 2015 May;93(3):253-7

TREATMENT

- **CORTICOSTEROIDS**

  Topical, intraarticular, intravitreal, oral or e.v.

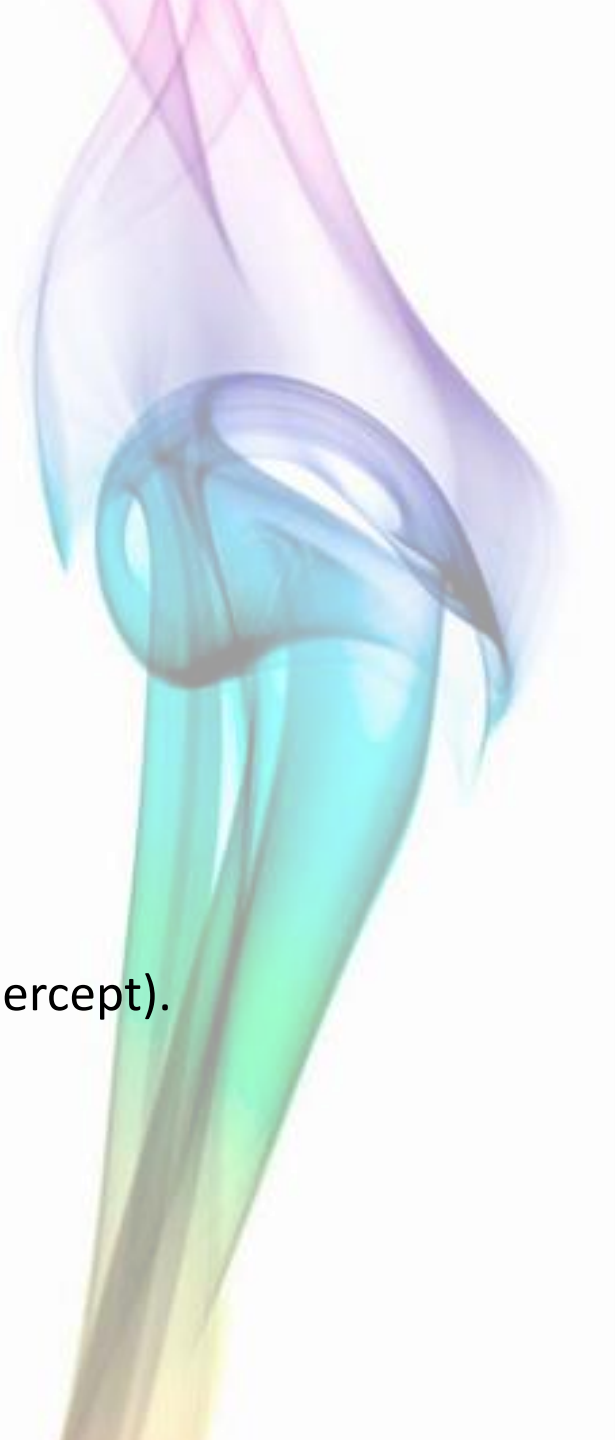
- **INMUNOSUPRESIVE**

  MTX, MMF, AZA, CsA.

- **BIOLOGICS**

1. ANTI TNFalpha: Infliximab, Adalimumab, (Etanercept).

2. ANTI IL-1: Anakinra, Canakimumab.



ARTHRITIS & RHEUMATISM
Vol. 56, No. 11, November 2007, pp 3805–3813
DOI 10.1002/art.22966

NOD2 Gene–Associated Pediatric Granulomatous Arthritis

Clinical Diversity, Novel and Recurrent Mutations, and Evidence of Clinical Improvement With Interleukin-1 Blockade in a Spanish Cohort

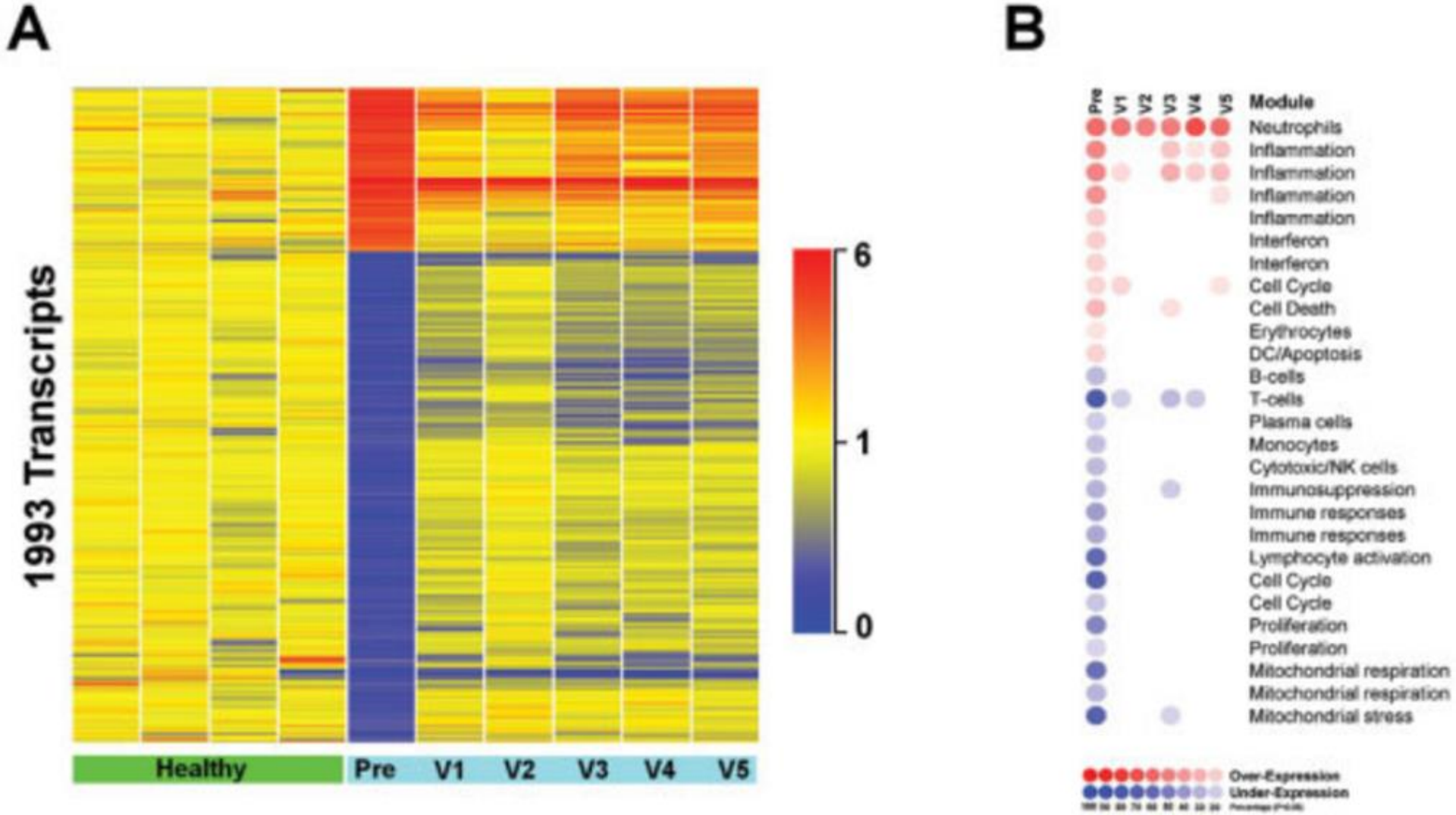
Juan I. Aróstegui,[1] Cristina Arnal,[2] Rosa Merino,[3] Consuelo Modesto,[2] María Antonia Carballo,[4] Purificación Moreno,[5] Julia García-Consuegra,[3] Antonio Naranjo,[6] Eduardo Ramos,[7] Pilar de Paz,[2] Josefa Rius,[1] Susana Plaza,[1] and Jordi Yagüe[1]

ARTHRITIS & RHEUMATISM
Vol. 60, No. 2, February 2009, pp 611–618
DOI 10.1002/art.24222

The *NOD2* Defect in Blau Syndrome Does Not Result in Excess Interleukin-1 Activity

Tammy M. Martin,[1] Zili Zhang,[1] Paul Kurz,[1] Carlos D. Rosé,[2] Hong Chen,[1] Huiying Lu,[1] Stephen R. Planck,[1] Michael P. Davey,[3] and James T. Rosenbaum[1]

ARTHRITIS & RHEUMATISM
Vol. 65, No. 2, February 2013, pp 513–518
DOI 10.1002/art.37776




Le Havre
Luxembourgo
Mannheim
Nuremberg
Plzen
REPÚBLICA TCHECA
Ostrava
Lviv
Paris
Karlsruhe
Strasbourg
Stuttgart
Brno
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Viena
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Peloponeso
Annaba
Tunis
Algiers
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Constantine
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Estreito de Gibraltar
Gibraltar
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MALTA
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Iraklion
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Rabat
Mar Mediterrâneo
Casablanca
Medenine
Tripoli

CASE REPORT

HOSPITAL CLINICO UNIVERSITARIO VIRGEN DE LA ARRIXACA

MURCIA

CASE 1

2007. Spain. Healthy female. American aboriginal ancestry (Ecuador).

2009. Return to Ecuador.

Fever + Rash + Arthritis.

Arthrotomy both ankles. (Typhoid fever).

Treatment for one month (antibiotics?)

2011. Return to Spain with her father (health related).

LORCA

2011(May) Hospitalization.

40 day fever + asthenia + abdominal pain + arthritis.

