#WCD2019

AEDV HIGHLIGHTS

24th World Congress of Dermatology (WCD)

10-15 JUNIO 2019

Milàn

Patrocina:

janssen Immunology
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organiza:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA
AEDV 1909

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24th World Congress of Dermatology (WCD)

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Milán

Psoriasis and inflammatory dermatosis

controversies in psoriasis

vasculitis and vasculopathy

other dermatosis: contact dermatitis-rosacea-HS

Mar Llamas Velasco.

Hospital Universitario de La Princesa. Madrid.

Patrocina: Janssen Immunology, Pharmaceutical Companies of Johnson & Johnson

Organiza: Academia Española de Dermatología y Venereología AEDV 1909

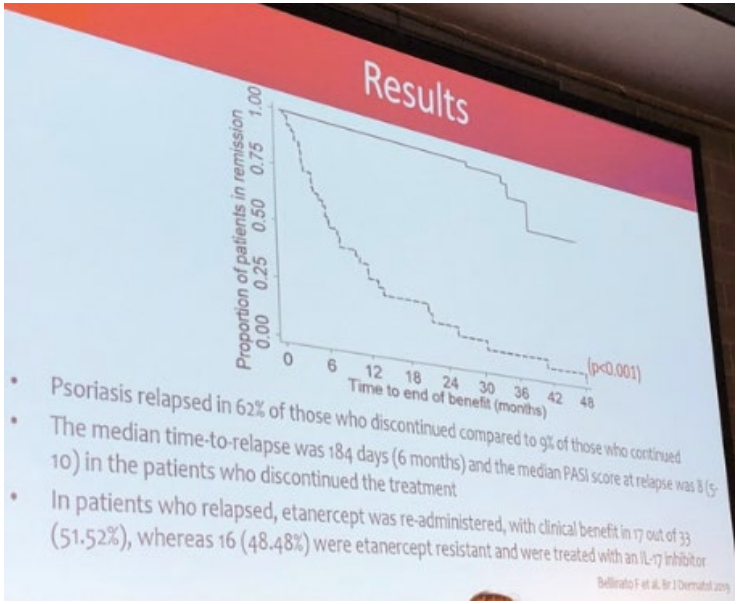
Topics to cover

- Can biologics ever been stopped?
- Vasculitis and vasculopathies
- Contact dermatitis- rosacea- hidrosadenitis.

Dr Gisondi Vs Dr Spuls. **Can biologics ever be stopped?**

- AGAINST (Dr Gisondi)

- Psicological stress
- Comorbidities control
- Percentage of patients relapsing after leaving medication
- Antibody risk formation in intermitent therapy



- PRO (Dr Spuls)

- Chronic treatments and low expectations may favor low adherence.
- Shared decision making (patient centered)
- Drug survival, many drugs but stil limited
- Costs and optimization of therapy
- If inflammation and Th17-IL17 pathway is involved in comorbidities long remission of inflammation as seen in the skin may correlate.

- Prediction model TRIPOD to safety cease antiTNF in Crohn´s disease and OPTIMAP study

Milàn

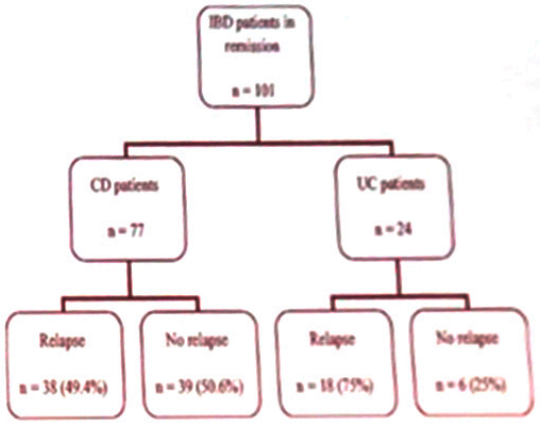
LESSONS LEARNED FROM GASTROENTEROLOGY

Relapse rates and predictors for relapse in a real-life cohort of IBD patients after discontinuation of anti-TNF therapy.

Bots SJ et al, Scand J Gastroenterol. 2019

IBD patients in remission receiving infliximab or adalimumab treatment for ≥1 year who discontinued treatment were included

Relapse rates and predictors for relapse were studied using survival and Cox regression analysis



THERAPEUTIC DRUG MONITORING

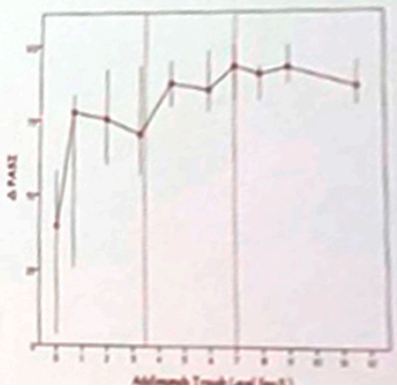
Developing a Therapeutic Range of Adalimumab Serum Concentrations in Management of Psoriasis. A Step Toward Personalized Treatment.

Menting SP et al, JAMA Dermatol. 2015

therapeutic range of adalimumab trough levels of 3.51 mg/L to 7.00 mg/L

One third of patients exceeded this window

One fifth of patients were below the window



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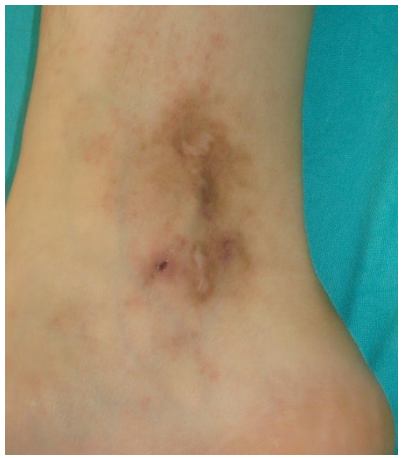
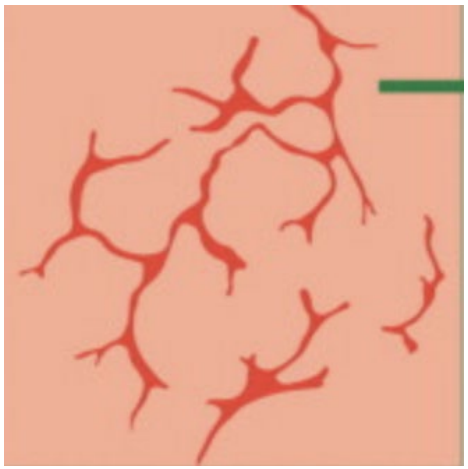
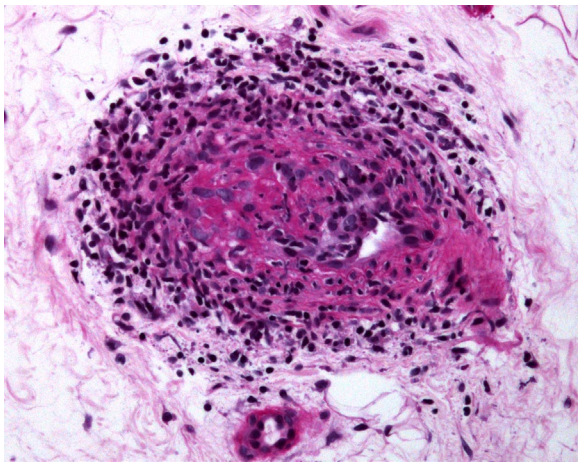
Vasculitis and vasculopathies

