Update of Frontal Fibrosing Alopecia

Curtis T. Thompson, M.D.
CTA Lab
And
Affiliate Professor of Dermatology and Pathology
Oregon Health & Sciences University

Lecture Overview

- History of FFA
- Causation of FFA
- New diagnostic techniques
  - 2mm punch
  - Mucin stain

Arch Dermatol. 1994 Jun;130(6):770-4.

Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution.

Kossard S[1].

Author information Papers

Erratum in
Arch Dermatol 1994 Nov;130(11):1407.

Abstract

BACKGROUND: Recession of the frontal hairline is a common event in postmenopausal women. This has been shown not to be a marker of gross androgenization, and is usually a progressive nonscarring alopecia. Six postmenopausal women, who developed a progressive frontal scarring alopecia, were studied and their clinical and laboratory data, as well as the results of scalp biopsy specimens in all six patients, were analyzed and compared with recognized forms of scarring alopecia and recently described findings in androgenetic alopecia.

OBSERVATIONS: The six postmenopausal women developed a progressive frontal hairline recession that was associated with perifollicular erythema within the marginal hairline, producing a frontal fibrosing alopecia extending to the temporal and parietal hair margins. Scalp biopsy specimens from the frontal hair margin showed perifollicular fibrosis and lymphocytic inflammation concentrated around the isthmus and infundibular areas of the follicles. Immunophenotyping of the lymphocytes showed a dominance of activated T-helper cells. Clinical review of all six cases showed a progressive marginal alopecia without the typical multifocal areas of involvement seen in lichen planopilaris or pseudopelade. None of the patients had mucous membrane or skin lesions typical of lichen planus. Hormonal studies, in five patients, showed no elevated androgen abnormalities.

CONCLUSIONS: Progressive frontal recession in postmenopausal women may show clinical features of a fibrosing alopecia. The histologic findings are indistinguishable from those seen in lichen planopilaris. However, the absence of associated lesions of lichen planus in all six women raises the possibility that this mode of follicular destruction represents a reaction pattern triggered by the events underlying postmenopausal frontal hairline recession.

Lichen Planopilaris (LPP)

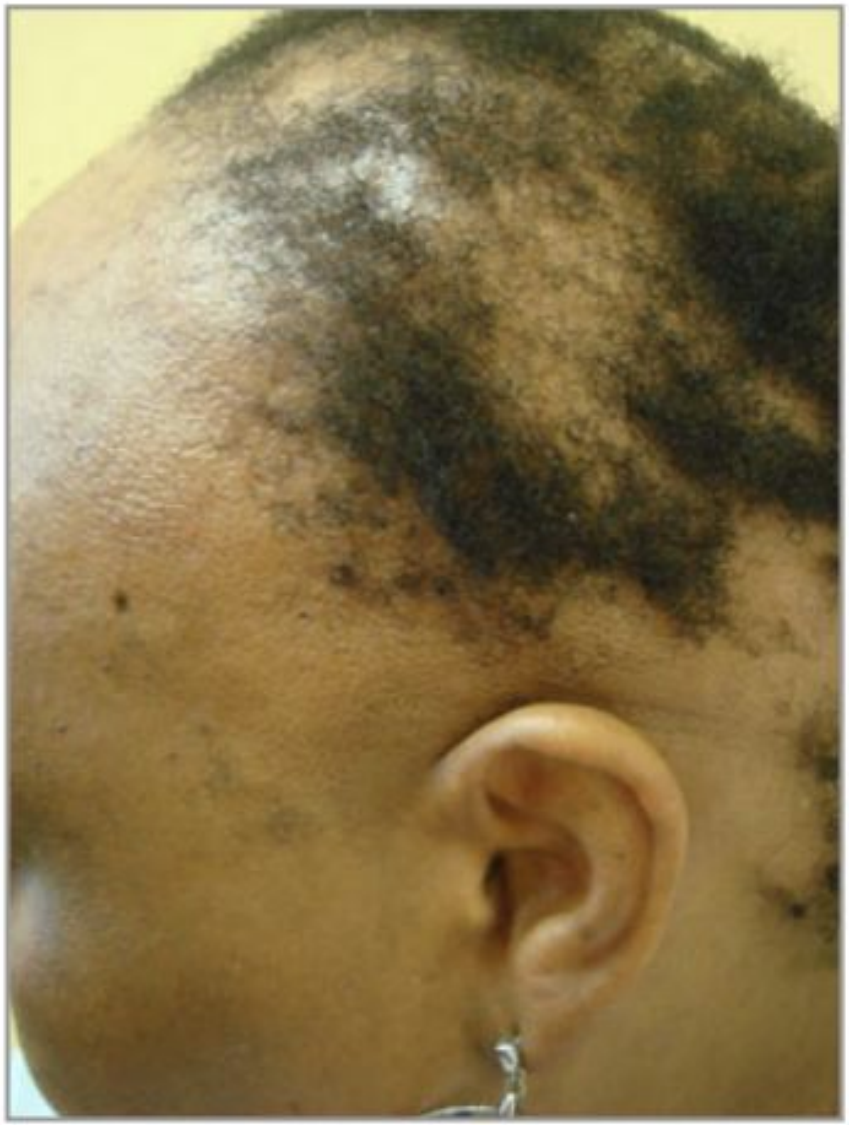
- Miniepidemic?
  - Hair loss clinicians observing increased incidence.
  - Traditionally West Coast > East Coast

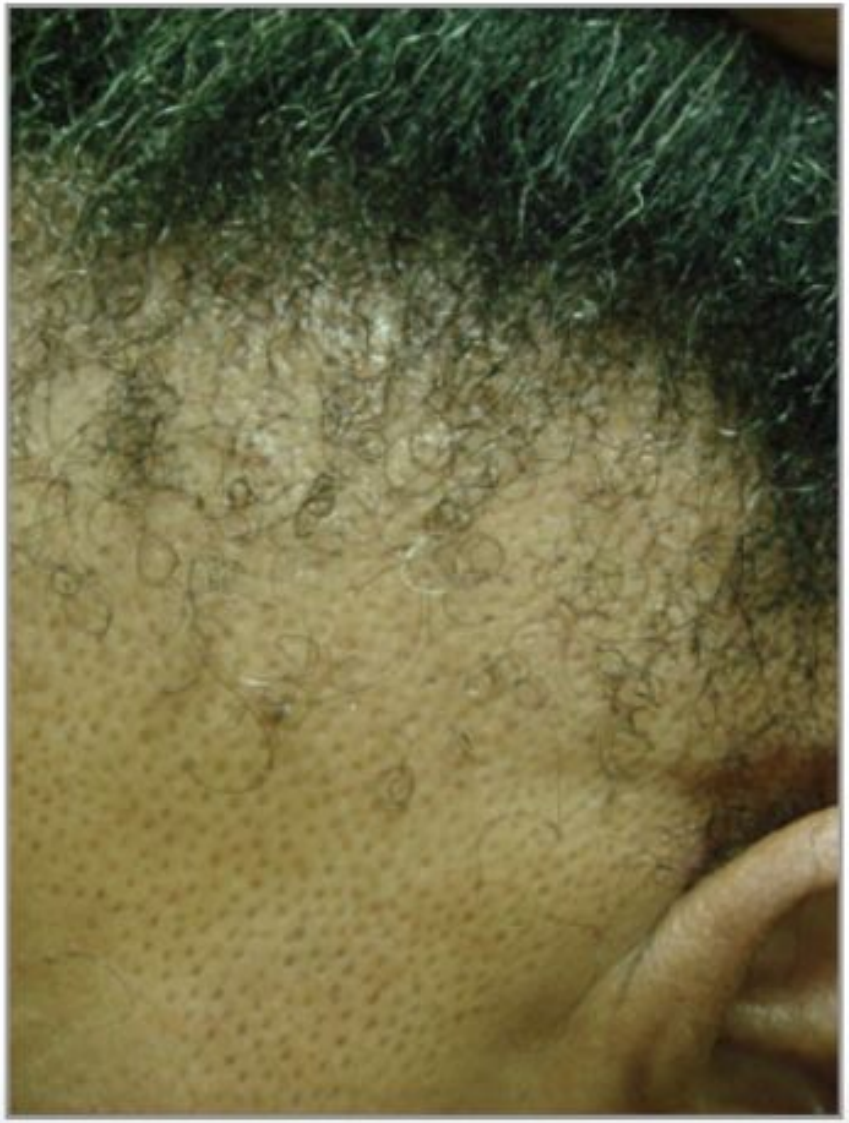
Lichen Planopilaris Increasing Incidence

- ?Nanoparticle?
  - Sunscreen?
  - Lichen planus—Metals, especially dental implicated
    - Gold, mercury—dental*
    - Nail LP associated with +metal patch test**

*Sasaki G et al. J Dermatol 23:890, 1996.
**Nishizawa A et al. J Eur Acad Dermatol Venerol 27:e231, 2013.

African people with FFA





Dlova NC *et al.* BRJ 169:939-41, 2013.

Br J Dermatol. 2016 Oct;175(4):762-7. doi: 10.1111/bjd.14535. Epub 2016 Jun 30.

Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study.

Aldoori N[1], Dobson K[1], Holden CR[1], McDonagh AJ[1], Harries M[2], Messenger AG[3].

Author information

Abstract

BACKGROUND: Since its first description in 1994, frontal fibrosing alopecia (FFA) has become increasingly common, suggesting that environmental factors are involved in the aetiology.

OBJECTIVES: To identify possible causative environmental factors in FFA.

METHODS: A questionnaire enquiring about exposure to a wide range of lifestyle, social and medical factors was completed by 105 women with FFA and 100 age- and sex-matched control subjects. A subcohort of women with FFA was patch tested to an extended British standard series of allergens.

RESULTS: The use of sunscreens was significantly greater in the FFA group compared with controls. Subjects with FFA also showed a trend towards more frequent use of facial moisturizers and foundations but, compared with controls, the difference in frequencies just failed to reach statistical significance. The frequency of hair shampooing, oral contraceptive use, hair colouring and facial hair removal were significantly lower in the FFA group than in controls. Thyroid disease was more common in subjects with FFA than controls and there was a high frequency of positive patch tests in women with FFA, mainly to fragrances.

CONCLUSIONS: Our findings suggest an association between FFA and the use of facial skin care products. The high frequency of sunscreen use in patients with FFA, and the fact that many facial skin care products now contain sunscreens, raises the possibility of a causative role for sunscreen chemicals. The high frequency of positive patch tests in women with FFA and the association with thyroid disease may indicate a predisposition to immune-mediated disease.

Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens

DOI: 10.1111/bjd.15311

Dear Editor, Frontal fibrosing alopecia (FFA) was first described by Kossard in 1994 in six postmenopausal women.[1] FFA remained rare during the 1990s, but in the last 10–15 years it has become increasingly common, a phenomenon observed worldwide. The recent onset and apparently rising incidence of FFA suggest involvement of environmental factors in the aetiology. We previously reported a questionnaire study in women with FFA that asked about a wide range of medical, social and environmental exposures. The results suggested an association between FFA and leave-on facial products, including moisturizers and sunscreens.[2] However, although the regular use of moisturizers was greater in women with FFA, these products are used by most women and we were unable to show a significant difference in their use between women with FFA and similarly aged controls. The use of primary sunscreens was significantly greater among women with FFA than in controls, but we were not able to assess whether patients were also exposed to sunscreens from other sources.

We have therefore repeated our questionnaire study in men with FFA, as we anticipated that their use of leave-on facial skincare products would be lower than in women.

As FFA is rare in men, patients were recruited from across the U.K. and one case was recruited from Belgium. In all cases the diagnosis was made by a clinician with special expertise in hair disease, and it was supported by histology in most cases. The clinical diagnosis was based on scarring alopecia affecting the frontal hairline causing recession of the hairline. Additional features included loss of eyebrows, follicular erythema of the frontal hairline and loss of sideburn and beard hair. Male controls aged 35–80 years were recruited from three sites (Sheffield, Salford and Glasgow). The patients completed a questionnaire similar to that used in our female study, but inviting more detailed information on the use of facial skincare and hair care products. Male patients with FFA were asked about the timing and distribution of hair loss, but otherwise the questionnaires completed by both groups were identical.

Seventeen men with FFA and 73 controls were recruited. The mean age of onset of hair loss in the patients with FFA was 54·5 years (range 35–77). All had loss of hair from the frontal hairline, and 16 (94%) had lost eyebrows. Twelve men (71%) reported loss of hair from the beard and 13 (76%) reported loss of hair from the limbs. All men with FFA reported using facial moisturizers, compared with 40% in the control group. Facial moisturizers were used at least twice a week by 94% of patients with FFA, but by only 32% of controls ($P < 0·001$) (Table 1). Sixteen patients reported using moisturizers for a period consistent with their use prior to the onset of FFA. The use of primary sunscreens by men with FFA was significantly more common than by controls. Overall 35% of men with FFA reported using a sunscreen at least twice a week all year round, compared with 4% of controls ($P = 0·0012$).

When moisturizers containing sunscreen chemicals were included in the analysis, at least 71% of men with FFA applied a product containing a sunscreen at least twice a week all year

Table 1 Reported use of skincare and hair care products by patients with frontal fibrosing alopecia (FFA) and controls

	Patients with FFA	Controls	P-value
Number of patients	17	73	
Age (years), mean (range)	63·1 (42–80)	59·1 (37–79)	
Age at onset of hair loss (years), mean (range)	54·5 (35–77)		
Facial moisturizer[a]	16 (94)	23 (32)	< 0·001
Primary sunscreen[b]	6 (35)	3 (4)	0·0012
Sunscreen[b]	12 (71)	8 (11)	< 0·001
Facial cleanser[a]	4 (24)	5 (7)	0·066
Facial scrub[a]	0	0	
Facial mask[a]	0	0	
Aftershave[a]	7 (41)	28 (39)	1·00
Shampoo[a]	13 (76)	62 (85)	0·27
Conditioner[a]	4 (24)	13 (18)	0·73
Hair spray[a]	1 (6)	2 (3)	0·48
Hair mousse[a]	0	0	
Hair gel[a]	2 (12)	10 (14)	1·00
Hair dye[c]	2 (12)	3 (4)	0·26

Values are n (%) unless stated otherwise. [a]Twice a week or more frequently. [b]Twice a week or more frequently all year round. [c]At least once a year. Sunscreen includes exposure to sunscreen chemicals in primary sunscreens and moisturizers. Analyses were performed after excluding subjects who failed to answer the question. Frequencies in the FFA and control groups were compared using Fisher's exact test.

© 2017 British Association of Dermatologists

Table 1 Reported use of skincare and hair care products by patients with frontal fibrosing alopecia (FFA) and controls

	Patients with FFA	Controls	P-value
Number of patients	17	73	
Age (years), mean (range)	63·1 (42–80)	59·1 (37–79)	
Age at onset of hair loss (years), mean (range)	54·5 (35–77)		
Facial moisturizer[a]	16 (94)	23 (32)	< 0·001
Primary sunscreen[b]	6 (35)	3 (4)	0·0012
Sunscreen[b]	12 (71)	8 (11)	< 0·001
Facial cleanser[a]	4 (24)	5 (7)	0·066
Facial scrub[a]	0	0	
Facial mask[a]	0	0	
Aftershave[a]	7 (41)	28 (39)	1·00
Shampoo[a]	13 (76)	62 (85)	0·27
Conditioner[a]	4 (24)	13 (18)	0·73
Hair spray[a]	1 (6)	2 (3)	0·48
Hair mousse[a]	0	0	
Hair gel[a]	2 (12)	10 (14)	1·00
Hair dye[c]	2 (12)	3 (4)	0·26

Values are n (%) unless stated otherwise. [a]Twice a week or more frequently. [b]Twice a week or more frequently all year round. [c]At least once a year. Sunscreen includes exposure to sunscreen

Debroy Kidambi A *et al.* Br J Dermatol 177:260-1, 2017.

Original article

CED
Clinical and Experimental Dermatology

Risk factors associated with frontal fibrosing alopecia: a multicentre case–control study

O. M. Moreno-Arrones,[1] D. Saceda-Corralo,[1] A. R. Rodrigues-Barata,[1] M. Castellanos-González,[2] M. A. Pugnaire,[3] R. Grimalt,[4] A. Hermosa-Gelbard,[1] C. Bernárdez,[5] A. M. Molina-Ruiz,[6] N. Ormaechea-Pérez,[7] P. Fernández-Crehuet[8] and S. Vaño-Galván[1,9]

[1]Dermatology Department, Hospital Universitario Ramon y Cajal, Madrid, Spain; [2]Dermatology Department, Hospital del Sureste, Madrid, Spain; [3]Dermatology Department, Hospital Universitario Campus de la Salud, Granada, Spain; [4]Dermatology Department, Universitat Internacional de Catalunya, UIC, Barcelona, Spain; [5]Dermatology Department, Hospital Ruber Juan Bravo, Madrid, Spain; [6]Dermatology Department, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [7]Dermatology Department, Hospital Universitario Donostia, San Sebastián, Spain; [8]Dermatology Department, Hospital Universitario Reina Sofía, Clínica Fernández-Crehuet, Córdoba, Spain; and [9]Department of Medicine and Medical Specialties, University of Alcalá, Alcalá de Henares-Madrid, Madrid, Spain

Alopécie frontale fibrosante post ménopausique : une réaction lichénoïde aux nanoparticules de dioxyde de titane présentes dans les follicules pileux?

Charlotte Gary[1], Florence Brunet-Possenti[1], Eduardo Marinho[2], Lydia Deschamps[2], Hester Colboc[3], Dominique Bazin[4], Vincent Descamps[1]

[1] Service de Dermatologie, Hôpital Bichat, Université Paris Diderot
[2] Service d'Anatomopathologie, Hôpital Bichat, Paris
[3]Service de Dermatologie, Hôpital Rothschild, Paris
[4]Synchrotron SOLEIL, Gif-sur-Yvette

Alopécie frontale fibrosante post ménopausique : une réaction lichénoïde aux nanoparticules de dioxyde de titane présentes dans les follicules pileux?

Charlotte Gary[1], Florence Brunet-Possenti[1], Eduardo Marinho[2], Lydia Deschamps[2], Hester Colboc[3], Dominique Bazin[4], Vincent Descamps[1]

[1] Service de Dermatologie, Hôpital Bichat, Université Paris Diderot
[2] Service d'Anatomopathologie, Hôpital Bichat, Paris
[3]Service de Dermatologie, Hôpital Rothschild, Paris
[4]Synchrotron SOLEIL, Gif-sur-Yvette

INTRODUCTION

L'alopécie frontale fibrosante (AFF) post ménopausique est une pathologie émergente dont l'incidence augmente dans l'ensemble des pays. Son origine reste inconnue. Nous rapportons la présence de dioxyde de titane dans les cheveux d'une patiente atteinte d'AFF.

OBSERVATION

Une patiente âgée de 79 ans était suivie en consultation depuis 2010 pour une alopécie progressive évoluant au moins depuis 12 ans soit depuis l'âge de 69 ans prédominant au niveau fronto-temporo-pariétal avec recul progressif de la ligne d'implantation des cheveux. Elle s'associait à une alopécie des sourcils. A l'examen la peau du front était scléreuse. Les cheveux présentaient à leur ostium folliculaire un léger érythème avec hyperkératose. Le tableau clinique était typique d'une AFF (Fig. 1). Une biopsie cutanée était réalisée confirmant le diagnostic d'alopécie cicatricielle lymphocytaire. Cette patient avait par ailleurs une forte héliodermie témoignant d'une exposition solaire importante tout au long de sa vie.

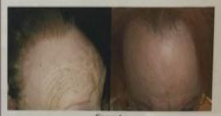


Figure 1

LAURÉAT PRIX

MÉTHODES ET RÉSULTATS

Une recherche de nanoparticules a été réalisée sur des follicules pileux extraits en zone atteinte par microscopie électronique à balayage par effet de champs combinée à une spectroscopie à dispersion énergétique.
Un jeu de clichés de microscopie électronique à balayage sur un microscope de dernière génération a été collecté sur un ensemble de cheveux mettant en évidence des dépôts anormaux de nanoparticules (Fig 2A, 2B).
En complément, les expériences de fluorescence X induites par des électrons sur le microscope électronique à balayage montraient distinctement un signal attribuable aux atomes de titane (Fig. 2C, 2D).

Cette observation met ainsi en évidence sans ambiguïté la présence de nanoparticules de dioxyde de titane au niveau des follicules pileux.