2011 to 2013

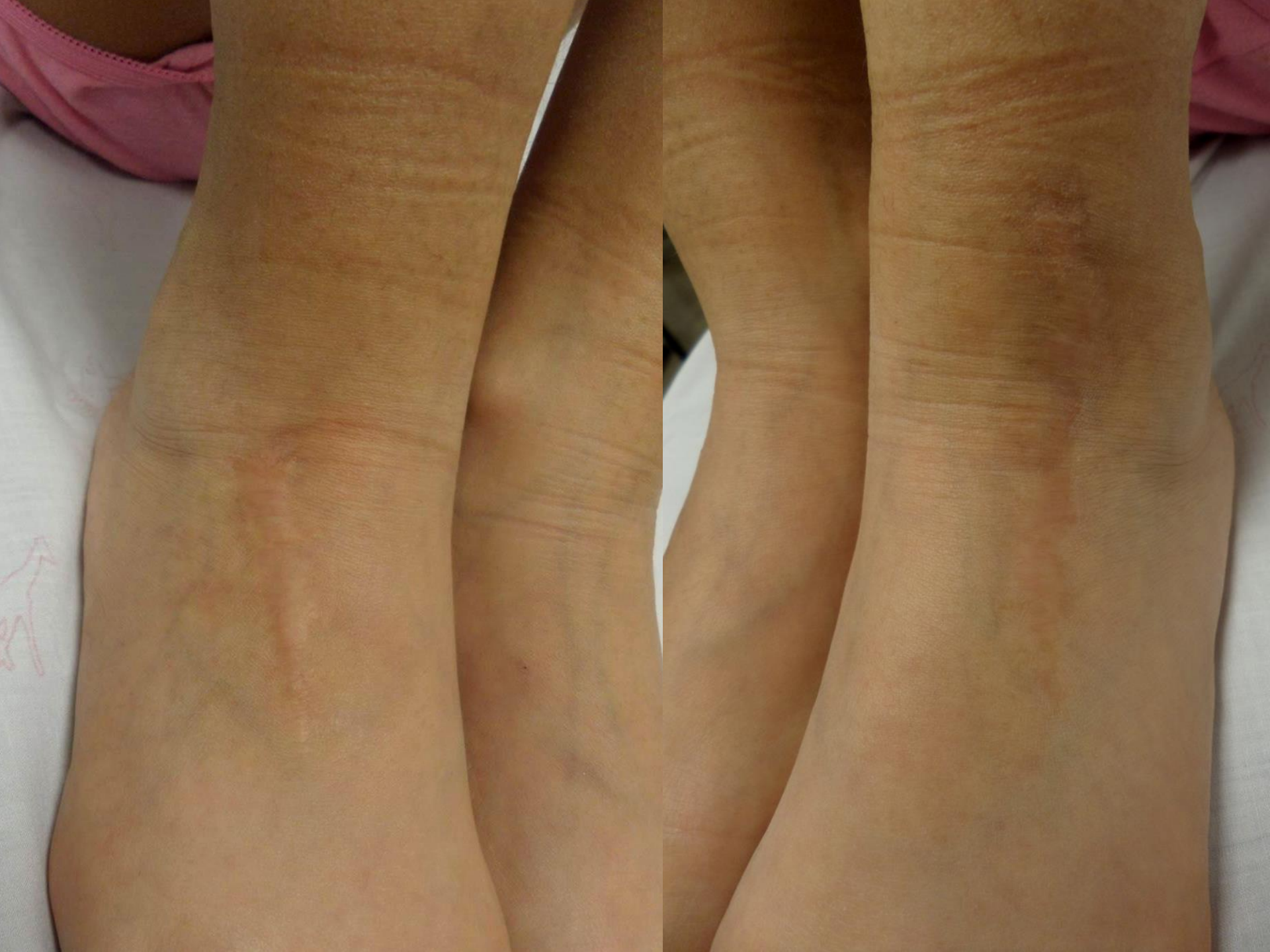
JIA Polyarticular RF-. Rheumatology dep.

Recurrent anterior uveitis. Ophtalmology dep.

3 joint injections (**knees**)

Topical steroids

Deflazacort + Metotrexate + Adalimumab



October 2013

Emergency room. 24 kg.

(Deflazacort 4 mg + Ada 20 mg + Mtx 2.5 mg/7d).

14 days of fever (max. 39.5ºC) + arthralgia + abdominal pain + vomiting + loss of well being. Acute phase reactants: CRP 14.56 mg/dL. ESR 112 mm/h.

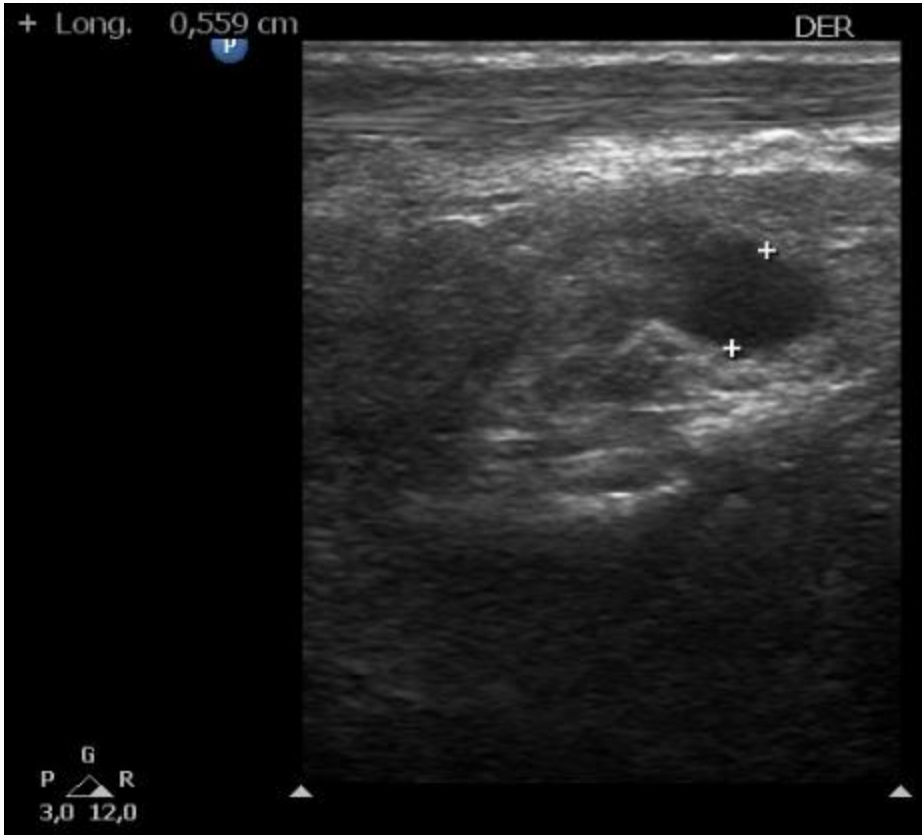
Hospitalization

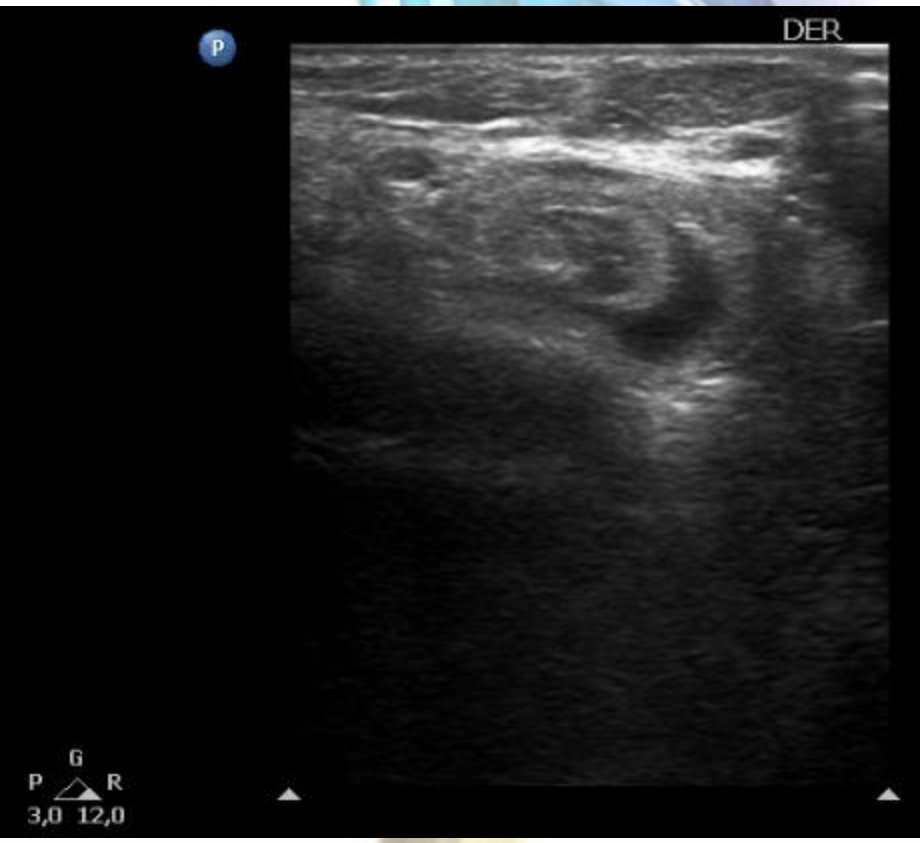
- Serology and cultures negative.
- Autoimmunity: ANA, ENA, Igs, Complement. NORMAL.
- Abdominal US, chest X-ray.