- Cord Sunderkoetter, Germany
- Warren Piette, United States
- Ko-Ron Chen, Japan
- Franscesco Tomasini, Italia
- Erkan Alpsoy, Turkey
- Tamihiro Kawakami, Japan
- David Wetter, United States
- Mar Llamas-Velasco, Spain

An exhaustive review of conceptual controversies, classification, histopathological diagnosis and therapeutic management







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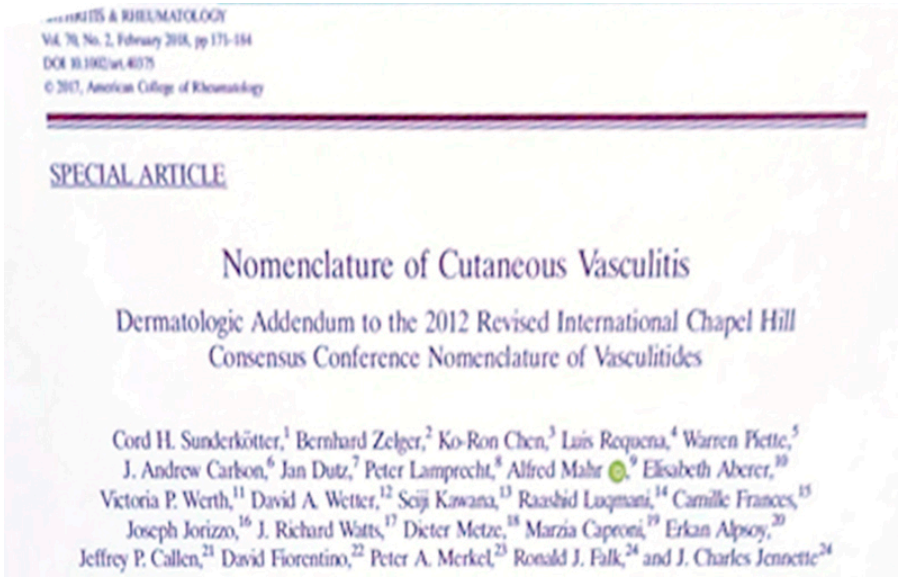
Cord Sunderkoetter, Germany



ARTHRITIS & RHEUMATOLOGY
Vol. 70, No. 2, February 2018, pp 171–184
DOI 10.1002/art.40375

SPECIAL ARTICLE

Nomenclature of Cutaneous Vasculitis

Dermatologic Addendum to the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides

Cord H. Sunderkötter,[1] Bernhard Zelger,[2] Ko-Ron Chen,[3] Luis Requena,[4] Warren Piette,[5] J. Andrew Carlson,[6] Jan Dutz,[7] Peter Lamprecht,[8] Alfred Mahr,[9] Elisabeth Aberer,[10] Victoria P. Werth,[11] David A. Wetter,[12] Seiji Kawana,[13] Rashid Luqmani,[14] Camille Francès,[15] Joseph Jorizzo,[16] J. Richard Watts,[17] Dieter Metze,[18] Marzia Caproni,[19] Erkan Alpsoy,[20] Jeffrey P. Callen,[21] David Fiorentino,[22] Peter A. Merkel,[23] Ronald J. Falk,[24] and J. Charles Jennette[24]

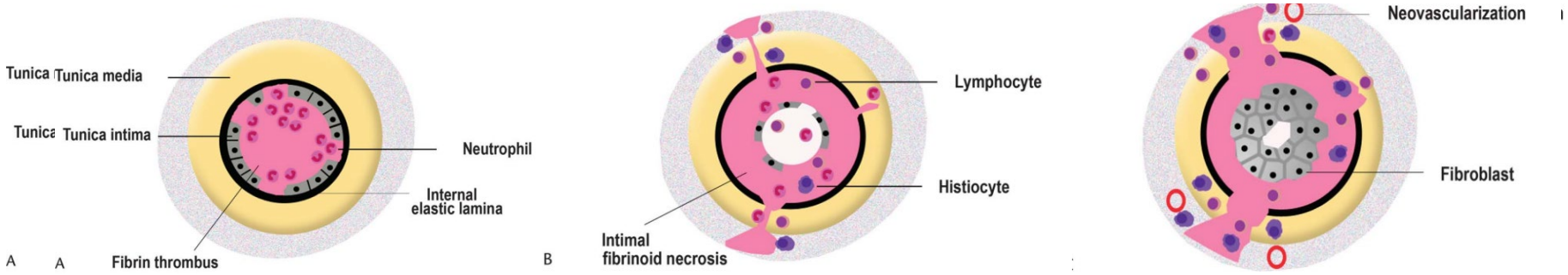
Summary
Clinical impact of new nomenclature / classification

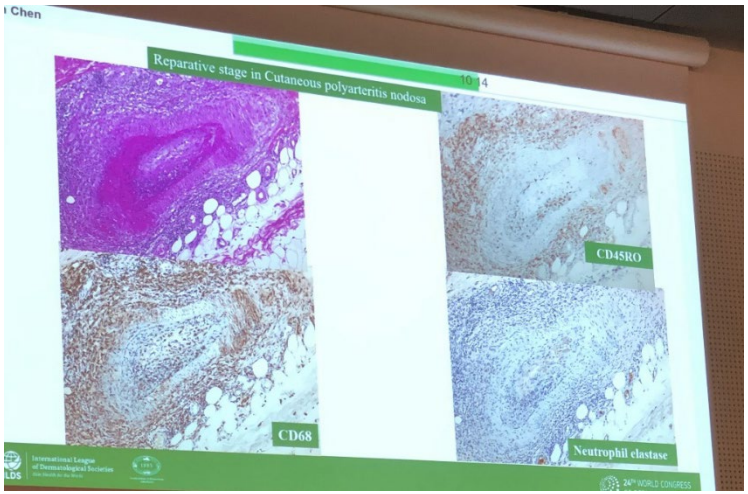
- Now defintions can be falsified or verified (and then modified or abandonned)
- Vasculitis of skin is
  - Cutaneous component of systemic vasculitides
  - Skin-limited variant of a systemic vasculitis
  - single-organ vasculitis of the skin
- To be solved
  - cases of pure IgG/IgM vasculitis
  - ANCA-associated vasculitides restricted to skin
- We need wider consensus on nomenclature of occlusive vasculopathy, but giid suggestions have been made