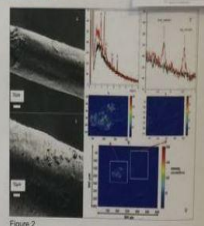


Figure 2

DISCUSSION

L'AFF est considérée comme une forme particulière de lichen folliculaire avec histologiquement un infiltrat lymphocytaire périfolliculaire. Des études épidémiologiques récentes associent la présence de cette alopécie à l'utilisation de cosmétiques en particulier de crème solaire.
En reprenant l'interrogatoire de cette patiente signalait l'utilisation quotidienne depuis 15 ans d'écrans solaires contenant du dioxyde de titane.
Du fait des propriétés anti-UV, la présence de nanoparticules (dioxyde de titane et oxyde de zinc) s'est très largement répandue au cours de ces dernières années dans les produits cosmétiques, et l'impact dermatologique à long terme de ces particules n'est pas encore bien connu chez l'homme.
L'hypothèse formulée est que la présence de dioxyde de titane au sein du follicule pileux soit responsable d'une réaction lichénoïde. Des réactions lichénoïdes sont connues avec d'autres métaux tels que le Nickel.
Des explorations complémentaires sont en cours chez cette patiente (tests épicutanés et tests in vitro de prolifération lymphocytaire et ELISPOT en présence de titane).

CONCLUSION

Nous présentons la première observation de présence de nanoparticules dans les follicules pileux d'une patiente atteinte d'AFF post-ménopausique.

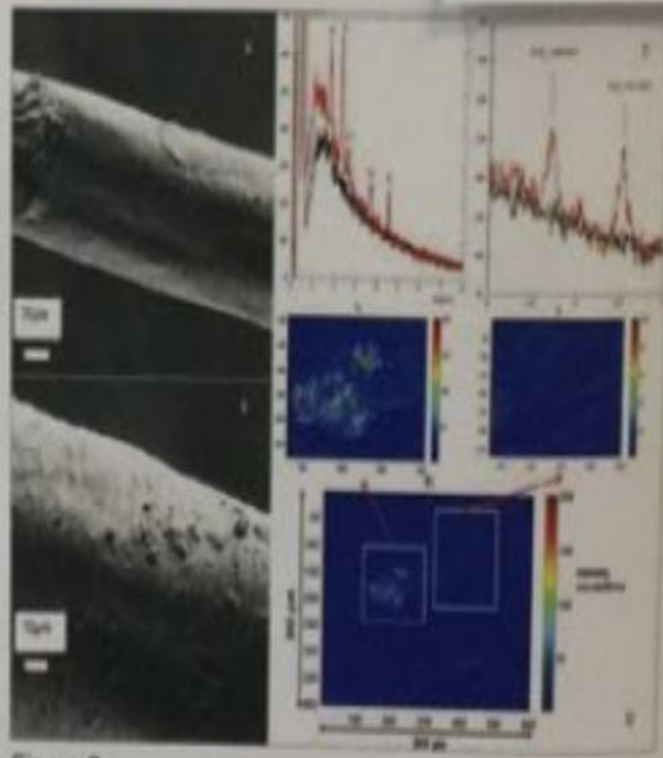
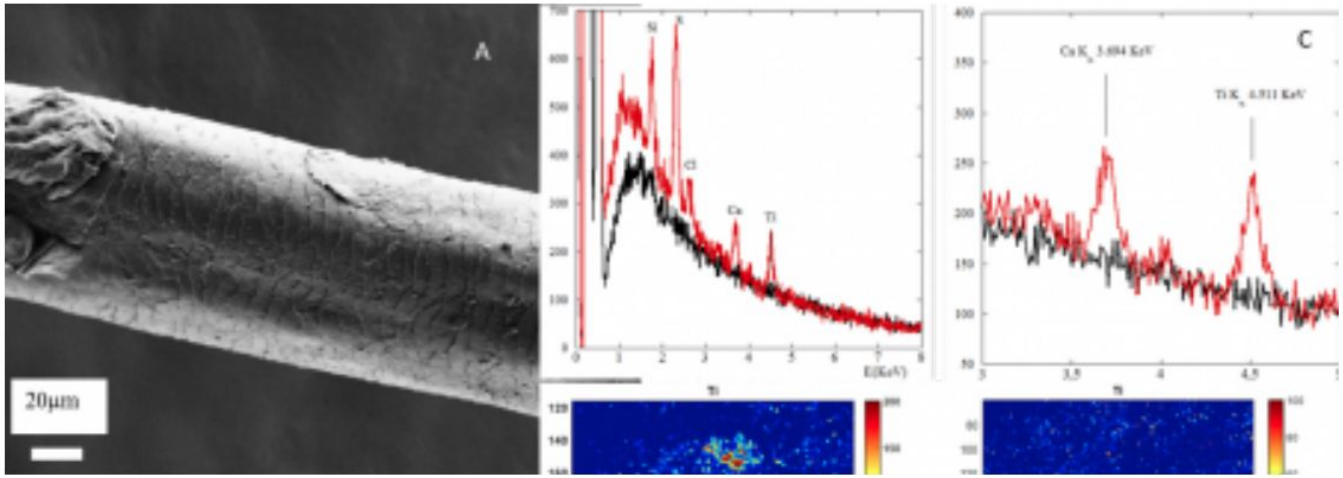


Figure 2

Titanium on the hair shaft

Le long des follicules, à leur surface, ont ainsi été mis en évidence des agrégats de microparticules de TiO_2 (0,5 – 1 μm) associées à des nanoparticules de TiO_2.



Brunet-Possenti F *et al.* JEADV 32:e442-3, 2018.

Br J Dermatol. 2019 Jan 16. doi: 10.1111/bjd.17639. [Epub ahead of print]

Identification of titanium dioxide on the hair shaft of patients with and without frontal fibrosing alopecia: A pilot study of 20 patients.

Thompson CT[1,2], Chen ZQ[3], Kolivras A[4], Tosti A[5].

Author information Papers

Abstract

Frontal fibrosing alopecia (FFA) has increased markedly in incidence since it was first reported in 1994. A possible role of cosmetic ingredients has been suspected, especially UV blockers, since these were added to products in the late 1980s. Daily, year-round use of facial moisturizers, most of which contain a sunscreen, has

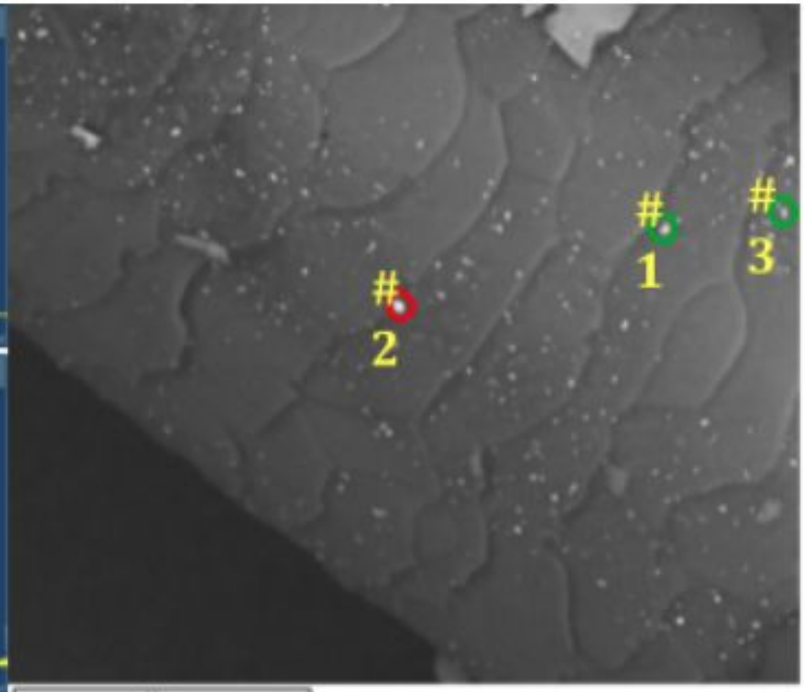


Fig. 1 Right: a backscattered electron image taken from one of typical hair shafts with SEM showing the presence of particles with brighter contrast on a hair shaft; Left: EDX spectra collected from particle 1-3 showing the presence of Ti species on particle 1 and 3.

EDX=Energy Dispersive X-ray Analysis

20 Patient Pilot Study

- 16 Female patients with FFA Positive Ti
- 3 Female patients without FFA Positive Ti
- 1 Male patient without FFA Negative Ti
  - No product usage on face or hair

Physical Properties of TiO_2

- **Pigment Form—Larger particles**
  - Paint, cosmetics, food
- **Non-Pigment Form--Nanoparticles**
  - Reduces unwanted shine. “Matte” type cosmetics.
  - **Texture** – Smoother more sheer but opaque formations—conceals blemishes
  - **UV**A/UVB absorption and scattering.
- **Waterproof and Long-lasting**

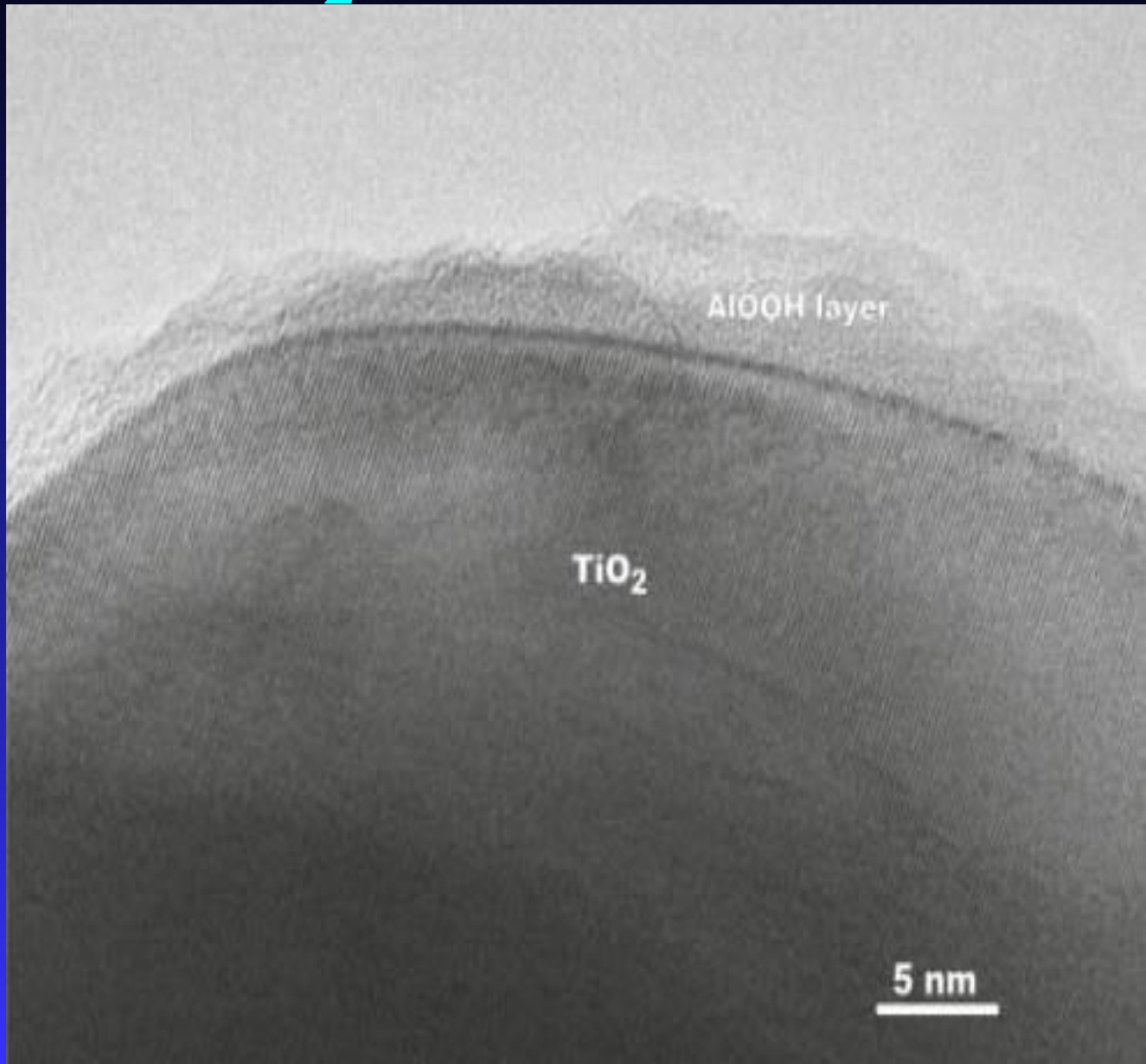
https://tdma.info/titanium-dioxide-the-cosmetic-industrys-best-kept-secret/

TiO_2 Nanoparticle Toxicity

- 1985—Mouse study—Chronic exposure led to lung bronchioloalveolar adenomas and cystic keratinizing squamous cell carcinomas
  - 5 days/week for 2 years

Lee KP, Trochimowicz HJ, Reinhardt CF, "Pulmonary response of rats exposed to titanium dioxide (TiO2) by inhalation for two years", Toxicol Appl Pharmacol. 1985;79:179–92.

Coating of TiO_2 Nanoparticles

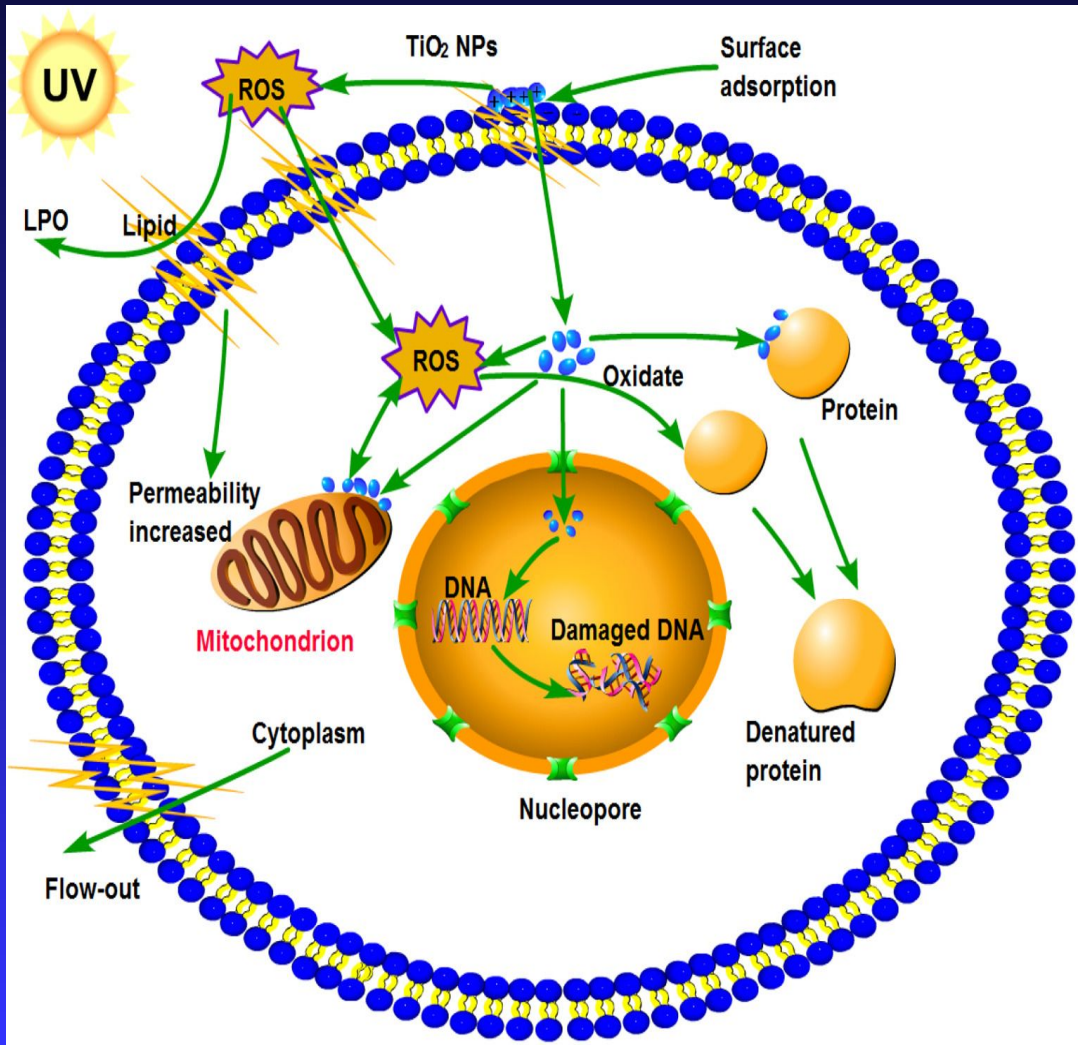


TiO_2 Nanoparticles—1990s

- 200-250nm in size but there are fragments 100nm
- Small enough to enter cells

Mechanism of TiO_2 nanoparticle toxicity

- Oxygen Radical Species upon UV exposure
  - O_2^-,
  - H_2O_2,
  - hydroxyl OH^-



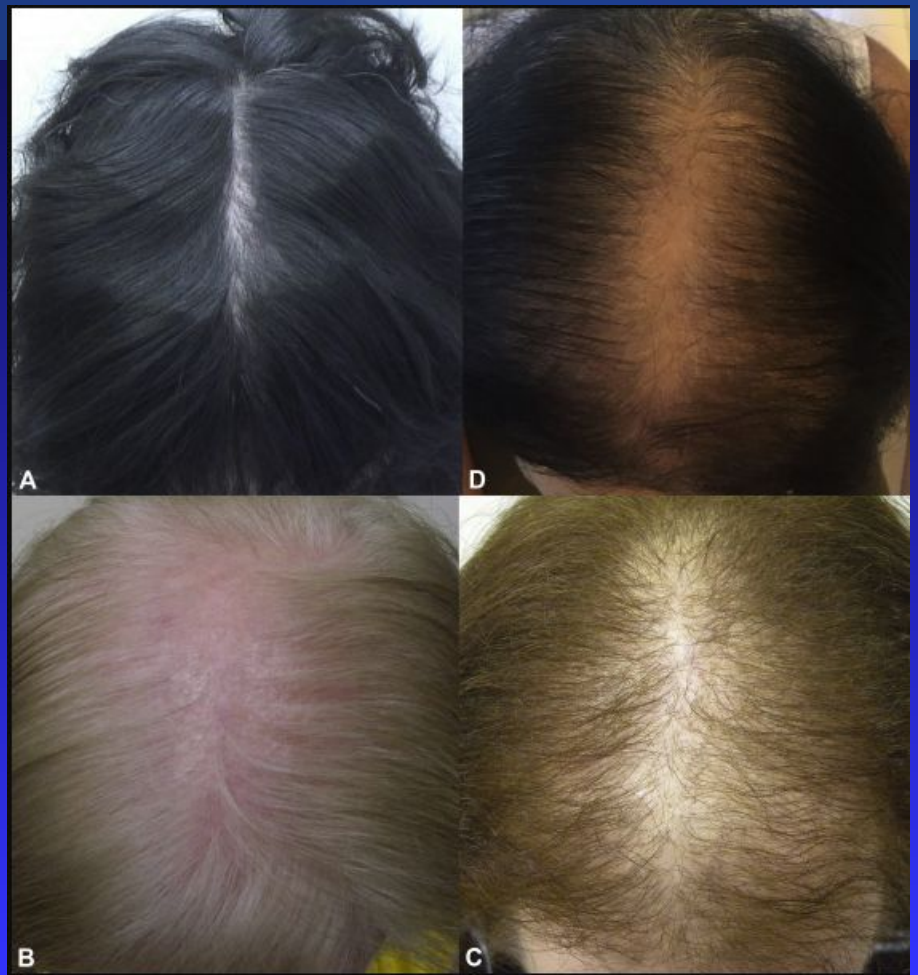
J. Hou *et al.* Toxicity and mechanisms of action of titanium dioxide nanoparticles in living organisms. J Environmental Sci 75:40-53, 2019.