(ADA y MTX stoped. EV Cefotaxime)

ARTHRALGIA

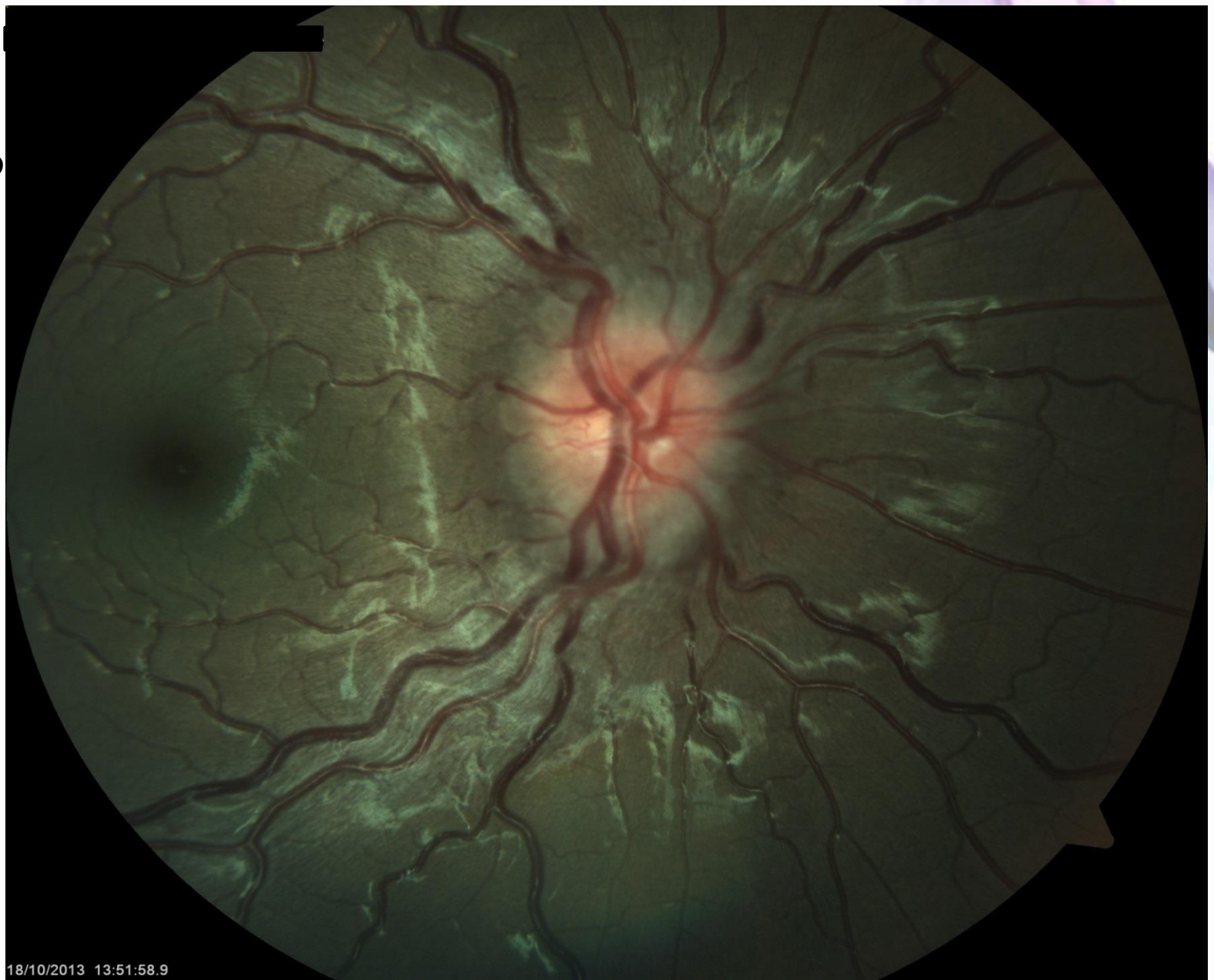
+ Arthritis (+ tenosynovitis both ankles).