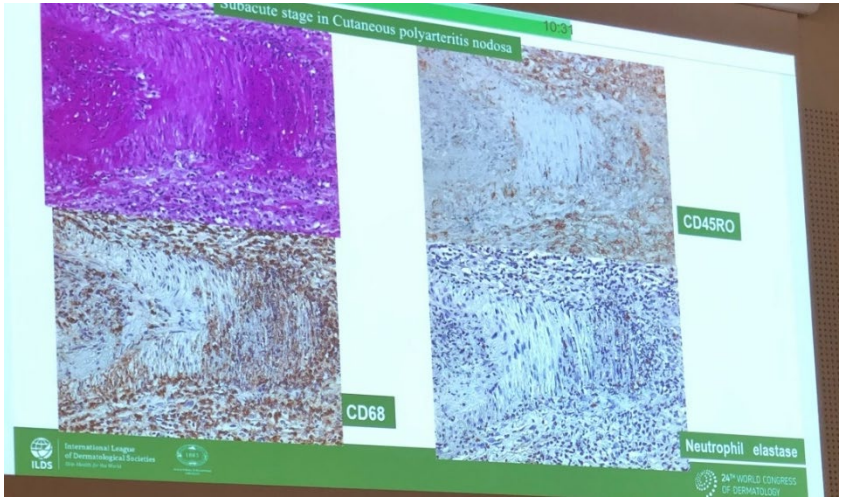
Milàn

Dr Chen and Dr Tomasini. **Dermatopathological diagnosis of vasculitis and vasculopathies**

Ishibashi and Chen. Am J Dermatopathol 2008;30:4:319-26







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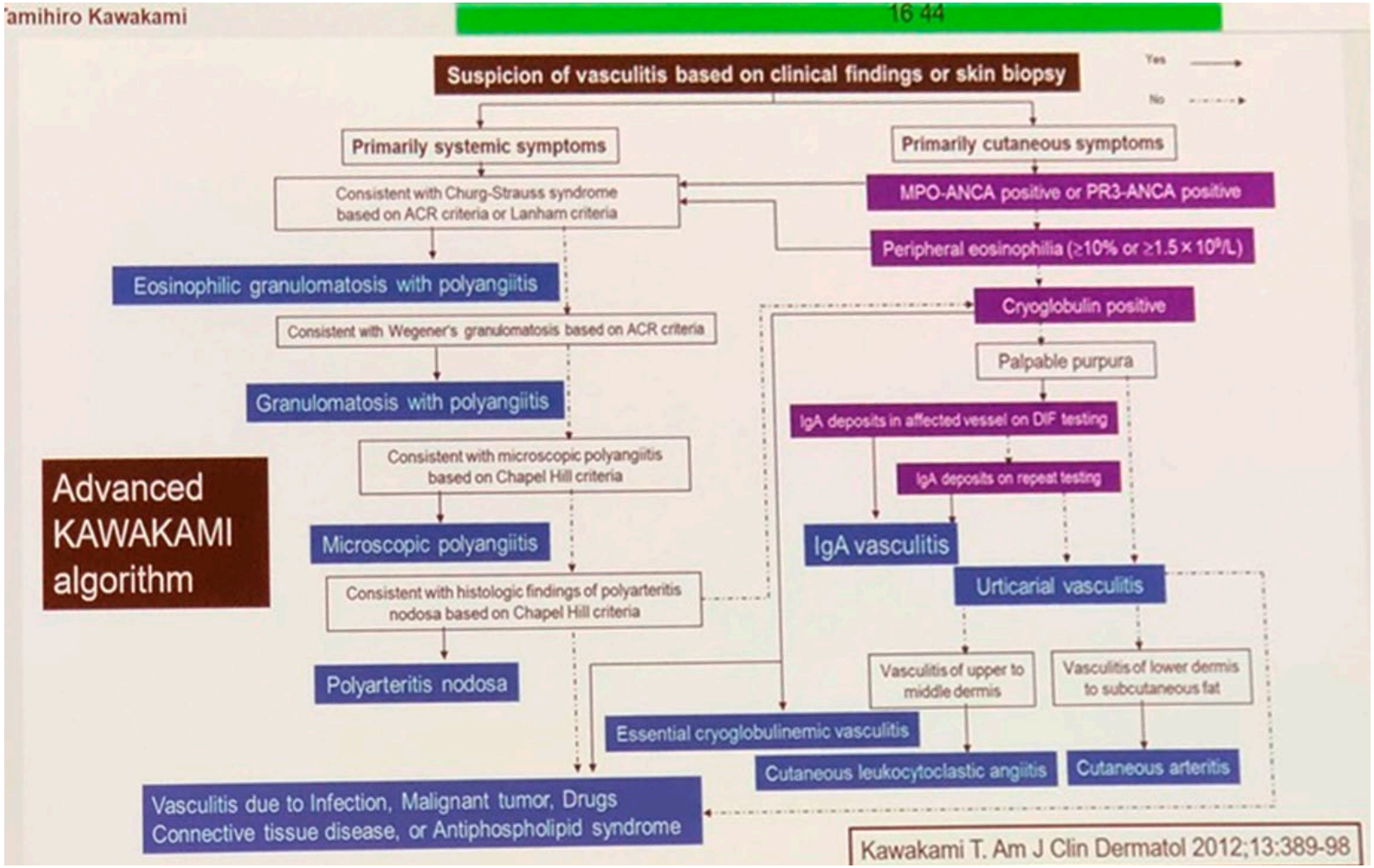
Dr Kawakami. **The evolution of the algorithmic approach to skin-limited vasculitis**