Inorganic Coatings	Organic Coatings	Natural coatings
silica	Stearate	Green tea
Alumina	butyl glycol dicaprylate + Stearate	Lignin
Silica + Alumina	Methicone	
Zirconium dioxide	Dimethicone	
Manganese oxide	Dimethicone / siloxane	
Iron oxide	Dimethicone / methicone copolymer	
Zinc oxide	Simethicone	
Aluminum hydroxide	Trimethylsiloxysilicone	
	Polyvinyl-pyrrolidone	
	Alkyl silane	
	Glycerin	

Fibrosing alopecia in a pattern distribution

Jacob Griggs, BA • Ralph M. Trüeb, MD • Maria Fernanda Reis Gavazzoni Dias, MD • Maria Hordinsky, MD • Antonella Tosti, MD

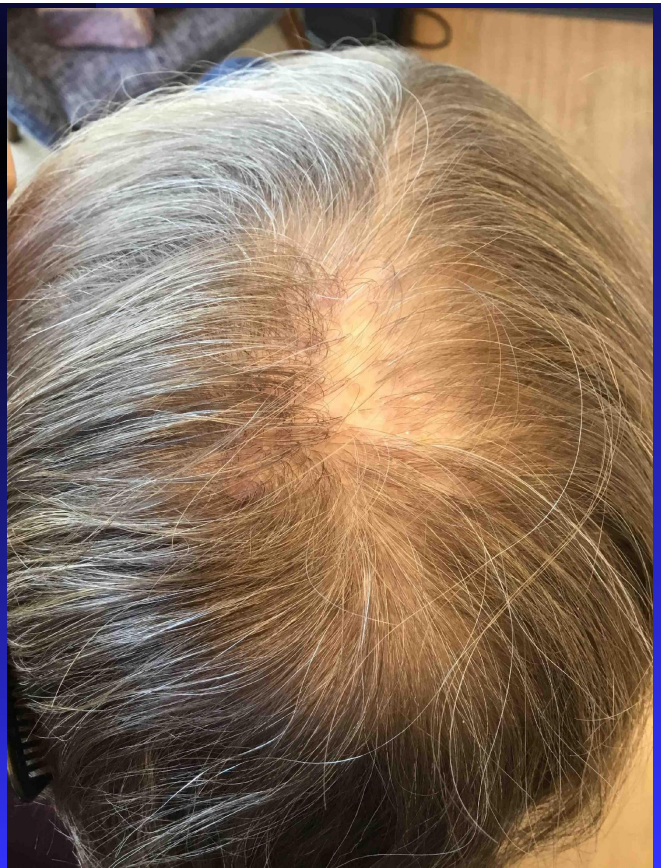
Published: January 08, 2020 • DOI: https://doi.org/10.1016/j.jaad.2019.12.056

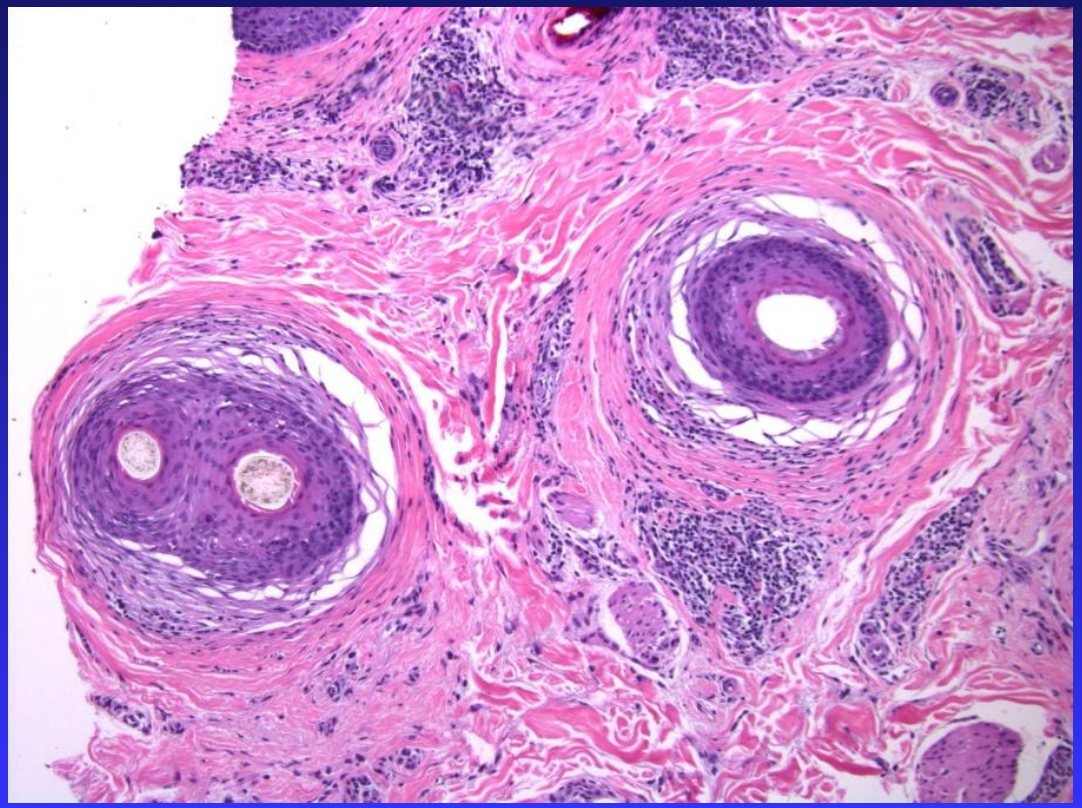


Is there a pathogenetic link between frontal **fibrosing alopecia**, androgenetic **alopecia** and **fibrosing alopecia** in a **pattern distribution**?

Katoulis AC, Diamanti K, Sgouros D, Liakou AI, Bozi E, Avgerinou G, Panayiotides I, Rigopoulos D.

J Eur Acad Dermatol Venereol. 2018 Jun;32(6):e218-e220. doi: 10.1111/jdv.14748. Epub 2018 Jan 15. No abstract available.

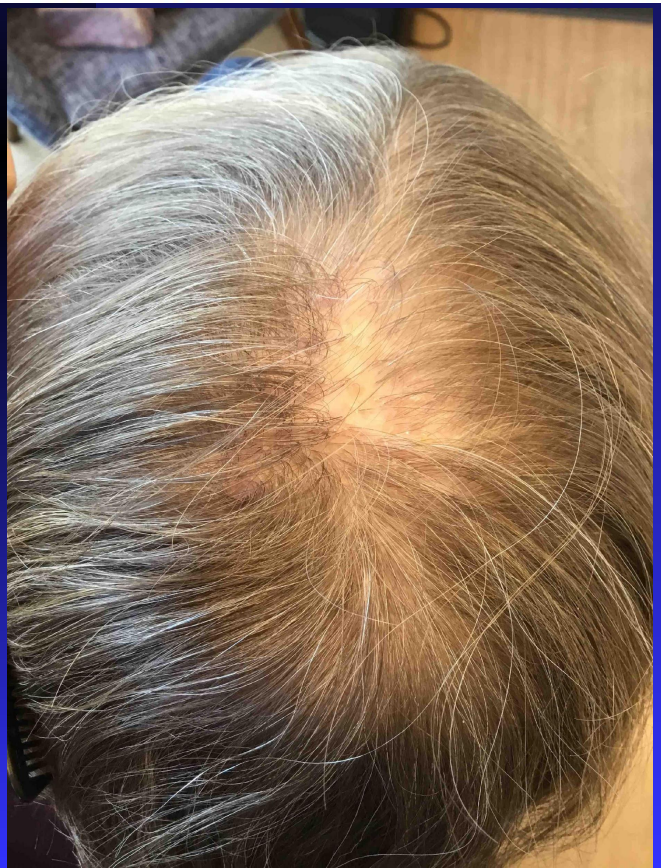




Is there a pathogenetic link between frontal **fibrosing alopecia**, androgenetic **alopecia** and **fibrosing alopecia** in a **pattern distribution**?

Katoulis AC, Diamanti K, Sgouros D, Liakou AI, Bozi E, Avgerinou G, Panayiotides I, Rigopoulos D.

J Eur Acad Dermatol Venereol. 2018 Jun;32(6):e218-e220. doi: 10.1111/jdv.14748. Epub 2018 Jan 15. No abstract available.



Fibrosing alopecia in a pattern distribution

Jacob Griggs, BA • Ralph M. Trüeb, MD • Maria Fernanda Reis Gavazzoni Dias, MD • Maria Hordinsky, MD • Antonella Tosti, MD

Published: January 08, 2020 • DOI: https://doi.org/10.1016/j.jaad.2019.12.056

The observation of familial occurrence of FAPD with FFA[8] and the presence of facial papules characterized by vellus follicle involvement[6] and/or extrafacial follicular red dots[10,21] in both FFA and FAPD suggest that these 2 conditions may be pathogenically related.

Sunscreen

- Avobenzone, Homosalate, Octinoxate, Octisalate, Octocrylene, Oxybenzone
- Inactive Ingredients: Sd Alcohol 40, C12-15 Alkyl Benzoate, Acrylates Octylacrylamide Copolymer, Caprylyl Glycol, Dimethyl Capramide, Aloe Barbadensis (**Aloe Vera**) Leaf Extract, Retinyl Palmitate, Tocopherol, Fragrance.

Sunscreen

- Avobenzone, Homosalate, Octinoxate, Octisalate, Octocrylene, Oxybenzone
- Sd Alcohol 40, C12-15 Alkyl Benzoate, Acrylates Octylacrylamide Copolymer, Caprylyl Glycol, Dimethyl Capramide, Aloe Barbadensis (**Aloe Vera**) Leaf Extract, Retinyl Palmitate, Tocopherol, Fragrance.

Present in 96% of the U.S. population

Skin Appendage Disorders

Novel Insights from Clinical Practice

Lichen Planopilaris in the Setting of Hair Sunscreen Spray

Canavan T.N.[a] · McClees S.F.[b] · Duncan J.R.[a] · Elewski B.E.[a]

Author affiliations

Keywords: Lichen planopilaris · Frontal fibrosing alopecia · Benzyl salicylate · Sunscreen · Scarring alopecia

Sunscreen for sure implicated

REVIEW | VOLUME 82, ISSUE 3, P723-728, MARCH 01, 2020

Sunscreen and frontal fibrosing alopecia: A review

Gabrielle Robinson, MD • Amy McMichael, MD • Steve Q. Wang, MD • Henry W. Lim, MD

Published: October 22, 2019 • DOI: https://doi.org/10.1016/j.jaad.2019.09.085 • Check for updates

Table I. Summary of case-control questionnaire studies regarding FFA and sunscreen use

Study (year)	Participants	Results
Aldoori et al[6] (2016)	Female (N = 205) 105 women with FFA and 100 age- and sex-matched controls	Higher rates of at least twice-weekly sunscreen use (48% vs 24%, $P < .001$)
Debroy et al[20] (2017) Research letter	Male (N = 90) 17 men with FFA and 73 age- and sex-matched controls	Higher rates of primary sunscreen use (35% vs 4%, $P = .0012$) Higher rates of either primary sunscreen use or a moisturizer containing sunscreen (71% vs 11%, $P < .001$) Higher rates of at least twice-weekly use of facial moisturizer with unspecified sunscreen content (94% vs 32%, $P < .001$)
Moreno-Arrones et al[17] (2018)	Female and male (N = 655) 308 cases (289 women and 19 men with FFA) and 347 age- and sex-matched controls (289 women, 58 men)	Higher rates of daily facial sunscreen among women (34.9% controls vs 48.1% cases, $P < .01$) and men (6.9% vs 31.6% $P < .01$)
Cranwell & Sinclair[21] (2019) Research letter	Female (N = 260) 130 women with FFA and 130 age- and sex-matched controls (women with any degree of androgenetic alopecia)	Higher rates of dedicated sunscreen use (92% vs 40%, $P < .001$) Higher rates of daily sunscreen use (88% vs 29%)

Is FFA a contact dermatitis?

Patch testing and contact allergen avoidance in patients with lichen planopilaris and/or frontal fibrosing alopecia: A cohort study

Sonya Prasad, BA • Dustin H. Marks, BS • Laura J. Burns, BA • ... JiaDe Yu, MD • Kristen LoSicco, MD • Maryanne M. Senna, MD • Show all authors

Published: January 18, 2020 • DOI: https://doi.org/10.1016/j.jaad.2020.01.026

Is FFA a contact dermatitis?

Table II Prevalence of allergens by cicatricial alopecia diagnosis, %

Allergen	LPP (n = 26)	FFA (n = 11)	LPP/FFA (n = 5)	Total (n = 42)
Positive reaction	76.9	81.8	60.0	76.2
Gallates	14.2	7.1	4.9	26.2
Fragrance mixes	19.2	27.3	0.0	19.0
Linalool	19.2	18.2	20.0	19.0

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-09117-w OPEN

Genome-wide association study in frontal fibrosing alopecia identifies four susceptibility loci including *HLA-B*07:02*

Christos Tziotzios et al.#

Table 1 Genome-wide significant loci for UK, Spain and meta-analysis

								UK cohort		Spanish cohort		Meta-analysis	
Locus	Gene	Position (hg19)	SNP ID	RA	PA	RAF_{Cases}	$RAF_{Controls}$	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
2p22.2	CYP1B1	38,298,139	rs1800440	T	C	0.87	0.81	1.62 (1.38-1.90)	5.89×10^{-9}	1.81 (1.28-2.58)	0.00090	1.65 (1.43-1.91)	2.44×10^{-11}
6p21.1	HLA-B	31,320,562	rs2523616	T	C	0.47	0.19	4.69 (4.07-5.40)	8.52×10^{-101}	4.97 (3.52-7.02)	8.09×10^{-20}	4.73 (4.15-5.39)	7.60×10^{-119}
8q24.22	ST3GAL1	134,503,229	rs760327	G	C	0.46	0.39	1.32 (1.18-1.47)	1.18×10^{-6}	1.50 (1.14-1.97)	0.00357	1.34 (1.21-1.49)	2.15×10^{-8}
15q26.1	SEMA4B	90,734,426	rs34560261	T	C	0.22	0.17	1.52 (1.32-1.76)	8.47×10^{-9}	1.51 (1.03-2.21)	0.03257	1.52 (1.22-1.74)	8.12×10^{-10}

Each SNP was tested for association by logistic regression using an additive regression model; total $N = 5161$ biologically independent subjects ($N_{cases} = 1044$ and $N_{controls} = 4145$)
RA risk allele, *PA* protective allele, *RAF* risk allele frequency, *OR* odds ratio, *RAF* risk allele frequency, *CI* confidence interval

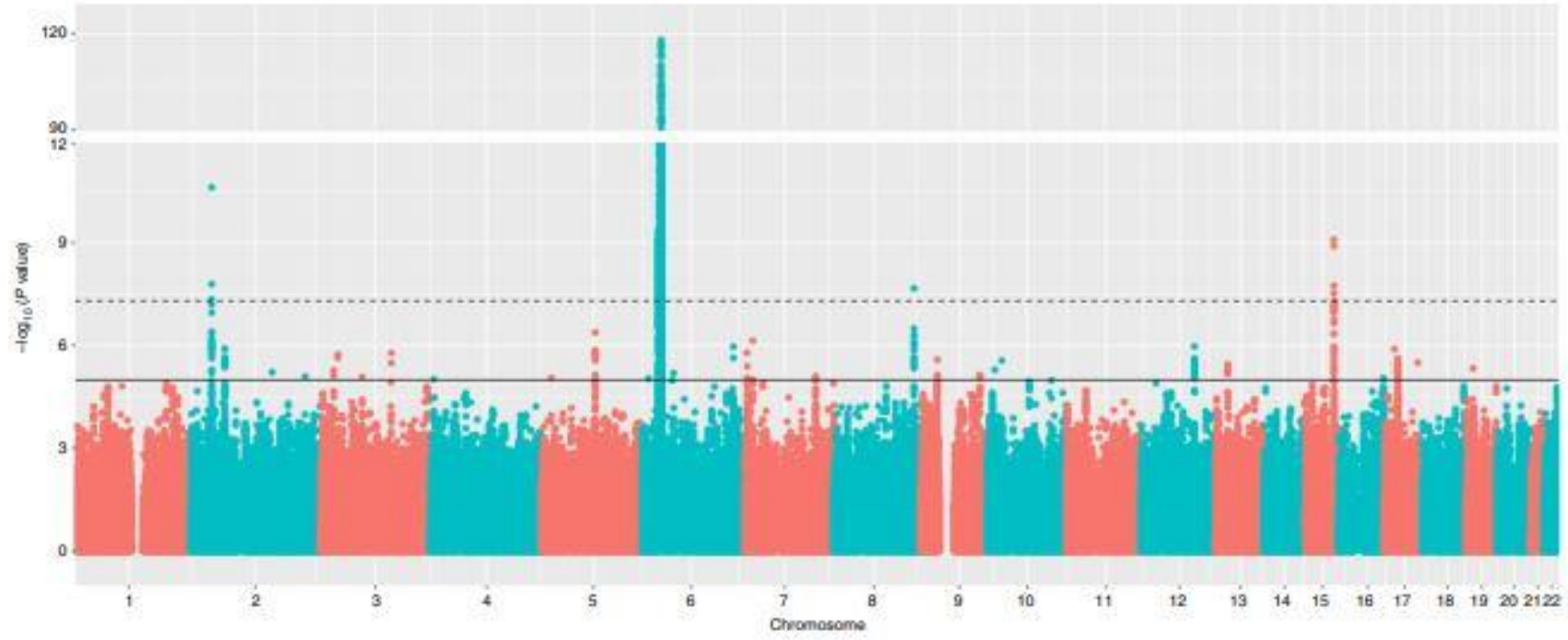


Fig. 2 Manhattan plot showing the *P* values for the meta-analysis genome-wide association study. Each SNP was tested for association by logistic regression using an additive regression model; the interrupted line indicates the threshold for genome-wide significance ($P = 5\times10^{-8}$); the *y* axis has been collapsed for better illustration of all genomic signals; the continuous line represents the threshold for suggestive significance ($P = 1\times10^{-5}$); $N = 5161$ biologically independent subjects ($N_{cases} = 1044$ and $N_{controls} = 4145$)

Journal of the American Academy of Dermatology

Available online 23 December 2018

In Press, Accepted Manuscript

A method for more precise sampling of the scalp and eyebrows in frontal fibrosing alopecia

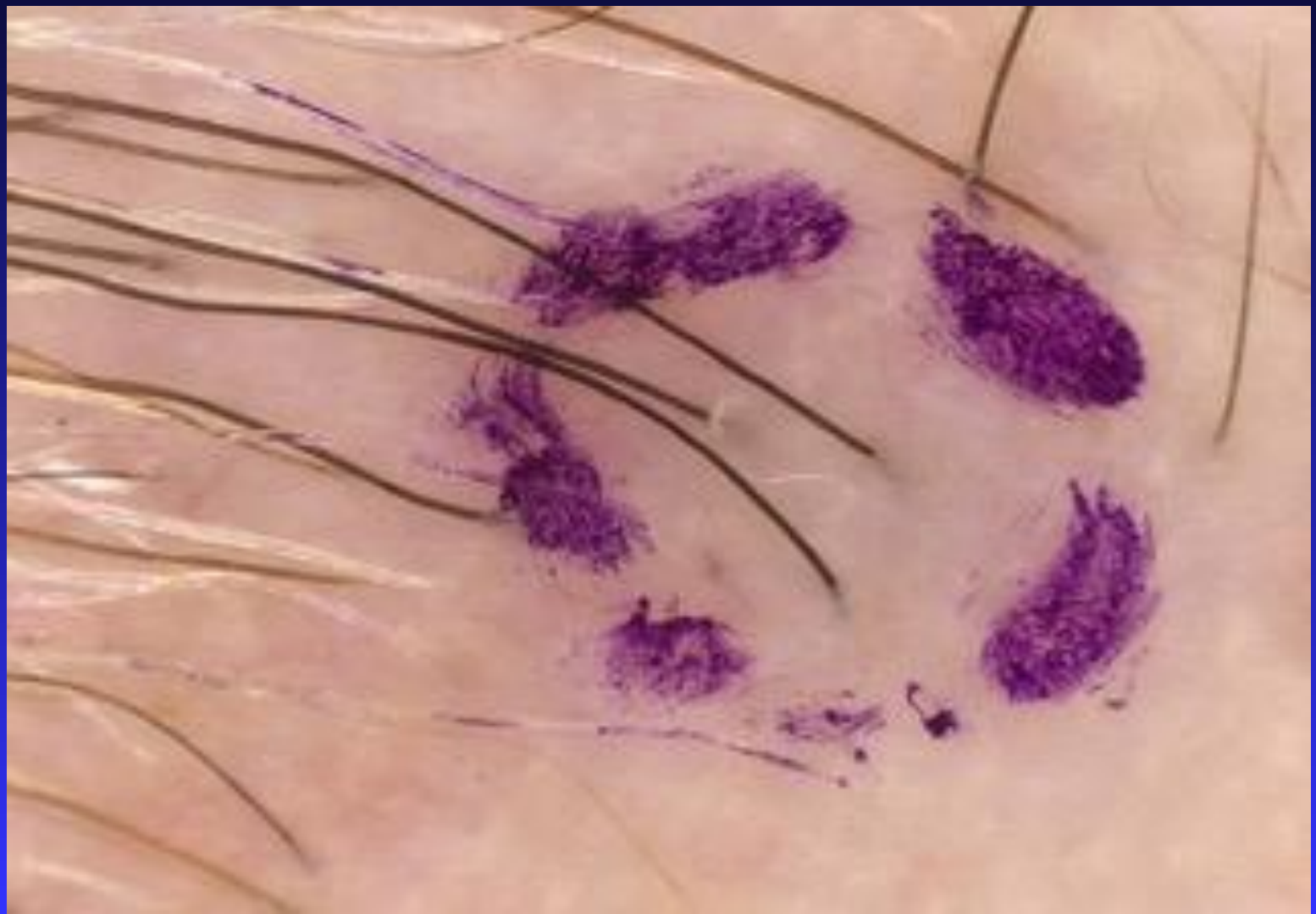
Curtis T. Thompson M.D. [1, 2], Antonella Tosti M.D. [3]