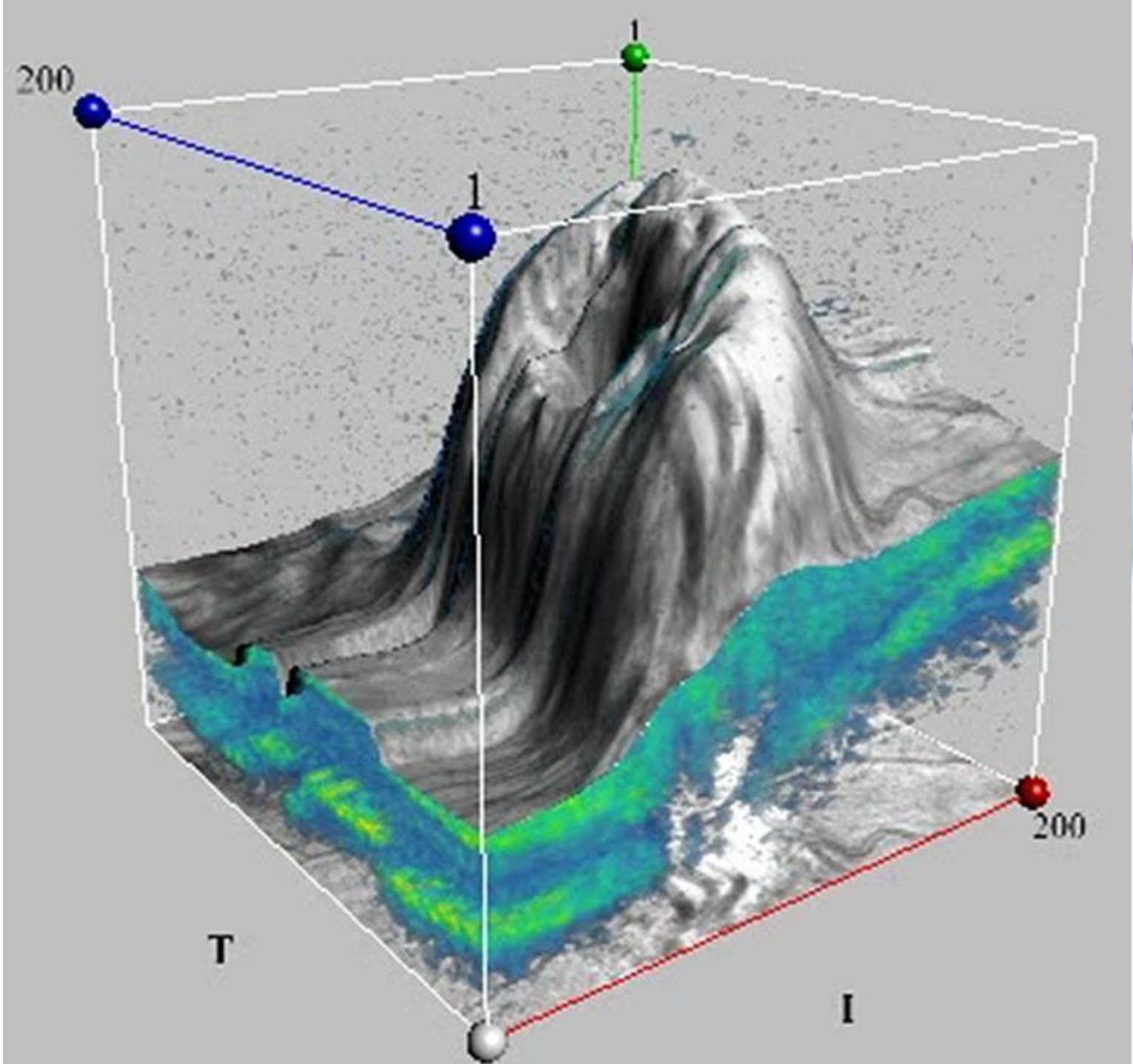




EYE

+ P

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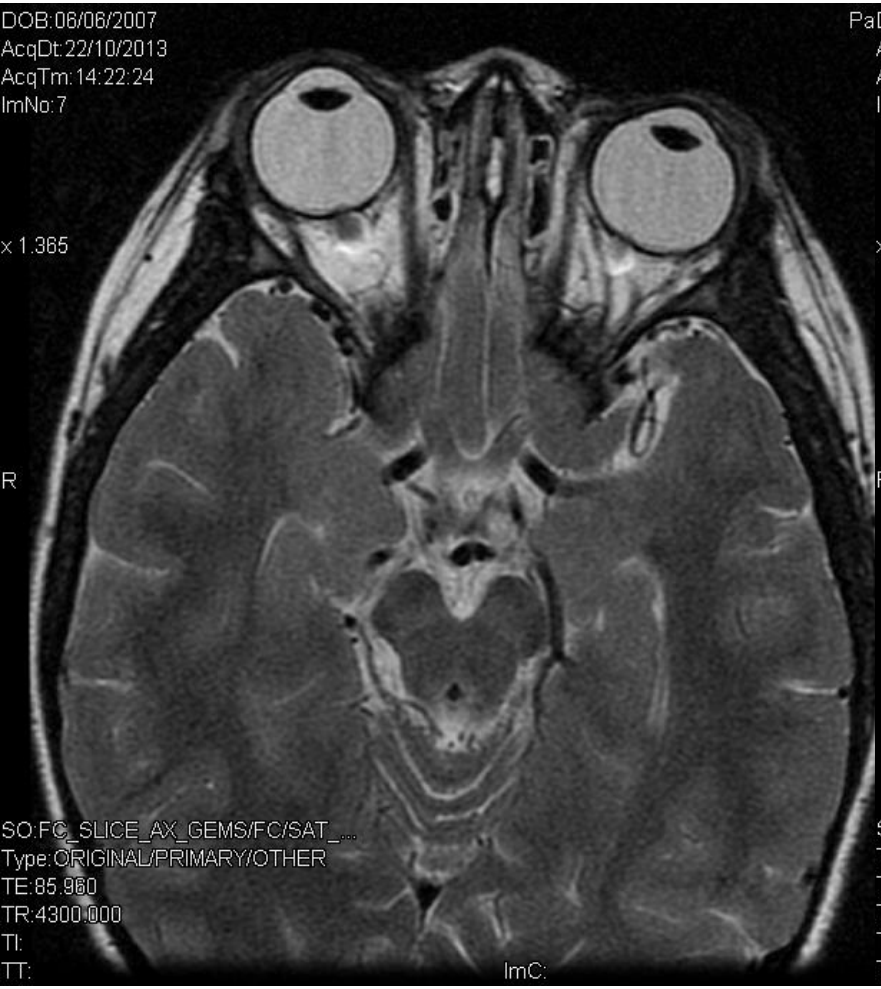
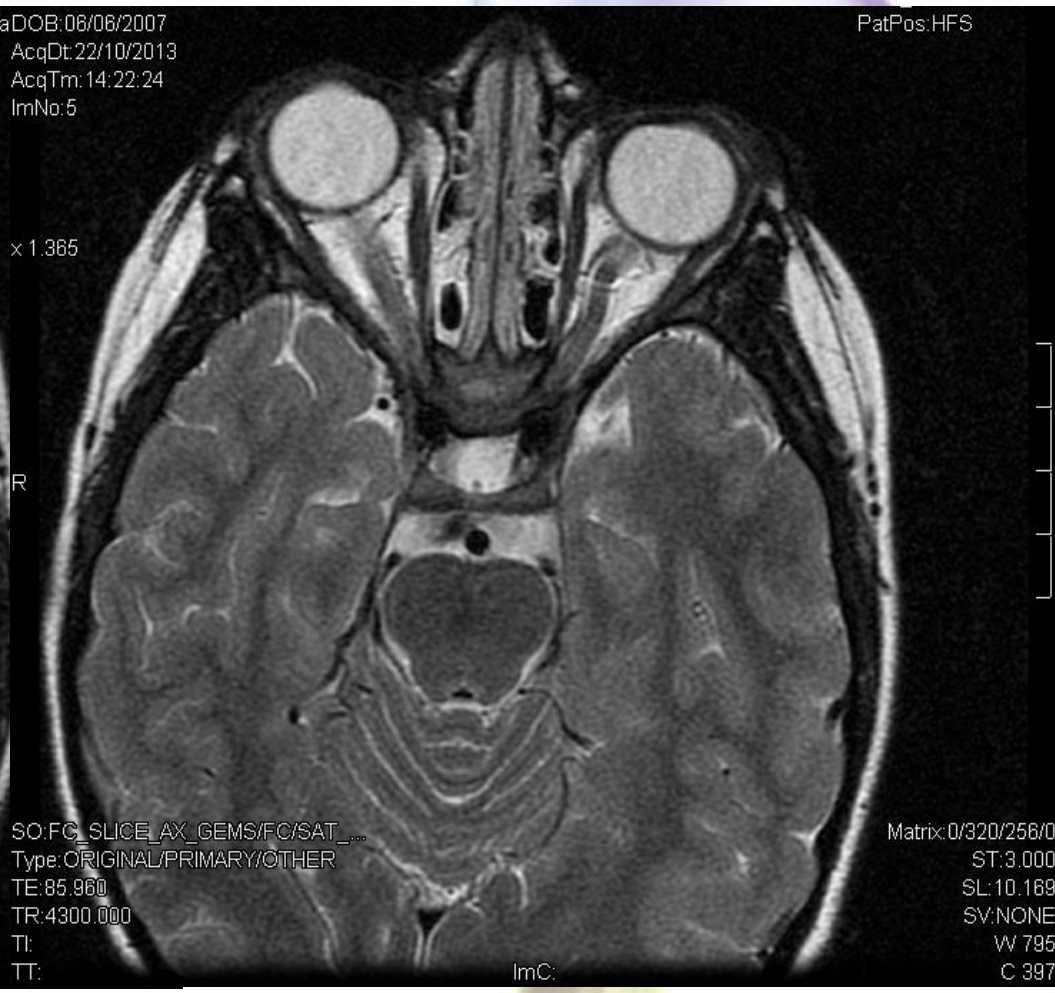
EYE/SINUPATHY





METOTREXATE 7.5 MG + PREDNISONE 5 MG + CEFUROXIME + TOPICAL STEROIDS + JOINT *INJECTION* (**ankle**)

NOV'13: STOP topical steroids. No papilar edema, no uveitis. Metotrexate 10 mg/7d.

DEC'13: STOP prednisone.

JAN'14: JOINT *INJECTION* (**both ankles**). ETANERCEPT **NOD-2**

FEB'14: Arthritis right ankle.

MAR'14: HOSPITALIZATION.

Fever 72 h (max 40ºC) + adominal pain + cephalea + arthritis **knees**.

ESR 115 mm/h. CRP 4.03 mg/dL.

Cefotaxime e.v + Cefuroxime oral 15 d.

APR'14: RESULTS NOD 2. **R334Q.**

PREDNISONE (0,5 mg/kg). Tonsil hypertrophy. Limph node enlargement.

<<< Back

We recommend that this information below should not be used as a reference for phenotype-genotype correlation.

R334Q	
Location in the gene	exon 4
Usual name Name as first published or submitted to Infevers. May be different from the HGVS edited protein and sequence names.	R334Q
HGVS protein name	p.Arg334Gln
HGVS sequence name	c.1001G>A
rs Number	rs104895461
Sequence	**cDNA:** TCCCATTCAGCTGCCGGCAGCTGCAGTGCAT
Alteration	Substitution
N base(s)	1
Base substituded	G>A
Consequence	Unknown
Functional tests	Yes
N Controls	206
Technique(s) used	Sequencing
Change/define RFLP	Unknown
Disease related symptoms in this patient	Symptomatic
Associated phenotype in this patient a variant observed in symptomatic subjects does not imply its causal role.	Blau syndrome
Country of origin / ***Ancestry***	France / *Unknown*
Reference	Miceli-Richard, C et al. Medline Abstract
Comment	Activation of the NF-kB response
Input date	2003-05-20
Contributed by	Suzanne LESAGE

MAY'14: Subtle arthritis. STOP prednisone.

JUL'14: Arthritis left knee. JOINT *INJECTION*.

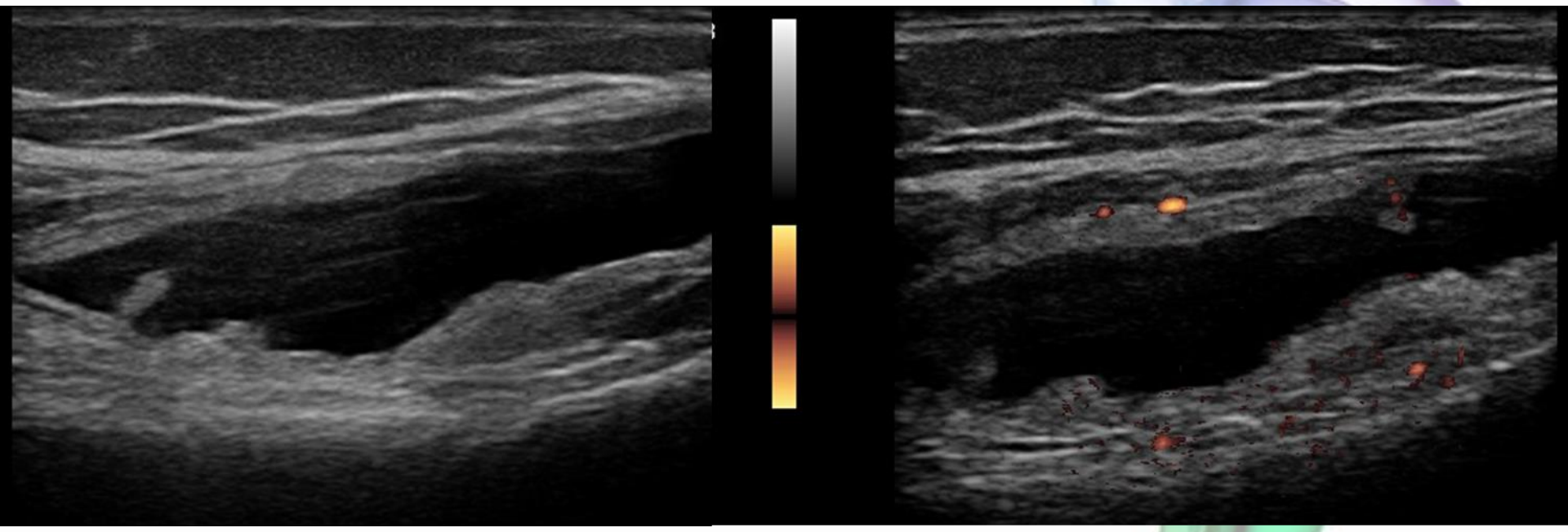
METOTREXATE 20 MG.