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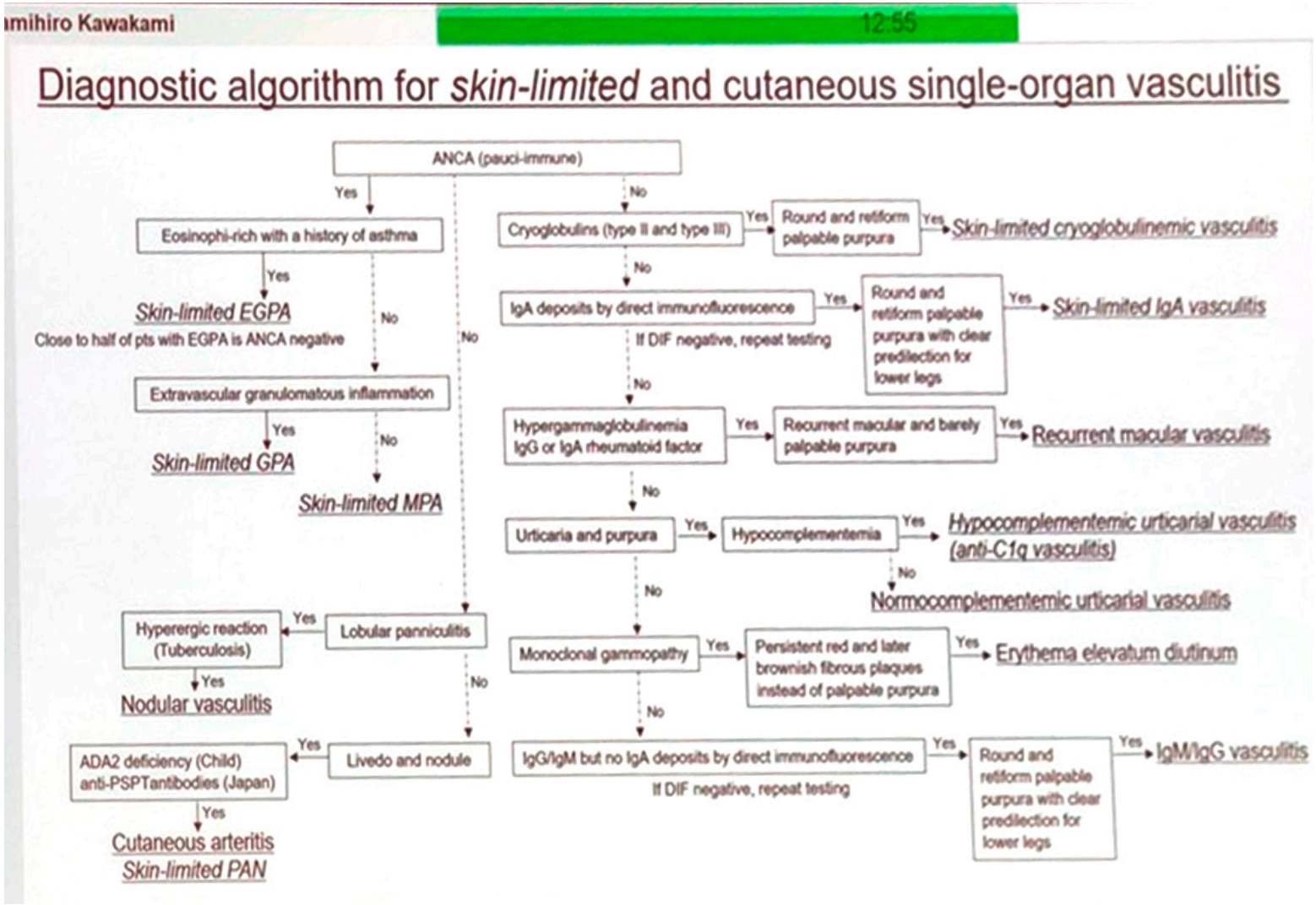
Dr Kawakami. **The evolution of the algorithmic approach to skin-limited vasculitis**



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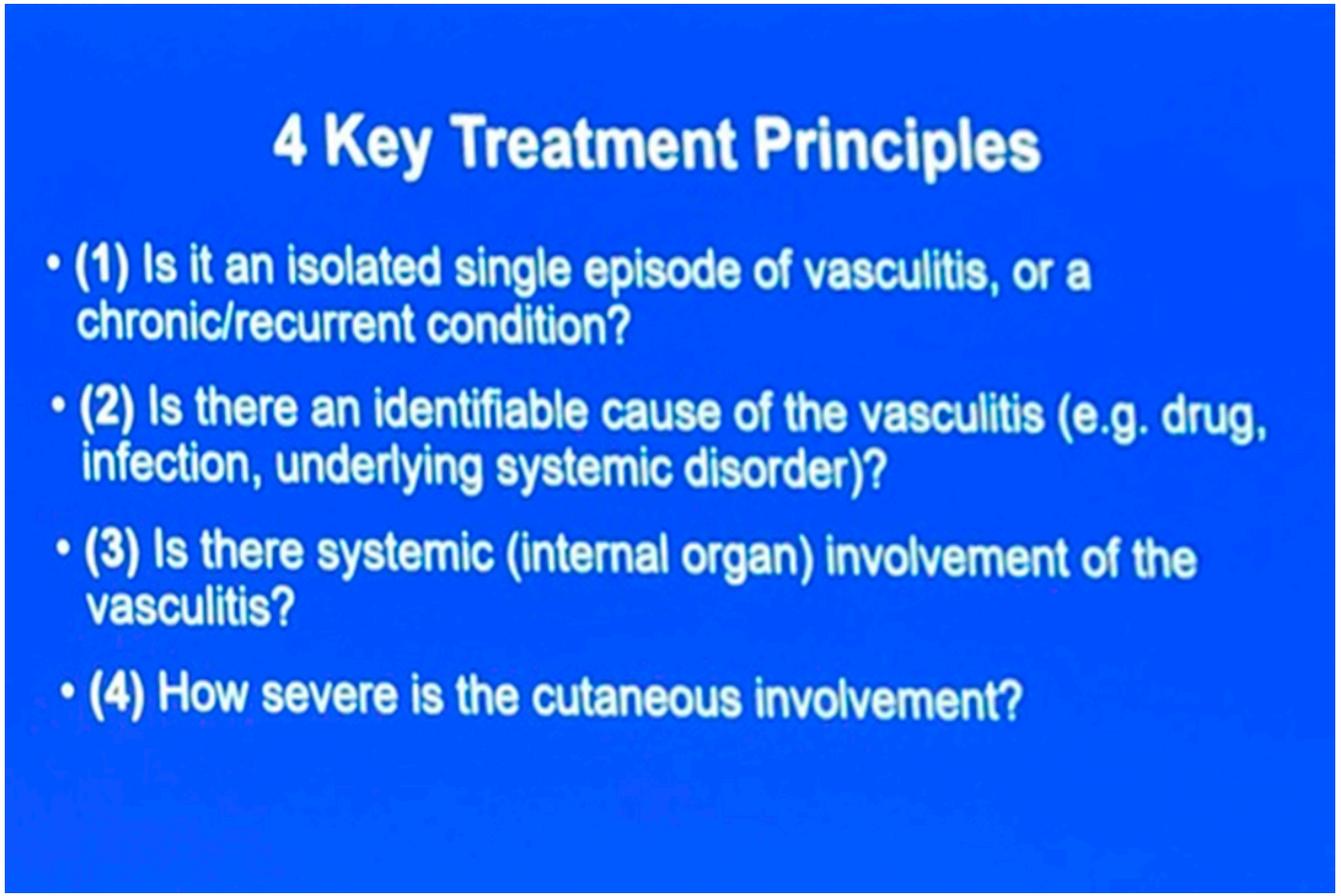
David Wetter, United States**. Management of vasculitis**