Show more

https://doi.org/10.1016/j.jaad.2018.12.033

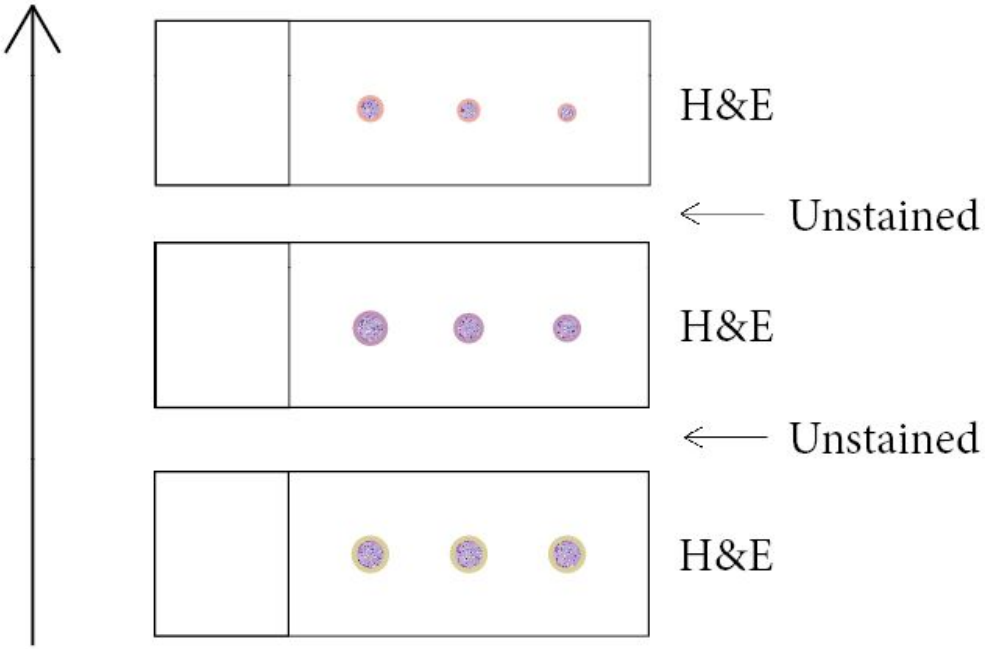
Get rights and content

Dermoscopic identification of disease



2mm punch—exhaust tissue

Skin Surface



3 slides total with 9 cross sections; 3 sections per slide

1. Tissue is embedded epidermis-down
2. Step through entire block on initial H&E stains
3. Obtain unstained slides

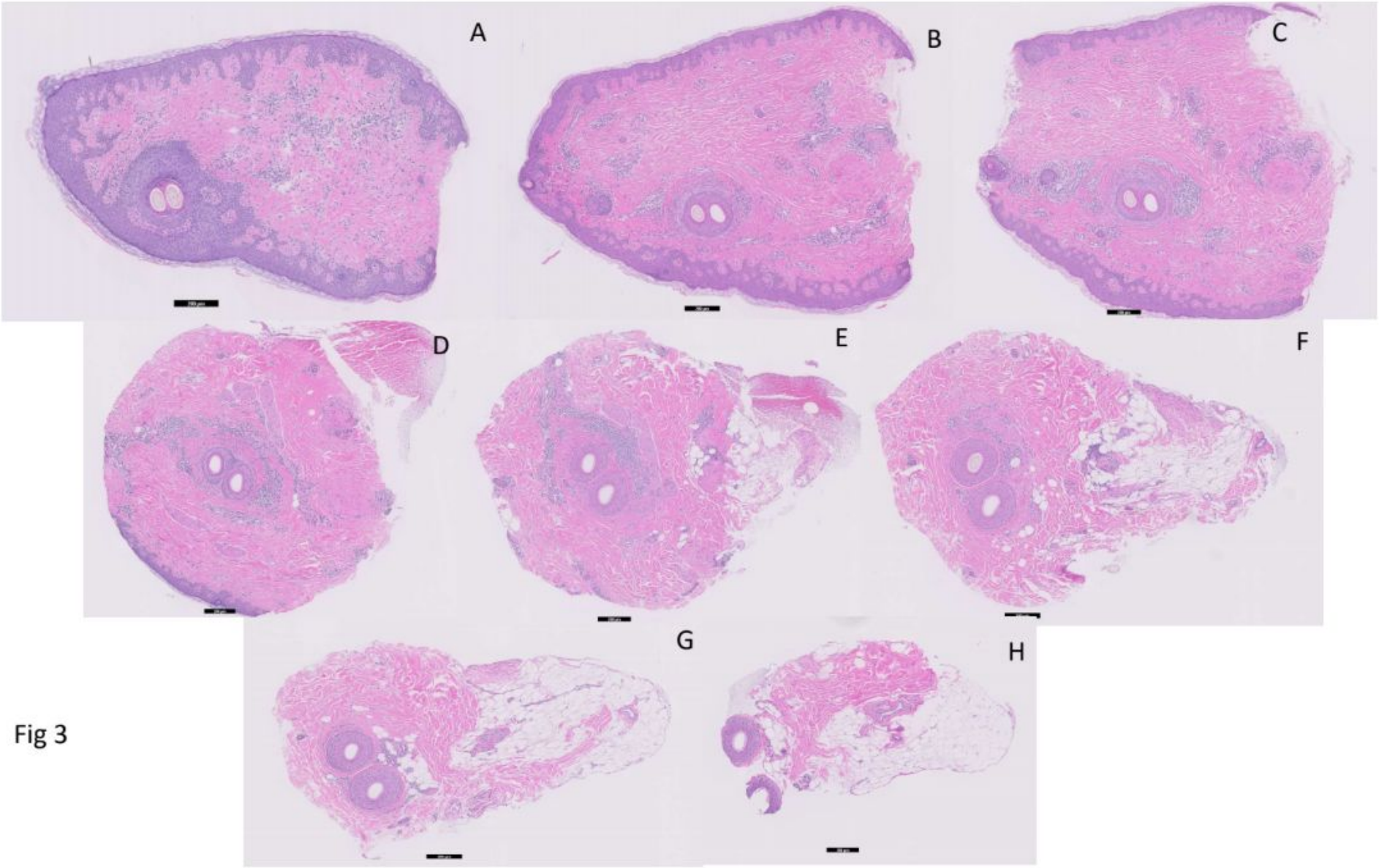
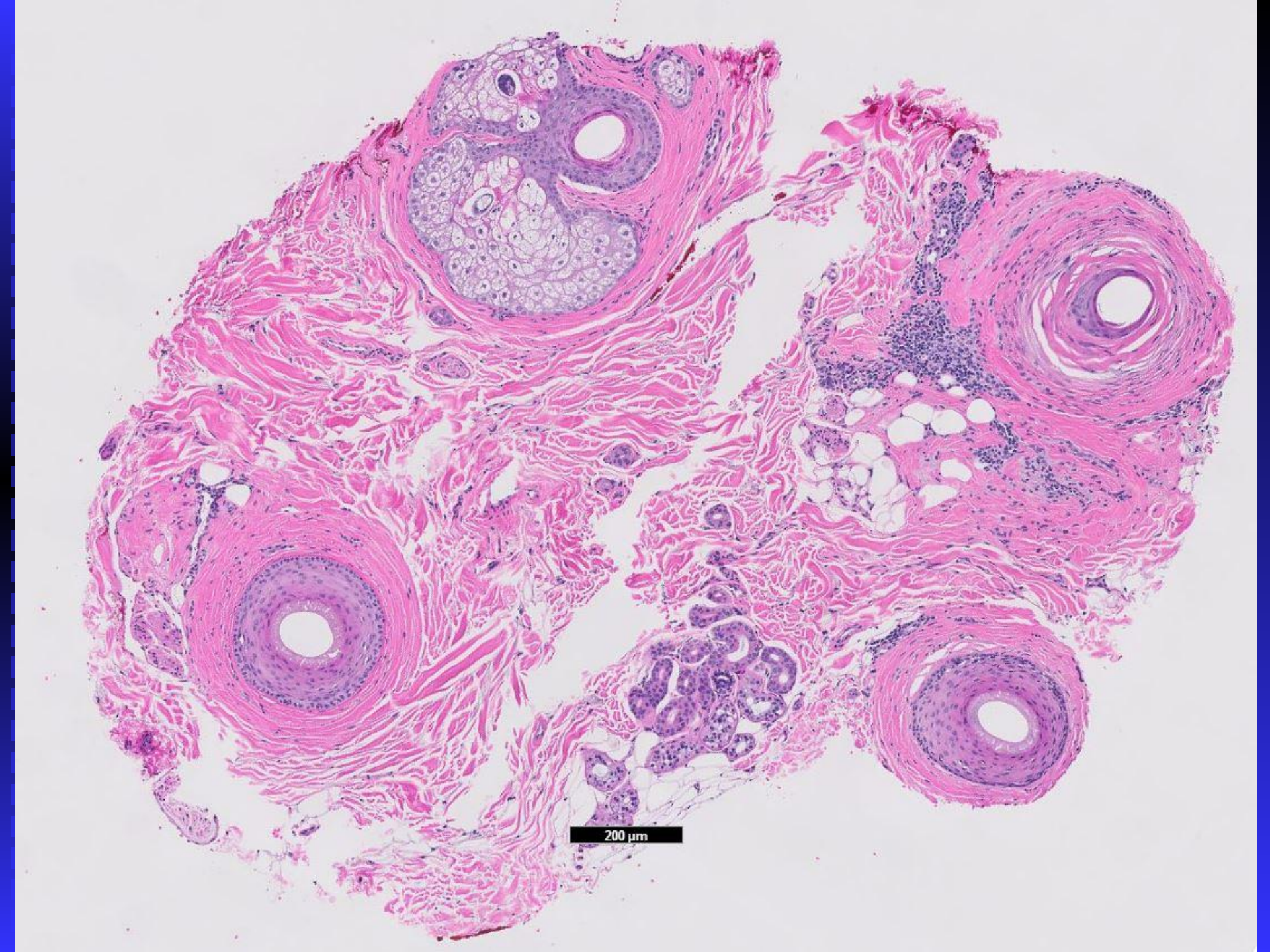
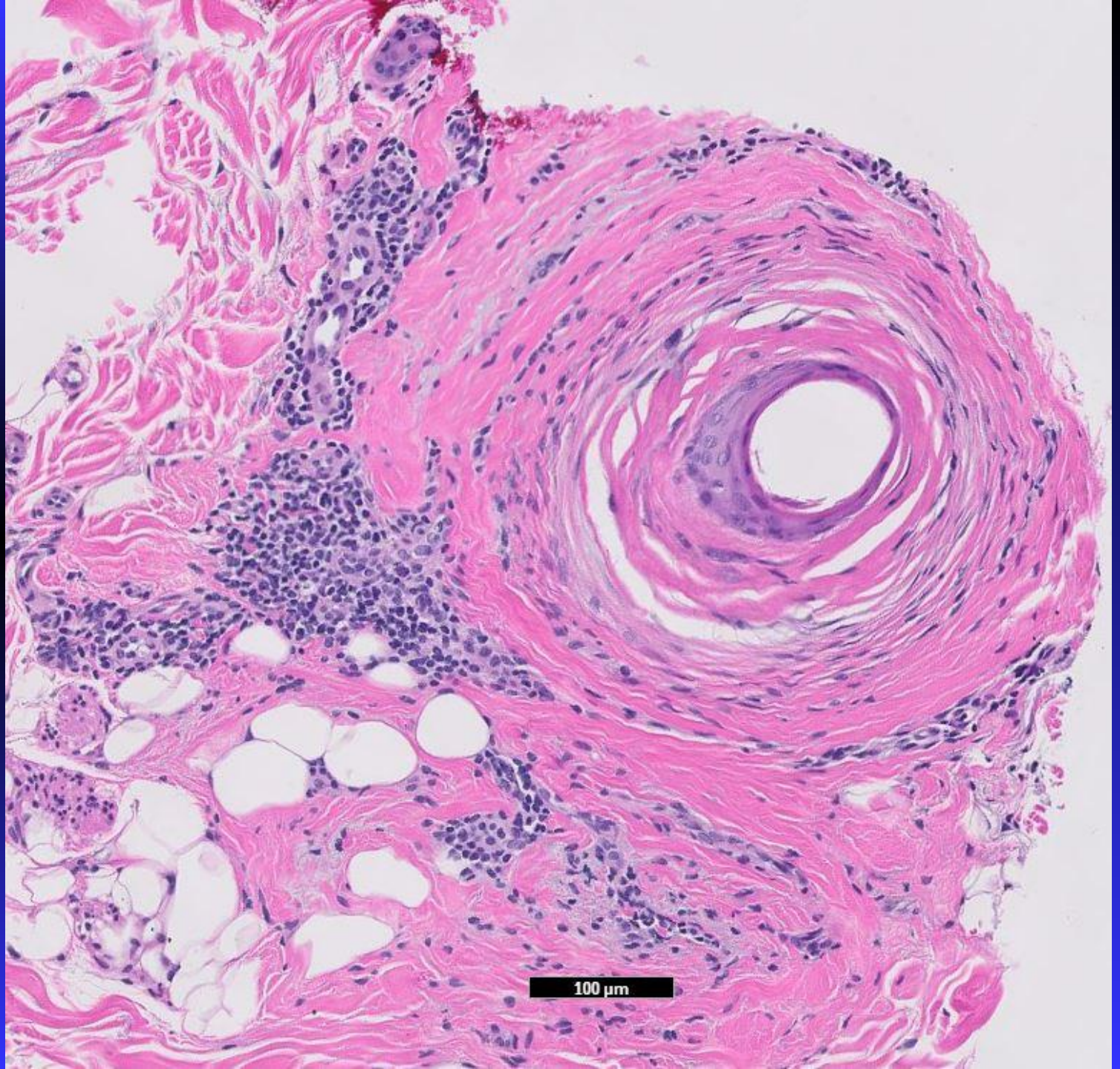
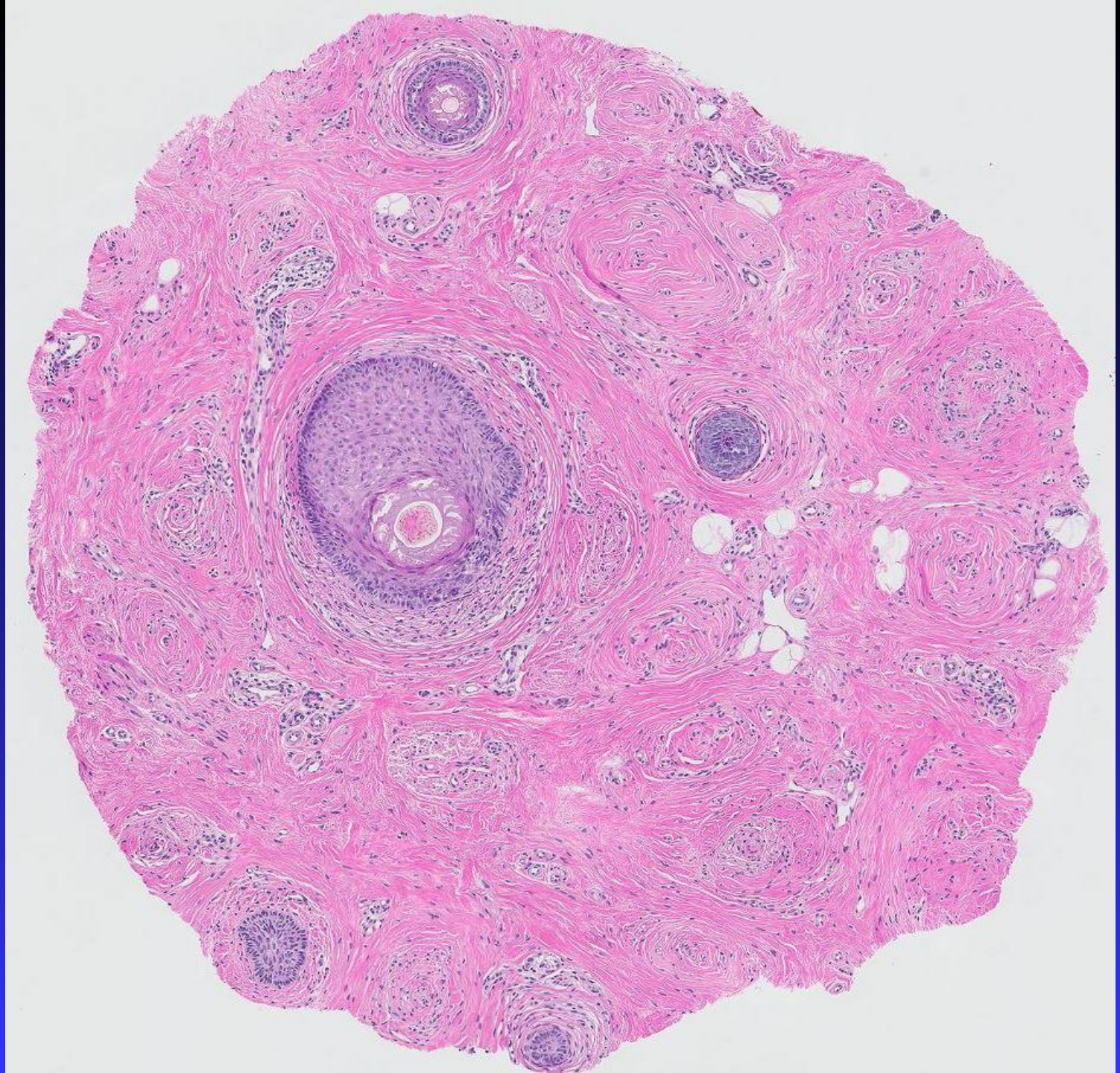