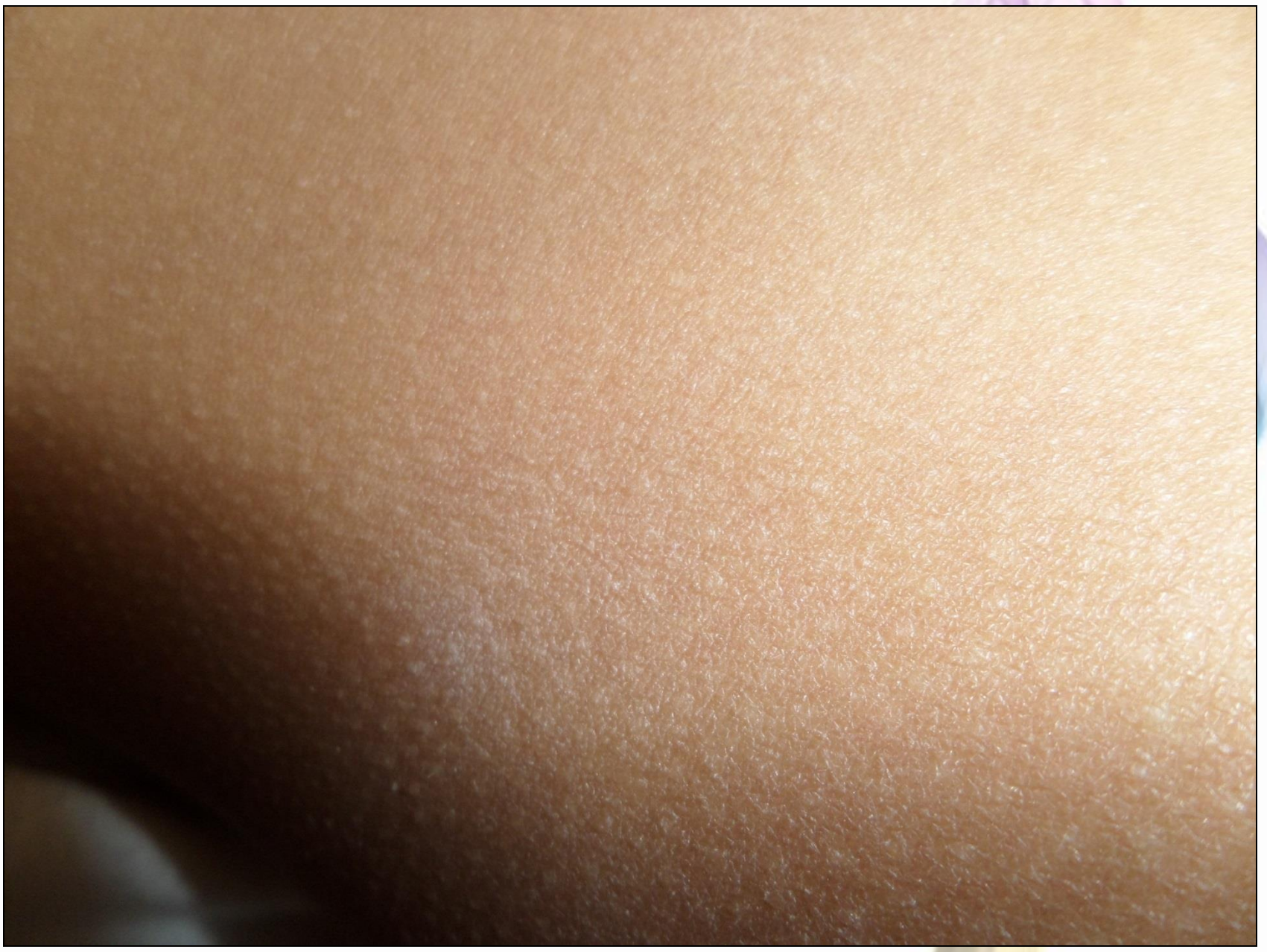
AUG'14: Arthritis **PIPs** 3, 4 left + ankles. PREDNISONE (0.5 mg/kg). ESR 40. CRP 2,08

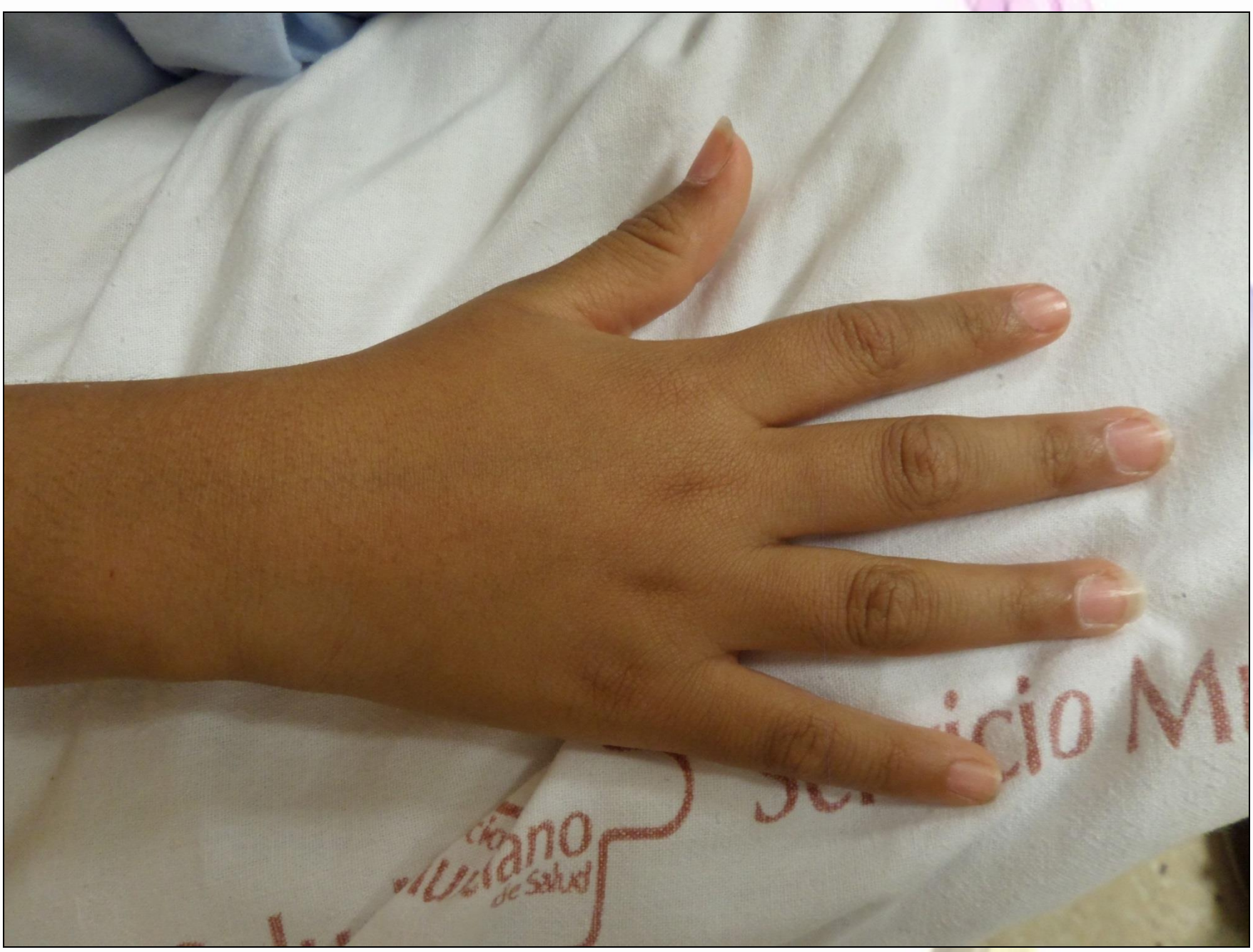
SEP'14: Arthritis ankles. STOP ETANERCEPT.

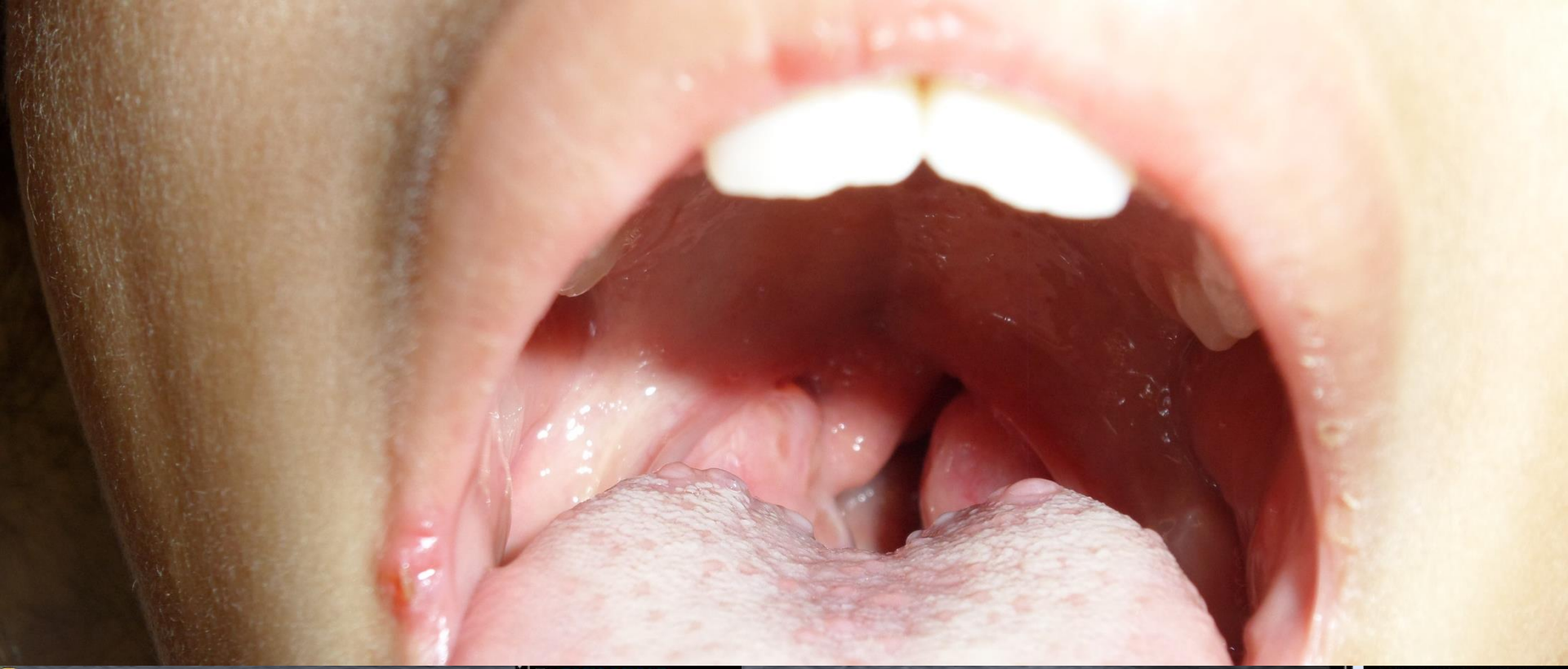
NOV'14: INFLIXIMAB 6 MG/KG 0, 2, 6, 14 wk and every 8 wk. ESR 19. CRP 0,04.