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David Wetter, United States. **Management Of Vasculitis**

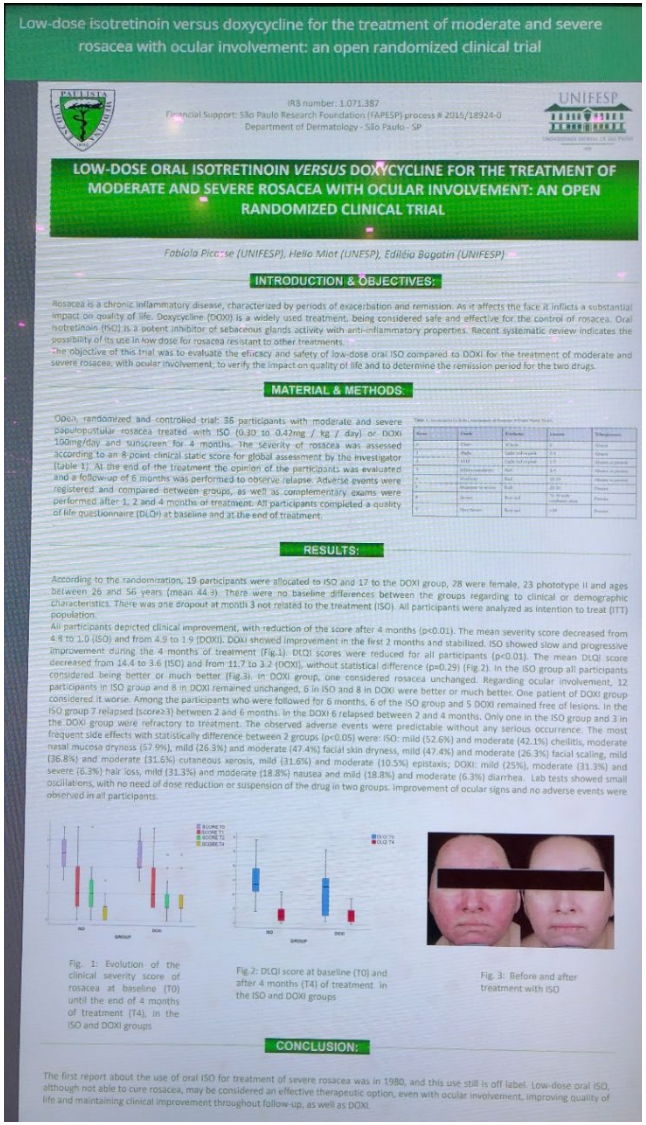
Treatment of Chronic Idiopathic CSVV (My Approach)

- ***First-line:***
  - **Colchicine** 0.6 mg 2-3 times daily
  - **Dapsone** 100-200 mg daily (check glucose-6-phosphate dehydrogenase [G6PD] prior to treatment)
  - Colchicine and dapsone **in combination**
- ***Second-line:***
  - **Mycophenolate mofetil** 2-3 grams daily (in divided doses)
  - **Azathioprine** 2-2.5 mg/kg/d if normal thiopurine methyltransferase [TPMT] level (typically 150 mg/d)
  - **Methotrexate** 10-25 mg weekly (note: has been reported to cause cutaneous vasculitis)
  - If severe disease, consider **short tapering course of prednisone** (2-3 months) while steroid-sparing agent fully kicks in

MAYO CLINIC

Milan

Rosacea



Low-dose isotretinoin versus doxycycline for the treatment of moderate and severe rosacea with ocular involvement: an open randomized clinical trial

IRB number: 1.071.387
Financial Support: São Paulo Research Foundation (FAPESP) process # 2015/18924-0
Department of Dermatology - São Paulo - SP

UNIFESP

LOW-DOSE ORAL ISOTRETINOIN *VERSUS* DOXYCYCLINE FOR THE TREATMENT OF MODERATE AND SEVERE ROSACEA WITH OCULAR INVOLVEMENT: AN OPEN RANDOMIZED CLINICAL TRIAL

Fabiola Piccase (UNIFESP), Helio Miot (UNESP), Ediléia Bagatin (UNIFESP)

INTRODUCTION & OBJECTIVES:

Rosacea is a chronic inflammatory disease, characterized by periods of exacerbation and remission. As it affects the face it inflicts a substantial impact on quality of life. Doxycycline (DOXI) is a widely used treatment, being considered safe and effective for the control of rosacea. Oral isotretinoin (ISO) is a potent inhibitor of sebaceous glands activity with anti-inflammatory properties. Recent systematic review indicates the possibility of its use in low dose for rosacea resistant to other treatments.

The objective of this trial was to evaluate the efficacy and safety of low-dose oral ISO compared to DOXI for the treatment of moderate and severe rosacea, with ocular involvement; to verify the impact on quality of life and to determine the remission period for the two drugs.

MATERIAL & METHODS:

Open, randomized and controlled trial: 36 participants with moderate and severe papulopustular rosacea treated with ISO (0.30 to 0.42mg / kg / day) or DOXI 100mg/day and sunscreen for 4 months. The severity of rosacea was assessed according to an 8-point clinical static score for global assessment by the investigator (table 1). At the end of the treatment the opinion of the participants was evaluated and a follow-up of 6 months was performed to observe relapse. Adverse events were registered and compared between groups, as well as complementary exams were performed after 1, 2 and 4 months of treatment. All participants completed a quality of life questionnaire (DLQI) at baseline and at the end of treatment.

RESULTS:

According to the randomization, 19 participants were allocated to ISO and 17 to the DOXI group, 28 were female, 23 phototype II and ages between 26 and 56 years (mean 44.3). There were no baseline differences between the groups regarding to clinical or demographic characteristics. There was one dropout at month 3 not related to the treatment (ISO). All participants were analyzed as intention to treat (ITT) population.