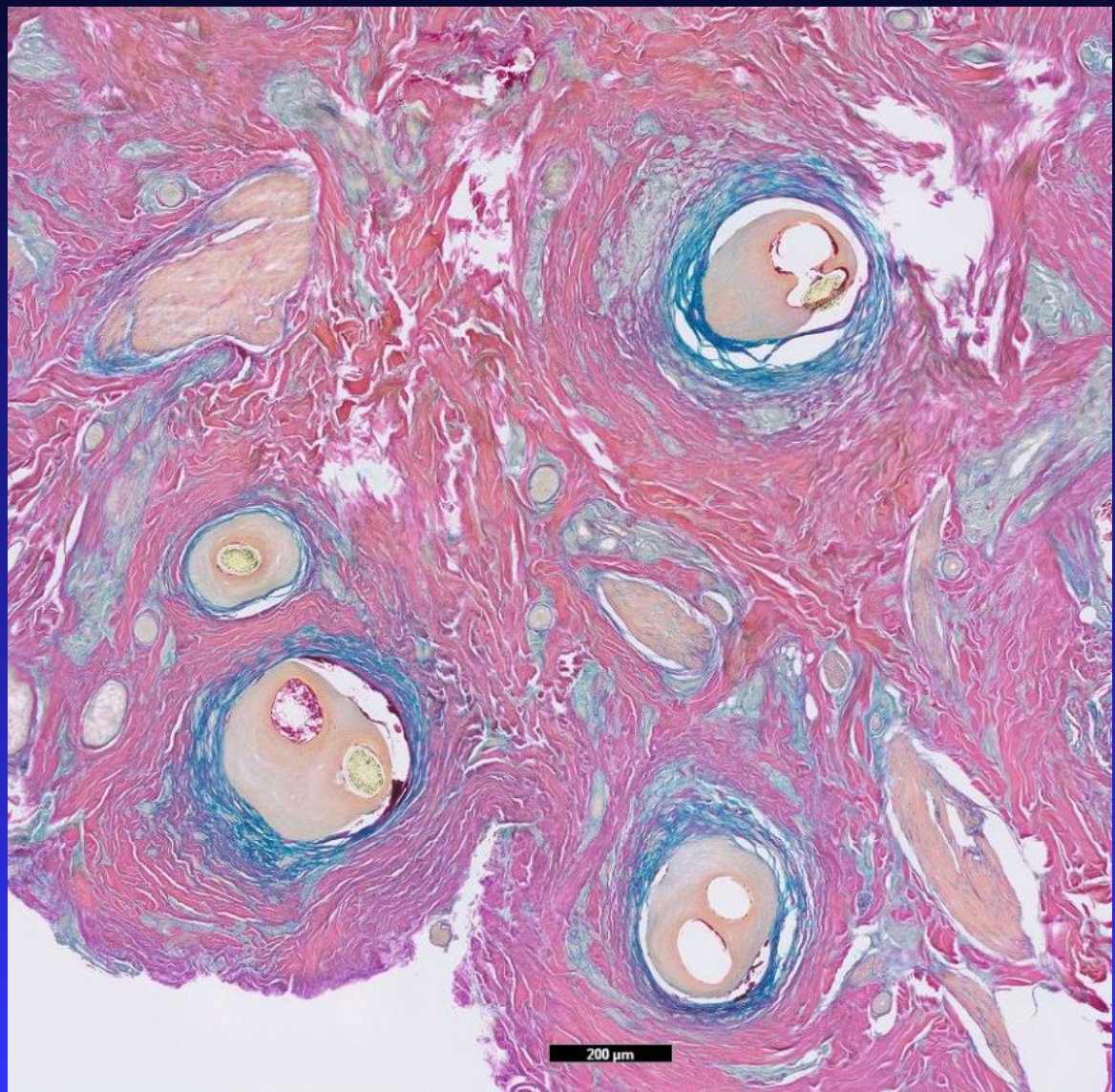
Fig 3


200 µm

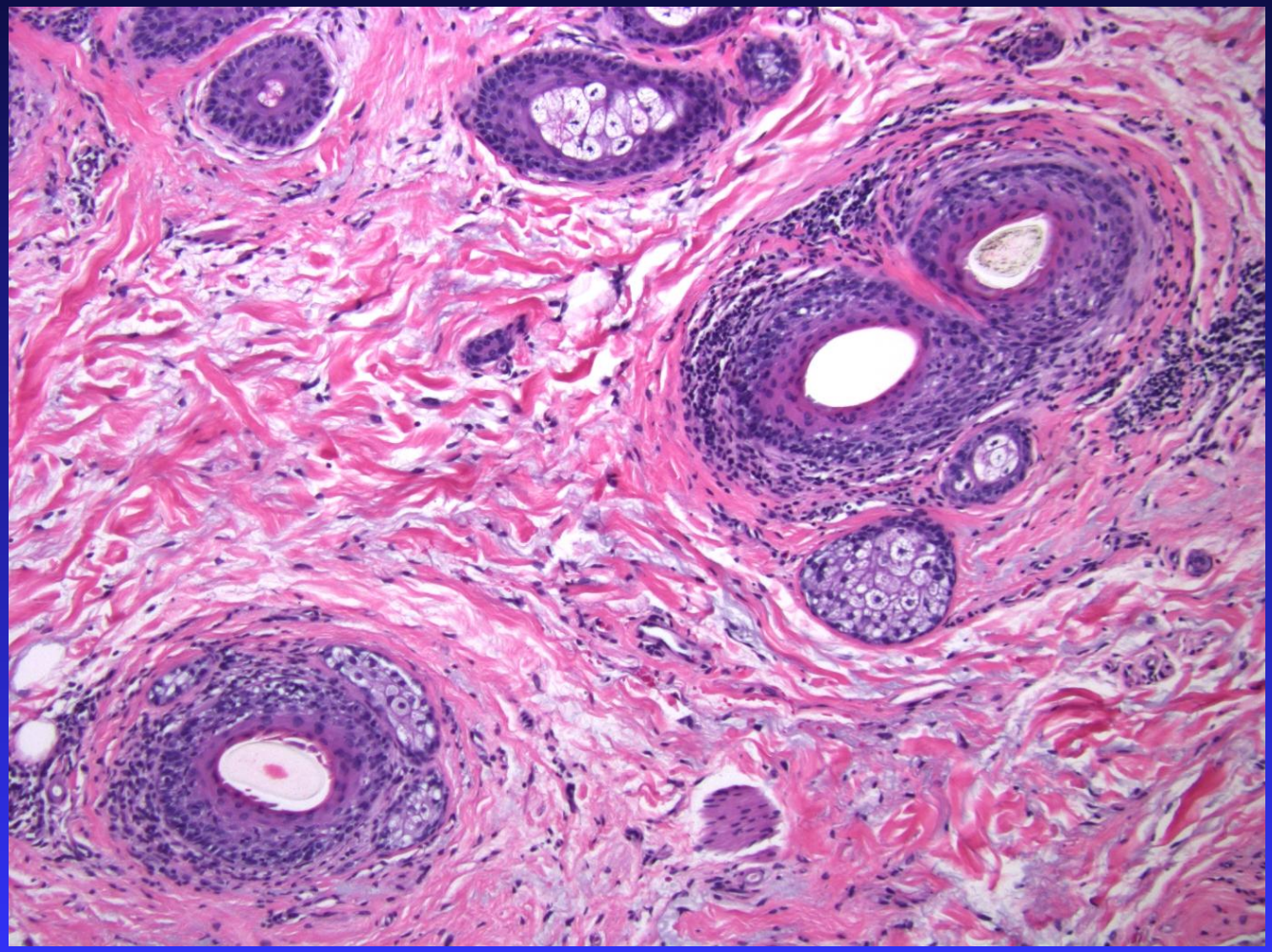

100 µm

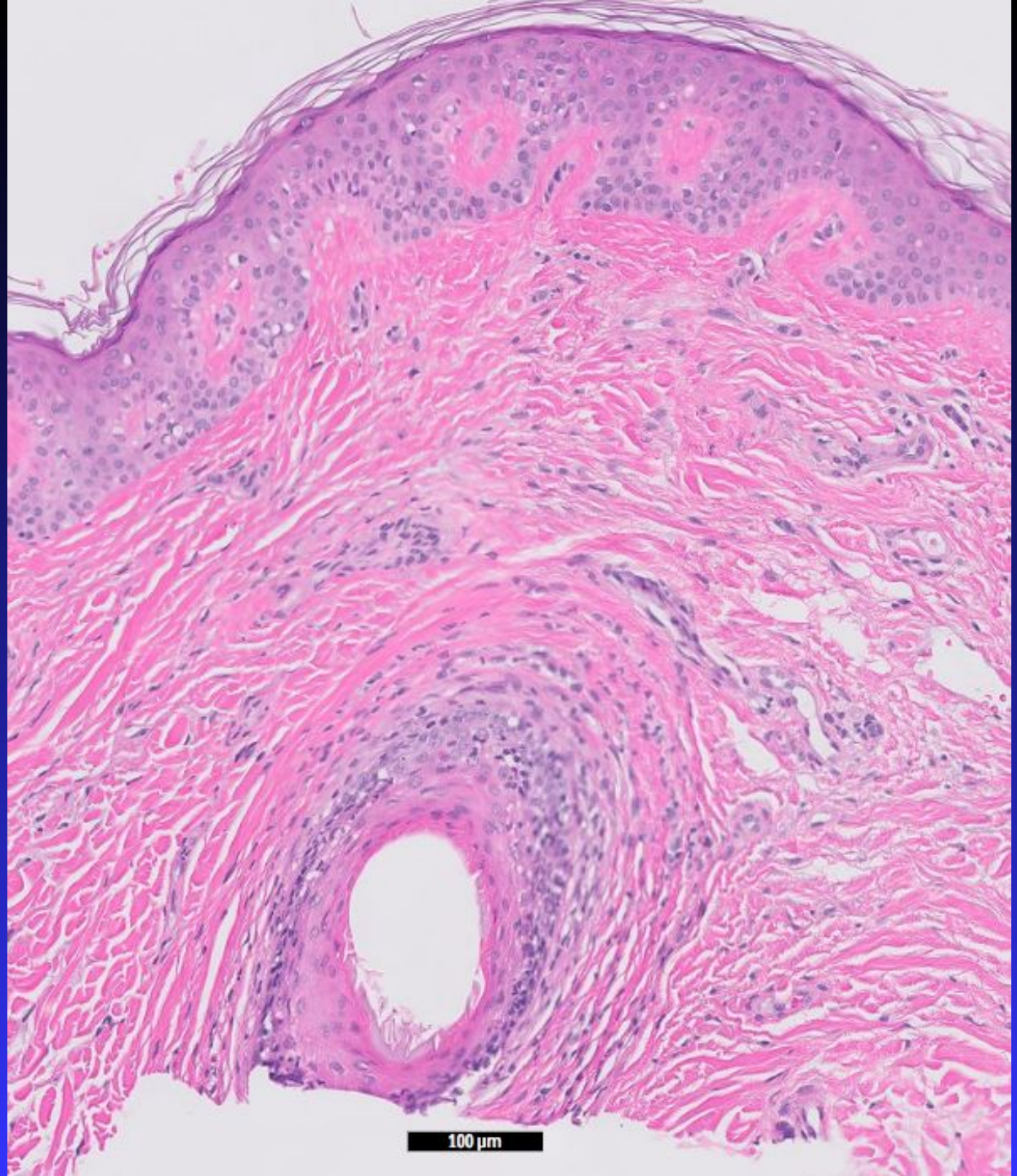


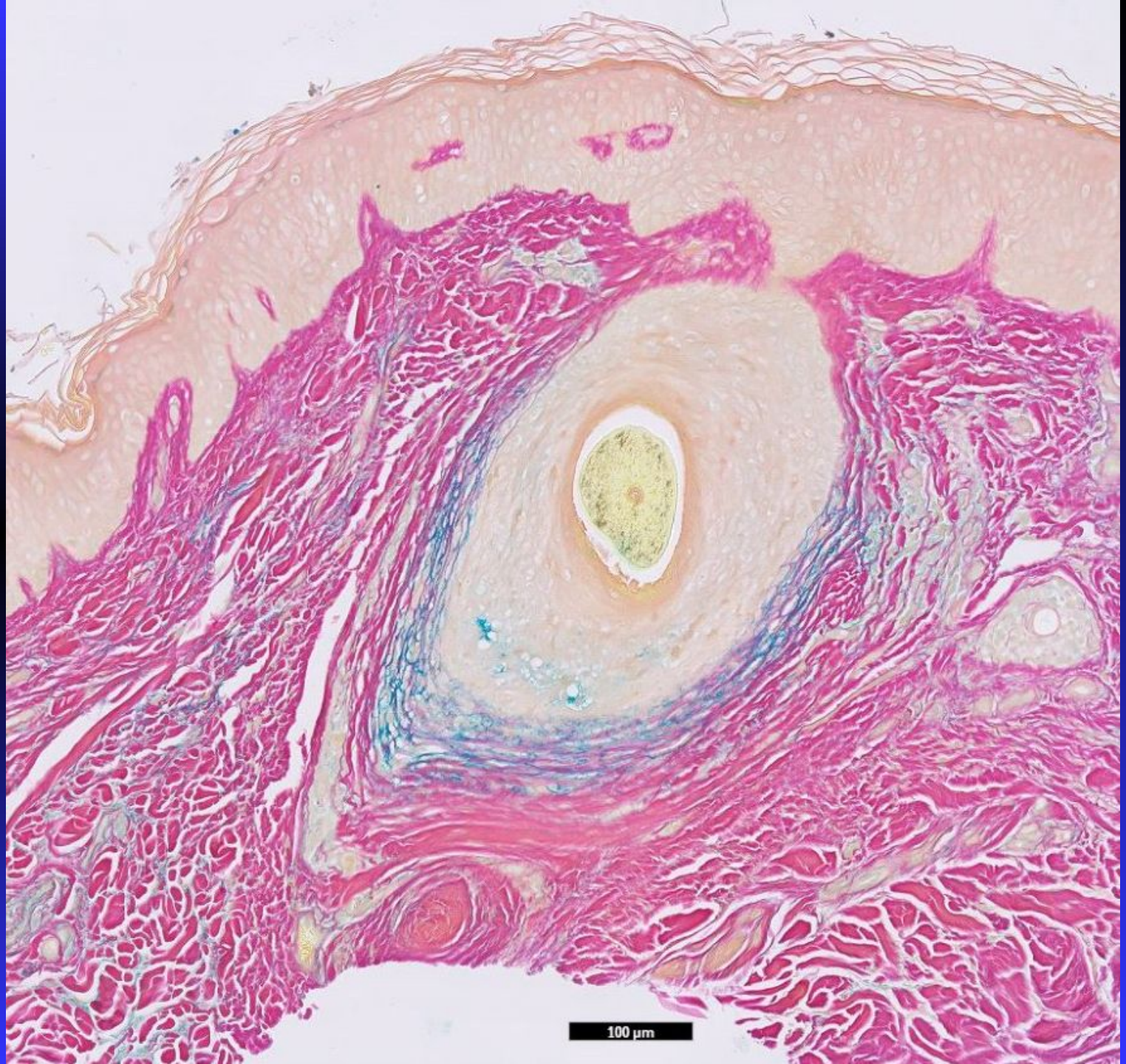
Identification of subtle, focal scarring in FFA