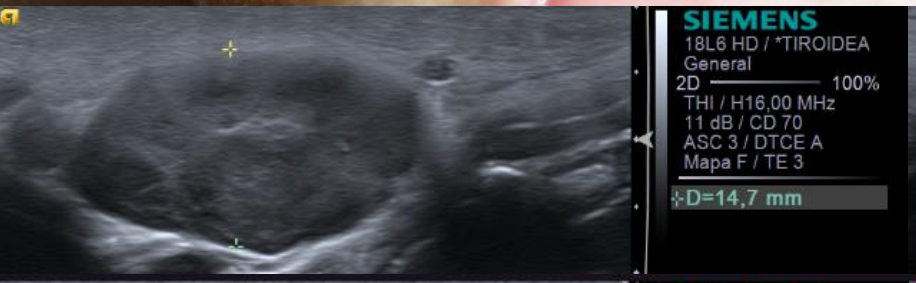
MAR'15: Asthenia, ESR 63, CRP 0,90. INFLIXIMAB 6 MG/KG every 6 wk.

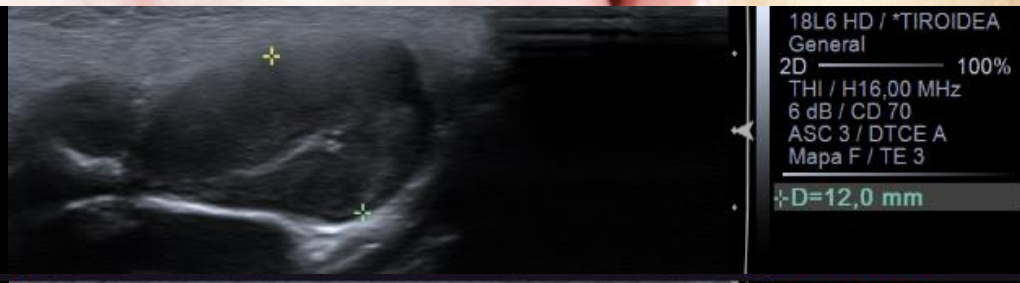


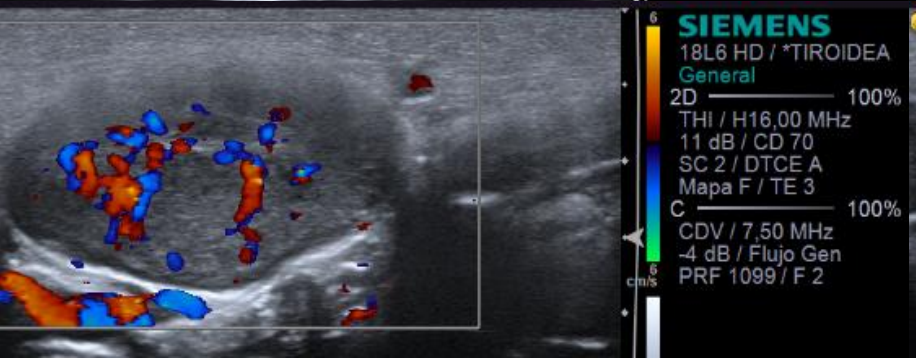


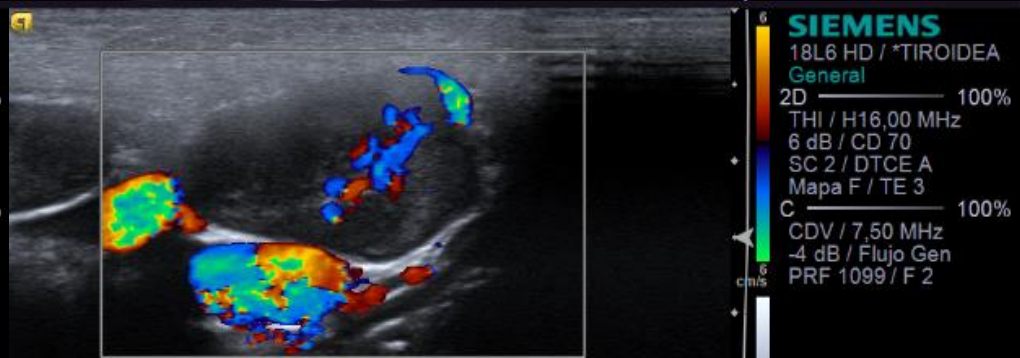





SIEMENS
18L6 HD / *TIROIDEA
General
2D 100%
THI / H16,00 MHz
11 dB / CD 70
ASC 3 / DTCE A
Mapa F / TE 3
D=14,7 mm


18L6 HD / *TIROIDEA
General
2D 100%
THI / H16,00 MHz
6 dB / CD 70
ASC 3 / DTCE A
Mapa F / TE 3
D=12,0 mm


SIEMENS
18L6 HD / *TIROIDEA
General
2D 100%
THI / H16,00 MHz
11 dB / CD 70
SC 2 / DTCE A
Mapa F / TE 3
C 100%
CDV / 7,50 MHz
-4 dB / Flujo Gen
PRF 1099 / F 2
cm/s


SIEMENS
18L6 HD / *TIROIDEA
General
2D 100%
THI / H16,00 MHz
6 dB / CD 70
SC 2 / DTCE A
Mapa F / TE 3
C 100%
CDV / 7,50 MHz
-4 dB / Flujo Gen
PRF 1099 / F 2
cm/s

BLAU/EOS

PARENTS NOD-2 SEQUENCING

(Family reengage)

NEGATIVE

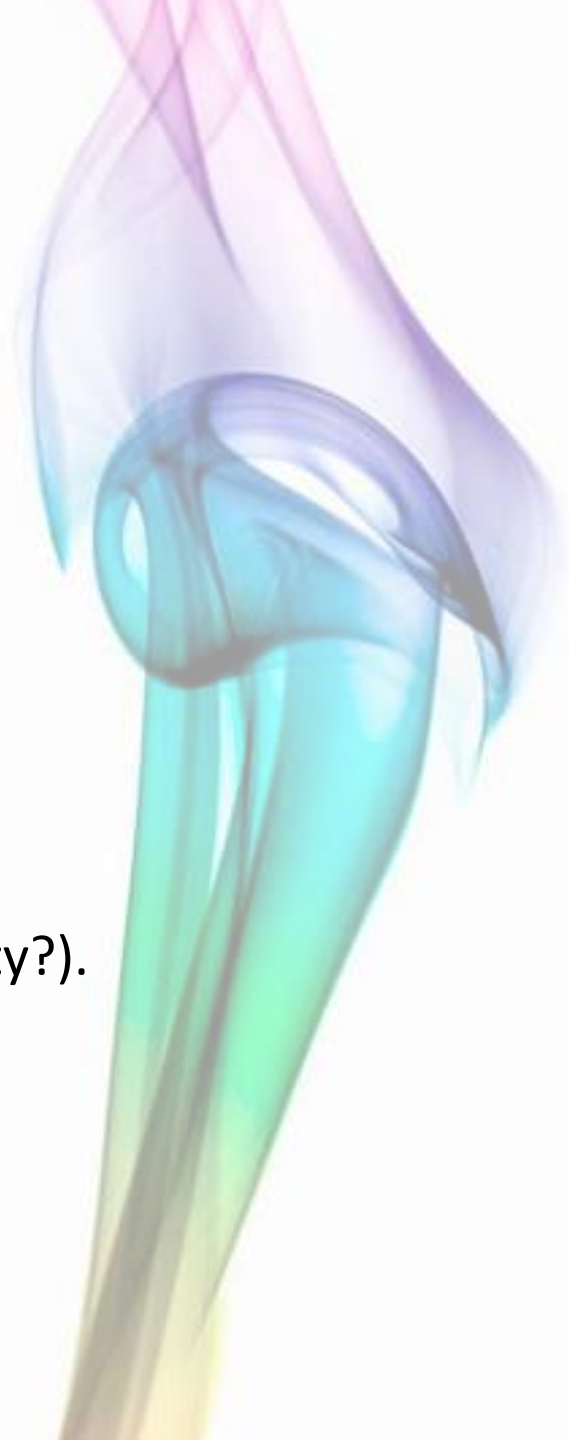
- SPORADIC JUVENILE SYSTEMIC GRANULOMATOSIS. (EARLY ONSET SARCOIDOSIS)

Summary

- **Arthtritis** + **Uveítis** +/- Skin.
- **Systemical disease** (fever, AFR)
- Limph node enlargement.