All participants depicted clinical improvement, with reduction of the score after 4 months ($p<0.01$). The mean severity score decreased from 4.8 to 1.0 (ISO) and from 4.9 to 1.9 (DOXI). DOXI showed improvement in the first 2 months and stabilized. ISO showed slow and progressive improvement during the 4 months of treatment (Fig.1). DLQI scores were reduced for all participants ($p<0.01$). The mean DLQI score decreased from 14.4 to 3.6 (ISO) and from 11.7 to 3.2 (DOXI), without statistical difference ($p=0.29$) (Fig.2). In the ISO group all participants considered being better or much better (Fig.3). In DOXI group, one considered rosacea unchanged. Regarding ocular involvement, 12 participants in ISO group and 8 in DOXI remained unchanged, 6 in ISO and 8 in DOXI were better or much better. One patient of DOXI group considered it worse. Among the participants who were followed for 6 months, 6 of the ISO group and 5 DOXI remained free of lesions. In the ISO group 7 relapsed (score≥3) between 2 and 6 months. In the DOXI 6 relapsed between 2 and 4 months. Only one in the ISO group and 3 in the DOXI group were refractory to treatment. The observed adverse events were predictable without any serious occurrence. The most frequent side effects with statistically difference between 2 groups ($p<0.05$) were: ISO: mild (52.6%) and moderate (42.1%) cheilitis, moderate nasal mucosa dryness (57.9%), mild (26.3%) and moderate (47.4%) facial skin dryness, mild (47.4%) and moderate (26.3%) facial scaling, mild (36.8%) and moderate (31.6%) cutaneous xerosis, mild (31.6%) and moderate (10.5%) epistaxis; DOXI: mild (25%), moderate (31.3%) and severe (6.3%) hair loss, mild (31.3%) and moderate (18.8%) nausea and mild (18.8%) and moderate (6.3%) diarrhea. Lab tests showed small oscillations, with no need of dose reduction or suspension of the drug in two groups. Improvement of ocular signs and no adverse events were observed in all participants.

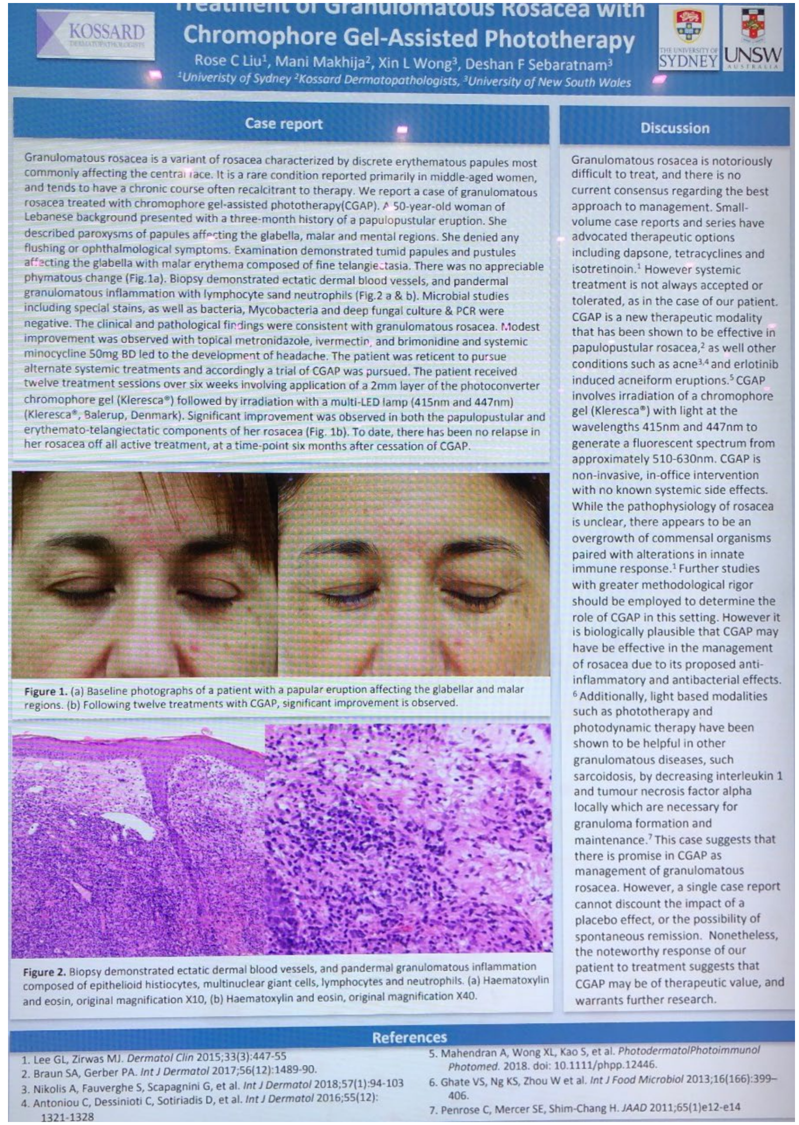
Fig. 1: Evolution of the clinical severity score of rosacea at baseline (T0) until the end of 4 months of treatment (T4), in the ISO and DOXI groups

Fig.2: DLQI score at baseline (T0) and after 4 months (T4) of treatment in the ISO and DOXI groups

Fig. 3: Before and after treatment with ISO

CONCLUSION:

The first report about the use of oral ISO for treatment of severe rosacea was in 1980, and this use still is off label. Low-dose oral ISO, although not able to cure rosacea, may be considered an effective therapeutic option, even with ocular involvement, improving quality of life and maintaining clinical improvement throughout follow-up, as well as DOXI.



KOSSARD DERMATOPATHOLOGISTS

Treatment of Granulomatous Rosacea with Chromophore Gel-Assisted Phototherapy

Rose C Liu[1], Mani Makhija[2], Xin L Wong[3], Deshan F Sebaratnam[3]
[1]Univeristy of Sydney [2]Kossard Dermatopathologists, [3]University of New South Wales

THE UNIVERSITY OF SYDNEY UNSW AUSTRALIA

Case report

Granulomatous rosacea is a variant of rosacea characterized by discrete erythematous papules most commonly affecting the central face. It is a rare condition reported primarily in middle-aged women, and tends to have a chronic course often recalcitrant to therapy. We report a case of granulomatous rosacea treated with chromophore gel-assisted phototherapy(CGAP). A 50-year-old woman of Lebanese background presented with a three-month history of a papulopustular eruption. She described paroxysms of papules affecting the glabella, malar and mental regions. She denied any flushing or ophthalmological symptoms. Examination demonstrated tumid papules and pustules affecting the glabella with malar erythema composed of fine telangiectasia. There was no appreciable phymatous change (Fig.1a). Biopsy demonstrated ectatic dermal blood vessels, and pandermal granulomatous inflammation with lymphocyte sand neutrophils (Fig.2 a & b). Microbial studies including special stains, as well as bacteria, Mycobacteria and deep fungal culture & PCR were negative. The clinical and pathological findings were consistent with granulomatous rosacea. Modest improvement was observed with topical metronidazole, ivermectin, and brimonidine and systemic minocycline 50mg BD led to the development of headache. The patient was reticent to pursue alternate systemic treatments and accordingly a trial of CGAP was pursued. The patient received twelve treatment sessions over six weeks involving application of a 2mm layer of the photoconverter chromophore gel (Kleresca®) followed by irradiation with a multi-LED lamp (415nm and 447nm) (Kleresca®, Balerup, Denmark). Significant improvement was observed in both the papulopustular and erythemato-telangiectatic components of her rosacea (Fig. 1b). To date, there has been no relapse in her rosacea off all active treatment, at a time-point six months after cessation of CGAP.