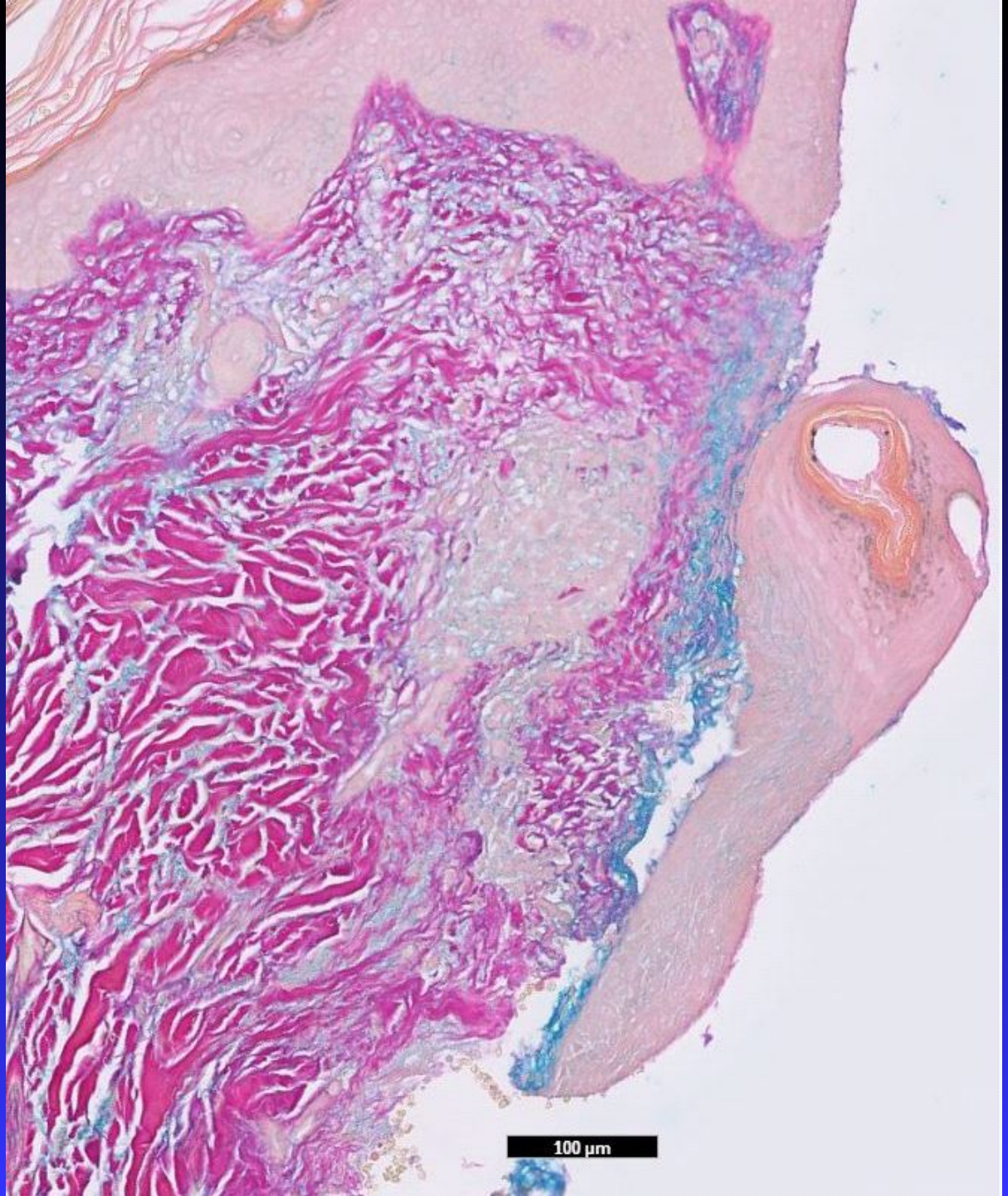


Frontal Fibrosing Alopecia Histology: Minimal scarring

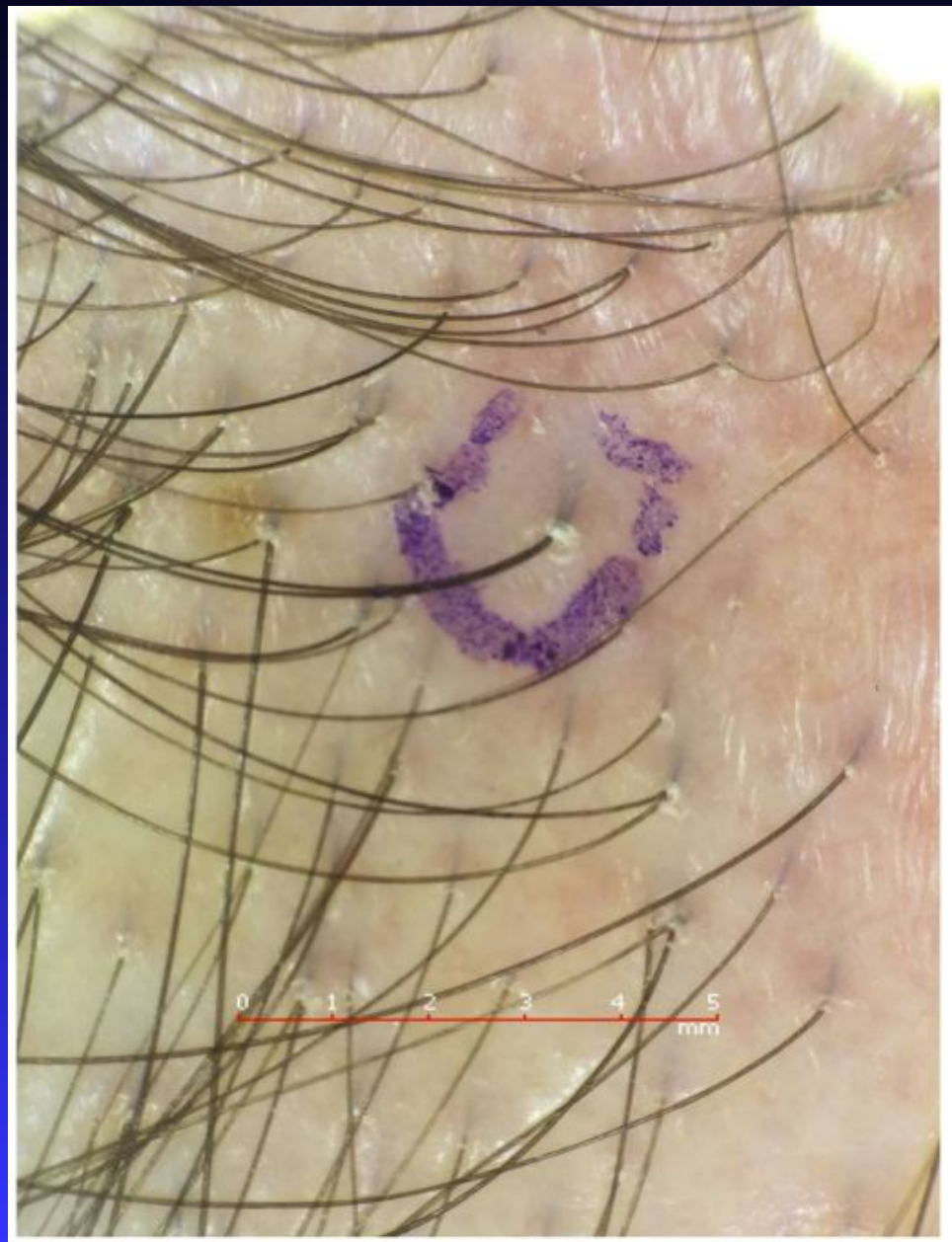



100 µm

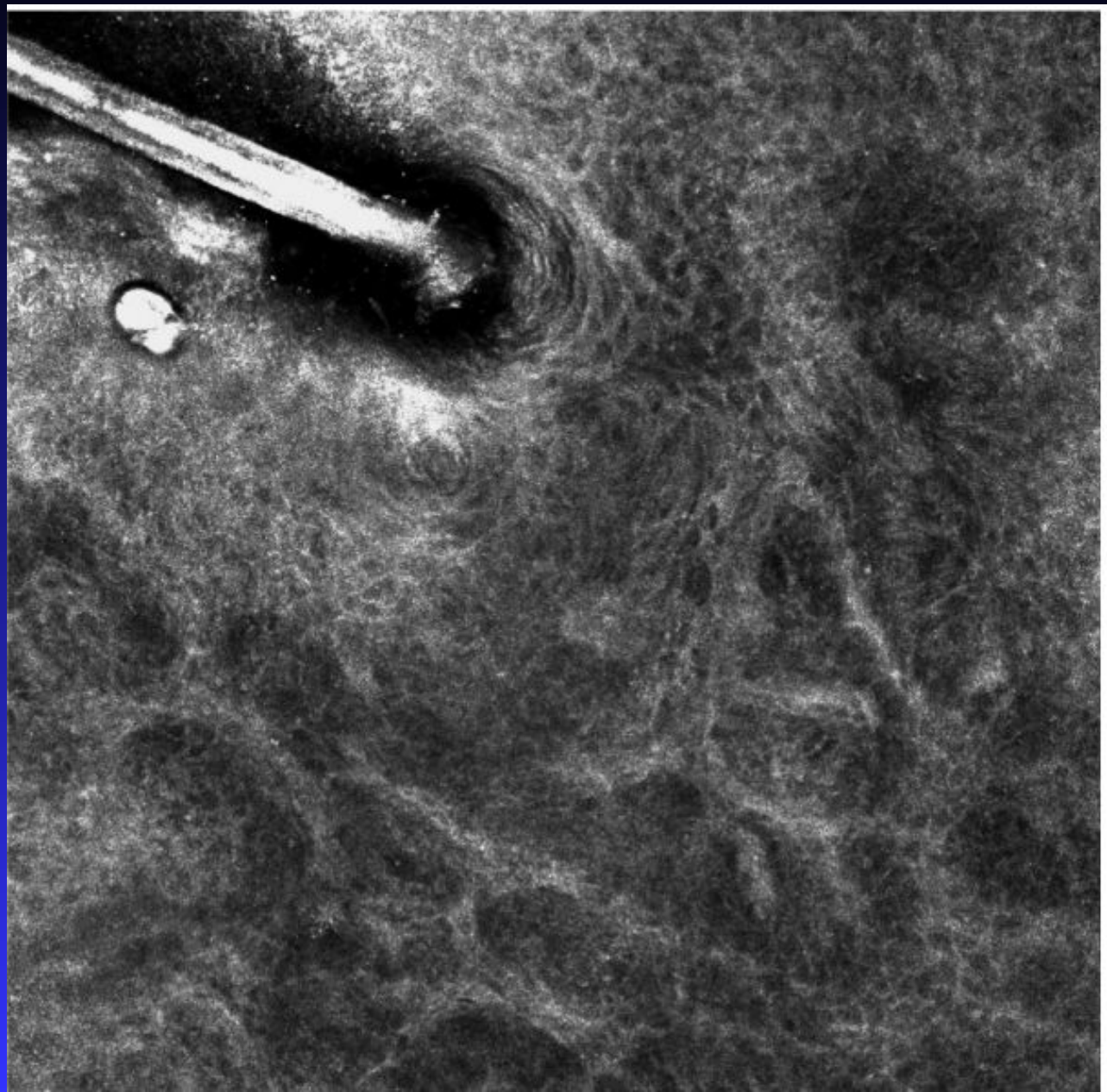

100 µm


100 µm

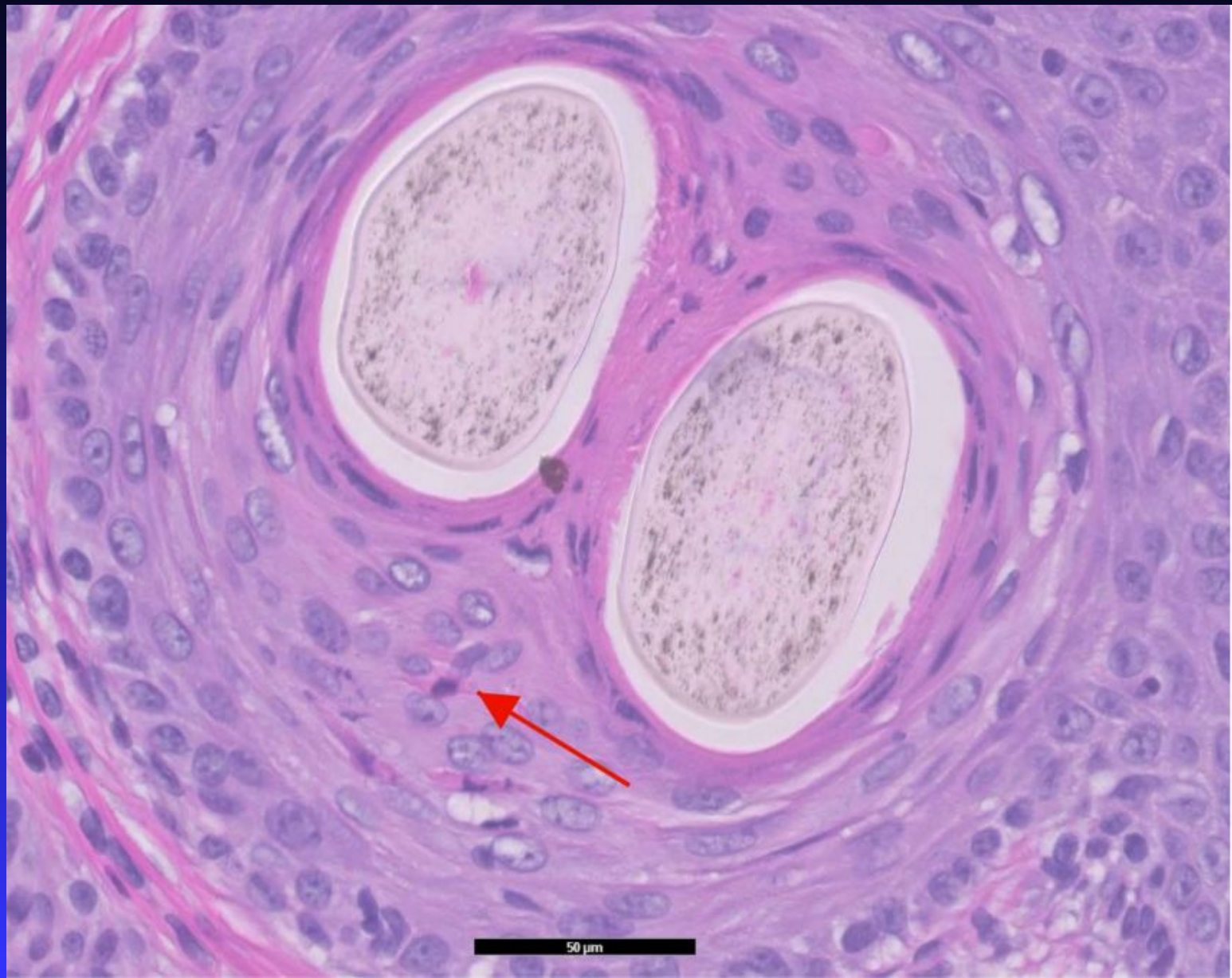
Peripilar Casts in FFA



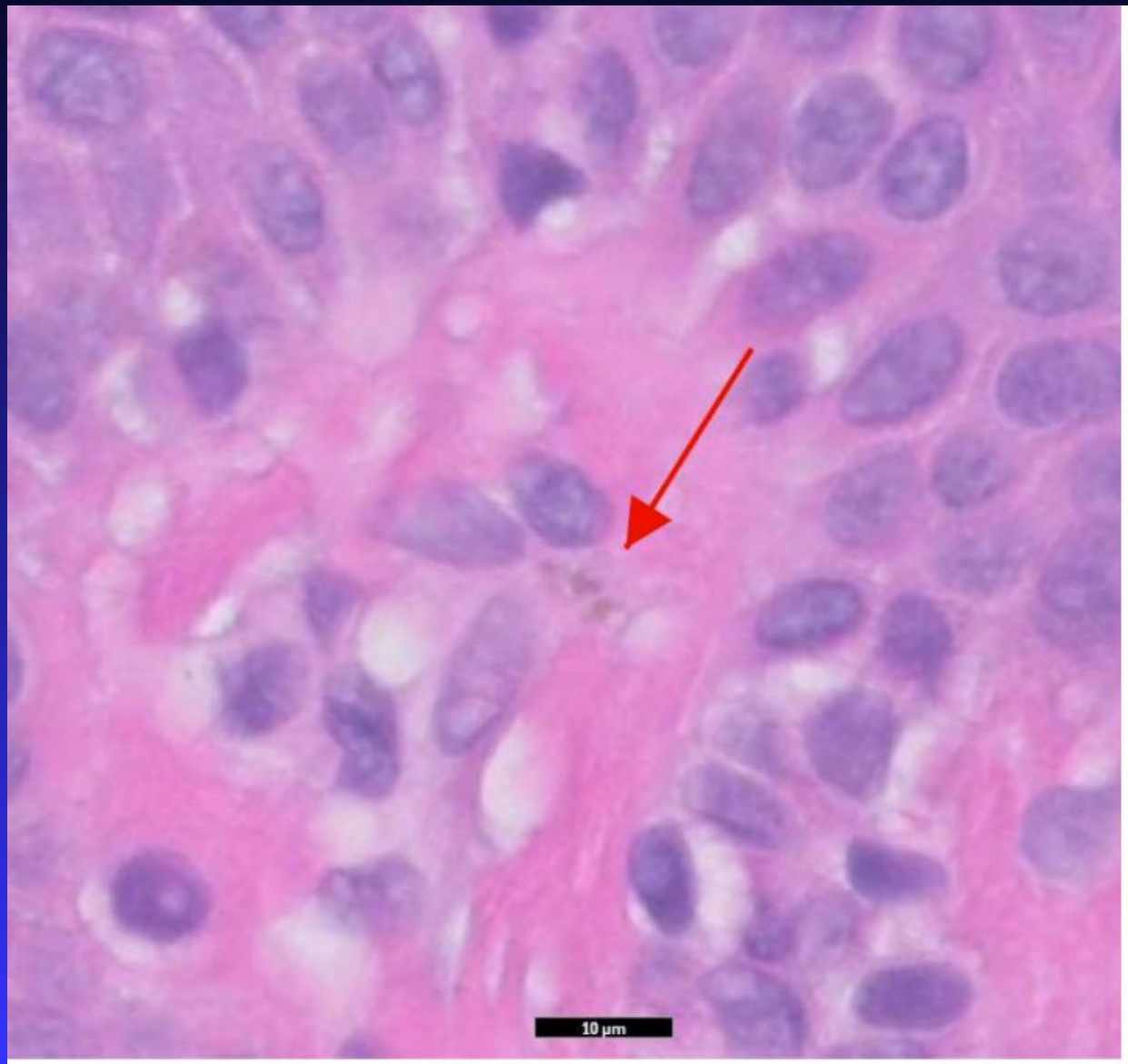
Peripilar Casts in FFA



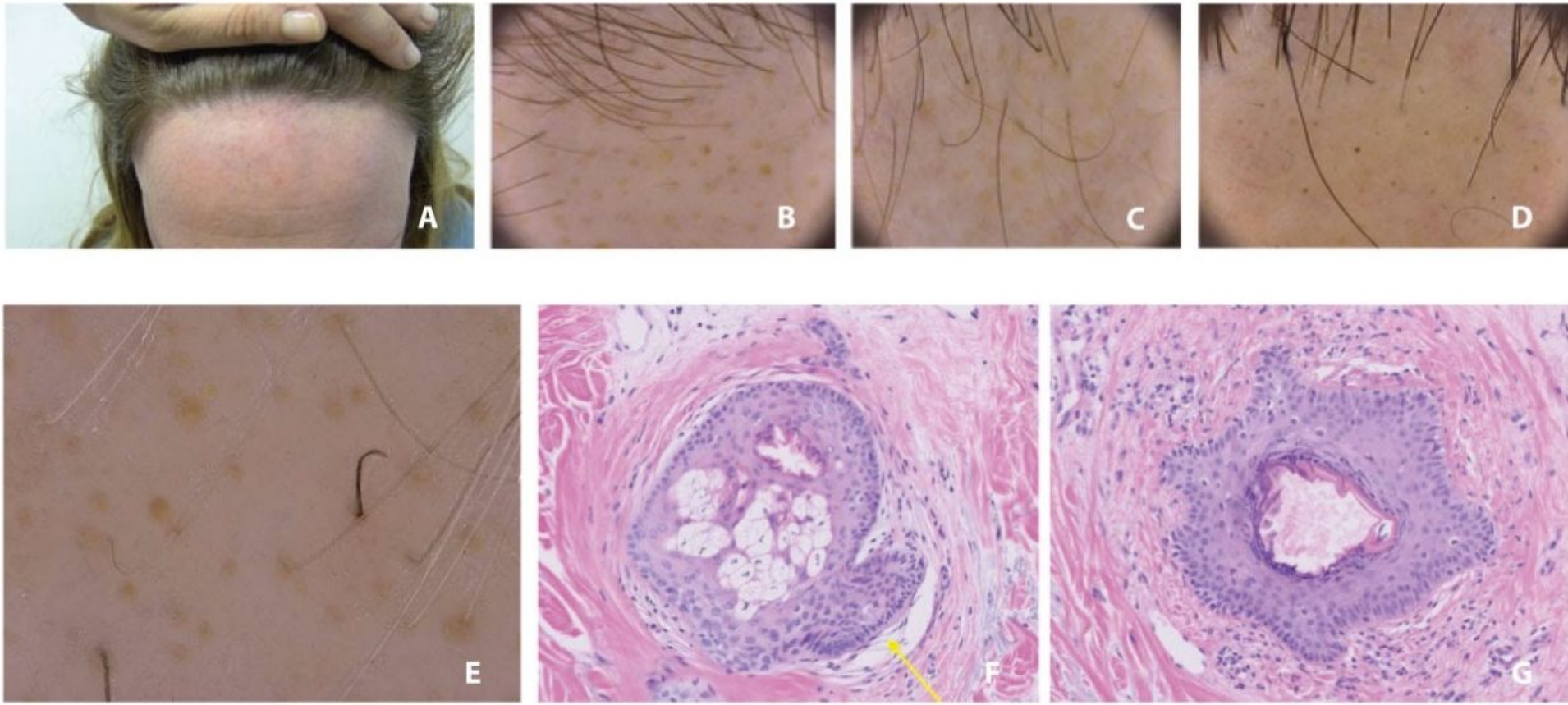
Folliculocentric interface change



Dyspigmentation in FFA

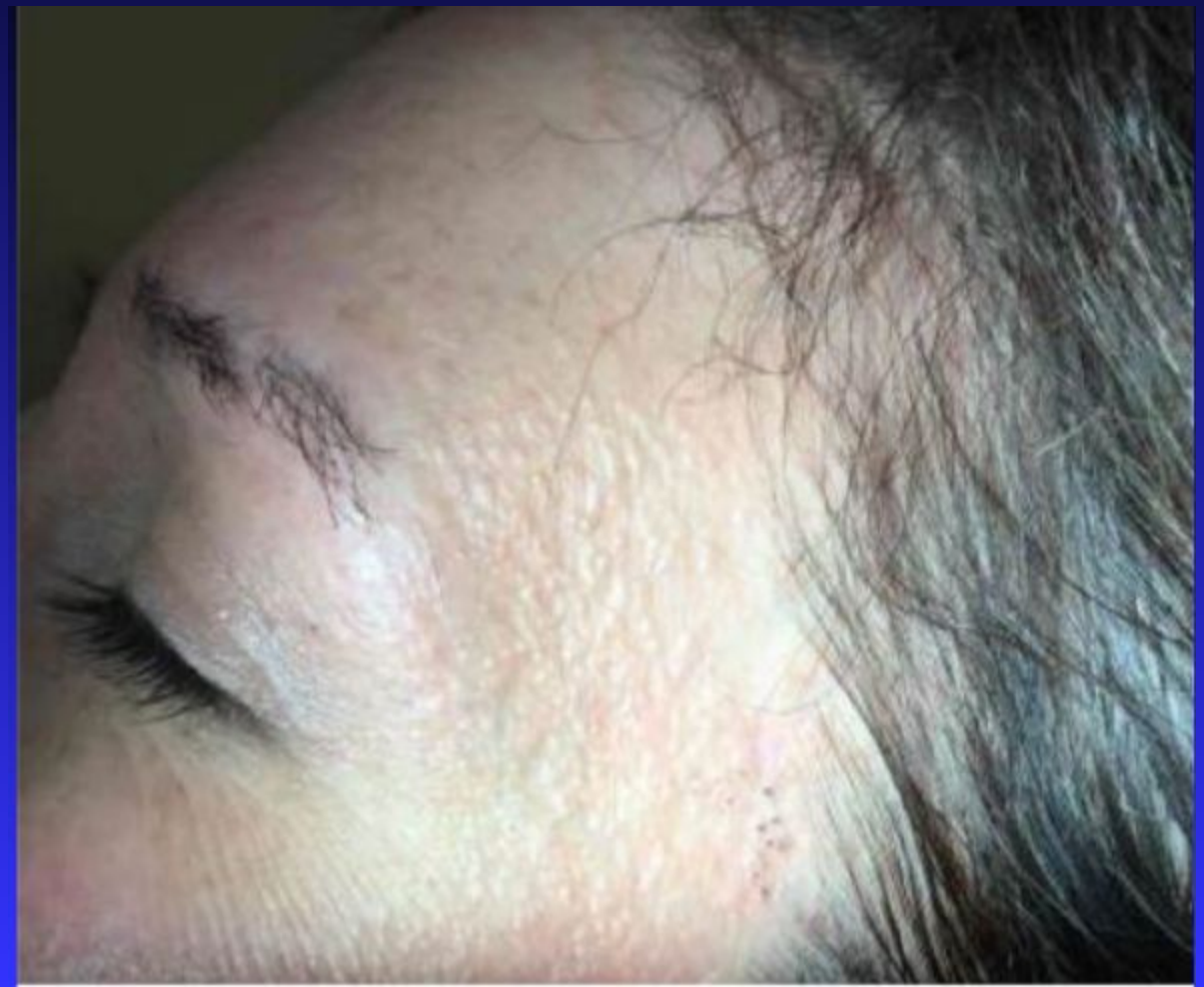


Dermascopic "Yellow Dots" in FFA

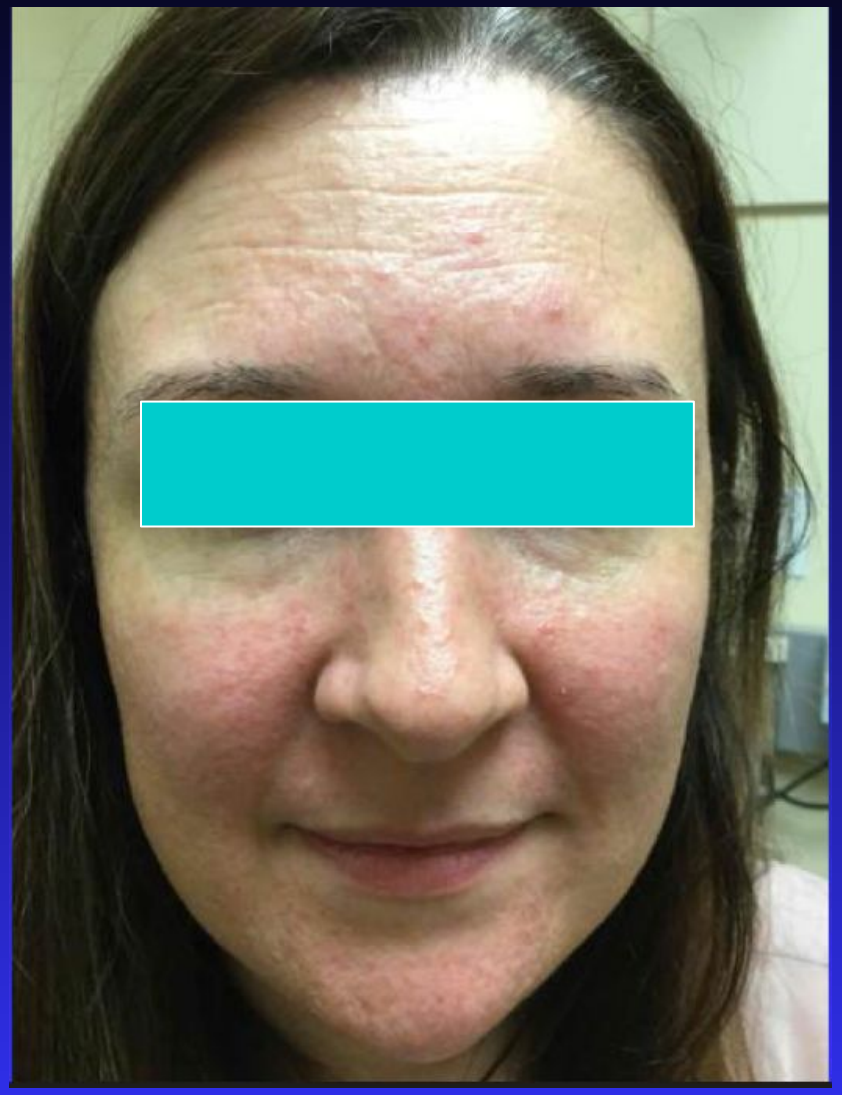


Velasco A, Thompson C and Tosti A. JEADV, In press, 2020

Rosacea?