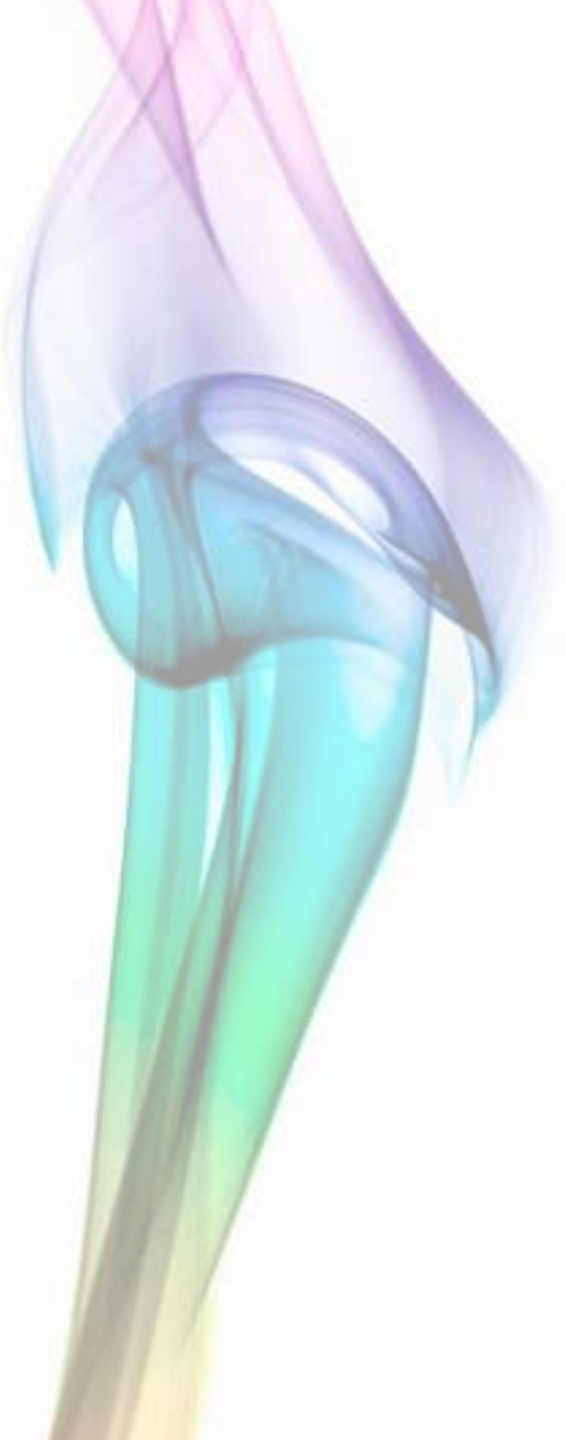
TREATMENT EXPERIENCE:

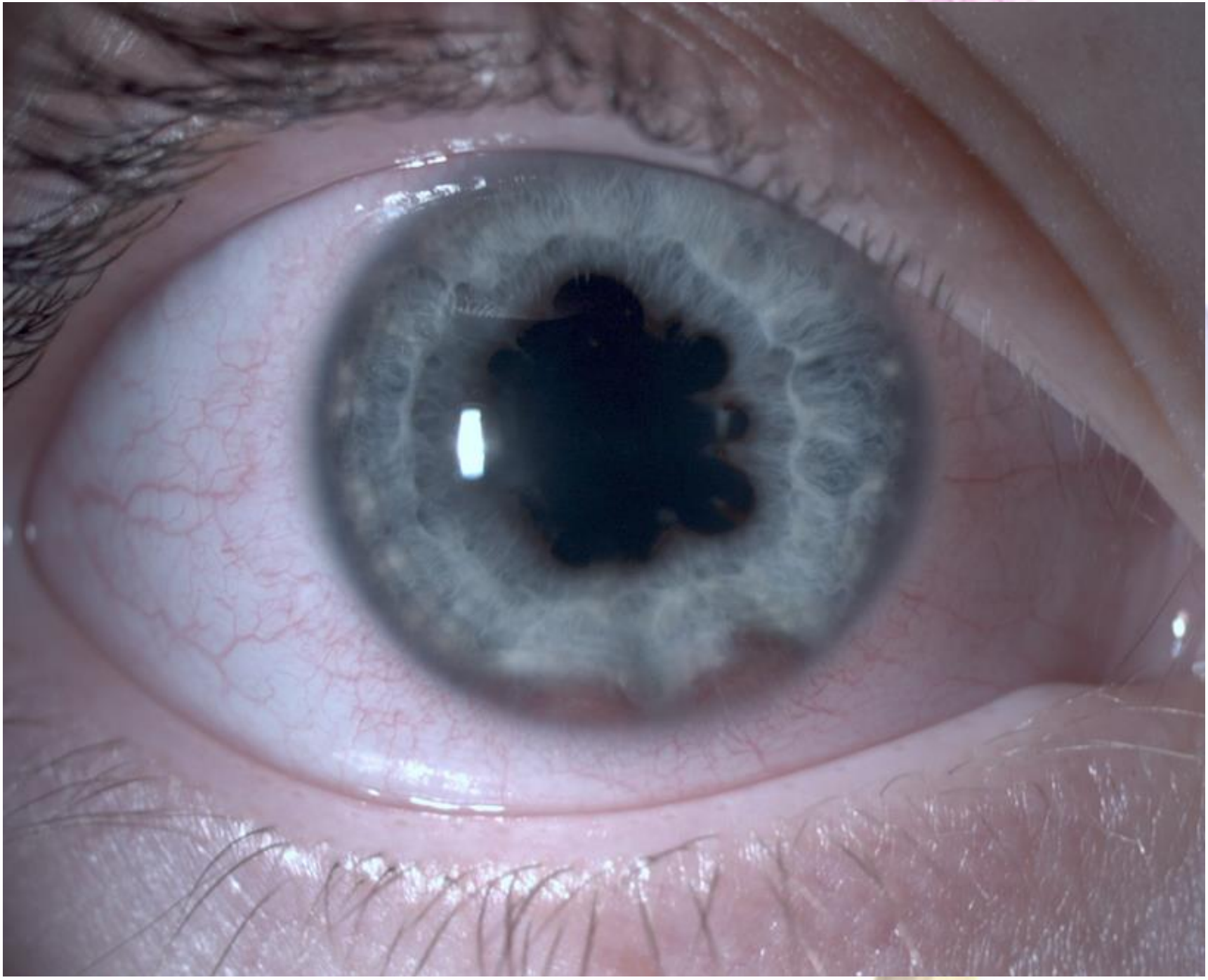
- Corticosteroids (good response).
- Adalimumab (secondary failure/immunogenicity?).
- Metotrexate (partial/no response)
- Etanercept (no response)
- Infliximab (response/limph nodes)