Figure 1. (a) Baseline photographs of a patient with a papular eruption affecting the glabellar and malar regions. (b) Following twelve treatments with CGAP, significant improvement is observed.

Figure 2. Biopsy demonstrated ectatic dermal blood vessels, and pandermal granulomatous inflammation composed of epithelioid histiocytes, multinuclear giant cells, lymphocytes and neutrophils. (a) Haematoxylin and eosin, original magnification X10, (b) Haematoxylin and eosin, original magnification X40.

Discussion

Granulomatous rosacea is notoriously difficult to treat, and there is no current consensus regarding the best approach to management. Small-volume case reports and series have advocated therapeutic options including dapsone, tetracyclines and isotretinoin.[1] However systemic treatment is not always accepted or tolerated, as in the case of our patient. CGAP is a new therapeutic modality that has been shown to be effective in papulopustular rosacea,[2] as well other conditions such as acne[3,4] and erlotinib induced acneiform eruptions.[5] CGAP involves irradiation of a chromophore gel (Kleresca®) with light at the wavelengths 415nm and 447nm to generate a fluorescent spectrum from approximately 510-630nm. CGAP is non-invasive, in-office intervention with no known systemic side effects. While the pathophysiology of rosacea is unclear, there appears to be an overgrowth of commensal organisms paired with alterations in innate immune response.[1] Further studies with greater methodological rigor should be employed to determine the role of CGAP in this setting. However it is biologically plausible that CGAP may have be effective in the management of rosacea due to its proposed anti-inflammatory and antibacterial effects.[6] Additionally, light based modalities such as phototherapy and photodynamic therapy have been shown to be helpful in other granulomatous diseases, such sarcoidosis, by decreasing interleukin 1 and tumour necrosis factor alpha locally which are necessary for granuloma formation and maintenance.[7] This case suggests that there is promise in CGAP as management of granulomatous rosacea. However, a single case report cannot discount the impact of a placebo effect, or the possibility of spontaneous remission. Nonetheless, the noteworthy response of our patient to treatment suggests that CGAP may be of therapeutic value, and warrants further research.

References

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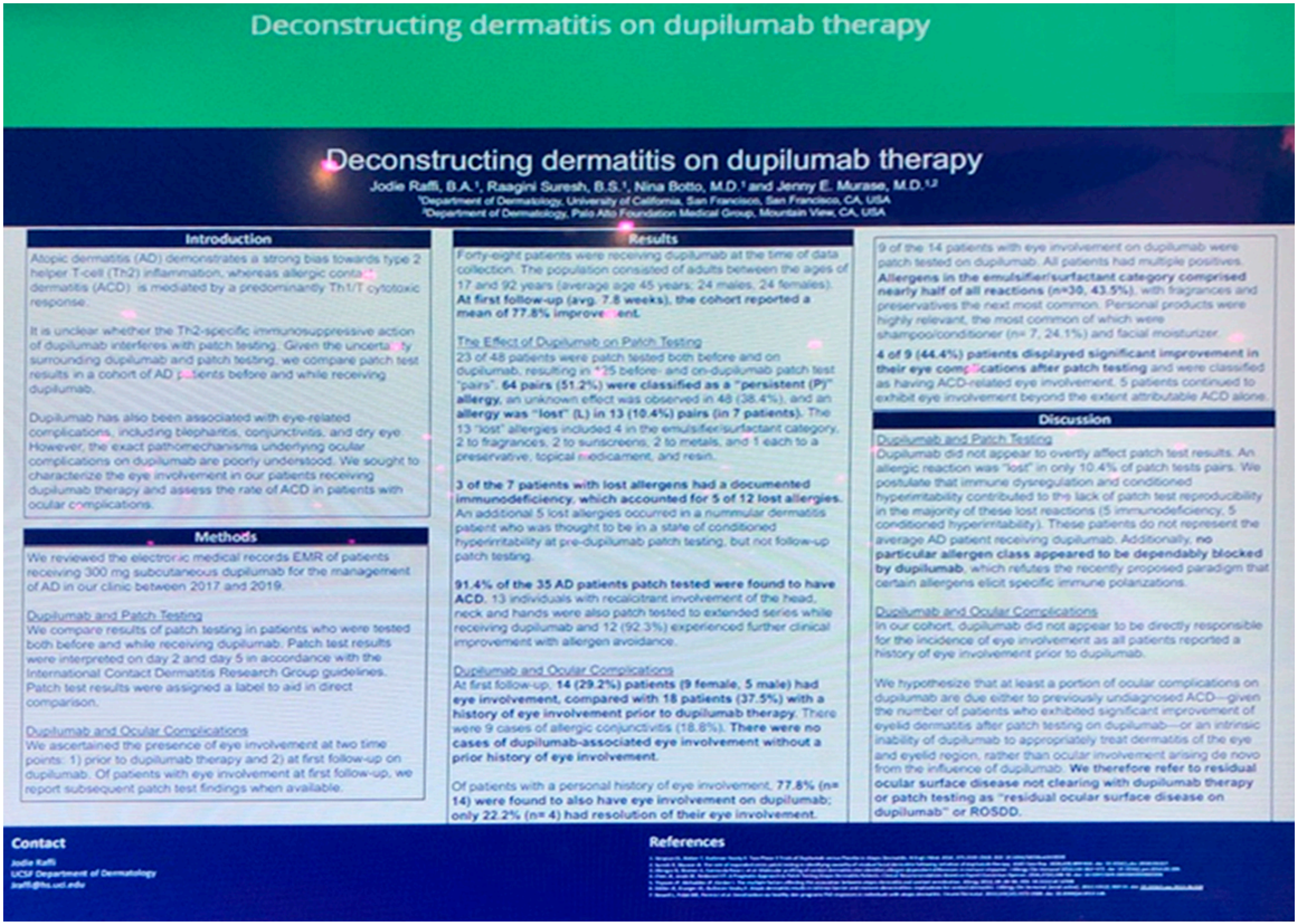
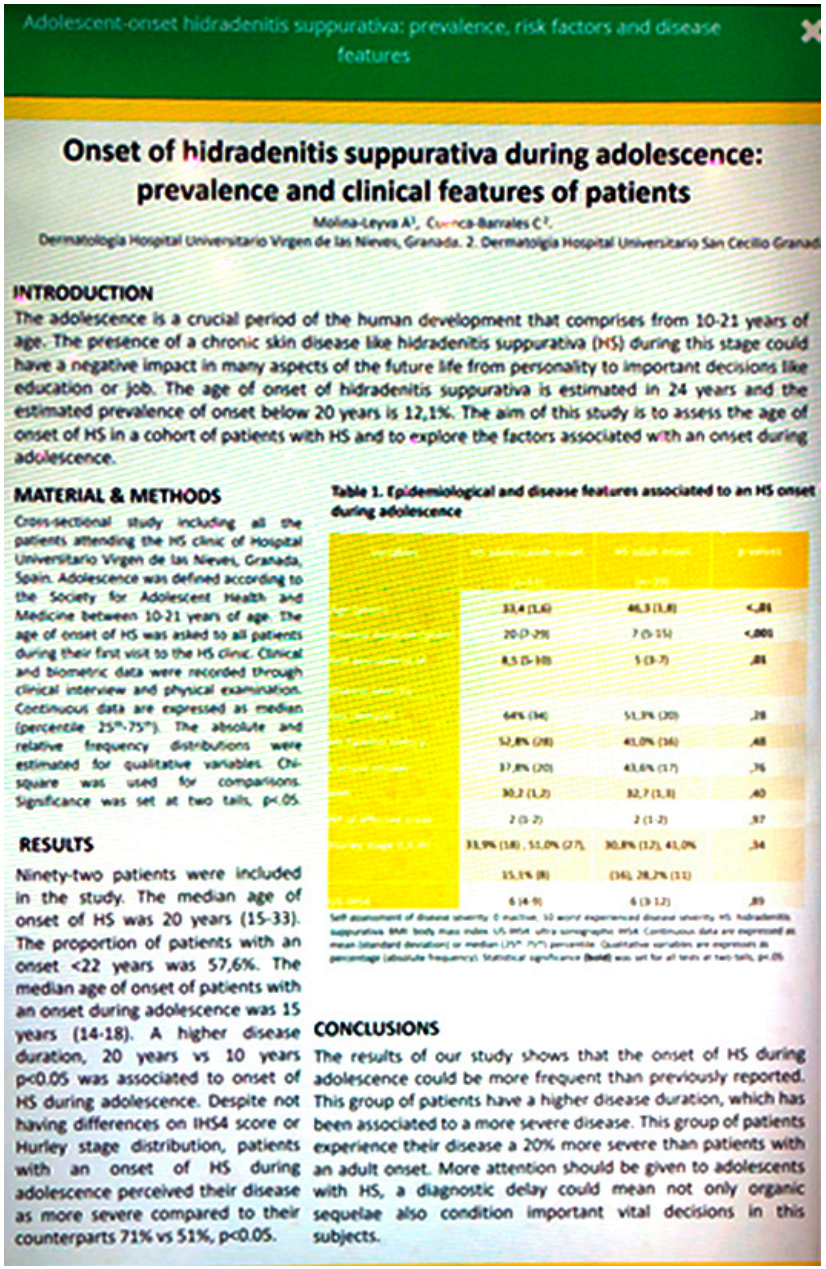
Contact dermatitis