Rosacea?



Skin Appendage Disorders

What Is Your Diagnosis?

Skin Appendage Disord 2020;6:190–193
DOI: 10.1159/000506749

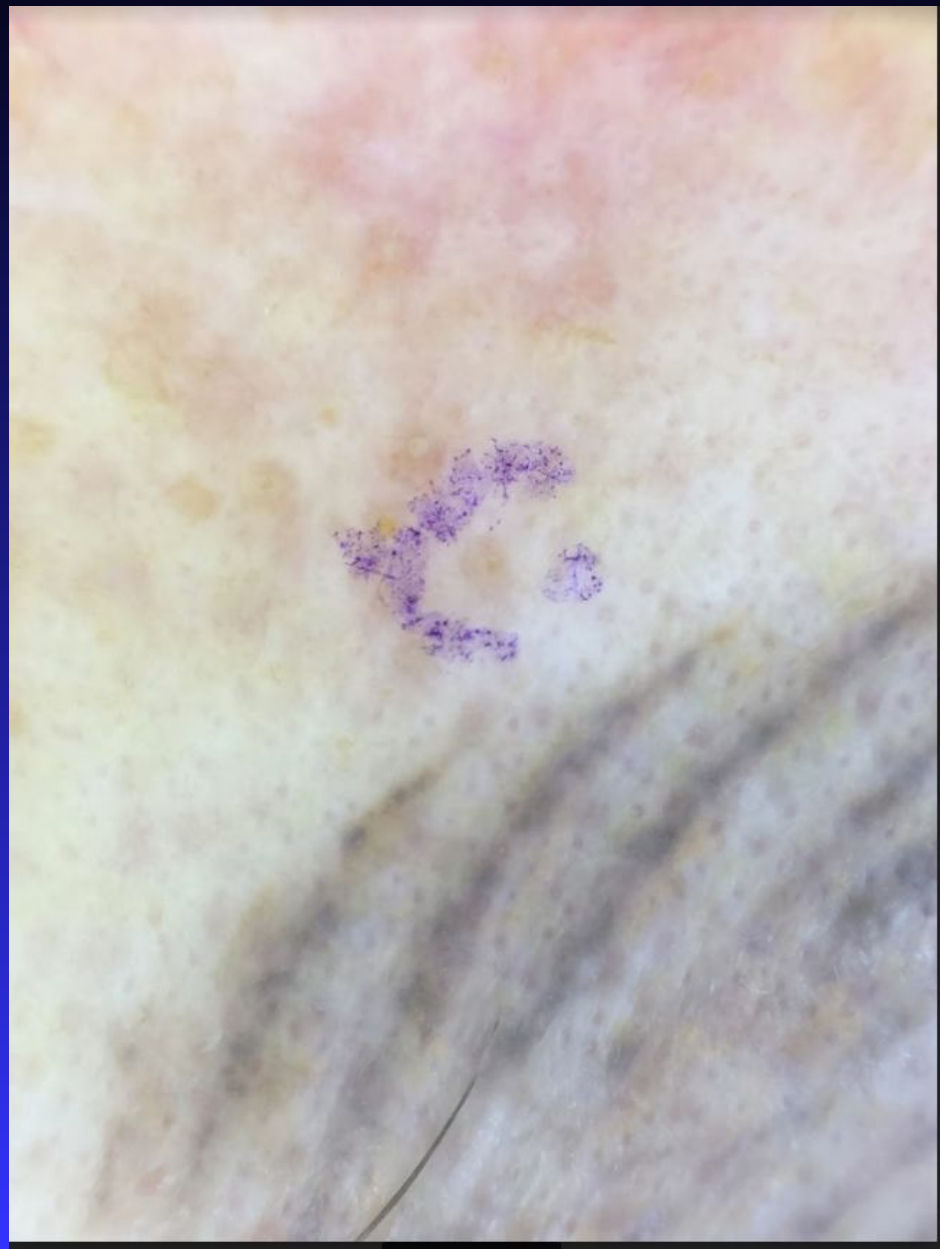
Received: January 31, 2020
Accepted: February 21, 2020
Published online: April 1, 2020

Erythematous Papules Involving the Eyebrows in a Patient with a History of Rosacea and Hair Loss

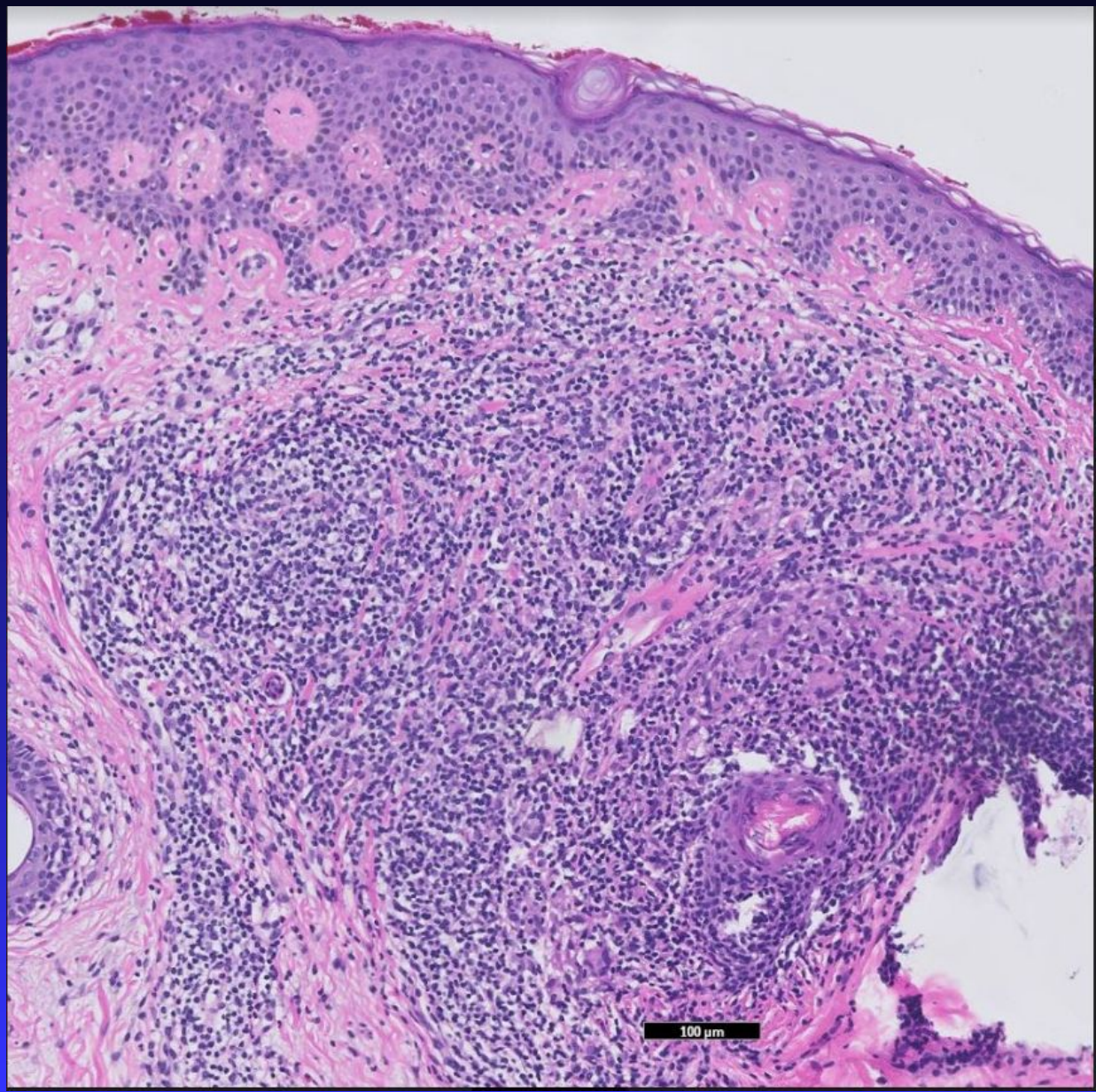
Agata Kłosowicz[a] Curtis Thompson[b] Antonella Tosti[c]

[a]Department of Dermatology, University Hospital in Kraków, Kraków, Poland; [b]CTA Lab, Portland, OR, USA; [c]Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL, USA

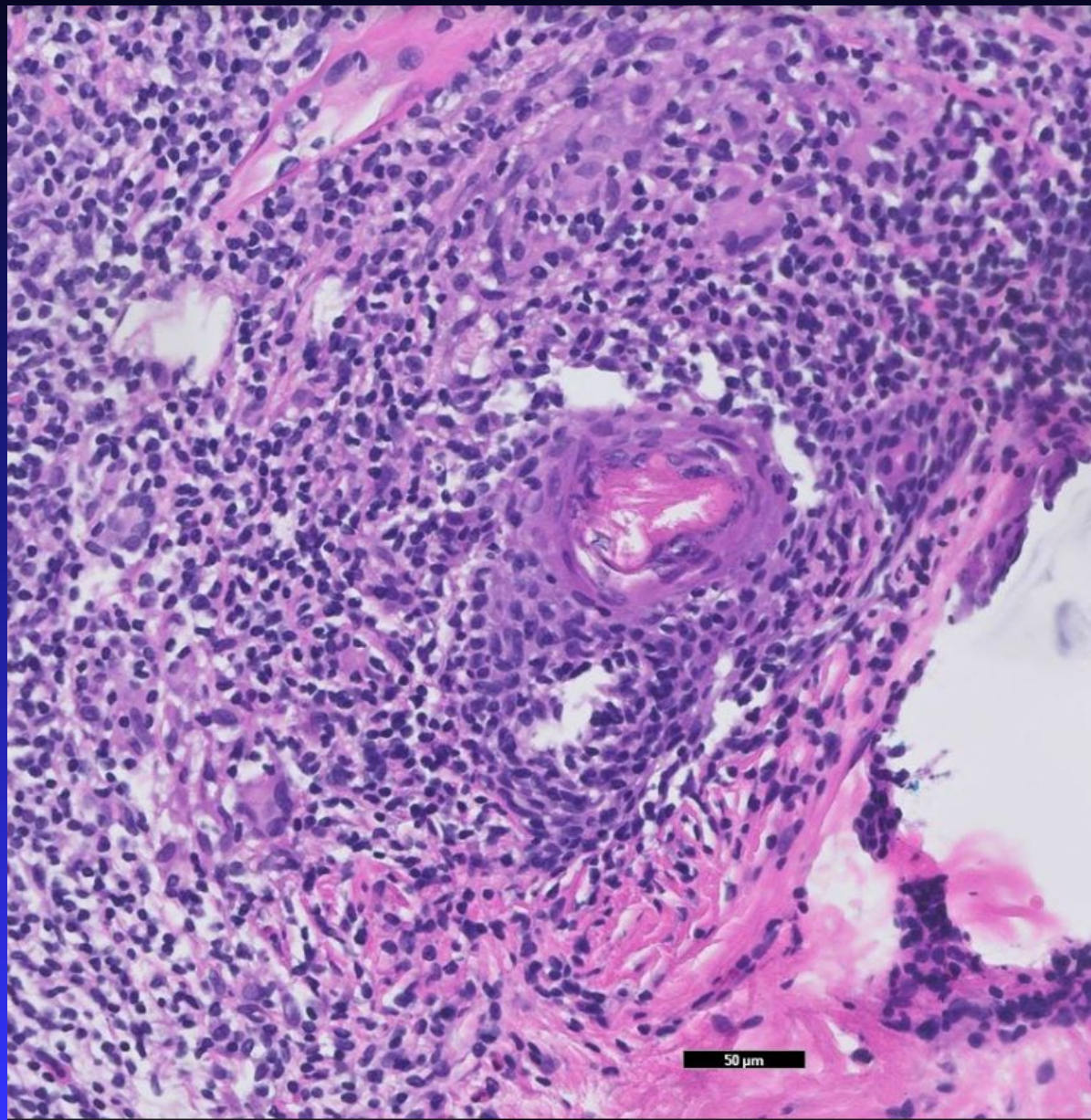
Facial papules in FFA



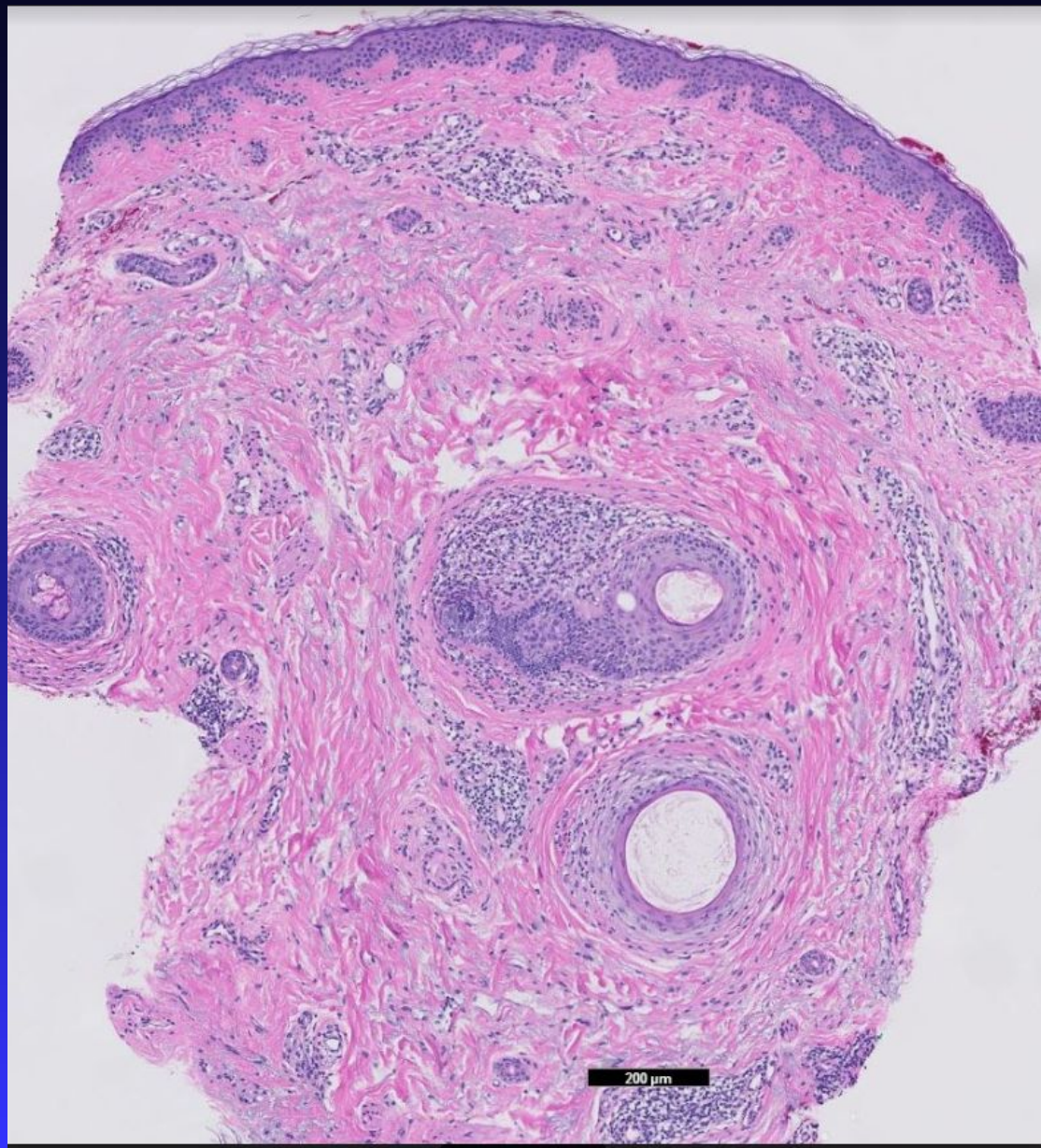
Facial papules in FFA



Facial papules in FFA



Facial papules in FFA



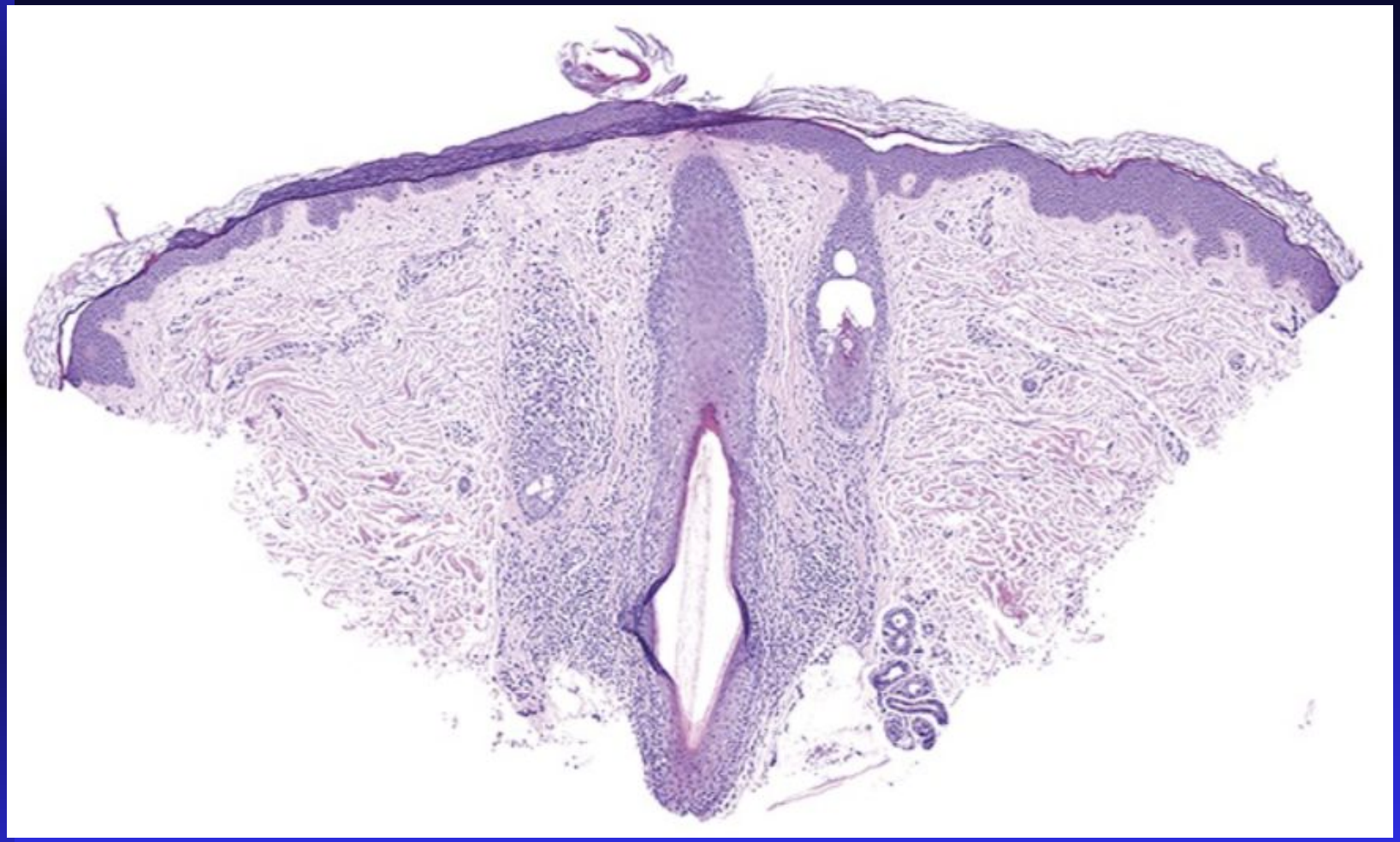
Alopecia away from the head

Frontal Fibrosing Alopecia Involving the Limbs Shows Inflammatory Pattern on Histology: A Review of 13 Cases

Miteva, Mariya MD **Author Information**

The American Journal of Dermatopathology: March 2020 - Volume 42 - Issue 3 - p 226-229
doi: 10.1097/DAD.0000000000001500