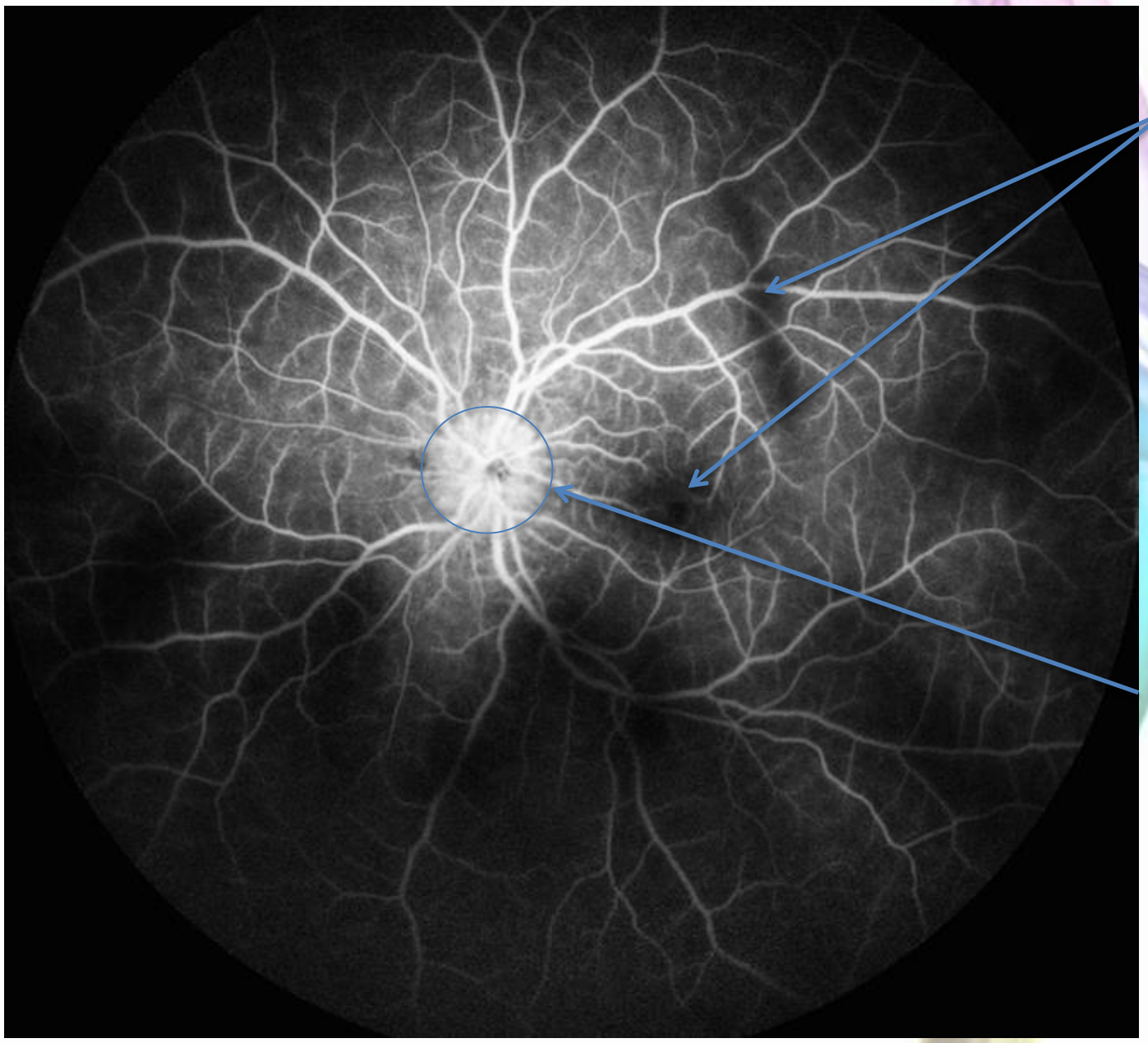


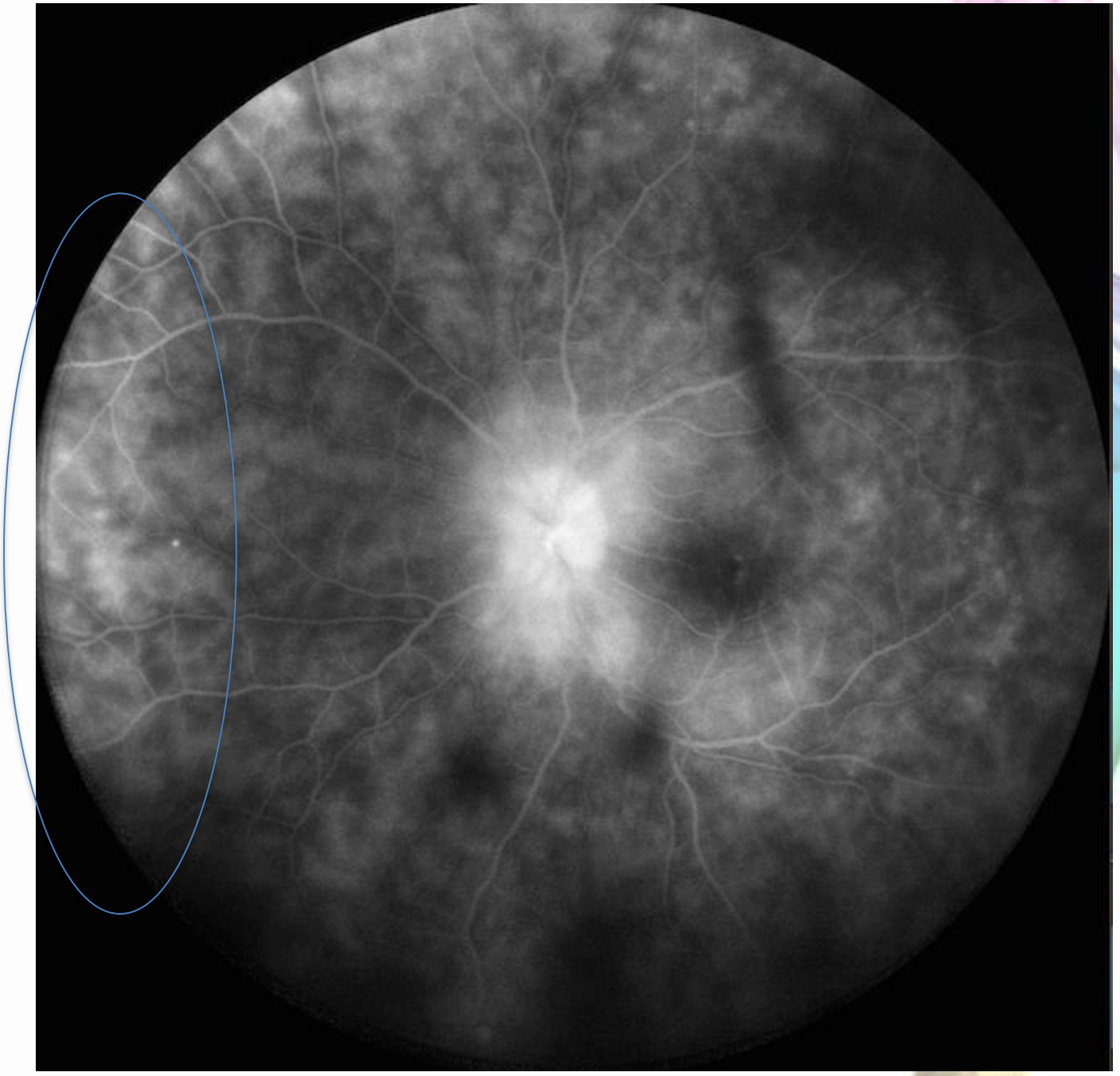
CASO 2

- 7 yrs.
- Caucasian (European).
- Ophtalmology referral.
- Granulomatous Pan-Uveítis.






Floculos vitreos
Nervio óptico



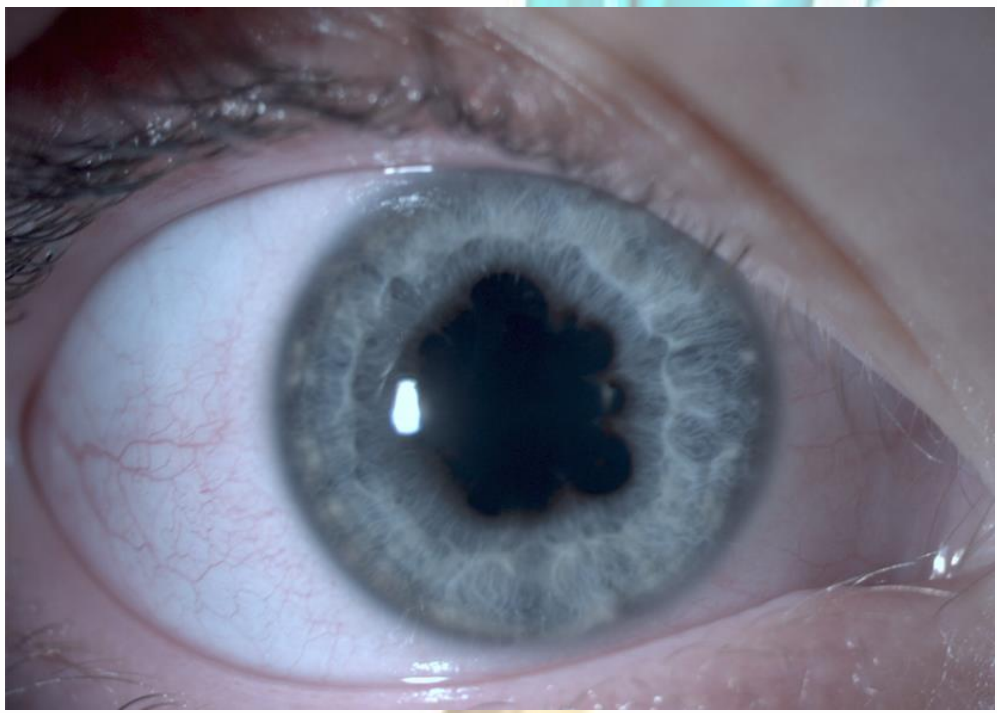
- Physical examination: Normal.
- Serology, negative.
- Chest X ray, Abd US, Cardio US: Normal.
- Fecal Calprotectine NEGATIVE.
- ACE: 77,4 U/L (18-55). ESR 18 mm/h. CRP 0,30 mg/dL.
- Corticosteroids 2 mg/kg. Metotrexato 15 mg s.c./7d. Adalimumab 40 mg s.c/14d.
- Dermatitis (paniculitis like): Biopsy (non specific perivascular dermatitis with mild eosinophyl infiltration).
- NOD-2 sequencing.

<<< Back

We recommend that this information below should not be used as a reference for phenotype-genotype correlation.

R702W/SNP8	
Location in the gene	exon 4
Usual name Name as first published or submitted to Infevers. May be different from the HGVS edited protein and sequence names.	R702W/SNP8
HGVS protein name	p.Arg702Trp
HGVS sequence name	c.2104C>T
rs Number	rs2066844
Sequence	**cDNA:** GAGAAGGCCCTGCTCCGGCGCCAGGCCTGTG
Alteration	Substitution
N base(s)	1
Base substituded	C>T
Consequence	Unknown
Functional tests	Yes
N Controls	174
Technique(s) used	ARMS Sequencing
Change/define RFLP	Unknown
Disease related symptoms in this patient	Unknown
Associated phenotype in this patient a variant observed in symptomatic subjects does not imply its causal role.	Crohn's disease Psoriatic Arthritis Rheumatoid Arthritis Spondylarthropathy Ulcerative Colitis
Country of origin / ***Ancestry***	Unknown / *Caucasian*
Reference	Hugot, JP et al. Medline Abstract
Comment	Diminution of both basal and PGN-induced potential of NF-kB activation
Input date	2003-06-04
Contributed by	Suzanne LESAGE

- ADALIMUMAB 40 MG.
- METOTREXATE 20 MG.
- CORTICOIDES stopped.



14-MAY-2015

FECAL CALPROTECTIN
369 ug/g (0-50)

FECAL BLOOD TEST
0 ng/ml

THANK YOU

Pablo Mesa del Castillo B.

mesacasti@gmail.com

Paula Alcañiz Rodríguez.

paulova81@hotmail.com

REUMATOLOGÍA PEDIÁTRICA

ARRIXACA.MURCIA