Hidrosadenitis



Adolescent-onset hidradenitis suppurativa: prevalence, risk factors and disease features

Onset of hidradenitis suppurativa during adolescence: prevalence and clinical features of patients

Molina-Leyva A[1], Cuenca-Barrales C[2].
Dermatología Hospital Universitario Virgen de las Nieves, Granada. 2. Dermatología Hospital Universitario San Cecilio Granada

INTRODUCTION

The adolescence is a crucial period of the human development that comprises from 10-21 years of age. The presence of a chronic skin disease like hidradenitis suppurativa (HS) during this stage could have a negative impact in many aspects of the future life from personality to important decisions like education or job. The age of onset of hidradenitis suppurativa is estimated in 24 years and the estimated prevalence of onset below 20 years is 12,1%. The aim of this study is to assess the age of onset of HS in a cohort of patients with HS and to explore the factors associated with an onset during adolescence.

MATERIAL & METHODS

Cross-sectional study including all the patients attending the HS clinic of Hospital Universitario Virgen de las Nieves, Granada, Spain. Adolescence was defined according to the Society for Adolescent Health and Medicine between 10-21 years of age. The age of onset of HS was asked to all patients during their first visit to the HS clinic. Clinical and biometric data were recorded through clinical interview and physical examination. Continuous data are expressed as median (percentile 25th-75th). The absolute and relative frequency distributions were estimated for qualitative variables. Chi-square was used for comparisons. Significance was set at two tails, p<.05.

Table 1. Epidemiological and disease features associated to an HS onset during adolescence

	33,4 (1,6)	46,3 (1,8)	<,01
	20 (7-29)	7 (5-15)	<,001
	8,5 (5-10)	5 (3-7)	,01
	64% (34)	51,3% (20)	,28
	52,8% (28)	41,0% (16)	,48
	37,8% (20)	43,6% (17)	,76
	30,2 (1,2)	32,7 (1,3)	,40
	2 (1-2)	2 (1-2)	,97
	33,9% (18) , 51,0% (27),	30,8% (12), 41,0%	,34
	15,1% (8)	(16), 28,2% (11)	
	6 (4-9)	6 (3-12)	,89

Self assessment of disease severity. 0 inactive, 10 worst experienced disease severity. HS: hidradenitis suppurativa. BMI: body mass index. US-IHS4: ultra sonographic IHS4. Continuous data are expressed as mean (standard deviation) or median (25th-75th percentile). Qualitative variables are expressed as percentage (absolute frequency). Statistical significance (**bold**) was set for all tests at two tails, p<.05.

RESULTS

Ninety-two patients were included in the study. The median age of onset of HS was 20 years (15-33). The proportion of patients with an onset <22 years was 57,6%. The median age of onset of patients with an onset during adolescence was 15 years (14-18). A higher disease duration, 20 years vs 10 years p<0.05 was associated to onset of HS during adolescence. Despite not having differences on IHS4 score or Hurley stage distribution, patients with an onset of HS during adolescence perceived their disease as more severe compared to their counterparts 71% vs 51%, p<0.05.

CONCLUSIONS

The results of our study shows that the onset of HS during adolescence could be more frequent than previously reported. This group of patients have a higher disease duration, which has been associated to a more severe disease. This group of patients experience their disease a 20% more severe than patients with an adult onset. More attention should be given to adolescents with HS, a diagnostic delay could mean not only organic sequelae also condition important vital decisions in this subjects.

Milàn