FFA Limbs

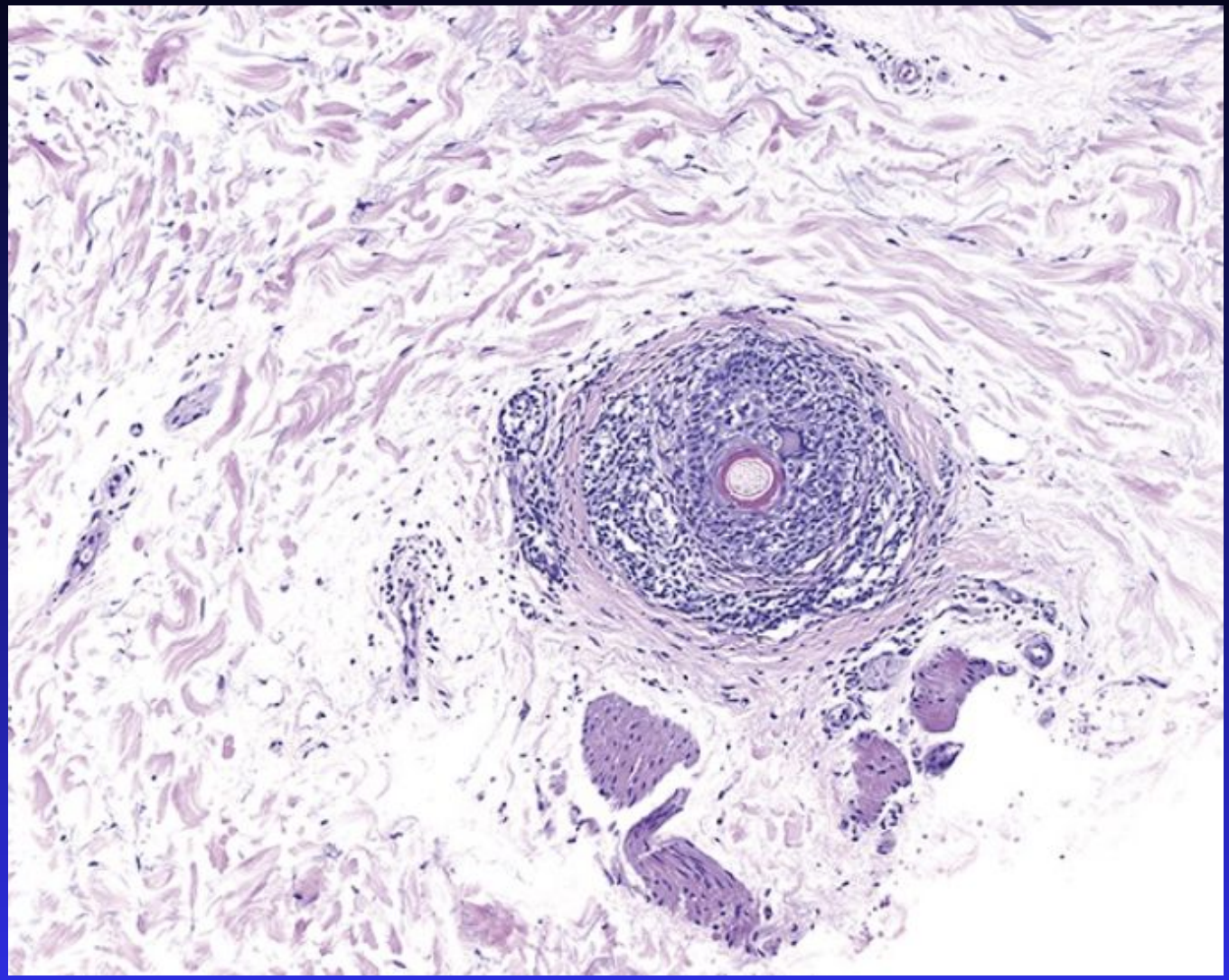


Frontal Fibrosing Alopecia Involving the Limbs Shows Inflammatory Pattern on Histology: A Review of 13 Cases

Miteva, Mariya MD Author Information

The American Journal of Dermatopathology: March 2020 - Volume 42 - Issue 3 - p 226-229
doi: 10.1097/DAD.0000000000001500

FFA Limbs

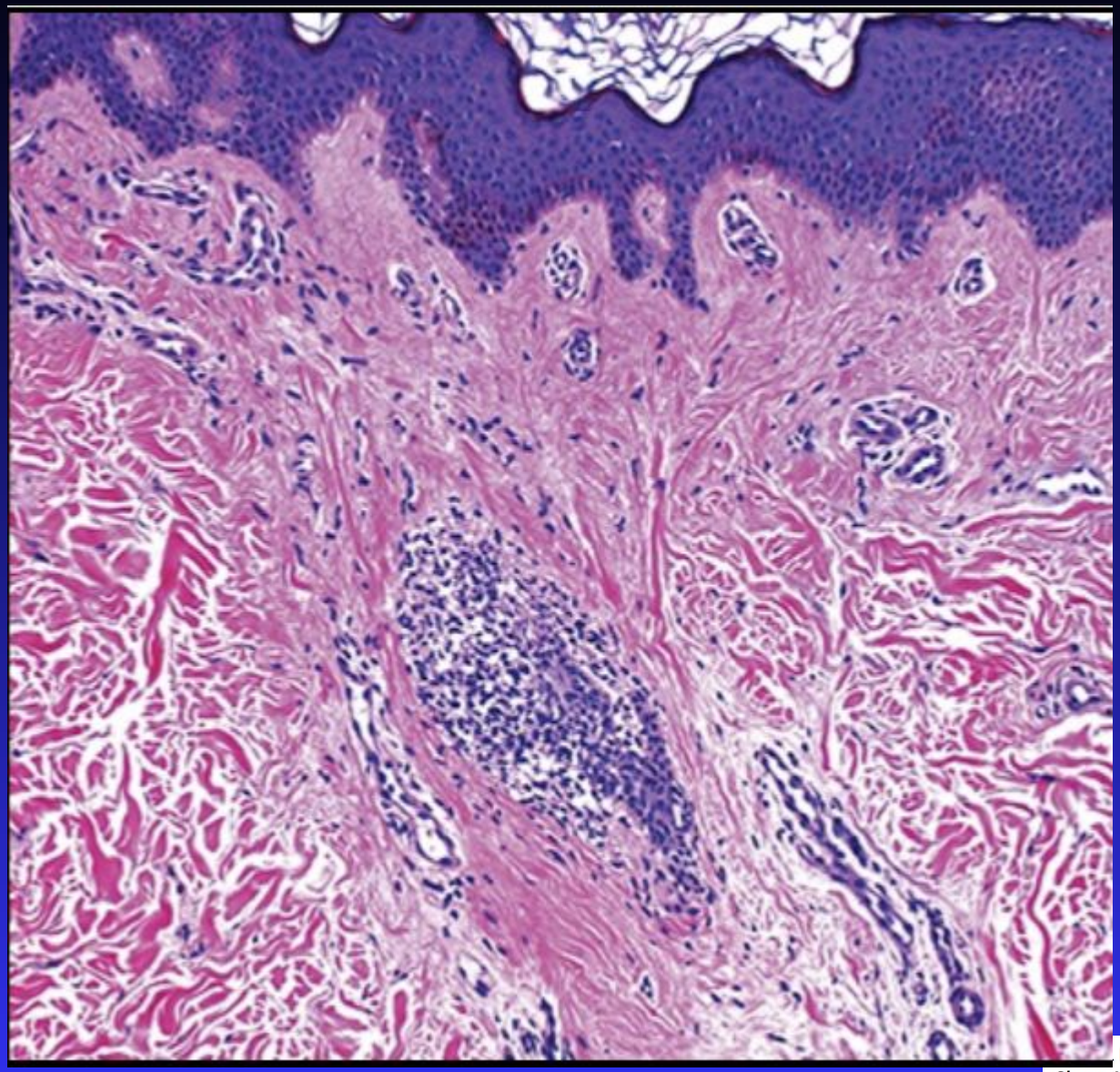


Frontal Fibrosing Alopecia Involving the Limbs Shows Inflammatory Pattern on Histology: A Review of 13 Cases

Miteva, Mariya MD Author Information

The American Journal of Dermatopathology: March 2020 - Volume 42 - Issue 3 - p 226-229
doi: 10.1097/DAD.0000000000001500

FFA Limbs

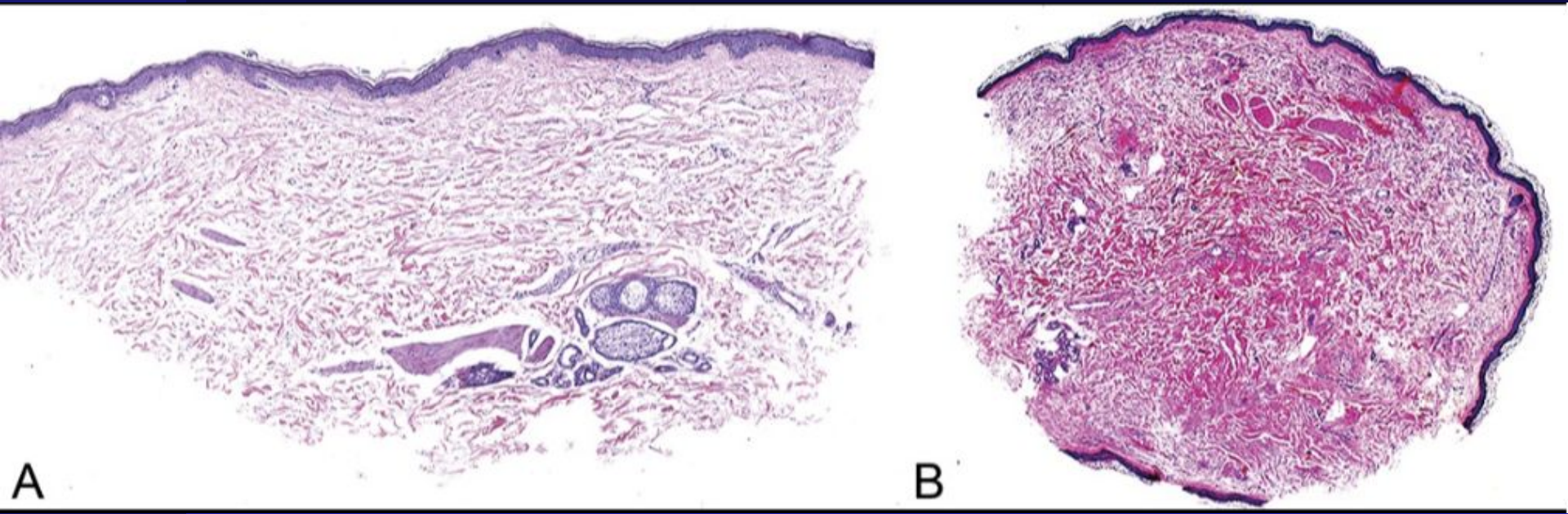


Fibrosing Alopecia Involving the Limbs Shows Inflammatory Pattern on Histology: A Review of 13 Cases

Miteva, Mariya MD Author Information

The American Journal of Dermatopathology: March 2020 - Volume 42 - Issue 3 - p 226-229
doi: 10.1097/DAD.0000000000001500

FFA Limbs



Frontal Fibrosing Alopecia Involving the Limbs Shows Inflammatory Pattern on Histology: A Review of 13 Cases

Miteva, Mariya MD **Author Information**

The American Journal of Dermatopathology: March 2020 - Volume 42 - Issue 3 - p 226-229
doi: 10.1097/DAD.0000000000001500

Summary of FFA Update

- 30% of cases can be credited to a chemical, possible nanoparticularized $Ti0_2$
  - Other ingredients should not yet be excluded
- 40% of cases are associated with certain genetic predisposition—HLA-B*07:02
- A 2mm punch with a mucin stain is the best tool for an accurate histopathologic diagnosis.

 doi: 10.1111/ajd.12833

LETTER TO THE EDITORS

Case Letter

Dear Editor,

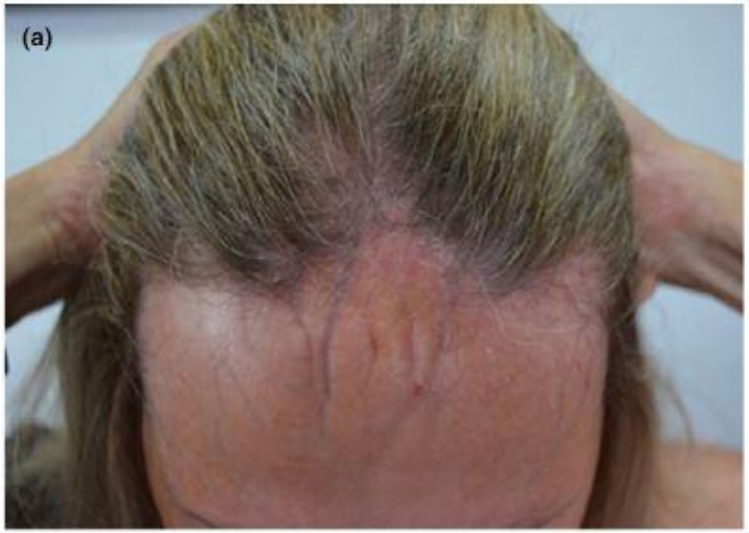
Frontal fibrosing alopecia: Regrowth following cessation of sunscreen on the forehead

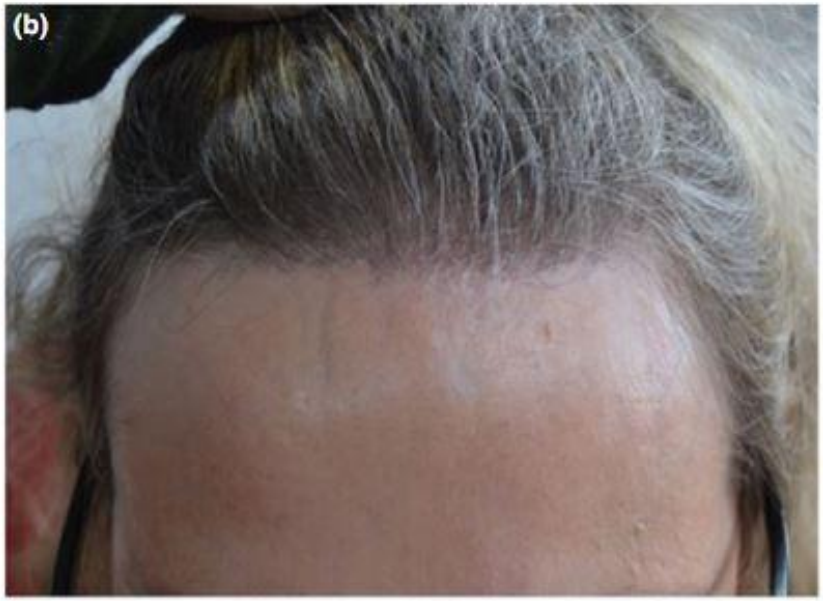
Frontal fibrosing alopecia is a progressive cicatricial alopecia that most commonly affects postmenopausal women. The prevalence of frontal fibrosing alopecia has increased ten-fold over the past decade.[1] The pathophysiology remains uncertain, although a key element appears to be destruction of the epithelial hair follicle stem cells located in the bulge region of the hair follicle.[2] Hormonal, genetic, autoimmune, inflammatory and environmental factors are thought to contribute the pathophysiology. Daily facial sunscreen use has been suggested as an important contributor to the pathophysiology of frontal fibrosing alopecia.[3,5]

We report the case of a 54-year-old perimenopausal woman referred by a dermatologist to our specialist hair clinic with a clinical diagnosis of frontal fibrosing alopecia. She presented with a 1-year history of frontotemporal and eyebrow hair loss. Current medications included daily hydroxychloroquine 200 mg and clobetasole diproprionate 0.05% ointment. Previous medications included dutasteride 0.1 mg oral daily and novasone 0.1% cream. Examination revealed erythema and perifollicular hyperkeratosis, anterior hairline skin atrophy and prominent vessels (Fig. 1a). Treatment for associated female pattern hair loss was commenced with daily spironolactone 100 mg and minoxidil 1 mg. For her frontal fibrosing alopecia, she continued hydroxychloroquine and dutasteride. Triamcinolone 5 mg/

regrowth along the anterior hairline. Skin atrophy reduced as a result of the cessation of intralesional and topical steroid use, and the forehead veins were less prominent (Fig. 2a). Ciclosporin and hydroxychloroquine were ceased, and hair regrowth was sustained after 12 months (Fig. 2b). Frontotemporal trichoscopy showed normal number of hairs and average hair shaft thickness. The patient continues to attend for review every 6 months and to date there has been no evidence of reactivation of her FFA (Fig. 2c).

How sunscreen contributes to the pathophysiology of frontal fibrosing alopecia is unknown. One hypothesis is that sunscreen enters the follicular infundibulum and elicits an immune reaction.[4] Low sebum production in





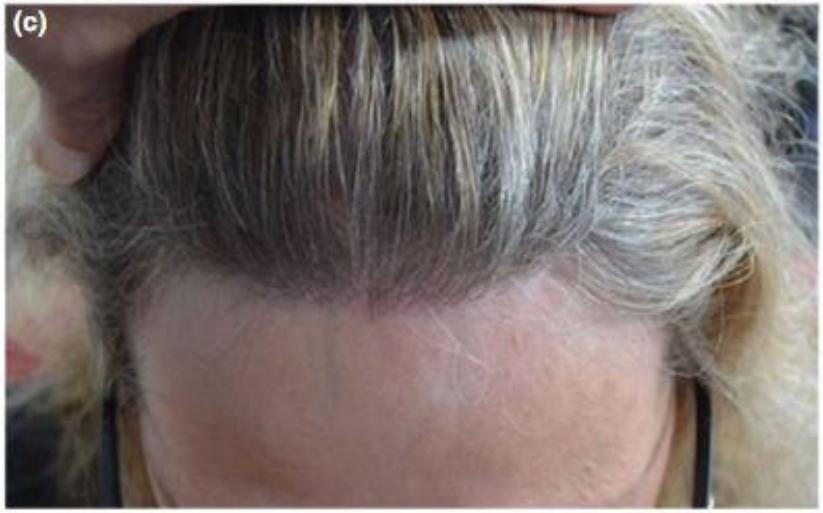


Figure 2 (a) At 24 months: increased frontotemporal hair density following cessation of sunscreen on the forehead. Reduced erythema, perifollicular hyperkeratosis, skin atrophy and prominent vessels. (b) At 30 months: sustained hair regrowth despite ceasing systemic and topical therapy for frontal fibrosing alopecia. (c) At 36 months: sustained hair regrowth 12 months after ceasing systemic and topical therapy for frontal fibrosing alopecia.

may improve frontal fibrosing alopecia.

We now recommend that patients with frontal fibrosing alopecia avoid applying sunscreen products on the forehead and use a cap or hat for sun protection.

William C Cranwell[1,2,3,4] | Rodney Sinclair[1,5,6]

[1]*Sinclair Dermatology, East Melbourne,* [2]*The Royal Melbourne Hospital, Parkville,* [3]*The Alfred Hospital, Melbourne,* [4]*Skin and Cancer Foundation Inc, Carlton,* [5]*Department of Medicine, University of Melbourne, Parkville, and* [6]*Epworth Dermatology, Melbourne, Victoria Australia*

REFERENCES

1. MacDonald A, Clark C, Holmes S. Frontal fibrosing alopecia: a review of 60 cases. *J. Am. Acad. Dermatol.* 2012; **67**: 955–61.
2. Lyakhovitsky A, Barzilai A, Amichai B. Frontal fibrosing alopecia update. *World J. Dermatol.* 2015; **4**: 35–43.
3. Aldoori N, Dobson K, Holden CR *et al.* Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. *Br. J. Dermatol.* 2016; **175**: 762–7.
4. Debroy Kidambi A, Dobson K, Holmes S *et al.* Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. *Br. J. Dermatol.* 2017; **177**: 260–1.
5. Cranwell WC, Sinclair R. *The role of sunscreen and facial skin care products in frontal fibrosing alopecia.* In: Proceedings of the 10th World Congress for Hair Research; 31 Oct–3 Nov 2017; Kyoto, Japan. Abstract PS1-1.

Hypotheses

- A chemical is causing a lichenoid reaction that results in IP breakdown.
- Sun protection promotes inflammation.
- Multiple entities are caused by the same chemical--FFA, LPP, FAPD, CCCA.
- Nanoparticles may be toxic.

Thanks to:

- Portland--Janet Roberts and Nisha Desai
- Miami et Bologna--Antonella Tosti and Colombina Vincenz
- Portland State University--Zhiqiang Chen
- Brussels--Athanassios Kolivras
- San Francisco--Vera Price

Thanks!

curtisinportland@gmail.com

CTA Lab

CURTIS THOMPSON, MD & ASSOCIATES

Skin, Hair and Nail Pathology Experts